INTRODUCTION: Disease modifying osteoarthritis (OA) drug (DMOAD) trials are hampered by the slow progression of OA. Drug companies address the issue by including patients that are at risk of progression (Early OA, Obesity, malalignment, older age, women, etc.); but current criteria have been proven to be very inefficient at predicting progression.

Purpose:
1) Identify X-Ray quantitative features that are typical of OA subjects who will progress during the next two years.
2) Develop an X-ray based OA progression index that can be used to screen for subjects who are at risk of radiological worsening.
3) Evaluate the standard response of the mean (SMR) of the set composed of subjects identified at risk of OA progression.

Methods: Quantitative joint space width (qJSW) measurements and semi-quantitative central readings of the knee for Kellgren & Lawrence (KL) grade and radiographic features of the tibio-femoral joint from fixed-flexion knee radiographs from the OAI were used in this study (https://oai.epi-ucsf.org/dataralease/ImageAssessments.asp). The qJSW set is composed of 21 continuous measurements and from those we derived 12 descriptive measurements for a total of 33 quantitative features. We used the qJSW and semi-quantitative assessment of the baseline, 12 month and 24 month x-rays. We also included the 36 and 48 month qJSW data. We complemented the data by including age, gender, weight, height, BMI, site information and the scan date from the clinical and enrollee OAI data sets. Only knees with complete qJSW data and KL scores were included. We used all the longitudinal data to detect and adjust for potential site-specific drift in qJSW. We adjusted qJSW data for height, age and gender using -subject-within-site regression analysis-

Results: 5211 knees (3109 females, age 61.8 ± 9.1) had complete qJSW and semi-quantitative KL scores at baseline. At baseline 988, 803, 2118, 1086 and 216 subjects had KL scores of 0, 1, 2, 3 and 4 respectively. The train set consisted of 745 subjects, 207 which had OARSI JSW progression. Figure 1 shows the heat map of features associated with OA progression. B:SWiMS identified that having an abnormal difference between medial and lateral JSW, or a large variance in the medial JSW or abnormal slope between the medial and lateral JSW measurements were z-transformed. Then, we split the subjects into a training set (1/3 of the population) and test set (the remaining 2/3). From the training set, we selected subjects that had a baseline KL score of 2 or 3. After that, we labeled subjects as progressors or non-progressors based on change between the baseline and 24-month exams of OARSI scores of medial and/or lateral joint space narrowing scores. The labeled train-set was explored by B:SWiMS (https://cran.r-project.org/web/packages/FRESA.CAD). B:SWiMS returned a set of compact features that were more common in subjects whose semi-quantitative scores worsened. B:SWiMS also returned a logistic model that can be used to gauge the risk of progression of any OA subject.

Conclusions: There are quantitative X-ray features that are unique in subjects that will progress during the ensuing two years. The logistic model composed by these features enabled the identification of subjects that are at risk of progression with a test sensitivity of 0.85. Screening for subjects with these features may boost the SRM of radiological features by 60%.