

MrOS Visit 2 Analyst Guide

HIP X-RAY

HX2

Note for BIOBANK: The HIP X-RAY images are in .dcm format. Each site has a folder with the images for participants from that site. For example:

MROS_XRAY/BI/BI0001. This participant has 5 .dcm images in their folder with the following naming convention: MRpptIDVISITlocation.dcm

Where PPT ID is the MROS ID.

Visit is either V1 or V2

Location is the scan location: H (hip), L (Lumbar spine) and T (Lateral thoracic)

All active MrOS participants that participated in the MrOS Visit 2 were invited to participate in an ancillary study for Hip Osteoarthritis. During visit 2 hip x-rays were taken of participants who agreed. The hip X-rays were read by a third party. All sites participated in the MrOS Hip OA study.

At the beginning of the second visit, exclusion criteria for the hip x-ray included previous knee and/or hip replacement. Within the first few months of recruitment, the exclusion criteria were updated to be only bilateral hip replacements. At the end of Visit 2, 4156 participants had completed a hip x-ray. At the start of MrOS visit 3, we asked all active participants that were originally excluded from having a hip x-ray because of the tighter exclusion criteria at the start of Visit 2 if they were willing to complete the hip x-ray as part of their third clinic visit. We were able to obtain 59 additional x-rays as part of Visit 3. Therefore, a total of 4,215 x-rays were obtained for the Hip OA study.

The date on which the hip x-ray was obtained can be found in the main V2 file (XRHDATE).

Out of the **4,530** visit 2 clinic visits completed, **4,218** X-Rays were administered indicated by the variable XRHIP in the main V2 dataset. However there are only **4,215** participants with a digital hip X-ray on file at the Coordinating Center and **312** had no hip X-rays due to;

Knee replacement	2
Hip replacement	21
Participant refused	208
Other	81

Participant

The reason for a participant not having an X-ray is located in the main V2 dataset by the variable XRHIPNO. The flag variable for if the digital hip X-ray is on file at the Coordinating Center "XRHIFLAG" can be found in the main V2 dataset.

Calculated Variables:

1. **Minimal joint space FOR EACH HIP SIDE was converted to millimeter as follows**

HXJSNR: $HXMINJSR \times 0.17$

HXJSNL: $HXMINJSL \times 0.17$

2. **Summary Grade for each hip**

HXCF1R : Croft for Right hip

HXCF1L: Croft for left hip

The summary grade was calculated for each hip separately;

Croft=0

Osteophytes and Joint space narrowing in any location and Cysts, deformity and Sclerosis are not ≥ 1 ;

Croft=1

Osteophyte in any location is mild, moderate or severe OR Joint space Narrowing in any location is greater than or equal to 1.

The following indicator variables (which are not included in the released dataset) were used to calculate croft score of 2, 3 and 4

OSTPOINT =1 if Osteophytes in any location is mild, moderate or severe
Else OSTPOINT=0

NARPOINT=1 if Joint space Narrowing in any location is greater than or equal to 1
Else NARPOINT=0

CYSPPOINT=1 if Cysts was mild, moderate or severe;
ELSE CYSPPOINT=0

SCLPOINT=1 if Sclerosis was mild, moderate or severe
ELSE SCLPOINT=0

DEFPOINT=1 if Deformity was mild, moderate or severe;
ELSE DEFPOINT=0

$G23POINT = \text{SUM}(\text{OSTPOINT}, \text{NARPOINT}, \text{CYSPPOINT}, \text{SCLPOINT})$;

Croft =2

Definition of croft 1 and $G23POINT \geq 2$

Croft =3

G23POINT > 2

Croft=4

G23POINT>2 AND DEFPOINT=1

3. Joint Space narrowing lateral >=2 OR Medial >=3 on either hip

For the right Hip;

If lateral JSN on either hip is >=2 or medial JSN on either hip is >=3 then
HX L23M =1.

If lateral JSN on either hip is <2 and medial JSN on either hip is < 3 then
HX L23M =0.

If both hips has no reading due to a total hip replacement, then
HXL23M=Not Applicable

If one hip has no reading due to a total hip replacement, HXL23M is equal
to the value of the other hip

4. Joint space narrowing >=2 AND Osteophytes anywhere >=2 on any hip

For the Right Hip;

If lateral of medial JSN >=2 and Osteophytes in any location >=2 then
indicatorR=1;

If lateral of medial JSN <2 or Osteophytes in any location <2 then
indicatorR=0;

For the Left Hip;

If lateral of medial JSN >=2 and Osteophytes in any location >=2 then
indicatorL=1;

If lateral of medial JSN <2 or Osteophytes in any location <2 then
indicatorL=0;

If JSN>=2 and Osteophytes >=2 is PRESENT on any hip, then
HXJSNOST=1

If JSN>=2 and Osteophytes >=2 is ABSENT on any hip, then
HXJSNOST=0

If both hips has no reading due to a total hip replacement then
HXJSNOST=Not applicable;

If one hip has no reading, HXJSNOST is equal to the value of the other
hip

5. Maximum Joint space narrowing lateral >=2 or medial >=3 OR Osteophytes anywhere >=2

HX L23M=1 or Osteophytes anywhere >=2 THEN HXJSNOS=1

HX L23M=0 AND Osteophytes anywhere < 2 THEN HXJSNOS=0

If both hips has no reading due to a total hip replacement then HXJSNOS=Not applicable.

