1	Presence and Extent of Severe Facet Joint Osteoarthritis Are Associated with Back
2	Pain in Older Adults
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34 ABSTRACT

35 **Objective**: To determine whether the presence and extent of severe lumbar facet joint 36 osteoarthritis (OA) is associated with back pain in older adults, accounting for disc height 37 narrowing and other covariates. 38 **Design**: 252 older adults from the Framingham Offspring Cohort (mean age 67 years) 39 were studied. Participants received standardized CT assessments of lumbar facet joint OA 40 and disc height narrowing at the L2-S1 interspaces using 4-grade semi-quantitative 41 scales. Severe facet joint OA was defined according to the presence and/or degree of joint 42 space narrowing, osteophytosis, articular process hypertrophy, articular erosions, 43 subchondral cysts, and intraarticular vacuum phenomenon. Severe disc height narrowing 44 was defined as marked narrowing with endplates almost in contact. Back pain was 45 defined as participant report of pain on most days or all days in the past 12 months. We 46 used multivariable logistic regression to examine associations between severe facet joint 47 OA and back pain, adjusting for key covariates including disc height narrowing, 48 sociodemographics, anthropometrics, and health factors. 49 **Results**: Severe facet joint OA was more common in participants with back pain than 50 those without (63.2% vs. 46.7%;p=0.03). In multivariable analyses, presence of any 51 severe facet joint OA remained significantly associated with back pain (odds 52 ratio[OR]2.15 (95% confidence interval [CI]1.13-4.08). Each additional joint with severe 53 OA conferred greater odds of back pain (OR per joint 1.20 (95% CI;1.02-1.41). 54 **Conclusions:** The presence and extent of severe facet joint OA on CT imaging is 55 associated with back pain in community-based older adults, independent of

56 sociodemographics, health factors, and disc height narrowing.

57 Key Words: zygapophyseal; lumbar; arthritis, intervertebral disc, spondylosis

58

60 INTRODUCTION

61

62	Back pain is a common reason prompting older adults to seek medical care, and a
63	leading cause of disability in developed countries [1-5]. The spinal facet
64	('zygapophyseal') joints are a widely treated source of back pain, and rates of
65	nonoperative yet invasive percutaneous facet joint procedures in older adults have
66	increased more than 4-fold over the past decade[6]. Facet joint osteoarthritis (OA) is
67	often presumed to be the cause of pain in some older adults with facet-mediated pain
68	confirmed by anesthetic blocks[7]. Nevertheless, some patients with facet joint OA may
69	have no back pain at all, and patients without facet joint OA may have substantial back
70	pain[8-10]. This discordance between the appearance of facet joint OA on imaging and
71	the symptom of pain is analogous to the high prevalence of asymptomatic radiographic
72	findings observed in the setting of knee OA[11, 12].
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82 as is seen in the context of knee OA[11]. Also, prior studies did not examine the number

83	of levels affected by severe facet joint OA, ignoring this important aspect of disease
84	burden. Furthermore, earlier studies examined younger and middle-aged samples. This
85	largely excludes older adults, in whom advanced facet joint OA on imaging as well as
86	facet-mediated pain is most prevalent[13, 14], and in whom facet joint interventions are
87	most commonly performed[6]. Last, some prior studies have not utilized well-described
88	and reliable scales for facet joint OA[8, 9].
89	< <table 1="">></table>
90	We attempted to overcome these limitations by conducting a study to examine
91	associations between lumbar facet joint OA on imaging and back pain in a sample
92	representative of community-based older US adults. The aim of this study was to
93	determine whether definitions of facet joint OA incorporating the presence and extent of
94	severe facet joint OA are associated with back pain in older adults, with and without
95	adjustment for other sociodemographic factors, clinical factors, and disc height
96	narrowing.
97	

