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DEVELOPMENT AND VALIDATION OF RISK STRATIFICATION TREES FOR INCIDENT SLOW GAIT SPEED IN PERSONS AT HIGH RISK FOR KNEE OSTEOARTHRITIS

Leena Sharma, MD[1], **Kent Kwoh, MD**[2], **Junghwa (Julia) Lee, PhD**[3], **Jane Cauley, DrPH**[4], **Rebecca Jackson, MD**[5], **Marc Hochberg, MD, MPH**[6], **Alison H. Chang, PT, DPT, MS**[7], **Charles B. Eaton, MD, MS**[8], **Michael Nevitt, PhD**[9], **Jing Song, MS**[10], **Orit Almagor, MA**[11], **Joan S. Chmiel, PhD**[12]

[1]Professor of Medicine and Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

[2]Professor of Medicine and Medical Imaging, University of Arizona, Tucson, AZ, USA

[3]Associate Professor of Preventive Medicine (Biostatistics), Northwestern University Feinberg School of Medicine, Chicago, IL, USA

[4]Professor of Epidemiology, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA, USA

[5]Professor, Division of Endocrinology, Diabetes and Metabolism, The Ohio State University Wexner Medical Center, Columbus, OH, USA

[6]Professor of Medicine and Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, MD, USA

[7]Associate Professor of Physical Therapy and Human Movement Sciences, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

[8]Professor of Family Medicine and Epidemiology, Brown University Alpert Medical School, Pawtucket, RI, USA

[9]Professor of Epidemiology and Biostatistics, University of California at San Francisco School of Medicine, San Francisco, CA, USA

[10]Statistical Analyst, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

[11]Statistical Analyst, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Corresponding Author: Leena Sharma, M.D., Division of Rheumatology, Northwestern University Feinberg School of Medicine, 633 N. St. Clair, 18-097, Chicago, IL 60611, USA, 919-265-4004, L-Sharma@northwestern.edu.

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[12]Professor of Preventive Medicine (Biostatistics), Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Abstract

Objectives: Disability prevention strategies are more achievable before osteoarthritis disease drives impairment. It is critical to identify high-risk groups, for strategy implementation and trial eligibility. An established measure, gait speed is associated with disability and mortality. We sought to develop and validate risk stratification trees for incident slow gait in persons at high risk for knee osteoarthritis, feasible in community and clinical settings.

Methods: Osteoarthritis Initiative (derivation cohort) and Multicenter Osteoarthritis Study (validation cohort) participants at high risk for knee osteoarthritis were included. Outcome was incident slow gait over up to 10-year follow-up. Derivation cohort classification and regression tree analysis identified predictors from easily assessed variables and developed risk stratification models, then applied to the validation cohort. Logistic regression compared risk group predictive values; AUCs summarized discrimination ability.

Results: 1870 (derivation) and 1279 (validation) persons were included. The most parsimonious tree identified 3 risk groups, from stratification based on age and WOMAC Function. A 7-risk-group tree also included education, strenuous sport/recreational activity, obesity, depressive symptoms; outcome occurred in 11%, varying 0-29% (derivation) and 2-23% (validation) depending on risk group. AUCs were comparable in the two cohorts [7-risk-group tree, 0.75, 95% CI 0.72-0.78 (derivation); 0.72, 95% CI 0.68-0.76 (validation)].

Conclusions: In persons at high risk for knee osteoarthritis, easily acquired data can be used to identify those at high risk of incident functional impairment. Outcome risk varied greatly depending on tree-based risk group membership. These trees can inform individual awareness of risk for impaired function, and define eligibility for prevention trials.

Keywords

Osteoarthritis; Knee osteoarthritis; Disability; Functional impairment; Prevention

INTRODUCTION

Knee osteoarthritis (OA) is a major cause of disability. Estimating that OA accounts for 2.4% of all years lived with disability (YLD), the World Health Organization ranked OA 10th among contributors to 1990-2013 global YLDs (1–3). Managing disability in knee OA is challenging, especially since beneficial approaches – e.g., physical activity, exercise – are difficult for persons with this disease. In these individuals, pain, deformity, deconditioning, and reduced aerobic capacity limit activity and exercise, and adaptations to avoid pain may be entrenched. Managing knee OA disability is costly, in part due to morbidity, loss of mobility, and effect on work. To reduce individual and societal burdens of knee OA, early prevention strategies may be more effective and less costly than managing established disability.

Effective prevention approaches could delay or reduce the ultimate severity of knee OA disability. Prevention trials are impeded by uncertainties regarding the population to study. First, should the target be persons with knee OA or with pre-OA, defined here as at high risk for knee OA but not yet with radiographic disease? Risk factors for functional impairment, a precursor of disability in knee OA have been identified (4–33). In persons with knee OA, OA disease and disease-exacerbated factors – e.g., pain (4, 5, 7–9, 28–30), buckling (21, 33), decreased confidence (15, 33), malalignment (6), proprioceptive inaccuracy (9) – have been associated with functional decline and may modify effects of factors like body weight. These disease-related factors complicate efforts to prevent decline, especially since interventions targeting them are inadequate. Further, these factors likely make lifestyle and behavioral modifications more difficult to achieve. In contrast, persons with pre-OA are at a stage when modification is more likely realizable and effective. Notably, their pathway to disability does not only go through knee OA; focus on pre-OA enables capturing individuals with chronic knee pain whether or not they develop OA (34).

Second, prevention trials optimally target persons at high risk for the outcome (35). However, to our knowledge, a method to stratify risk of functional impairment has not been reported, either for pre-OA or existing knee OA. Risk stratification methods are critical to identify high-risk groups, for trial eligibility and dissemination of prevention strategies.

An established measure of functional impairment, slow gait speed is associated with disability, increased morbidity, and excess mortality in older individuals (36–40). Our objective was to develop and validate a practical, user-friendly method of risk stratification for incident slow gait speed in persons with pre-OA, applicable to community and clinical settings. A cohort study of persons with or at high risk for knee OA, the Osteoarthritis Initiative (OAI) offered a unique opportunity to follow individuals with pre-OA; we leveraged the OAI to study this group by extending their follow-up to 10 years. The Multicenter Osteoarthritis Study (MOST), which also includes a large cohort at high risk for knee OA, provided the best current opportunity to validate this method.

METHODS

Derivation and Validation Cohorts.

