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Appendix 1. PICOS table and search

Frame	Description	Key words and medical subject headings*
Patient	Patients underwent lumbar fusion regardless of the types of surgery or the length of the fused construct	#1: lumbar OR low back OR lower back OR lx OR spine OR spinal OR vertebra* OR thoracolumbar OR lumbosacral OR lumbopelvic #2: fusion OR internal fixat* OR arthrodes* OR instrumentation OR stabilization OR stabilisation
Exposure	Symptomatic or clinical adjacent segment disease (ASD) (diagnosed based on both radiological and clinical findings)	#3: adjacent segment disease* OR adjacent level disease* OR adjacent disc disease* OR adjacent disk disease* OR adjacent level disc disease* OR adjacent level disk disease* OR ASDis OR ASDz #4: adjacent segment degeneration OR adjacent level degeneration OR adjacent disc degeneration OR adjacent disk degeneration OR adjacent level disc degeneration OR ASDeg
Comparison	Patients without ASD	/
Outcome	Risk factors for adjacent segment disease (The primary article needs to provide statistical information (e.g., mean difference between patients with and without ASD, odds ratio, hazard ratio) regarding the risk of patients with ASD or enough raw data so that the relevant statistics can be calculated.	#5: risk factor* OR prognostic factor* OR predictive factor* OR odds ratio* OR hazard ratio*
Study design	Retrospective or prospective cohort studies, case-control studies, cross-sectional studies, randomized controlled trials that reported risk factors for ASD.	

Embase

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#42	#11 AND #18 AND #35 AND #41	401
#41	#36 OR #37 OR #38 OR #39 OR #40	2,260,416
#40	hazard AND ratio*	180,392
#39	odds AND ratio*	338,757
#38	predictive AND factor*	189,569
#37	prognostic AND factor*	238,946
#36	risk AND factor*	1,745,293
#35	#27 OR #34	14,009
#34	#28 OR #29 OR #30 OR #31 OR #32 OR #33	3,381
#33	asdeg	17
#32	adjacent AND level AND disc AND degeneration	1,091
#31	adjacent AND disk AND degeneration	1,928
#30	adjacent AND disc AND degeneration	2,057
#29	adjacent AND level AND degeneration	1,815
#28	adjacent AND segment AND degeneration	1,860
#27	#19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26	12,613
#26	asdz	4
#25	asdis	62
#24	adjacent AND level AND disk AND disease*	1,004
#23	adjacent AND level AND disc AND disease*	1,219
#22	adjacent AND disk AND disease*	2,124
#21	adjacent AND disc AND disease*	2,381
#20	adjacent AND level AND disease*	9,385
#19	adjacent AND segment AND disease*	3,458
#18	#12 OR #13 OR #14 OR #15 OR #16 OR #17	513,791
#17	stabilisation	11,923
#16	stabilization	124,711
#15	instrumentation	75,122
#14	arthrodes*	20,223
#13	internal AND fixat*	29,667
#12	fusion	283,044
#11	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10	941,883
#10	lumbopelvic	943
#9	lumbosacral	17,667
#8	thoracolumbar	13,186
#7	vertebra*	259,831
#6	spinal	453,047
#5	spine	316,990
#4	lx	5,050
#3	lower AND back	40,095
#2	low AND back	93,894
#1	lumbar	175,229

Academic Search Premier, CINAHL, MEDLINE

EBSCOhost

#	Query	Limiters/Expanders
S42	S11 AND S18 AND S35 AND S41	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S41	S36 OR S37 OR S38 OR S39 OR S40	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S40	TX hazard ratio*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S39	TX odds ratio*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S38	TX predictive factor*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S37	TX prognostic factor*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S36	TX risk factor*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S35	S27 OR S34	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S34	S28 OR S29 OR S30 OR S31 OR S32 OR S33	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S33	TX ASDeg	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S32	TX adjacent level disc degeneration	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S31	TX adjacent disk degeneration	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S30	TX adjacent disc degeneration	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S29	TX adjacent level degeneration	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S28	TX adjacent segment degeneration	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S27	S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase

