Creation and Validation of Algorithms to Identify Patients with Moderate-to-Severe Osteoarthritis of the Hip and/or Knee and Inadequate/Intolerable Response to Multiple Pain Medications

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BACKGROUND

- Osteoarthritis (OA) is a degenerative joint disease that impacts ~32.5 million US adults:[1]
  - It is more common in women than men; for all persons, risk increases with age.[2]
  - 27.8% of those aged >45 years have radiographic OA of the knee(s) (24.3% of men, 30.1% of women); 27.0%, of the hip(s) (25.7% in men; 26.9% in women).[3]
- Deleterious impacts of OA are substantial and are experienced disproportionately among those with moderate-to-severe disease and/or with relatively high levels of pain.[4,5] Quantification of these impacts would help inform development of new therapeutics to alleviate their burden; the approach to such a study is complicated by limitations of existing data sources:
  - Healthcare claims databases provide comprehensive information on use and cost of care but lack information on disease severity/progression and pain levels; conversely, medical records provide clinical detail but lack complete data on use and cost of care.
  - If case-selection algorithms of sufficient reliability can be developed, healthcare claims databases could be used to address these and related questions.

OBJECTIVE

- To determine preliminarily whether case-selection algorithms can be developed for use in electronic healthcare databases to identify with reasonably good accuracy patients with: (1) hip/knee OA; (2) moderate-to-severe OA; and (3) inadequate/intolerable response to ≥2 pain-related medications.

METHODS

Data Source

- Data were obtained from Reliant Medical Group, a large, private, multispecialty group practice (>250 physicians in >20 locations) in central Massachusetts:
  - 62% of patients have commercial insurance and 38% are insured through Medicare and/or Medicaid; 14% are aged ≥65 years.
  - Institutional Review Board approval was obtained before chart abstraction or analyses of electronic health data was undertaken.

Study Population

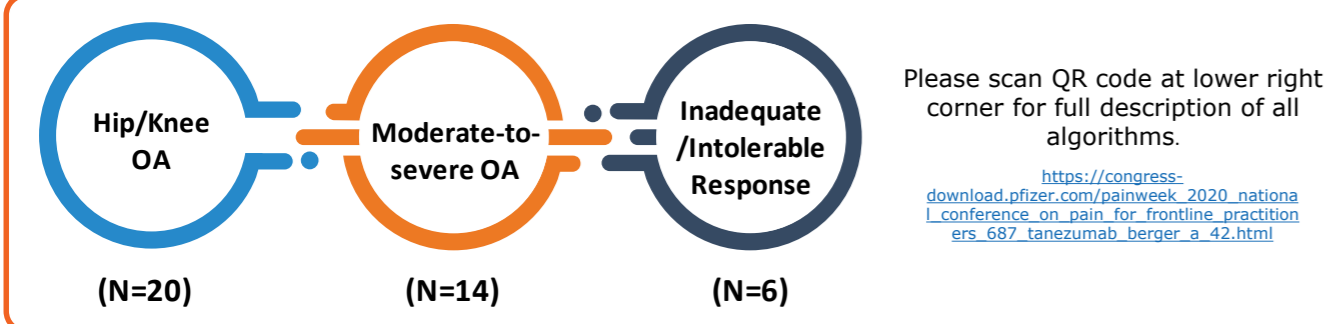- 50 adults (i.e., aged ≥18 years), selected at random based on presence of defining characteristics between January 1, 2014 and December 31, 2019.

Defining Characteristic	Selection Criteria	N
Hip/knee OA	≥1 claims with relevant diagnoses	46
Back/other joint pain	≥1 claims with relevant diagnoses **AND** no diagnoses of hip/knee OA	2
No OA	No diagnoses of OA (and site) **AND** no receipt of HA/IA steroids **AND** no hip/knee arthroplasty	2

Abbreviations: HA = hyaluronic acid; IA = intra-articular; OA = osteoarthritis

Case Selection Algorithms

- 40 case-selection algorithms developed based on targeted review of published literature, relevant treatment guidelines, and professional organizations.

Hip/Knee OA (N=20) — Moderate-to-severe OA (N=14) — Inadequate/Intolerable Response (N=6)

Please scan QR code at lower right corner for full description of all algorithms.

https://congress-download.pfizer.com/painweek_2020_national_conference_on_pain_for_frontline_practitioners_687_tanezumab_berger_a_42.html

Statistical Analysis

- Patients' medical records used to ascertain "true status" with respect to each characteristic of interest.
- Case-selection algorithms then applied, with performance assessed vs. true status in terms of sensitivity analysis, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy:
  - Ability of algorithms to collectively correctly identify those with moderate-to-severe OA with inadequate/intolerable response to pain-related medications (i.e., all three criteria) also assessed.