- **METHODS**

101	Participants: This study was an ancillary investigation to the Framingham Heart Study,
102	and was approved by the Institutional Review Board of New England Baptist Hospital.
103	The Offspring cohort of the Framingham Heart Study was initiated in 1971 as a
104	prospective epidemiologic study of 5124 young adults [15]. 1418 individuals from the
105	Offspring cohort underwent computed tomography (CT) scanning as part of the
106	multidetector CT (MDCT) substudy of Framingham, which has been described elsewhere
107	^[16, 17] . Two hundred and seventy-two participants randomly selected from the MDCT
108	cohort study received standardized CT assessments of facet joint OA as part of this
109	ancillary study (Figure 1). Of this subgroup, 252 participants also attended Framingham
110	Examination 8, and comprised our study sample. This represents a separate study sample
111	from that reported in an earlier publication on facet joint OA by our research group [10].
112	Whereas the earlier study examined participants from both the Offspring and Generation
113	3 cohorts of Framingham, the present study sample is drawn from the Offspring cohort
114	only, enriching the sample for older adults. Furthermore, the present study includes
115	separate CT assessments conducted by different readers, and different pain assessments.
116	In addition, our <i>a priori</i> analytic approach is distinct from that taken in our earlier work
117	in that it examines the presence and extent of severe facet joint OA, rather than the
118	finding of any moderate FJ facet joint OA.
119	<< Figure 1>>
120	

121 Assessment of Facet Joint Osteoarthritis: All CT imaging assessments were performed 122 using eFilm Workstation (Version 2.0.0) software, with blinding to sociodemographic 123 and health-related factors, and pain information. Facet joint OA was graded at both the 124 left and the right side at the spinal levels L2-L3, L3-L4, L4-L5, and L5-S1. We applied 125 the Framingham Scale for grading of facet joint OA, a semi-quantitative measure we 126 designed for these research purposes, based on earlier scales by Pathria et al.[19] and 127 Weishaupt et al.[20] The Framingham Scale grades facet joint OA according to the 128 degree of pathoanatomic change in the separate subcategories of joint space narrowing, 129 osteophytosis, articular process hypertrophy, sclerosis, subarticular erosion, subchondral 130 cystic change, and presence of vacuum phenomenon (Appendix 1). Because we were 131 specifically focused on examining associations with severe or advanced facet joint OA, 132 we considered the presence of severe facet joint OA to be at least grade IV facet joint OA 133 in either the left or right facet joints at one or more lumbar spinal levels L2-S1 (Appendix 134 1). We defined the extent of severe facet joint OA as the number of joints with severe 135 facet joint OA at the lumbar spinal levels L2-S1 (range 0-8). The Framingham CT scans 136 did not consistently include the L1-L2 level, and this level therefore was not read as part 137 of these structured assessments.

138

Assessment of Disk Height Narrowing: Disc height narrowing was graded at spinal
levels L2-L3, L3-L4, L4-L5, and L5-S1, using grading criteria developed for research
purposes by Videman et al., that have been used previously in studies of spinal
degeneration on MRI[21-23]. Using sagittal CT reformatting, the midsagittal plane was
identified at each level, and measurements of disc height narrowing were made at the

144 midpoint of the anteroposterior diameter of the disk. This method was intended to 145 account for degenerative scoliosis, which is common in older adults and may influence 146 interpretations of disc height. These measurements were then used in applying the 147 grading system of Videman: disc height narrowing was graded as 'normal' (disk height 148 greater than level immediately superior), 'mild' (disk height equal to level immediately 149 superior), 'moderate' (disk height narrowed as compared to level immediately superior), 150 and 'severe' (endplates almost in contact)[24]. In instances where the reference level 151 exhibited apparent disc height narrowing, the first 'normal' interspace superior to the 152 index level was used as a reference. Since there is greater variability in disk height at the 153 L5-S1 level as compared to L4-L5 [25], L5-S1 was graded based on reader experience, 154 but was generally considered normal if comparable to, or slightly narrowed, as compared 155 to L4-L5. Further details of the disc grading methods employed are provided 156 elsewhere[24].