6. Validated Total hip replacement

All cases with a problem preventing the reading of the X-ray were reevaluated for presence of a total hip replacement. A validated THR variable for each hip was created based on evidence from the X-ray. In addition cases where there was no problem reported for reading the X-ray but the participant had self reported a THR were also confirmed for the absence of a THR before creating the THR variable.

Standard definition for OA

OA is defined as Men with Croft ≥ 2 on the worst hip or having a total hip replacement (THR) as assessed from the hip OA dataset using the Validated Total hip replacement variable. Men without OA are defined as having croft scores of 0 or 1 and NO THR.

The following manuscript should be referenced in future papers using the Hip OA dataset and this definition.

Chaganti RK, Parimi N, Lang T, Orwoll E, Stefanick ML, Nevitt M, Lane NE; Osteoporotic Fractures in Men (MrOS) Study Group. **Bone mineral density and prevalent osteoarthritis of the hip in older men for the Osteoporotic Fractures in Men (MrOS) Study Group.** *Osteoporos Int.* 2010 Aug;21(8):1307-16. Epub 2010 Jan 26.

Reliability scores of Hip X-rays for Mr.OS

A random sample of 472 X-rays were re-read independently by the same reader to measure reliability of the Hip X-ray readings. The following are the intra rater scores for some X-ray readings.

Definition	Intra-class correlation
Minimal joint space	
Right	0.856
Left	0.740
Total Osteophytes Score	0.591
Lateral JSN	
Right	0.796
Left	0.781
Medial JSN	
Right	0.734
Left	0.781

Variables	Kappa(Disease=1)
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Summary grade ≥ 2 on either hip Weighted (0-4)	0.565 0.477
Joint space narrowing lateral ≥ 2 or medial ≥ 3	0.809
JSN ≥ 2 Weighted (0-4)	0.792 0.715
Osteophytes score ≥ 2 Weighted (0-4)	0.398 0.375
Femoral Osteophytes ≥ 2 Weighted (0-4)	0.711 0.518
Joint space narrowing ≥ 2 and osteophytes anywhere ≥ 2	0.809

Funding Sources

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Vertebral Fracture Assessment Data (SQ grading)

Data set name: XM1XXX##, XM2XXX##

Original authors:

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Introduction

The XM datasets contains results from semi-quantitative (SQ) readings of lateral spine x-rays. SQ is used as an assessment of vertebral fracture from a spine radiography. XM1 contains data from x-rays collected at Visit 1 and XM2 data from Visit 2. All V1 and V2 x-rays have SQ readings.

Study population

At Visit 1, all 5994 participants had lateral spine x-rays completed.

Films for three participants were lost during the digitization process (the variable XRSIFLAG=3 in V1XXX## dataset indicates that images are missing) and an additional 29 men had films that were not suitable for reading for vertebral fracture leaving 5962 men with data in the XM1XXX## dataset.

At Visit 2, 4401 (of the 5229 men at the visit) have data in the XM2XXX## dataset.

To be included in the XM2XXX## dataset, men must have had both baseline and Visit 2 images available and suitable for reading for vertebral fractures.

There are several reasons for why men did not have data in the XM2XXX## dataset (N=828):

- o 699 men did not have x-rays taken at Visit 2 because they had self-administered questionnaire data only (as noted by the variable V2TYPE=1 in the V2XXX## dataset)
- o 105 men had a clinic visit but did not have spine x-rays (as noted by the variables V2TYPE in (2,3) and XRSIFLAG=.M in the V2XXX## dataset);
- o 3 had lost spine films at visit 2 (XRSIFLAG=3 in the dataset V2XXX## dataset)
- o 21 men had images that were not suitable for reading (XRSIFLAG in(1,2) but do not have records in the XM2XXX## dataset).

See XM_VertFxFlowChart.ppt for flowchart of vertebral fracture assessment data.