The OAI (4796 persons, 45-79 years) and MOST (3026 persons, 50-79 years) provided our derivation and validation cohorts. OAI and MOST are prospective, observational, longitudinal cohort studies of individuals with or at high risk to develop knee OA (Supplemental Table 1 for study details) (41). We additionally required baseline absence of OA in both knees [Kellgren and Lawrence (KL) radiographic grade <2]. OAI and MOST used the same radiographic acquisition protocol and centralized reading site (42, 43). Persons with slow gait speed (<1 meter/second) at baseline were excluded. The Institutional Review Board at each site approved the study.

Predictors.

In the derivation cohort, 40 baseline variables were considered (Table 1), including age, sex, race, ethnicity, education, health insurance, marital status, and living alone. Physical activity

variables included sitting, walking, light-, moderate-, and strenuous-sport/recreation, and muscle strength/endurance using Physical Activity Scale for the Elderly (PASE) (44) subscales. Knee pain frequency in both knees was considered. Frequent medication use was for knee symptoms most days of 1 month (m) in the past 12m. WOMAC Pain, WOMAC Stiffness, WOMAC Function (45), KOOS Pain, and KOOS Symptoms (46) were included, worse of the 2 knees. Individual KOOS Quality of Life items were: ≥weekly aware of problems with knees; and ≥moderate, for modified lifestyle to avoid damaging activities to knees, how much troubled with lack of confidence in knees, and general difficulty with knees. Whether a participant had limited activities due to knee symptoms in the past 1m was included. OA or OA symptoms in other joints included observation of hard bumps on joints closest to fingertips, back pain (any, past 1m), and hip, ankle, and foot pain (most days of 1m during the past 12m). Comorbidity variables included overweight, obesity, depressive symptoms [Center for Epidemiologic Studies Depression Scale (47), score ≥16], a questionnaire version of the Charlson Index (48) (score ≥2), and falls (any, past year). BMI [weight (kg)/height (m^2)] was overweight if ≥25 ≤BMI<30 and obese if BMI ≥30. Other variables included previous knee injury (ever so badly that it was difficult to walk for ≥1 week), previous knee surgery (ever any surgery to either knee), family history of knee replacement, and smoking (current). All variables were self-report except BMI (49, 50). MOST generally employed similar methods (differences noted in Table 1 footnotes).

Outcome.

The outcome was incident slow gait speed (<1 meter/second) (51–53) at any follow-up, excluding persons with slow gait speed at baseline. Gait speed was measured using a timed 20 meter walk in the OAI at baseline and 12m, 24m, 36m, 48m, 72m, 96m, and 120m, and in MOST at baseline and 30m, 60m, and 84m follow-up visits.

Statistical Analysis.

Classification and regression tree (CART) methods were used in the derivation cohort to identify the best predictor set and develop risk stratification models (54–56). CART, in contrast to logistic regression models, can generate classification/decision trees, following *a priori* decisions to maximize predictive accuracy based on cross-validation, and classify persons into risk groups. Briefly, CART segregates different values of the predictors (classification) through a decision tree composed of progressive binary splits based on recursive partitioning analysis. Every value of each predictor is considered as a potential split, and the optimal split is selected based on an impurity criterion (the reduction in the residual sum of squares due to a binary split of the data at that tree node). When missing values are encountered in considering a split, probability and impurity measures are calculated from surrogates. CART includes all records with outcomes; for any missing predictors “surrogate splitters” are substituted, back-up rules that mimic primary splitting rules. Each parent node produces two child nodes, which in turn can become parent nodes, with tree building and pruning until the statistical criterion indicates tree fit without overfitting. Terminal nodes, created if no further split was made, are mutually exclusive and exhaustive sample subgroups. Nodes were constrained to a minimum of 60 persons in parent and 30 in child nodes. To avoid overfitting, tree models were evaluated for predictive ability using 10-fold cross-validation. Outcome rates for each terminal node were used to create

risk stratification groups in the derivation cohort. The predictive value of the risk stratification models was assessed by odds ratios (ORs) and 95% confidence intervals (CIs) using logistic regression to compare risk group pairs.

Derived trees were then prospectively applied to the validation cohort to independently test their ability to identify participants in different risk groups. Incidence outcome rates for these risk groups and ORs and 95% CIs comparing risk groups were calculated.

The discrimination ability of the prediction models was compared using area under receiver operating characteristic curves (AUCs). Salford Predictive Modeler's CART® v8.0 was used for CART and SAS v9.4 for logistic regression and AUC analyses.

Patient and Public Involvement.

We did not involve patients or the public in our work.

RESULTS

The number of persons who had KL 0/0 (KL 0 in both knees), 0/1, or 1/1, and without slow gait speed at baseline was 1870 in the derivation cohort and 1279 in the validation cohort (Supplemental Figures 1A-1B). Incident slow gait speed occurred at a study visit within 10-year follow-up in 206/1870 (11.0%) persons in the derivation cohort and within 7-year follow-up in 143/1279 (11.2%) in the validation cohort. Baseline characteristics of each cohort are shown in Table 1. In derivation cohort participants without and with the outcome, mean (SD) baseline gait speed (meters/second) was 1.40 (0.18) and 1.19 (0.14), and change in gait speed (baseline minus final observation) was −0.05 (0.16) and −0.27 (0.18). In validation cohort participants without and with the outcome, baseline gait speed was 1.31 (0.16) and 1.16 (0.12), and change in gait speed was 0.004 (0.14) and −0.25 (0.16).

In the derivation cohort, the most parsimonious model was a 3-risk-group tree including age and WOMAC Function, shown with outcome frequency for each risk group in Figure 1. Seven-, 9-, 11-, and larger risk-group trees were within 1 SE of the measured performance of the most parsimonious tree, but trees with 11 or more risk groups were complex and difficult to interpret. The 7-risk-group tree included age, WOMAC Function, education, strenuous activity, obesity, and high depressive symptoms as discriminators; risk groups are shown in Figure 2. Table 2 summarizes characteristics of these 7 risk groups in both cohorts. The 9-risk-group tree additionally included overweight or obesity.

For risk groups identified by the 3-risk-group tree (Figure 1), ORs comparing risk groups were significant for High Risk-1 vs. Low Risk groups (OR 5.24, 95% CI 3.80, 7.24) and for High Risk-2 vs. Low Risk groups (OR 7.13, 95% CI 4.35, 11.69) but not for High Risk-2 vs. High Risk-1 groups (OR 1.36, 95% CI 0.84, 2.21). For risk groups identified by the 7-risk-group tree, comparisons are shown in Supplemental Table 2.

The trees generated by analysis of the derivation cohort were then tested for their ability to risk stratify persons in the validation cohort; Figures 3 and 4 depict the 3-risk-group tree and 7-risk-group tree, respectively.