157

158 Quality and Reliability of CT Assessments: CT assessments of facet joint OA and disc 159 height narrowing were performed by a board-certified, fellowship-trained nonoperative 160 spine care specialist (PS), who was trained by a musculoskeletal radiologist (AG). 161 Assessments of facet joint OA and disc height narrowing were performed at separate 162 periods in time (i.e. disc height narrowing assessments were completed for all 163 participants in the sample prior to the start of facet joint OA assessments), and participants were blinded to the results of these assessments. A reference atlas for each 164 165 degenerative parameter was used throughout the reading process. The spine specialist 166 reader calibrated to the standard of the radiologist prior to the start of formal reads using

167 training sets of CT scans, and inter-observer reliability was calculated between the 168 radiologist and spine specialist at the start of the reading process. All CT scans were 169 interpreted by the spine specialist in a blinded fashion. Recalibration of the spine 170 specialist was repeated during the reading process, either by direct interactions with the 171 radiologist, or by review of images previously interpreted by the radiologist. To evaluate 172 for reader-drift, reliability was reassessed periodically. Inter-observer reliability using the 173 weighted κ statistic ranged between 0.68 and 0.84 for facet joint OA, and 0.70 and 0.84 174 for disc height narrowing, representing moderate to excellent reproducibility.

175

176 Assessment of Back Pain: All participants in the Framingham Offspring cohort 177 underwent a standardized interview as part of the recurring Framingham clinical 178 examinations. Participants were asked the question, 'Have you had back pain in the past 179 12 months?' Response categories included 'no back pain', or back pain on 'a few days', 180 'some days', 'most of the days', or 'all days'. Because most individuals reported having 181 at least some back pain, and we were interested in associations with frequent or persistent 182 back pain specifically, individuals who reported having back pain on 'all days' or 'most 183 of the days' were considered to have frequent back pain, and individuals who reported having no back pain, back pain on 'a few days', or 'some days' were considered to be 184 185 without frequent back pain. Back pain and covariate data were taken from the 186 Framingham examination that best coincided with the timing of the CT scan 187 (Examination 8); this examination was conducted an average of 20 months after the CT 188 scan (range: -1 to 58 months).

190 **Covariates:** Covariates examined in this study included those of particular relevance to 191 older adults at or beyond retirement age[26-28]. Data were collected on participant age 192 calculated according to birth date, and participant-reported sex, race, ethnicity, and 193 educational background. Participants reported on current employment or volunteering 194 activities, retirement from primary occupation or career, marital status, and whether or 195 not they currently lived alone. Height and weight were measured at each clinical 196 examination, and body mass index (BMI) was calculated as weight (kg) divided by height 197 (meters²). Participants who reported smoked regularly within the past year were defined 198 as current smokers.

199

200 Statistical analysis:

201 We characterized the sample using descriptive statistics. We compared 202 sociodemographics, health-related factors, and prevalence of facet joint OA and disc height 203 narrowing between participants with and without frequent back pain, using the Student's t-204 test for continuous variables or the chi-square test for categorical variables. We used a series 205 of logistic regression models to determine unadjusted associations between single 206 independent variables, including facet joint OA, and the outcome of frequent back pain. We 207 examined correlations between independent variables using Spearman correlation 208 coefficients. Next, we created a 'core' multivariable logistic regression model that included 209 those sociodemographic and health-related factors that demonstrated at least a statistical 210 trend towards an association with frequent back pain in the unadjusted regression models (p 211 ≤ 0.15). We then added the variables of any severe facet joint OA and any severe disc height 212 narrowing to the core multivariable model. We then repeated this process, treating the facet

213	joint OA and disc height narrowing variables as the number of joints with severe OA or the
214	number of disc levels with severe narrowing, rather than as dichotomous variables. We also
215	conducted secondary multivariable analyses choosing covariates based on conceptual
216	importance, adjusting for the factors of age, sex, BMI, and education. All analyses were
217	performed using SPSS software, version 20.0.0) (IBM Corporation, Armonk, NY).
218	
219	RESULTS
220	Two hundred and fifty-two participants comprised the study sample (Table 2).
221	The mean age of participants was 67.4 ± 9.1 years and approximately half of participants
222	were female. Reflecting the demographics of Framingham, Massachusetts at the time of the
223	Offspring cohort's inception, almost all participants were of white race and of non-Latino
224	ethnicity. Roughly half of the sample were neither working nor volunteering, or had retired
225	from their primary career occupation, reflecting the older age of the study sample. The study
226	sample was slightly older than the main MDCT cohort (67.4 vs. 65.9 years; p=0.02), but
227	otherwise without significant differences with respect to sociodemographic factors or back
228	pain (data not shown).
229	<< Table 2>>
230	Table 3 presents a comparison of individuals with and without frequent back pain.
231	Individuals with back pain were significantly older than those without (69.6 vs. 66.7 years;
232	p=0.03); this association was driven mainly by a higher prevalence of back pain in those
233	adults age \geq 75 years. Self-report of neither working nor volunteering currently, and
234	retirement from usual occupation, were significantly associated with a higher prevalence of

back pain, and individuals with back pain were also somewhat more likely to live alone.