S26	TX ASDz	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S25	TX ASDis	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S24	TX adjacent level disk disease*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S23	TX adjacent level disc disease*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S22	TX adjacent disk disease*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S21	TX adjacent disc disease*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S20	TX adjacent level disease*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S19	TX adjacent segment disease*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S18	S12 OR S13 OR S14 OR S15 OR S16 OR S17	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S17	TX stabilisation	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S16	TX stabilization	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S15	TX instrumentation	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S14	TX arthrodes*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S13	TX internal fixat*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S12	TX fusion	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S11	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S10	TX lumbopelvic	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S9	TX lumbosacral	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase

S8	TX thoracolumbar	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S7	TX vertebra*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S6	TX spinal	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S5	TX spine	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S4	TX lx	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S3	TX lower back	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S2	TX low back	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S1	TX lumbar	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase

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#1	lumbar	Limits	15698
#2	low back	Limits	14411
#3	lower back	Limits	6736
#4	lx	Limits	1084
#5	spine	Limits	17606
#6	spinal	Limits	26808
#7	vertebra*	Limits	9444
#8	thoracolumbar	Limits	676
#9	lumbosacral	Limits	1344
#10	lumbopelvic	Limits	233
#11	#1 or #2 or #3 or #4 or #5 or #6 or #7 r #8 or #9 or #10	Limits	55715
#12	fusion	Limits	7284
#13	internal fixat*	Limits	2783
#14	arthrodes*	Limits	508
#15	instrumentation	Limits	23928
#16	stabilization	Limits	6503
#17	stabilisation	Limits	6506
#18	#12 or #13 or #14 or #15 or #16 or #17	Limits	38709
#19	adjacent segment disease*	Limits	257
#20	adjacent level disease*	Limits	811
#21	adjacent disc disease*	Limits	305
#22	adjacent disk disease*	Limits	305
#23	adjacent level disc disease*	Limits	220
#24	adjacent level disk disease*	Limits	220
#25	ASDis	Limits	2
#26	ASDz	Limits	0
#27	#19 or #20 or #21 or #22 or #23 or #24 or #25 or #26	Limits	953
#28	adjacent segment degeneration	Limits	193
#29	adjacent level degeneration	Limits	237
#30	adjacent disc degeneration	Limits	277
#31	adjacent disk degeneration	Limits	277
#32	adjacent level disc degeneration	Limits	197
#33	ASDeg	Limits	2
#34	#28 or #29 or #30 or #31 or #32 or #33	Limits	331
#35	#27 or #34	Limits	1057
#36	risk factor*	Limits	102249
#37	prognostic factor*	Limits	11771
#38	predictive factor*	Limits	12419
#39	odds ratio*	Limits	28039
#40	hazard ratio*	Limits	24341
#41	#36 or #37 or #38 or #39 or #40	Limits	145585
#42	#11 and #18 and #35 and #41	Limits	59

Row #1 also shows: 5 ▾ | MeSH ▾

Web of Science

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Search History:

Set	Results	Save History / Create Alert · Open Saved History	Edit Sets	Combine Sets (AND / OR, Combine)	Delete Sets (Select All, Delete)
# 42	397	#41 AND #35 AND #18 AND #11 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 41	1,600,978	#40 OR #39 OR #38 OR #37 OR #36 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 40	125,889	**ALL FIELDS:** (hazard ratio*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 39	252,974	**ALL FIELDS:** (odds ratio*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 38	128,070	**ALL FIELDS:** (predictive factor*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 37	191,940	**ALL FIELDS:** (prognostic factor*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 36	1,196,012	**ALL FIELDS:** (risk factor*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 35	10,589	#34 OR #27 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 34	2,516	#33 OR #32 OR #31 OR #30 OR #29 OR #28 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 33	14	**ALL FIELDS:** (ASDeg) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 32	973	**ALL FIELDS:** (adjacent level disc degeneration) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 31	277	**ALL FIELDS:** (adjacent disk degeneration) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 30	1,573	**ALL FIELDS:** (adjacent disc degeneration) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 29	1,573	**ALL FIELDS:** (adjacent level degeneration) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 28	1,635	**ALL FIELDS:** (adjacent segment degeneration) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 27	9,336	#26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 26	3	**ALL FIELDS:** (ASDz) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 25	69	**ALL FIELDS:** (ASDis) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 24	199	**ALL FIELDS:** (adjacent level disk disease*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 23	1,018	**ALL FIELDS:** (adjacent level disc disease*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 22	363	**ALL FIELDS:** (adjacent disk disease*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 21	1,619	**ALL FIELDS:** (adjacent disc disease*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 20	7,295	**ALL FIELDS:** (adjacent level disease*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		

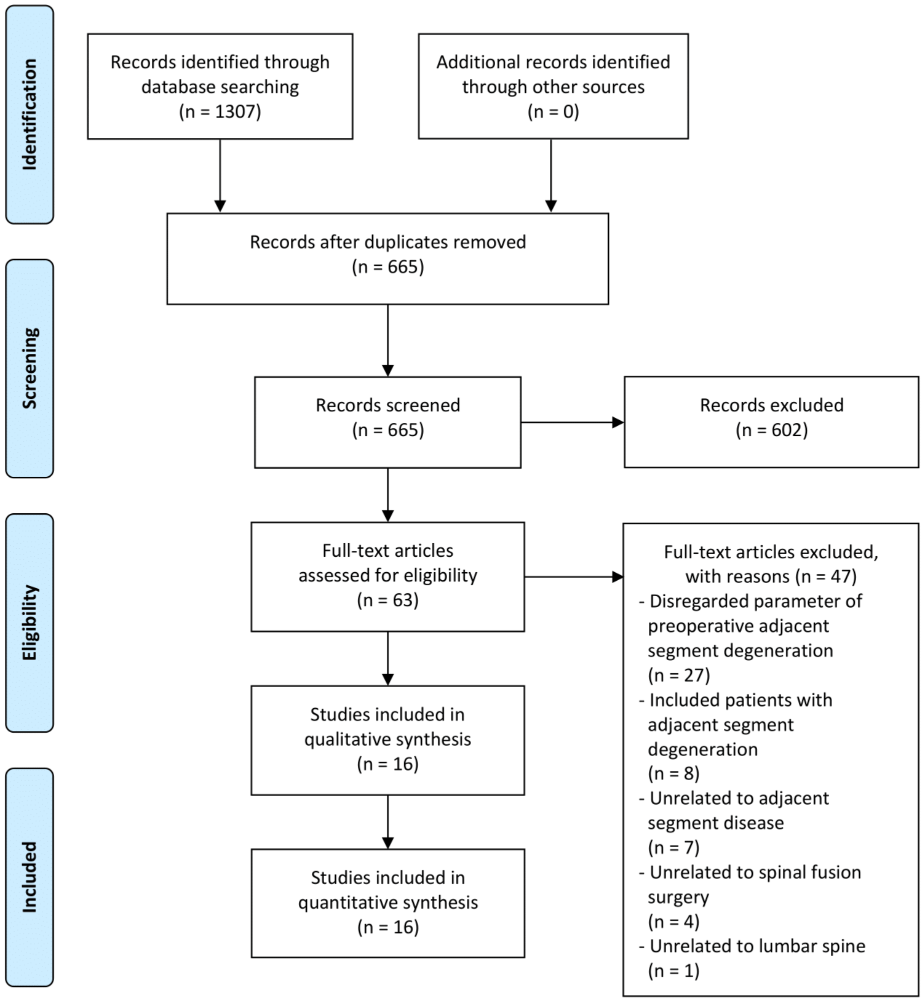
# 19	2,822	**ALL FIELDS:** (adjacent segment disease*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 18	1,179,704	#17 OR #16 OR #15 OR #14 OR #13 OR #12 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 17	18,468	**ALL FIELDS:** (stabilisation) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 16	264,025	**ALL FIELDS:** (stabilization) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 15	438,343	**ALL FIELDS:** (instrumentation) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 14	12,473	**ALL FIELDS:** (arthrodes*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 13	24,674	**ALL FIELDS:** (internal fixat*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 12	460,144	**ALL FIELDS:** (fusion) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 11	840,710	#10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 10	931	**ALL FIELDS:** (lumbopelvic) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 9	10,338	**ALL FIELDS:** (lumbosacral) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 8	9,097	**ALL FIELDS:** (thoracolumbar) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 7	227,614	**ALL FIELDS:** (vertebra*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 6	311,274	**ALL FIELDS:** (spinal) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 5	182,668	**ALL FIELDS:** (spine) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 4	79,409	**ALL FIELDS:** (lx) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 3	135,698	**ALL FIELDS:** (lower back) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 2	134,991	**ALL FIELDS:** (low back) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
# 1	103,322	**ALL FIELDS:** (lumbar) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI Timespan=All years*	Edit		
				AND OR Combine	Select All Delete