In the validation cohort, for risk groups identified by the 3-risk-group tree, ORs comparing risk groups were significant for High Risk-1 vs. Low Risk groups (OR 4.28, 95% CI 2.94, 6.24) and for High Risk-2 vs. Low Risk groups (OR 2.29, 95% CI 1.22, 4.27), but not for High Risk-2 vs. High Risk-1 groups (OR 0.53, 95% CI 0.29, 1.00). For risk groups identified by the 7-risk-group tree, comparisons are shown in Supplemental Table 3. Distribution of incident outcomes, and Kaplan-Meier estimates of probability of outcome-free follow-up, overall and by 3-risk-group trees is shown in Supplemental Tables 4A–4D for both cohorts.

AUCs to summarize discrimination ability were comparable in the derivation and validation cohorts: for the 3-risk-group tree, AUC 0.70, 95% CI 0.67, 0.74 and AUC 0.67, 95% CI 0.62, 0.71; for the 7-risk-group tree, AUC 0.75, 95% CI 0.72, 0.78 and AUC 0.72, 95% CI 0.68, 0.76; and for the 9-risk-group tree, AUC 0.77, 95% CI 0.74, 0.80 and AUC 0.73, 95% CI 0.69, 0.77. The AUCs for the 7-risk-group tree were better than for the 3-risk-group tree, for both cohorts (each $p < 0.0001$). The AUCs for the 9-risk-group tree were better than for the 7-risk-group tree, for both the derivation and validation cohorts: $p < 0.0001$ and $p = 0.02$.

DISCUSSION

In analyses considering 40 baseline variables, a 3-risk-group tree (including age and WOMAC Function) was identified as the most parsimonious model. A 7-risk-group tree (including age, WOMAC Function, education, strenuous activity, obesity, and high depressive symptoms) and a 9-risk-group tree performed comparably to the parsimonious tree; AUCs were best for the 9-risk-group tree but were not substantially different from the 7-risk-group tree. Overall, incident slow gait speed occurred in 11%, but the risk varied greatly, between 0% and 29% in the derivation cohort and between 2% and 23% in the validation cohort, depending on risk group membership using the 7-risk-group tree. In both cohorts, ORs comparing risk groups from the 3-risk-group tree were significantly different from 1.0 for High Risk-1 vs. Low Risk and for High Risk-2 vs. Low Risk. AUCs to summarize discrimination ability were comparable in the two cohorts. These findings suggest that in persons at high risk for knee OA, risk of functional decline can be estimated using easily acquired data.

Methods to stratify risk of functional decline have not been reported, for persons with knee OA or pre-OA. Previous longitudinal studies of functional outcome have evaluated persons with knee OA, frequent knee pain, or a pool of persons with or at high risk to develop knee OA. These studies have identified risk factors including age, female sex, socioeconomic status, BMI, pain, comorbidity, depressive symptoms, knee buckling, low knee confidence, falls, laxity, malalignment, disease severity, proprioceptive inaccuracy, sleep disturbance, and community mobility barriers, while greater physical activity, less sedentary time, aerobic exercise, strength, self-efficacy, and social support were associated with a reduced risk (4–33). These studies have not separately examined pre-OA. While risk stratification in persons with knee OA is important, focusing only on this stage bypasses a compelling stage for prevention, before disease consequences become dominant. Persons with pre-OA are at a stage when lifestyle and behavioral modification to prevent decline are more likely

achievable and effective. Further, our findings are relevant to the large pool at high risk for knee OA, including those with chronic knee pain, whether or not they develop knee OA.

The findings in MOST provided some, albeit not perfect, validation. Outcome frequency was consistently higher in MOST high-risk than low-risk groups, but was sometimes lower in MOST than in the OAI. Possible reasons include fewer follow-up visits, shorter follow-up duration, and higher baseline prevalence of no frequent pain in both knees in MOST (Table 1). High-risk groups with the greatest difference in outcome frequency between OAI and MOST differed in at least two ways (Table 2). First, baseline prevalence of no frequent pain in both knees was higher in these MOST vs. OAI groups. Second, while only persons with bilateral KL <2 were included, frequency of KL 0 in both knees was higher in the MOST groups; OAI high-risk groups included more individuals with KL 1 in one or both knees.

Outcome frequency in low risk groups was similar between the two cohorts, reinforcing the concept of a resilient phenotype. Risk of incident slow gait speed was low in persons <66.5 years, with a WOMAC Function score ≤23.7, if above the education threshold. Being younger and with a better WOMAC Function score and *below* the education threshold could be overcome, by one of two routes – any strenuous activity ≥2 days/week, or not being obese and not having high depressive symptoms (Figures 2 and 4). The findings demonstrate the importance of validation, and that comparable performance cannot be assumed even when studies are similarly designed. Comparability of AUCs in the two cohorts provides further evidence of validation and generalizability.

This study has limitations. We used easily assessed variables, deliberately to maximize application of these trees. However, other variables may influence risk discrimination. The validation cohort had a shorter follow-up duration. Both OAI and MOST were designed to study community-dwelling individuals at high risk for knee OA and recruited from population lists but did not use random sampling; to accrue a comparably sized random sample would require this data collection in a very large population study. We included persons without radiographic knee OA. These findings should be validated in a high-risk population without self-reported knee OA. These results may not be generalizable to a non-U.S. population. As an objective performance measure associated with disability and survival (36–40), gait speed was a logical choice to measure outcome. A threshold is more interpretable than change. However, an inherent issue is that individuals closer to a threshold may be more likely to cross it, and predictors may be weighted towards variables associated with being closer to it. Notably, change also has limitations, e.g., with interpretability, how to incorporate from where a person starts, and what magnitude of change is meaningful at different starting points.

This prognostic stratification could be applied in community and clinical settings to promote awareness of risk and motivate efforts to prevent poor outcome. This would involve identifying persons at high risk for knee OA, and then among them, those at high risk for functional impairment. The approach to identify the former, carefully developed and very similar in the OAI and MOST, is translatable into a short paper or electronic form; this with a tree would yield an easily completed, simple, and inexpensive tool. The current findings suggest that the 3- and 7-risk-group trees are reasonable alternatives. If simplicity is

required, the smaller tree may suffice. The 7-risk-group tree is slightly more burdensome but had better AUCs; in theory, the modifiable factors (strenuous activity, high depressive symptoms, obesity) in the 7-risk-group tree could serve to motivate. These findings have impact at two levels, first as a tool to enhance awareness of risk of impaired function at an early stage, which may motivate steps to prevent decline, and second, to help define eligibility for functional decline prevention trials. For a sense of magnitude, among 1000 with pre-OA, 299 would be classified high risk (High Risk-1 or −2 using the 3-risk-group tree), of whom 72 (24.1%) would be expected to experience incident slow gait speed over the coming 7-10 years. Of the other 701 persons not classified high risk, 38 (5.4%) would be expected to experience this outcome. There are several potential interventions to prevent disability in pre-OA; an abundant literature suggests the most cost-effective and scalable may include physical activity promotion. Awareness of risk at the stage of our sample, not yet afflicted by knee OA, would be information at a point when these individuals are well enough to act and to perceive such action as a preservation of wellness.