Acquisition of the spine x-ray

Lateral thoracic and lumbar spine radiographs were obtained in accordance with the 1995 National Osteoporosis Foundation guidelines (NOF 1995) at baseline and Visit 2. All clinical centers acquired conventional films at the baseline exam. Two clinical centers (Portland and Birmingham) collected images digitally while all other centers used conventional films at Visit 2. All conventional films were scanned to create digital images. The visit date is the same as the x-ray date, so a separate variable for x-ray date is not included in the dataset.

Spine Analyzer software

Data is collected using SpineAnalyzer Software (Optasia Medical, Ltd, Cheadle, United Kingdom) using digital images. SpineAnalyzer™ aids the identification of even subtle vertebral deformities by efficiently and comprehensively facilitating the annotation of spine anatomy. This novel software workflow solution enables assessment of the accepted quantitative standard (6 point morphometry), while simultaneously providing full contours outlining vertebral shape (95-point morphometry). The software facilitates annotation of the lateral vertebral margins of the spine on selected vertebrae from T4 to L4.

Triage process

A triage process (the process of determining the priority of patients' treatments based on the severity of their condition) was used to reduce the total number of films that required review by an expert reader for fracture. A trained technician (Lisa Christensen) reviewed Visit 2 films (or Visit 1 films if follow-up was not completed) for the presence of any possible fracture or abnormality. Participants with completely normal films were classified as “triage negative.” Participants with any possible fracture or whose films were difficult to assess were classified as “triage positive.” Differential diagnoses such as degenerative disease were not considered during the triage process unless such differential diagnosis suggested a fracture or required additional time to review the image. The triage process was purposefully designed to have a high sensitivity with a low specificity; that is, we aimed to include all fractures in the triage positive sample. As expected, the sensitivity of the triage process was excellent, as assessed in a random sample of 500 participants. At visit 1, for prevalent fractures of $SQ \geq 1$, the sensitivity of triage was 96.8% and the specificity was 46.3%. At visit 1, for prevalent fractures with an $SQ \geq 2$, the sensitivity of triage was 98.3% and the specificity was 42.9%. Similar results were seen for Visit 2 prevalent fractures.

Triage positive participants then had all available films from both visits analyzed for SQ grading by an expert reader (John Schousboe, staff id=CC96). The SpineAnalyzer software automatically generated both 6-point and 95-point morphometry with minimal adjustment by the reader for these participants.

Participants with Visit 1 and 2 x-rays considered “triage negative” had a random subset of images reviewed by a trained technician (Aldric Chau, staff id=CC13) only for QM point placement in order to calculate Cobb angle. SQ measures for these triage negative images were not completed and were set to 0=NORMAL for all levels. These triage negative films only had the differential diagnosis code of 6=unevaluable completed for any levels that were unreadable; no other differential diagnosis codes for triage negative participants were completed. The remaining “triage negative” images were not read. Subject-level SQ outcomes were set to 0=NORMAL based on triage (staff id= CC95).

The flag variable XMTRIAGE indicates the results of triage.

SQ Grading

The Genant semi-quantitative (SQ) grade (Genant 1998) is the main analysis variable (variables for vertebral level specific data are XMSQL1-L4, XMSQT4-T12). The variables have the following values:

0= NORMAL

1= MILD

2= MODERATE

3= SEVERE

At Visit 2, variables for change in SQ grade (Visit 2 – Visit 1) are also available (Variables XMDSQL1-L4, XMDSQT4-T12).

More detailed scores for prevalent fracture were recorded for each vertebral levels (variables XMSSL1-L4, XMSST4-T12). These variables may be used as secondary analyses and were coded as follows:

0=NORMAL

1=MILD BICONCAVE

2=MILD WEDGE

2.5=MILD CRUSH

3=MODERATE BICONCAVE

4=MODERATE WEDGE

4.5=MODERATE CRUSH

5=SEVERE BICONCAVE

6=SEVERE CRUSH

7=SEVERE WEDGE

For both sets of variables, if the film was not triaged the variable will have a value of .M, and should be considered 0=Normal.

Quantitative morphometry (QM)

Quantitative morphometric (QM) points were placed using the automated software with minor adjustments by the reader. QM data includes traditional 6-point morphometry per the SOF protocol (Genant 1998) and a software-dependent 95-point morphometry generated by the SpineAnalyzer software. QM data is not included in the XM datasets, but is available upon request from the Coordinating Center. However, the 6-point morphometry from selected vertebra were used to calculate the Cobb angle data (see XC_Information).

Differential diagnosis

Variables XMDDL1-L4, XMDDT4-T12

In addition to SQ measures for each vertebrae, a differential diagnosis (DD) to identify non-osteoporotic problems was recorded. These were only assessed in the triage positive participants, with the exception of 6=unevaluable in the triage negative participants. These variables may be used to complete sensitivity analyses but should not be used as primary outcomes individually. These were recorded as follows:

1= CONGENITAL ANOMALY

2= DEGENERATIVE DISEASE

3= NORMAL

4= OTHER

5= SCHEURMANN'S DISEASE

6= UNEVALUABLE

Levels with DD=6: UNEVALUABLE have SQ grades and scores set to SAS special missing value code=.N (cannot evaluate).