http://dx.doi.org/10.2106/JBJS.20.00408

Appendix 2. Strength of evidence.[25]

Strength of evidence	**Description**
Strong	Consistent (or pooled) findings with statistical significance from multiple studies with low risk of bias
Moderate	Consistent (or pooled) findings with statistical significance from multiple high risk of bias studies, and/or significant findings from one study with low risk of bias
Limited	Significant findings from one study with high risk of bias
Conflicting	Inconsistent findings among multiple studies
No evidence	No study(ies) showed statistical significance

Appendix 3. PRISMA flow diagram



http://dx.doi.org/10.2106/JBJS.20.00408

Appendix 4. Newcastle-Ottawa Scale.

A) Cohort Studies

Study	NOS_1	NOS_2	NOS_3	NOS_4	NOS_5	NOS_6	NOS_7	NOS_8	NOS_9	Score	Risk of bias
Bagheri SR et al., 2019[26]	1	1	1	1	1	1	1	1	1	9	Low
Wang H et al., 2017[29]	0	1	1	0	1	0	1	0	0	4	High
Wang S et al., 2017[30]	0	1	1	0	0	0	1	0	0	3	Very high
Zhong ZM et al., 2017[31]	0	1	1	1	0	0	1	0	0	4	High
Yugue I et al., 2016[32]	1	1	1	0	1	0	1	0	0	5	High
Heo Y et al., 2015[33]	1	1	0	0	0	0	0	0	1	3	Very high
Lee YS et al., 2015[34]	0	1	0	0	0	0	1	0	0	2	Very high
Cho TK et al., 2014[36]	0	1	1	0	1	0	1	0	1	5	High
Sakaura H et al., 2013[38]	0	1	1	0	0	0	1	1	0	4	High
Kaito T et al., 2010[39]	0	1	1	0	0	1	1	0	1	5	High
Okuda S et al., 2004[41]	0	1	0	0	0	1	1	0	1	4	High
Percentage of rating 1	27%	100%	73%	18%	36%	27%	91%	18%	45%	Mean: 4.7	

Note. NOS_1 = Representativeness of the exposed cohort; NOS_2 = Selection of the non-exposed cohort; NOS_3 = Ascertainment of exposure; NOS_4 = Demonstration that outcome of interest was not present at start of study; NOS_5 = Study controls for diagnosis of index surgery in degenerative diseases; NOS_6 = Study controls for no radiological and symptomatic symptoms in non-ASD exposure group; NOS_7 = Assessment of outcome; NOS_8 = Was follow-up long enough for outcomes to occur; NOS_9 = Adequacy of follow up of cohorts.