In conclusion, in persons at high risk for knee OA, easily acquired data can be used to identify those at high risk of incident slow gait speed. Outcome risk varied greatly depending on risk group identified using the trees. These trees can inform an individual's awareness, at an early stage, of risk for impaired function, and define eligibility for prevention trials.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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KEY MESSAGES

- This is the first report to develop and validate risk stratification trees for incident functional impairment in persons with pre-osteoarthritis, defined as at high risk but not yet with radiographic disease.
- Our derivation and validation cohorts are from carefully designed, prospective, longitudinal cohort studies in which participants were comprehensively characterized and with multi-year follow-up.
- Forty potential predictors were consider to develop the trees; all predictors considered and in the final trees are easily assessed.
- The frequency of incident functional impairment varied according to tree-based risk group membership. AUCs were comparable in the derivation and validation cohorts.
- The identified trees are feasible for clinical settings to stratify risk and motivate prevention efforts at a stage when such efforts are most likely to be realizable and effective.

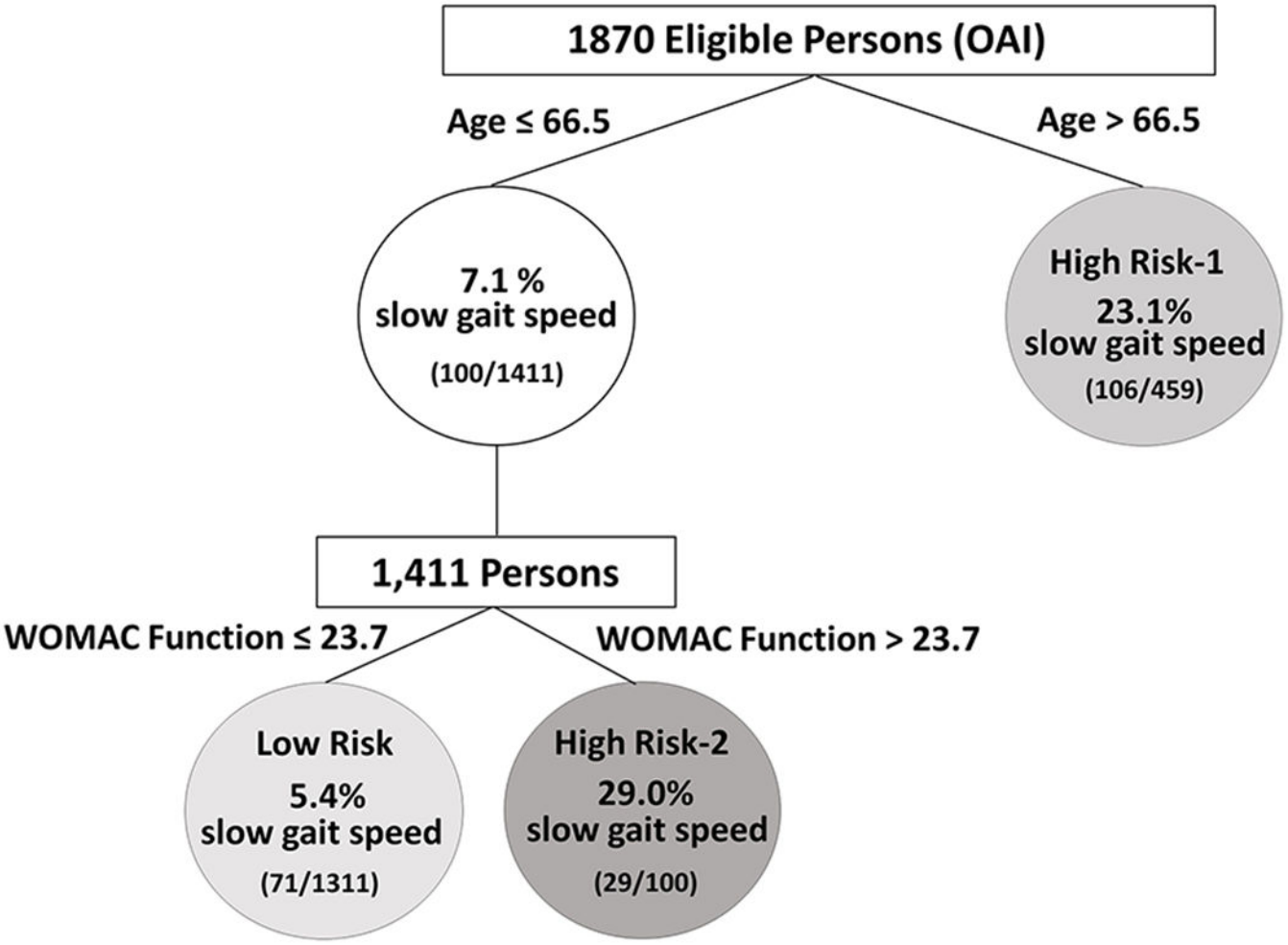

FIGURE 1. Predictors of Incident Slow Gait Speed and Risk Stratification, Derivation Cohort (OAI).