LIMITATIONS

- Relatively small sample (n=50) from single health system; while promising, additional research required to verify and potentially expand upon algorithm combinations identified herein.
- Information available from patients' medical records was extremely variable and often lacking OA-specific severity scales; clinical experience required to fully interpret available information.

RESULTS

Patient Characteristics

- Most patients were aged ≥65 years, female, and Caucasian; use of pain-related therapies was common.

DEMOGRAPHICS
Female 66.0%
Mean Age: 70.0 Years
Caucasian, 82.0%
Unknown, 14.0%
Hispanic, 4.0%

BMI
Mean: 32.0 kg/m²
IQR: 28.5-36.0 kg/m²

ANALGESIC USE
86.0% IA steroids
42.0% Opioids
40.0% NSAIDs

Abbreviations: BMI = body mass index; IA = intra-articular; IQR = interquartile range; NSAIDs = non-steroidal anti-inflammatory drugs
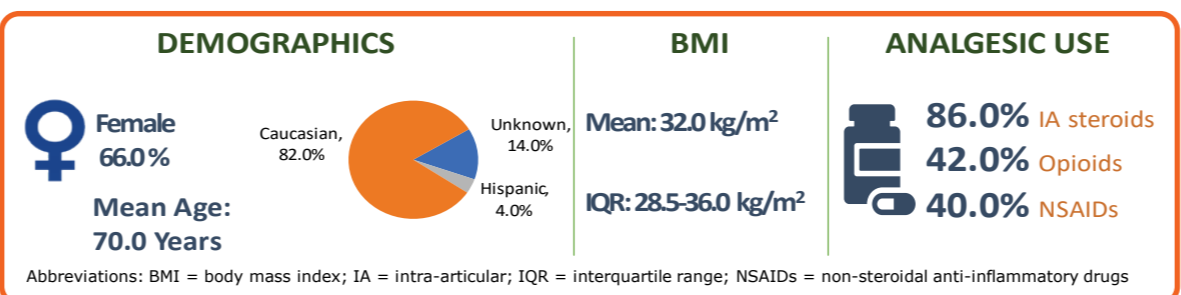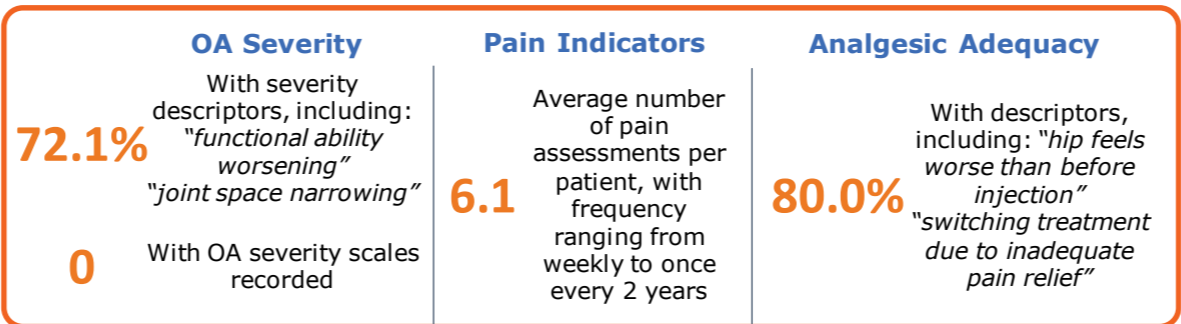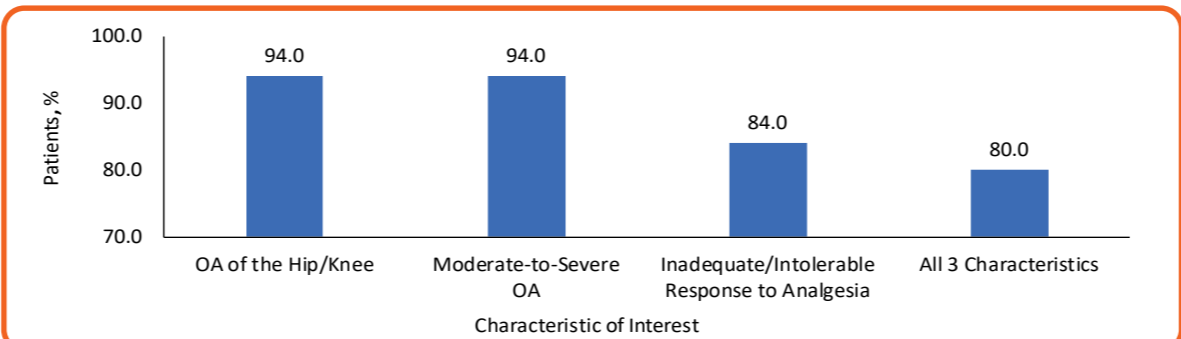
Chart Review

- Evidence of disease severity limited to descriptive text and unavailable for most patients; levels of pain estimated based on descriptors and numeric (but unnamed) pain scales; most patients had information on reason(s) for changes to therapy.

