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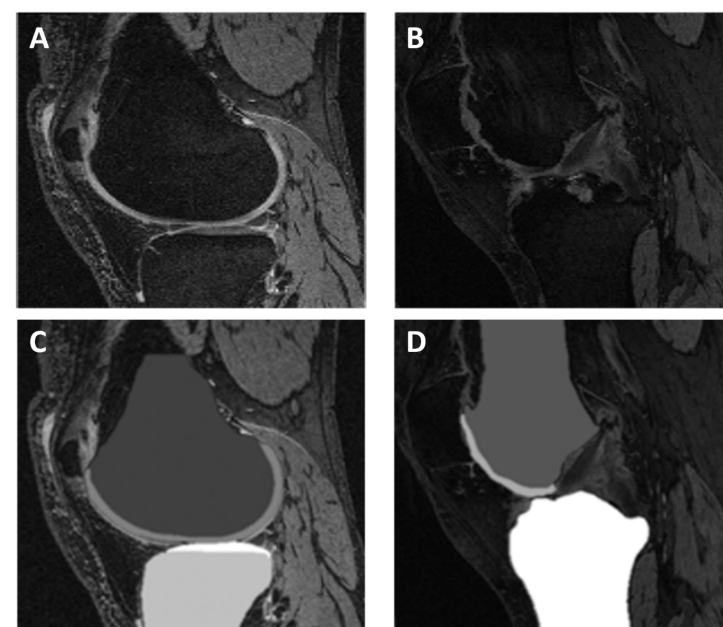
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### BACKGROUND

- Knee osteoarthritis (OA) is a major cause of pain, disability, and structural joint deterioration.
- Predicting radiographic progression may support earlier risk stratification and targeted intervention.
- Clinical variables and biospecimen biomarkers alone may not fully capture whole-joint structural risk.
- Purpose: develop and compare multimodal machine-learning models using clinical variables, biomarkers, MOAKS, and MRI radiomics.

### METHODS

- Nested case-control analysis from the Osteoarthritis Initiative / FNIH OA Biomarkers Consortium.
- Included 600 knees with baseline KL grade 1-3, biospecimen biomarkers, baseline MRI, and 24-month radiographs.
- Outcome: radiographic progression, defined as  $\geq 0.7$  mm loss in minimum medial tibiofemoral joint space width at 24 months.
- Feature sets: M1 BioClinical; M2 BioClinical + MOAKS; M3 BioClinical + radiomics; M4 combined all domains.
- Algorithms: logistic regression, XGBoost, random forest, and SVM with nested 10x5-fold cross-validation.



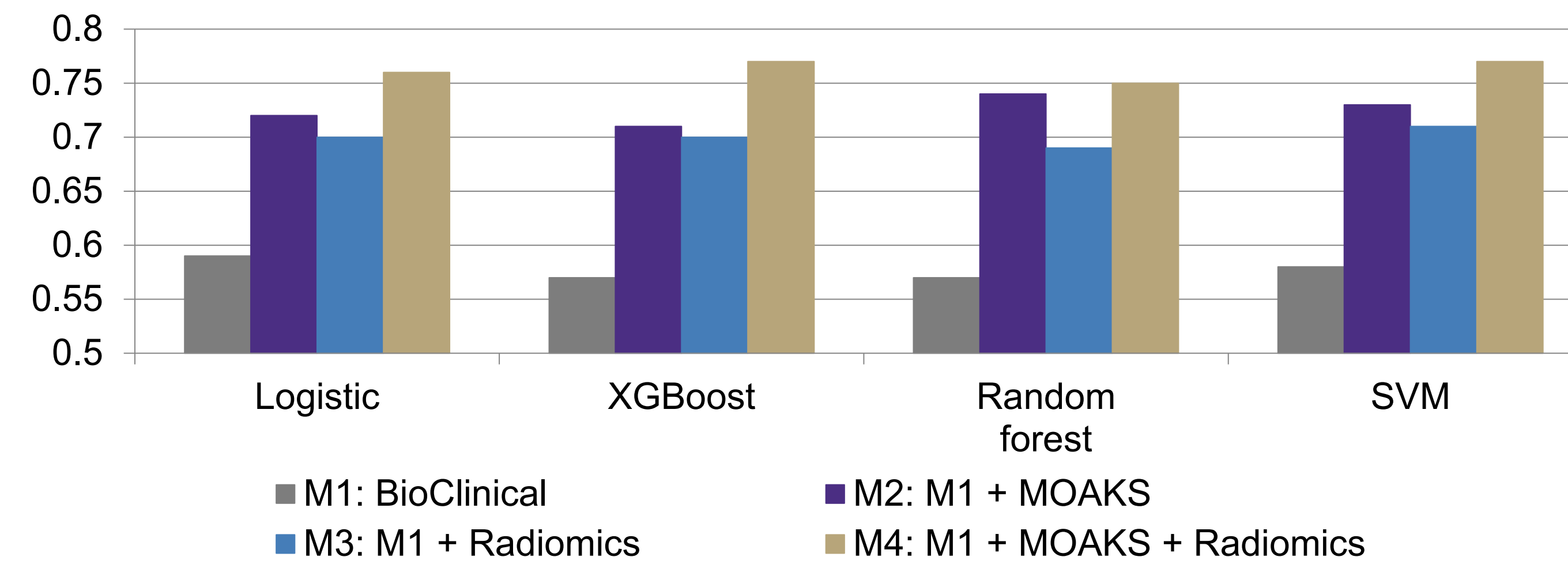
- **Automated segmentation enabled extraction of 100 radiomics features from each femoral/tibial bone and cartilage region.**