The figure depicts the optimal (most parsimonious) tree and frequency of outcome for each terminal node (risk group):

- age >66.5 years (High Risk-1)
- age ≤66.5 and WOMAC Function >23.7 (High Risk-2)
- age ≤66.5 and WOMAC Function ≤23.7 (Low Risk)

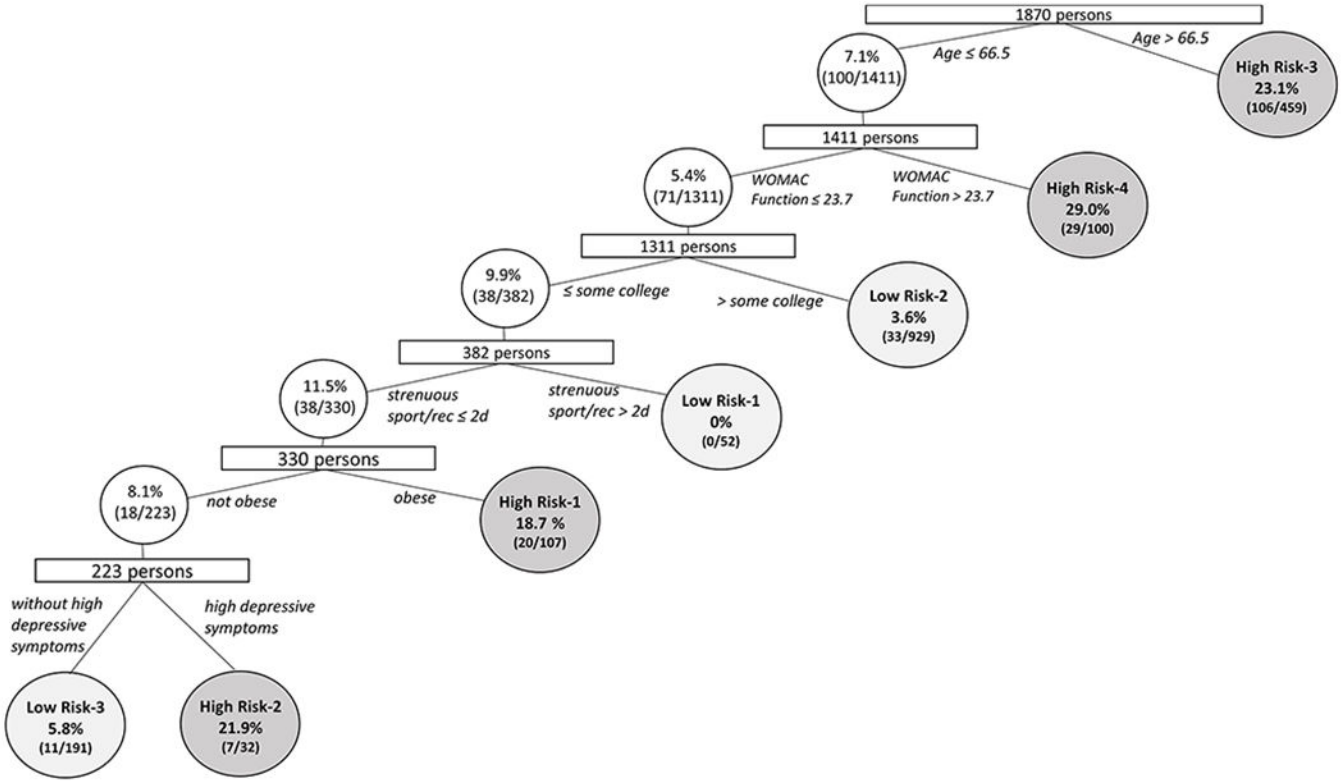

FIGURE 2. Predictors of Incident Slow Gait Speed and Risk Stratification, Derivation Cohort (OAI).

The figure depicts the 7-risk-group tree and frequency of outcome for each risk group:

- age >66.5 (High Risk-3)
- age ≤66.5, WOMAC Function >23.7 (High Risk-4)
- age ≤66.5, WOMAC Function ≤23.7, education >some college (Low Risk-2)
- age ≤66.5, WOMAC Function ≤23.7, education ≤some college, strenuous activities >2 days (Low Risk-1)
- age ≤66.5, WOMAC Function ≤23.7, education ≤some college, strenuous activities ≤2 days, obese (High Risk-1)
- age ≤66.5, WOMAC Function ≤23.7, education ≤some college, strenuous activities ≤2 days, nonobese, with high depressive symptoms (High Risk-2)
- age ≤66.5, WOMAC Function ≤23.7, education ≤some college, strenuous activities ≤2 days, nonobese, without high depressive symptoms (Low Risk-3)