Other sociodemographic and health factors, including higher BMI, were not associated with
back pain. The presence of moderate facet joint OA was not associated with back pain, but
both the presence of any severe facet joint OA (46.7% vs. 63.2%; p=0.03), and the number of
joints with severe facet joint OA (p=0.006), were significantly associated with back pain.
No associations were seen between disc height narrowing and back pain, regardless of the
severity or extent of disc height narrowing.

242

<<suggested position of Table 3>>

243 Table 4 presents odds ratios (ORs) and 95% confidence intervals (95% CI) for 244 associations between predictor variables and frequent LBP. Retirement and 245 working/volunteering status were highly intercorrelated, and therefore only retirement status 246 was included in the multivariable analyses. In the core multivariable model including the 247 sociodemographic factors of age \geq 75, retirement, and living alone, retirement showed a weak 248 and non-significant trend towards an association with back pain (odds ratio [OR] 1.82 [95% 249 confidence interval [95% CI] 0.95-3.48]), but other variables showed no independent 250 association with back pain (data not shown). When the variables of any severe facet joint OA 251 and any severe disc height narrowing were added to the core model, the presence of any 252 severe facet joint OA was significantly and independently associated with back pain (OR 253 2.15 [95% CI 1.13-4.08]), but no association was seen for disc height narrowing. When the 254 variables of number of joints with severe facet joint OA and number of spinal levels with 255 severe disc height narrowing were added to the core model, the number of joints with severe 256 OA was significantly and independently associated with back pain (OR 1.22 [95% CI 1.04-257 1.42]), but no such association was seen for number of spinal levels with severe disc height 258 narrowing. In secondary multivariable analyses, when adjusting for factors based on

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259 conceptual importance alone (age, sex, BMI, and education), any severe facet joint OA (259	conceptual importance	llone (age, sex, BMI.	, and education), an	y severe facet	joint OA (OR
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260 1.96 [95% CI 1.01-3.77]), and number of joints with severe OA (OR 1.21 [95% CI 1.03-

- 261 [1.42]), were significantly associated with back pain, although the corresponding measures for
- 262 disc height narrowing were not. Last, in sensitivity analyses to examine the effects of
- 263 imprecise temporal concordance between the date of the CT scans and the clinical
- examination (during which back pain frequency in the prior 12 months was assessed), we
- found no material differences in the association between facet joint OA and back pain when
- 266 including the covariate of time delay between CT scan and clinical examination, or when
- restricting the analyses to those participants with less than a 20 month (mean) delay between
- the CT scan and the clinical examination (data not shown).
- 269

<< Table 4>>

270 In *post-hoc* analyses, we examined relevant interactions between age and features of 271 severe spinal degeneration by addition of interaction terms to the multivariable models from 272 Table 3. In order to examine whether relationships between facet joint OA and back pain 273 would be stronger in older adults, we tested for an interaction between facet joint OA and age 274 > 75 years. We found no interaction between age and the presence of any severe facet joint 275 OA, or the number of joints with severe facet joint OA (data not shown), indicating that facet 276 joint OA was associated with back pain across the age spectrum of the sample. In order to 277 examine whether relationships between disc height narrowing and back pain would be 278 stronger in younger and middle-aged adults, we tested for an interaction between disc height 279 narrowing and age ≥ 60 years. We found a statistically significant interaction between any 280 severe disc height narrowing and age ≥ 60 (p=0.02), with a main effect for any severe disc

height narrowing of OR 3.72 (95% CI 0.85-16.3). This interaction is depicted graphically in

Figure 2, which shows that disc height narrowing is associated with back pain in participants < 60 years, but not in participants ≥ 60 years. We found a similar interaction between the number of spinal levels with severe disc height narrowing and age ≥ 60 (p=0.04), with disc height narrowing associated with back pain only in the younger group. Severe facet joint OA remained significantly associated with back pain in all models including an interaction term (data not shown).