### TAKE-HOME

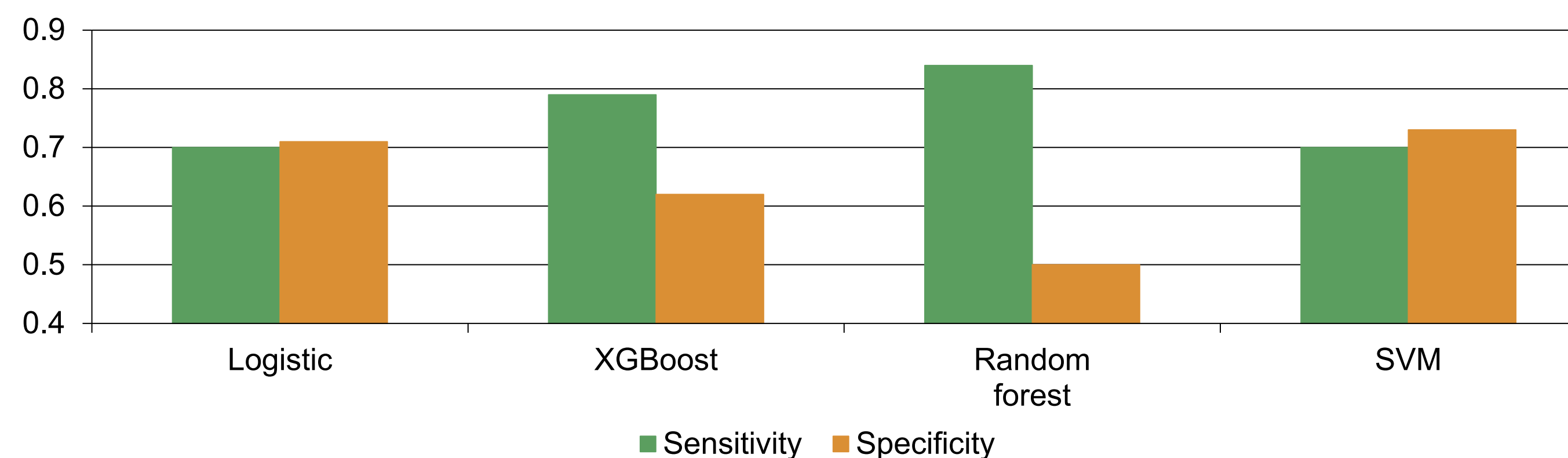
- MRI-derived structural features markedly improved prediction beyond clinical and biospecimen biomarkers.
- MOAKS and radiomics performed similarly; combining all domains achieved the best discrimination.

### RESULTS

#### AUC by algorithm and feature set



#### Combined model test-fold sensitivity and specificity



- BioClinical model showed modest discrimination (AUC 0.57-0.59).
- Adding MOAKS features improved AUC to 0.71-0.74; adding radiomics improved AUC to 0.69-0.71 (all vs M1  $p < 0.0001$ ).
- MOAKS and radiomics models were not significantly different across algorithms.
- Combined model achieved the highest AUCs (0.75-0.77), with XGBoost and SVM highest at 0.77.
- Decision curve analysis favored the combined model across most threshold probabilities.

### DISCUSSION

- Baseline MRI captured structural disease signals relevant to 24-month radiographic progression risk.
- MOAKS provides expert-derived whole-joint structural assessment, while radiomics offers automated quantitative texture, intensity, and shape information.
- Best performance with the combined model suggests that clinical, biochemical, semiquantitative MRI, and radiomics domains provide complementary information.
- SHAP analysis of the combined (M4) SVM model highlighted cartilage lesions, meniscal extrusion, KL grade, bone marrow lesions, cartilage turnover biomarkers, and radiomics texture/shape features.
- Limitations: internal validation only; whole-bone/cartilage radiomics rather than subregional extraction; external validation is needed.

### CONCLUSIONS

- Clinical and biospecimen biomarkers alone provided only modest prediction of radiographic knee OA progression.
- Adding MRI-derived features substantially improved model discrimination.
- MOAKS and radiomics showed broadly comparable predictive value.
- Integrating all predictor domains achieved the best overall performance, supporting multimodal baseline risk stratification.

### REFERENCES

Selected: Hunter et al. Osteoarthritis Cartilage 2011; Roemer et al. BMC Musculoskelet Disord 2016; Collins et al. Osteoarthritis Cartilage 2025; Li et al. Arthritis Rheumatol 2024; Wang et al. PLoS Med 2025.