B) Case-control studies

Study	NOS_1	NOS_2	NOS_3	NOS_4	NOS_5	NOS_6	NOS_7	NOS_8	NOS_9	Score	Risk of bias
Kim WJ et al., 2019[27]	0	0	1	1	1	0	1	1	0	5	High
Mastsumoto T et al., 2017[28]	0	0	1	1	1	0	0	0	0	4	High
Rothenfluh DA et al., 2015[35]	0	0	1	1	1	0	0	0	0	4	High
Liang J et al., 2014[37]	0	1	1	0	1	0	1	1	0	5	High

Lee CS et al., 2009[40]	0	1	1	0	1	0	0	0	0	3	Very high
Percentage of rating 1	0%	40%	100%	60%	100%	0%	40%	40%	0%	Mean: 4.2	

Note. NOS_1 = Is the case definition adequate; NOS_2 = Representativeness of the cases; NOS_3 = Selection of controls; NOS_4 = Definition of controls; NOS_5 = Study controls for diagnosis of index surgery in degenerative diseases; NOS_6 = Study controls for no radiological and symptomatic symptoms in non-ASD exposure group; NOS_7 = Ascertainment of exposure; NOS_8 = Same method of ascertainment for cases and controls; NOS_9 = Non-Response rate.

Appendix 5. Various risk factors for adjacent segment disease (ASD) investigated by the included studies that showed no statistical significance or conflicting results. If a potential factor consistently showed non-significant results in the relevant included studies, no meta-analysis was conducted because the pooled result would show no evidence for that factor to be a significant risk factor.

Potential Risk factor	Study	Number of patients	Statistics	ASD	Control (Ctrl)	Results	*P*-value	Pooled data (95%CI)	Level of evidence
Demographic									
Older age (years)	#Bagheri SR et al., 2019[26]	ASD: 76 Ctrl: 554	Independent t-test	61.4 ± 4.1	62.4 ± 3.9	MD: -1.00 (95%CI: -1.9 to -0.1)	0.038	Pooled MD = 1.3 (-0.8 to 3.4) (*P*=0.22)	Conflicting
	#Wang H et al., 2017[29]	ASD: 15 Ctrl: 222	Independent t-test	55.3 ± 10.5	53.1 ± 10.9	MD: 2.2 (95%CI: -3.5 to 7.9)	0.449		
	#Wang S et al., 2017[30]	ASD: 21 Ctrl: 96	Independent t-test	56.4 ± 8.8	54.6 ± 12.3	MD: 1.83 (95%CI: -3.8 to 7.4)	0.518		
	#Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Independent t-test	59.8 ± 14.1	58.2 ± 13.4	MD: 1.6 (95%CI: -5.1 to 8.3)	0.637		
	Yugue I et al., 2016[32]	ASD: 44 Ctrl: 117	Log rank test	NA	NA	NA	0.399*		
	#Heo Y et al., 2015[33]	ASD: 33 Ctrl: 345	Independent t-test	62.8 ± 8.2	58.7 ± 9.9	MD: 4.1 (95%CI: 0.6 to 7.6)	0.021		
	Lee YS et al., 2015[34]	ASD: 16 Ctrl: 99	Log rank test	NA	NA	NA	NS*		
	Cho TK et al., 2014[36]	ASD: 10 Ctrl: 144	Independent t-test	58.8 ± SD not reported	64.5 ± SD not reported	NA	0.006*		
	#Sakaura H et al., 2013[38]	ASD: 4 Ctrl: 36	Independent t-test	53.5 ± 12.6	59.1 ± 15.1	MD: -5.6 (95%CI: -21.5 to 10.3)	0.481		
	#Kaito T et al., 2010[39]	ASD: 13 Ctrl: 58	Independent t-test	66.0 ± 8.3	63.4 ± 8.6	MD: 2.6 (95%CI: -2.6 to 7.8)	0.325		
	#Okuda S et al., 2004[41]	ASD: 4 Ctrl: 58	Independent t-test	64.0 ± 5.0	64.1 ± 10.2	MD: 0.0 (95%CI: -10.1 to 10.1)	1.000		
History of alcohol drinking	#Wang S et al., 2017[30]	ASD: 21 Ctrl: 96	Chi-square test	Yes: 6 / No: 15	Yes: 54 / No: 42	OR: 0.3 (95%CI: 0.1 to 0.9)	0.026	Pooled OR	Conflicting