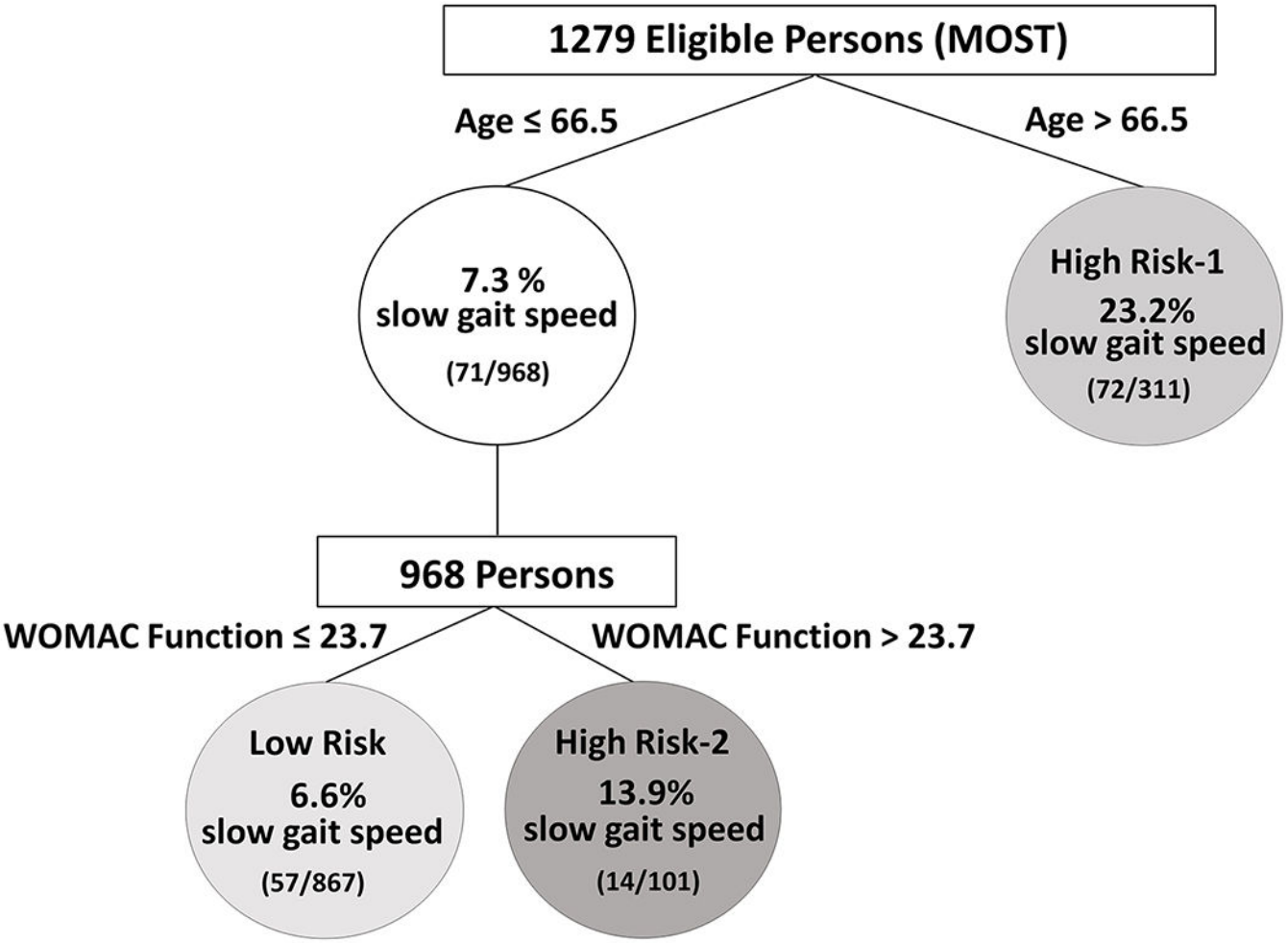

FIGURE 3. Predictors of Incident Slow Gait Speed and Risk Stratification, Validation Cohort (MOST).

The figure depicts the findings when the most parsimonious tree generated by analysis of the derivation cohort was tested for its ability to risk stratify persons in the validation cohort (MOST).

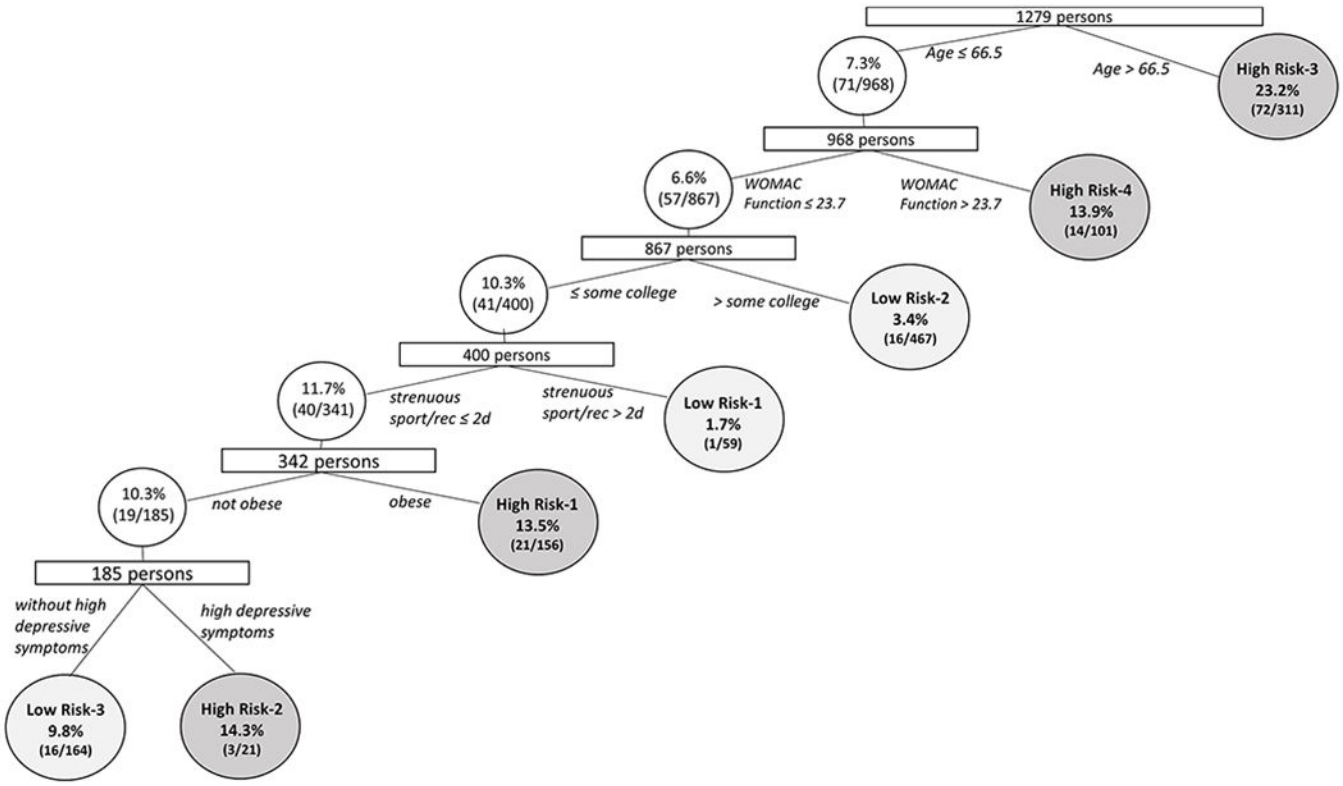

FIGURE 4. Predictors of Incident Slow Gait Speed and Risk Stratification, Validation Cohort (MOST).

The figure depicts the findings when the 7-risk-group tree generated by analysis of the derivation cohort was tested for its ability to risk stratify persons in the validation cohort (MOST).

TABLE 1.

CHARACTERISTICS OF THE DERIVATION AND VALIDATION COHORTS[a]

	Derivation Cohort n = 1870 persons	Validation Cohort n = 1279 persons
Demographic		
Age, mean (SD), years	59.0 (9.0)	60.4 (7.8)
Female	1093 (58)	727 (57)
Race (African-American)	234 (13)	148 (12)
Hispanic	22 (1)	6 (0.5)
Education		
less than high school graduate	35 (2)	29 (2)
high school graduate	192 (10)	257 (21)
some college	409 (22)	348 (27)
college graduate	418 (23)	280 (22)
some graduate school	168 (9)	116 (9)
graduate degree	635 (34)	249 (19)
Live alone	357 (19)	224 (18)
Married	1316 (70)	966 (76)
Health insurance	1799 (96)	Not available
Knee history		
Knee injury	650 (35)	407 (32)
Knee surgery	200 (11)	125 (10)
Family history knee replacement	263 (14)	Not available
Knee OA disease severity		
KL 0 in both knees	1206 (64)	874 (68)
KL 0 in one knee, 1 in one knee	388 (21)	230 (18)
KL 1 in both knees	276 (15)	175 (14)
Pain/OA other sites[b]		
Back pain	1082 (58)	889 (70)
Hip pain	435 (23)	603 (47)
Ankle pain	162 (9)	269 (21)
Foot pain	181 (10)	502 (40)