The recording of a differential diagnosis and an SQ grade or score are not mutually exclusive. Levels can have both an SQ score and a differential diagnosis, or an SQ score and no differential diagnosis (that is, the differential diagnosis set to .M) or a differential diagnosis and no SQ score

(that is, the SQ score set to .M) . The differential diagnosis variables can have a value of .M if the participants' images were triage negative, or if there was no differential diagnosis noted upon review of the level.

Image Type

Variables XMIML1-XMIML4, XMIMT4-XMIMT12

These variables explain on which film the vertebral level was evaluated (lumbar or thoracic). In general, readers attempted to read all thoracic vertebrae on thoracic images and all lumbar vertebrae on lumbar images, but this was not always possible. In paired longitudinal readings, the SQ grade and score were completed on the same image type at each visit. The variable XMLONT indicates the number of lumbar levels that were read on the thoracic image; the variable XMTONL indicates the number of thoracic levels that were read on the lumbar image.

General data structure

The data contains both vertebra-specific variables and subject-specific variables. The dataset is in wide format, with one observation per ID.

There are vertebra-specific variables for SQ grade (0-3), SQ score (0-7), DD, and image type (lumbar or thoracic). Each variable ends with L4 to T4.

Subject-specific variables include staff id and summary variables for SQ grade ≥ 1 , SQ grade ≥ 2 , maximum SQ grade, change in SQ grade ≥ 1 and 2 and maximum change (V2), any of each type of SQ scores, and any of each type of DD values. Some of the summary variables are to help identify subsets of data. These include number of levels with SQ readings, whether lumbar vertebra are read on thoracic x-ray or thoracic vertebra are read on lumbar x-ray, etc. We recommend that analysts use data where ≥ 10 levels have SQ readings for analyses of prevalent or incident fractures unless SQ is based on triage (XMNSQLV=.M). Therefore all subject-level outcome variables have been set to .N when number of levels <10 .

Analysis of prevalent fracture

The simple SQ grade (0,1,2,3), in most cases, will be the primary variable of interest in prevalent data analyses. Generally, primary analyses for prevalent fracture should use an SQ grade ≥ 2 as a prevalent fracture. Thus, the primary analysis variable is XMSQGE2. Secondary or sensitivity analyses should include "mild" SQ grades (SQ=1) as a prevalent fracture (variable XMSQGE1).

Analysis of incident fracture

The main variable for incident fracture analysis should be XMDSQGE1, which indicates a change of SQ grade ≥ 1 for at least one vertebral level for a participant, regardless of SQ grade at baseline. Such a change in SQ grade is generally considered a fracture and would include both new fractures (for example, going from an SQ of 0 at Visit 1 to an SQ of 1, 2, or 3 at Visit 2) and worsening fractures (going from an SQ of 1 or 2 at Visit 1 to an SQ of 2 or 3 at Visit 2). Various methods to analyze the incident fracture data are available and should be considered for sensitivity analyses. The variables to use for these situations (including XMDSQGE1) are:

XMDSQGE1	This variable indicates at least 1 level changed from 0 to ≥ 1 , regardless of the status of other levels at V1.
XMDSQNW1	This variable indicates <u>new</u> fractures with an SQ change of ≥ 1 in those who had an V1 SQ of 0. In other words, this indicates a change in SQ grade of at

	least 1 for people who had an SQ grade of 0 at baseline. These values are calculated for each vertebra separately and then expressed as a person level variable. To subset analyses to those without any prevalent fracture (defined as SQ ≥ 1), analysts must use the variable XMSQGE1 or XMSQGE2 from the XM1 file to identify those with a prevalent fracture at baseline.
XMDSQNW2	This variable indicates <u>new</u> fractures with an SQ change of ≥ 1 in those who had a V1 SQ of 0 or 1. In other words, this indicates a change in SQ grade of at least 1 for people who had an SQ grade of 0 at baseline. This variable is calculated for each vertebra separately and then expressed as a person level variable. To subset analyses to those without any prevalent fracture (defined as SQ ≥ 1), analysts must use the variable XMSQGE1 or XMSQGE2 from the XM1 file to identify those with a prevalent fracture at baseline.
XMDSQW11	This variable indicates a worsening fracture with an SQ change ≥ 1 for men who had an SQ grade of at least 1 at baseline.
XMDSQW12	This variable indicates a worsening fracture with an SQ change ≥ 2 for men who had an SQ grade of at least 1 at baseline.

References

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