	#Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	Yes: 8 / No: 10	Yes: 68 / No: 68	OR: 0.8 (95%CI: 0.3 to 2.2)	0.658	= 0.5 (0.2 to 1.3) (*P*=0.15)	
Anemia	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Fisher's exact test	Yes: 1 / No: 17	Yes: 5 / No: 131	OR: 1.54 (95%CI: 0.2 to 14.0)	0.701		No evidence
Bone mineral density (T score; -4.0 to 0.5)	#Wang H et al., 2017[29]	ASD: 15 Ctrl: 222	Independent t-test	-1.0 ± 0.2	-1.2 ± 0.3	MD: 0.2 (95%CI: 0.1 to 0.4)	0.012	Pooled MD = -0.1 (-0.6 to 0.5) (*P*=0.85)	Conflicting
	#Wang S et al., 2017[30]	ASD: 21 Ctrl: 96	Independent t-test	-1.3 ± 0.9	-0.9 ± 1.2	MD: -0.4 (95%CI: -0.9 to 0.1)	0.145		
	Lee YS et al., 2015[34]	ASD: 16 Ctrl: 99	Log rank test	NA	NA	NA	NS*		
	Cho TK et al., 2014[36]	ASD: 10 Ctrl: 144	Independent t-test	-3.7 ± SD not reported	-4.0 ± SD not reported	NA	0.997*		
Comorbidity index	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test (ASAPSC system; out of 6 grades)	≥ 3: 1 / < 3: 17	≥ 3: 19 / < 3: 117	OR: 0.4 (95%CI: 0.1 to 2.9)	0.337		No evidence
Depression	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	Yes: 3 / No: 15	Yes: 28 / No: 108	OR: 0.8 (95%CI: 0.2 to 2.9)	0.697		No evidence
Diabetes mellitus	Bagheri SR et al., 2019[26]	ASD: 76 Ctrl: 554	Chi-square test	Yes: 14 / No: 62	Yes: 146 / No: 408	OR: 0.6 (95%CI: 0.3 to 1.2)	0.139		No evidence
	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	Yes: 1 / No: 17	Yes: 12 / No: 124	OR: 0.6 (95%CI: 0.1 to 5.0)	0.643		
Duration of disease from first symptoms to index surgery (months)	Wang H et al., 2017[29]	ASD: 15 Ctrl: 222	Independent t-test	15.1 ± 9.7	12.1 ± 7.8	MD: 3.0 (95%CI: -1.2 to 7.2)	0.157		No evidence
	Wang S et al., 2017[30]	ASD: 21 Ctrl: 96	Independent t-test	5.95 ± 4.84	5.78 ± 5.70	MD: 0.2 (95%CI: -2.5 to 2.8)	0.899		
Female sex	Bagheri SR et al., 2019[26]	ASD: 76 Ctrl: 554	Chi-square test	Female: 43 Male: 33	Female: 284 Male: 270	OR: 1.2 (95%CI: 0.8 to 2.0)	0.385		No evidence
	Wang H et al., 2017[29]	ASD: 15 Ctrl: 222	Chi-square test	Female: 9 Male: 6	Female: 122 Male: 100	OR: 1.2 (95%CI: 0.4 to 3.6)	0.704		
	Wang S et al., 2017[30]	ASD: 21 Ctrl: 96	Chi-square test	Female: 10 Male: 11	Female: 50 Male: 46	OR: 0.8 (95%CI: 0.3 to 2.2)	0.711		
	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	Female: 13 Male: 5	Female: 97 Male: 39	OR: 1.1 (95%CI: 0.4 to 3.1)	0.937		