	Derivation Cohort n = 1870 persons	Validation Cohort n = 1279 persons
Hand OA (observed hard bumps on joints closest to fingertips)	554 (30)	Not available
Comorbid conditions		
BMI, mean (SD), kg/m^2	27.2 (4.4)	29.0 (4.8)
Overweight	752 (40)	527 (41)
Obese	477 (26)	487 (38)
High depressive symptoms	170 (9)	140 (11)
Comorbidity (2 or more)	132 (7)	111 (9)
Smoking (current)	131 (7)	81 (6)
Falls	599 (32)	Not available
Knee symptoms/function		
Frequent knee symptoms		Frequent knee symptoms
no pain either knee	393 (21)	no frequent pain either knee 924 (72)
infrequent pain, no pain	284 (15)	no frequent pain, frequent pain 230 (18)
infrequent pain, infrequent pain	436 (23)	frequent pain both knees 124 (10)
frequent pain, no pain	247 (13)	
frequent pain, infrequent pain	195 (10)	
frequent pain both knees	314 (17)	
Medication use for knee symptoms[c]	364 (19)	260 (46)
KOOS Pain,[d] mean (SD), range 0-100 (higher better)	84.8 (15.5)	Not available
KOOS Symptoms,[d] mean (SD), range 0-100 (higher better)	87.8 (12.1)	Not available
KOOS item, aware of problems with knees, at least weekly	1005 (54)	Not available
KOOS item, modified lifestyle to avoid damaging activities to knees, moderate or worse	391 (21)	Not available
KOOS item, how much troubled with lack of confidence in knees, moderate or worse	266 (14)	Not available
KOOS item, general difficulty with knees, moderate or worse	344 (18)	Not available
WOMAC Pain,[d] mean (SD), range 0-20, higher worse	2.4 (2.9)	2.9 (3.3)
WOMAC Function,[e] mean (SD), range 0-68, higher worse	6.8 (9.2)	9.6 (10.4)
WOMAC Stiffness,[d] mean (SD), range 0-8, higher worse	1.5 (1.5)	1.7 (1.6)

	Derivation Cohort n = 1870 persons	Validation Cohort n = 1279 persons
Either knee, limit activities due to pain, aching or stiffness, past 30 days	356 (19)	205 (16)
Gait speed, mean (SD), m/s	1.4 (0.2)	1.3 (0.2)
Physical activity (past 7 days)		
Sitting		
Never	5 (0.3)	1 (0.1)
Seldom (1-2 days)	71 (4)	46 (3.6)
Sometimes (3-4 days)	178 (10)	154 (12)
Often (5-7 days)	1616 (86)	1078 (84)
Walking		
Never	276 (15)	127 (10)
Seldom (1-2 days)	348 (19)	196 (15)
Sometimes (3-4 days)	414 (22)	303 (24)
Often (5-7 days)	832 (44)	653 (51)
Light sport/recreation		
Never	1602 (86)	988 (77)
Seldom (1-2 days)	184 (10)	198 (15)
Sometimes (3-4 days)	58 (3)	63 (5)
Often (5-7 days)	26 (1)	30 (2)
Moderate sport/recreation		
Never	1545 (83)	1021 (80)
Seldom (1-2 days)	203 (11)	146 (11)
Sometimes (3-4 days)	86 (5)	37 (3)
Often (5-7 days)	36 (2)	75 (6)
Strenuous sport/recreation		
Never	1216 (65)	880 (69)
Seldom (1-2 days)	241 (13)	147 (11)
Sometimes (3-4 days)	270 (14)	163 (13)
Often (5-7 days)	143 (8)	89 (7)
Muscle strength/endurance		
Never	1009 (54)	705 (55)
Seldom (1-2 days)	324 (17)	170 (13)
Sometimes (3-4 days)	362 (19)	231 (18)
Often (5-7 days)	175 (9)	173 (14)

[a] Values are expressed as number (percentage) unless otherwise indicated. Data are based on participants with available data for each characteristic.

[b] OAI and MOST used different questions. In OAI, hip, ankle, and foot pain were queried as most days of 1 month during the past 12 months. In MOST, hip pain was queried as any pain, past 30 days, and foot pain as pain on most of the past 30 days; ankle pain was present if participants answered yes to "on most days, do you have pain, aching or stiffness in any joints", and then selected either ankle on a drawing of a human figure.

[c] In OAI, all participants were asked about medication use: “Either knee, used medication for pain, aching or stiffness more than half the days of a month, past 12 months”. In MOST, only persons who answered yes to the question “Has a doctor ever told you that you have arthritis” were asked about medication use: “Are you taking any of the following medications for your arthritis every day or almost every day? (Aspirin, Ibuprofen, Acetaminophen, Cox2 inhibitors, other nonsteroidal/anti-inflammatories)”

[d] Worse of the two knees

[e] OAI assessed WOMAC Function separately for each knee; the worse value was used. MOST assessed WOMAC Function considering both knees at once.

TABLE 2.

CHARACTERISTICS OF THE DERIVATION AND VALIDATION COHORTS IN RISK GROUPS FROM THE 7-RISK-GROUP MODEL[a]

		Low Risk-1	Low Risk-2	Low Risk-3	High Risk-1	High Risk-2	High Risk-3	High Risk-4
		DERIVATION COHORT (1870 PERSONS)						
Number of persons with incident slow gait speed/number in group		0/52 (0)	33/929 (3.6)	11/191 (5.8)	20/107 (18.7)	7/32 (21.9)	106/459 (23.1)	29/100 (29.0)
Demographic								
	Age, mean (SD), years	55.7 (6.2)	54.7 (5.6)	55.4 (6.3)	55.6 (6.0)	56.0 (6.0)	71.7 (3.3)	54.3 (6.1)
	Female	32 (62)	482 (52)	153 (80)	72 (67)	21 (66)	265 (58)	68 (68)
	Education							
	less than high school graduate	2 (4)	0	2 (1)	7 (7)	4 (13)	12 (3)	8 (8)
	high school graduate	12 (24)	0	49 (26)	29 (27)	6 (20)	79 (17)	17 (18)
	some college	37 (73)	0	140 (73)	71 (66)	20 (67)	96 (21)	45 (46)
	college graduate	0	308 (33)	0	0	0	94 (21)	16 (17)
	some graduate school	0	120 (13)	0	0	0	42 (9)	6 (6)
	graduate degree	0	497 (54)	0	0	0	133 (29)	5 (5)
Knee history								
Knee OA disease severity								
KL 0 in both knees		40 (77)	632 (68)	133 (70)	59 (55)	22 (69)	267 (58)	53 (53)
KL 0 in one knee, 1 in one knee		9 (17)	183 (19)	32 (16)	28 (26)	4 (13)	107 (24)	25 (25)
KL 1 in both knees		3 (6)	114 (12)	26 (14)	20 (19)	6 (19)	85 (19)	22 (22
Comorbid conditions								
	BMI, mean (SD), kg/m^2	27.3 (4.4)	26.9 (4.5)	25.2 (2.9)	33.3 (2.7)	24.7 (3.4)	26.6 (3.7)	29.5 (5.0)
	Overweight	23 (44)	350 (38)	106 (56)	0	16 (50)	216 (47)	41 (41)
	Obese	13 (25)	233 (25)	0	107 (100)	0	82 (18)	42 (42)