288

<< Figure 2>>

290 **DISCUSSION**

Severe facet joint OA was significantly associated with frequent back pain in this study of community-based US older adults, adjusting for sociodemographics and health factors, and disc height narrowing. Furthermore, a greater number of joints with severe facet joint OA conferred greater odds of having frequent back pain. Disc height narrowing was independently associated with back pain in younger adults < age 60 years, but not in older adults.

297 To our knowledge, this is the first study demonstrating a clear association 298 between facet joint OA on advanced spinal imaging and the presence of back pain. Prior 299 studies examining this relationship have either found no association[8, 10], or 300 associations that were not statistically significant[9]. Our study had various 301 distinguishing features from prior work that may explain our positive findings and our 302 ability to detect an association between facet joint OA and back pain. First and most 303 importantly is the substantially older age of our study sample, including participants of 304 mean age 67 years, as compared to prior studies where mean age ranged between 36 to 305 53 years. Since OA is an age-related degenerative process, it follows logically that advanced OA might be associated with pain in older adults, but not in younger adults[30, 306 307 31]. Indeed, prior studies using comparative diagnostic anesthetic blocks to identify the 308 source of back pain have demonstrated that the proportion of back pain attributable to the 309 facet joints is high in older adults, and low in younger adults [13, 14]. Second, our study 310 applied thresholds for facet joint OA severity that identified severe OA in particular, 311 inspired by findings from the knee OA literature, where a closer association between 312 radiographic OA and pain is often seen in the setting of more severe radiographic

changes[11, 32, 33]. Earlier studies, including work from our group conducted in another
sample of Framingham participants[10], used thresholds of mild or moderate facet joint
OA[8, 9]. This is likely inappropriate, since mild facet joint OA is essentially ubiquitous
by middle age[34-36], and moderate facet joint OA is nearly so[10, 36]. Third, our study
used a well-characterized and reliable scale for facet joint OA, in contrast to some earlier
studies[8, 9].

319 Various prior studies have reported associations between disc height narrowing on 320 advanced spinal imaging and back pain, and these have largely included samples of 321 younger and middle-aged adults [37-39]. A noteworthy finding of this study was the 322 association between disc height narrowing and back pain in adults < 60 years, but not in 323 older adults. This observation supports the view held by some clinicians that discogenic 324 back pain predominates in the young and middle-aged, but may become less symptomatic 325 (or 'burn out') for individuals over the course of time[40]. This hypothesis has been 326 difficult to test empirically due to the paucity of prior longitudinal imaging studies of 327 back pain that include both middle-age and elderly persons. Furthermore, the 328 overwhelming majority of prior cross-sectional studies using advanced spinal imaging 329 such as CT or MRI examine only the anterior spinal structures of the intervertebral discs 330 and endplates in young to middle-aged adults- not including older individuals [41]. Our 331 data suggest the possibility that nonspecific back pain may shift from being discogenic-332 predominant in middle age to facetogenic-predominant in older adults, and this 333 speculation warrants examination in future research. 334 Our study has other features that distinguish it from earlier works. Studies

335 attempting to link spinal pain to specific posterior spinal structures on imaging (such as

336 facet joint OA) generally come in two categories: 1) examinations of associations 337 between imaging findings and spinal pain (including subjects with and without pain[8-338 10]), or 2) examinations of associations between imaging findings and the results of 339 diagnostic anesthetic blocks to spinal structures (including only subjects with pain, 340 usually from clinical convenience samples [7, 42]). Our study falls into the former 341 category. We view this as a study strength, in light of continuing controversy regarding 342 the validity of comparative diagnostic blocks[43]. In addition, we included both 343 assessments of posterior spinal structure degeneration (facet joint OA) and anterior spinal 344 structure degeneration (disc height narrowing) in the same multivariable models. Such an 345 approach has been suggested since disc height narrowing might serve as a surrogate for 346 facet joint OA when only the anterior structures are taken into account[44, 45]. 347 Our study detected a modest magnitude association between facet joint OA and 348 back pain (OR 2.2), which is generally comparable to odds ratio point estimates ranging 349 from 2.0 - 2.5 for the most commonly studied parameters of intervertebral disk 350 degeneration on imaging, including disc height narrowing, anular tears, and others[37, 351 41]. Similar to the case of both disc degeneration and extremity OA, however, the 352 presence of any severe facet joint OA has limited discriminatory capability: many people 353 with severe facet joint OA have no back pain, and some with back pain have no severe 354 facet joint OA. This does not mean, however, that facet joint OA is not a potential cause 355 of back pain. In fact, modest associations between spinal pathoanatomy and back pain 356 should be expected due to the myriad confounding factors also contributing to the highly 357 subjective experience of pain, including genetics, sociocultural factors, pain beliefs, 358 mood, and other factors [46-49]. Our study, like the majority of prior imaging studies of