OA Severity
72.1% With severity descriptors, including: "functional ability worsening" "joint space narrowing"
0 With OA severity scales recorded

Pain Indicators
6.1 Average number of pain assessments per patient, with frequency ranging from weekly to once every 2 years

Analgesic Adequacy
80.0% With descriptors, including: "hip feels worse than before injection" "switching treatment due to inadequate pain relief"

- 94.0% (n=47) had confirmatory evidence of hip/knee OA in medical records; 94.0% (n=47), of moderate-to-severe disease; and 84.0% (n=42), of inadequate/intolerable response:
  - Most patients (80.0% [n=40]) had evidence of all three characteristics.

Algorithms for Identifying Hip/Knee OA

- Each algorithm resulted in 100% PPV and specificity, respectively; "≥1 outpatient visits resulting in diagnoses of OA of the hip/knee" (algorithm #4) and "≥1 medical encounters resulting in diagnoses of OA of the hip/knee" (#15) had the greatest accuracy and sensitivity.
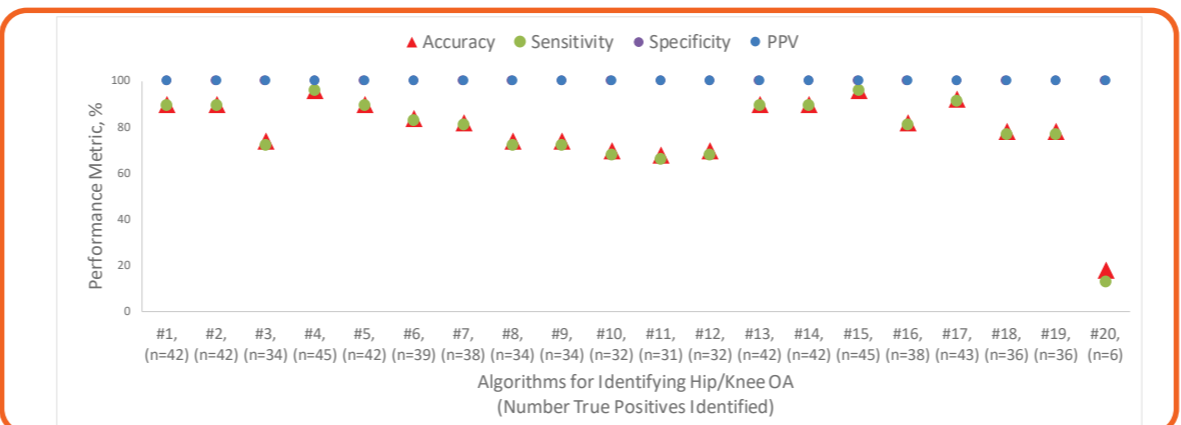
Algorithms for Identifying Moderate-to-Severe OA

- Algorithms with 100% PPV and 100% specificity required presence of: OA-related surgeries (algorithm #1); multiple X-ray examinations (#14); nerve block (#9); multiple opioid prescriptions (#4), receipt of NSAIDs (#5, #6); relatively high OA-related costs (#12); and/or use of mobility aids (#10).
  - Receipt of ≥1 HA/IA steroid injections (algorithm #7) had greatest accuracy and sensitivity.
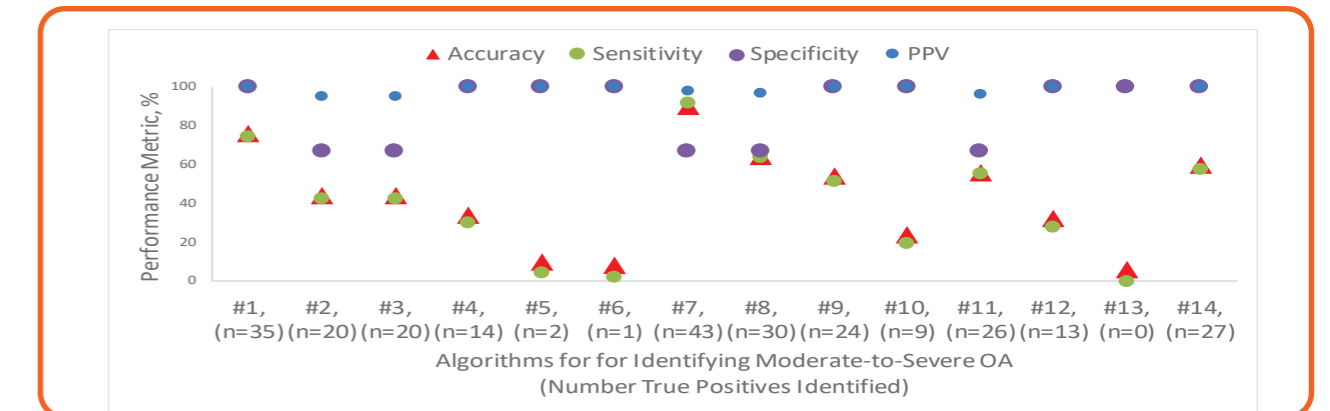
Algorithms for Identifying Inadequate/Intolerable Response