		Low Risk-1	Low Risk-2	Low Risk-3	High Risk-1	High Risk-2	High Risk-3	High Risk-4
	High depressive symptoms	1 (2)	68 (7)	0	16 (15)	31 (100)	25 (5)	29 (29)
Knee symptoms/function								
	No frequent symptoms either knee	27 (52)	581 (62)	116 (61)	57 (54)	18 (57)	305 (66)	9 (9)
	WOMAC Pain,[b] mean (SD)	2.2 (2.2)	1.7 (2.0)	2.4 (2.5)	2.7 (2.7)	3.1 (3.1)	2.1 (2.7)	9.3 (2.8)
	WOMAC Function,[c] mean (SD)	5.3 (6.7)	4.5 (5.9)	6.2 (6.6)	7.3 (7.2)	8.9 (6.9)	6.2 (8.7)	31.8 (6.4)
	Gait speed, mean (SD), m/s	1.4 (0.1)	1.4 (0.2)	1.4 (0.2)	1.3 (0.2)	1.4 (0.2)	1.3 (0.2)	1.3 (0.2)
Physical activity (past 7d)								
	Strenuous sport/recreation							
	Never	0	529 (57)	166 (87)	93 (87)	31 (97)	314 (68)	83 (83)
	Seldom (1-2 days)	0	141 (15)	25 (13)	14 (13)	1 (3)	53 (12)	7 (7)
	Sometimes (3-4 days)	40 (77)	155 (17)	0	0	0	66 (14)	9 (9)
	Often (5-7 days)	12 (23)	104 (11)	0	0	0	26 (6)	1 (1)
		VALIDATION COHORT (1279 PERSONS)						
Number of persons with incident slow gait speed/number in group		1/59 (1.7)	16/467 (3.4)	16/164 (9.8)	21/156 (13.5)	3/21 (14.3)	72/311 (23.1)	14/101 (13.9)
Demographic								
	Age, mean (SD), years	58.6 (5.1)	56.3 (4.8)	58.2 (5.1)	56.7 (5.0)	56.0 (5.6)	71.3 (3.5)	57.2 (5.3)
	Female	31 (53)	236 (51)	111 (68)	94 (60)	13 (62)	176 (57)	66 (65)
	Education							
	less than high school graduate	1 (2)	0	6 (4)	4 (3)	1 (5)	14 (5)	3 (3)
	high school graduate	23 (39)	0	59 (36)	65 (42)	9 (43)	76 (24)	25 (25)
	some college	35 (59)	0	99 (60)	87 (56)	11 (52)	84 (27)	32 (32)
	college graduate	0	199 (43)	0	0	0	61 (20)	20 (20)
	some graduate school	0	83 (18)	0	0	0	25 (8)	8 (8)
		0	185 (40)	0	0	0	51 (16)	13 (13)

		Low Risk-1	Low Risk-2	Low Risk-3	High Risk-1	High Risk-2	High Risk-3	High Risk-4
	graduate degree							
Knee history								
Knee OA disease severity								
KL 0 in both knees	42 (71)	329 (70)	120 (73)	103 (66)	16 (76)	195 (63)	69 (68)	
KL 0 in one knee, 1 in one knee	10 (17)	87 (19)	23 (14)	28 (18)	4 (19)	64 (21)	14 (14)	
KL 1 in both knees	7 (12)	51 (11)	21 (13)	25 (16)	1 (5)	52 (17)	18 (18)	
Comorbid conditions								
	BMI, mean (SD), kg/m^2	28.3 (4.4)	28.8 (4.8)	26.2 (2.7)	34.0 (3.7)	26.0 (2.6)	28.1 (4.1)	30.3 (5.5)
	Overweight	27 (46)	184 (39)	120 (73)	0	14 (67)	151 (49)	31 (31)
	Obese	19 (32)	170 (36)	0	156 (100)	0	91 (29)	51 (51)
	High depressive symptoms	5 (8)	32 (7)	0	31 (20)	21 (100)	20 (6)	31 (31)
Knee symptoms/function								
	No frequent symptoms either knee	45 (76)	354 (76)	128 (78)	122 (78)	14 (67)	230 (74)	31 (31)
	WOMAC Pain,[b] mean (SD)	2.3 (2.8)	1.9 (2.3)	2.5 (2.5)	2.5 (2.6)	3.2 (2.6)	3.0 (3.4)	8.7 (3.2)
	WOMAC Function,[c] mean (SD)	6.5 (6.4)	5.6 (6.5)	7.1 (6.2)	8.4 (7.0)	12.1 (8.8)	10.6 (10.9)	31.5 (7.0)
	Gait speed, mean (SD)	1.3 (0.2)	1.3 (0.2)	1.3 (0.2)	1.2 (0.1)	1.3 (0.2)	1.2 (0.1)	1.2 (0.1)
Physical activity (past 7d)								
	Strenuous sport/recreation							
	Never	0	275 (59)	143 (87)	142 (91)	20 (95)	220 (71)	80 (79)
	Seldom (1-2 days)	0	68 (15)	21 (13)	14 (9)	1 (5)	33 (11)	10 (10)
	Sometimes (3-4 days)	41 (69)	82 (18)	0	0	0	33 (11)	7 (7)
	Often (5-7 days)	18 (31)	42 (9)	0	0	0	25 (8)	4 (4)

[a]Values are expressed as number (percentage) unless otherwise indicated. Data are based on participants with available data for each characteristic.

[b] Worse of the two knees

[c] OAI assessed WOMAC Function separately for each knee; the worse value was used. MOST assessed WOMAC Function considering both knees at once