back pain[50], accounted for only some of these potential confounding factors. On the
contrary, our results showing significant associations between both severity and extent of
facet joint OA and back pain provide some preliminary support for a causal link worthy
of further examination in longitudinal studies.

363 Some limitations of our study are worthy of mention. First, we used a general 364 back pain question which did not specify locations of lumbar pain corresponding to the 365 levels that were imaged by CT (L2-S1). Therefore, our definition of frequent back pain 366 may include not only lumbar pain, but also thoracic pain, which is prevalent in 2-6% of 367 older adults[51]. Second, our study lacked precise concordance between the timing of 368 CT scans and assessment of back pain frequency. Given that quantitative changes in 369 lumbar spinal degeneration on advanced imaging are less than 1-2 % per year [52], we 370 would expect any delay between CT scan and assessment of back pain to result in low 371 rates of misclassification, which is supported by the results of our sensitivity analyses. 372 Importantly, any misclassification in back pain locations or delays between imaging and 373 pain assessments would be expected to bias towards the null, and would not explain the 374 positive associations between facet joint OA and back pain detected in this study. Third, 375 our imaging assessments utilized CT, a modality which is optimal for the cardinal 376 features of facet joint OA (joint space narrowing, articular process hypertrophy, 377 osteophytosis, and sclerosis) [13], but may be inferior for visualization of secondary 378 features of facet joint OA, including joint effusions and articular process bone marrow 379 lesions[53]. However, CT is currently not recommended as the first choice for advanced 380 spinal imaging in situations where MRI is available, due in part to the known risks of 381 ionizing radiation. MRI assessments of facet joint OA show moderate agreement with

382 CT assessments of facet joint OA[20], but it remains to be seen whether severe facet joint

383 OA on MRI associates with back pain in older adults in the manner seen here when using

384 CT. Of note, our CT reads did not assess the L1-L2 spinal level, in contrast to most prior

385 lumbar imaging studies, which include the entire lumbar region. Fourth, sample size in

386 this study was not determined in advance based on power calculations related to the main

387 research question pursued here. Nevertheless, the fact that we detected statistically

388 significant results would suggest against type II error. Fifth, the cross-sectional nature of

389 our study makes identifying potential confounding factors on conceptual grounds

- 390 especially challenging, since temporal order between many of our measures cannot be
- 391 determined. Future longitudinal studies of severe facet joint OA and associations with
- 392 back pain are needed.

393 In conclusion, the results of this study demonstrate a significant but modest

394 association between the presence and extent of severe facet joint OA on CT imaging and

395 back pain in a sample of community-based older adults, independent of

396 sociodemographics, health factors, and disc height narrowing. Further research is needed

397 to determine whether imaging of facet joint OA may have a role in refining back pain

398 case definition or directing back pain treatment for older adults.

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- 400

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406 **CONTRIBUTIONS**

408 PS was involved with study concept and design, acquisition of data, analysis of data,

409 interpretation of data, and drafting of the manuscript. DJH was involved with study

410 concept and design and manuscript preparation. JR was involved with study concept,

411 design, and manuscript preparation. AG was involved with study design, acquisition of

412 data, and manuscript preparation. JNK was involved with study design, analysis of data,

413 interpretation of data, and manuscript preparation. All authors were involved with critical

414 revision of the manuscript for important intellectual content and approved the final

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436 **REFERENCES**

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