- "Receipt of nerve block" (algorithm #4) resulted in 96% PPV and 62% accuracy; "receipt of either HA/IA corticosteroid injection or nerve block following receipt of 2 different analgesic classes" (#1) resulted in 100% specificity but identified 0 true positives.
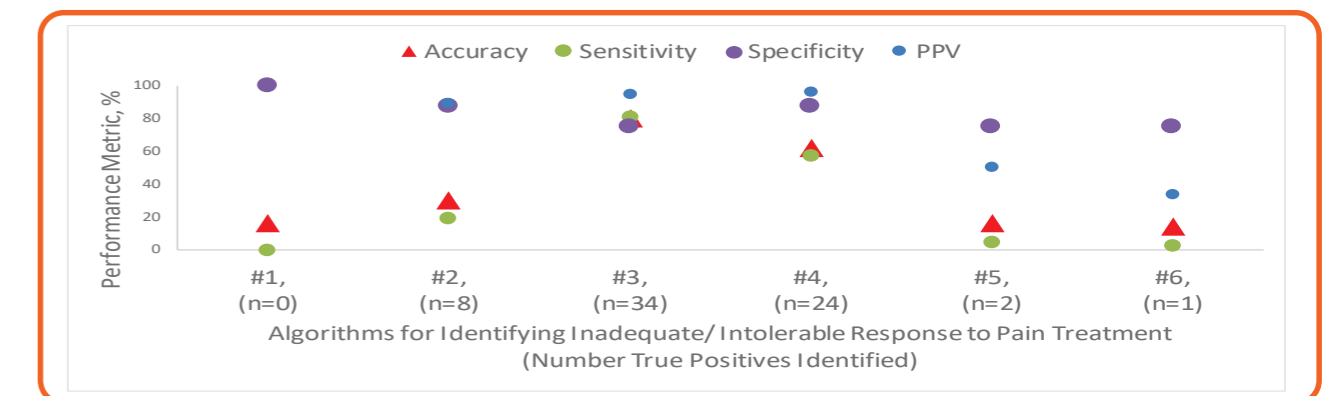
Algorithm Combinations for Identifying All Three Characteristics

- Ability of algorithms to identify patients with all 3 characteristics varied substantially:
  - While several algorithm combinations resulted in estimates of PPV ≥90% and accuracy ≥80%, no single combination identified all patients with these characteristics (range of true positives identified was 0.0% to 82.5%).
  - Combination that identified largest number of true positives also resulted in misclassification of 2 patients.
  - Overall accuracy ranged from 16.0% to 82.0%.

Well-Performing Algorithm Combinations

Hip/Knee OA: #4 Severity: #1 Inadequacy: #3		Chart Review	
Algorithms		Yes	No
	Yes	33	2
	No	7	8

PPV: 94.3%; NPV: 53.3%
Sen: 85.5%; Spec: 80.0%
Accuracy: 82.0%

Hip/Knee OA: #4 Severity: #7 Inadequacy: #3		Chart Review	
Algorithms		Yes	No
	Yes	32	2
	No	8	8

PPV: 94.1%; NPV: 50.0%
Sen: 80.0%; Spec: 80.0%
Accuracy: 80.0%

Poor-Performing Algorithm Combination

Hip/Knee OA: #1 Severity: #10 Inadequacy: #6		Chart Review	
Algorithms		Yes	No
	Yes	0	2
	No	40	8

PPV: 0.0%; NPV: 16.7%
Sen: 0.0%; Spec: 80.0%
Accuracy: 16.0%

Abbreviations: PPV = positive predictive value; NPV = negative predictive value; Sen = sensitivity; Spec = specificity

CONCLUSIONS

- Algorithms based on literature review and expert opinion can identify relevant OA patient subgroups, although those used to identify hip/knee OA are more reliable than those used for disease severity or inadequate/intolerable response to pain-related therapies:
  - Machine learning may improve algorithm performance.
- No one algorithm combination could identify all true cases; multiple combinations will likely be required to comprehensively capture cohorts:
  - Pragmatic assessment required that considers trade-offs between increasing number of true positives vs. risk of misclassification of false negatives.
  - Pending this assessment, algorithms of high PPV may prove an efficient tool to enable analyses of large healthcare databases to increase knowledge of these important OA subgroups.

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