	Yugue I et al., 2016[32]	ASD: 44 Ctrl: 117	Log rank test	NA	NA	NA	0.353*		
	Heo Y et al., 2015[33]	ASD: 33 Ctrl: 345	Chi-square test	Female: 19 Male: 14	Female: 234 Male: 111	OR: 0.6 (95%CI: 0.3 to 1.3)	0.235		
	Lee YS et al., 2015[34]	ASD: 16 Ctrl: 99	Log rank test	NA	NA	NA	NS*		
	Cho TK et al., 2014[36]	ASD: 10 Ctrl: 144	Chi-square test	Female: 5 Male: 5	Female: 100 Male: 44	OR: 0.4 (95%CI: 0.1 to 1.6)	0.212		
	Sakaura H et al., 2013[38]	ASD: 4 Ctrl: 36	Chi-square test	Female: 2 Male: 2	Female: 12 Male: 24	OR: 2.0 (95%CI: 0.3 to 16.0)	0.513		
	Kaito T et al., 2010[39]	ASD: 13 Ctrl: 58	Chi-square test	Female: 6 Male: 7	Female: 41 Male: 17	OR: 0.4 (95%CI: 0.1 to 1.2)	0.099		
Gastrointestinal diseases	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	Yes: 6 / No: 12	Yes: 35 / No: 101	OR: 1.4 (95%CI: 0.5 to 4.1)	0.495		No evidence
Genitourinary diseases	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	Yes: 3 / No: 15	Yes: 17 / No: 129	OR: 1.5 (95%CI: 0.4 to 5.8)	0.541		No evidence
Heart diseases	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	Yes: 1 / No: 17	Yes: 4 / No: 132	OR: 1.9 (95%CI: 0.2 to 18.4)	0.563		No evidence
Hyperlipidemia	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	Yes: 5 / No: 13	Yes: 37 / No: 99	OR: 1.0 (95%CI: 0.3 to 3.1)	0.959		No evidence
Hypertension	Bagheri SR et al., 2019[26]	ASD: 76 Ctrl: 554	Chi-square test	Yes: 22 / No: 54	Yes: 124 / No: 430	OR: 1.4 (95%CI: 0.8 to 2.4)	0.205		No evidence
	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	Yes: 7 / No: 11	Yes: 43 / No: 93	OR: 1.4 (95%CI: 0.5 to 3.8)	0.537		
Hypothyroidism	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	Yes: 4 / No: 14	Yes: 23 / No: 113	OR: 1.4 (95%CI: 0.4 to 4.7)	0.579		No evidence
Myelopathy (out of 18)	Sakaura H et al., 2013[38]	ASD: 4 Ctrl: 36	Independent t-test (JOA grade)	13.3 ± 6.8	16.0 ± 3.7	MD: -2.7 (95%CI: -7.0 to 1.6)	0.212		No evidence
	Kaito T et al., 2010[39]	ASD: 13 Ctrl: 58	Independent t-test (JOA grade)	16.4 ± 3.8	15.1 ± 4.2	MD: 1.3 (95%CI: 1.2 to 3.8)	0.309		
Osteoarthritis	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	Yes: 4 / No: 14	Yes: 37 / No: 99	OR: 0.8 (95%CI: 0.2 to 2.5)	0.654		No evidence
Osteoporosis	Bagheri SR et al., 2019[26]	ASD: 76 Ctrl: 554	Chi-square test	Yes: 23 / No: 53	Yes: 174 / No: 380	OR: 1.0 (95%CI: 0.6 to 1.6)	0.840		No evidence

	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	Yes: 0 / No: 18	Yes: 12 / No: 124	OR: 0.3 (95%CI: 0.0 to 4.7)	0.370		
	Cho TK et al., 2014[36]	ASD: 10 Ctrl: 144	Independent t-test	15.1 ± SD not reported	12.1 ± SD not reported	NA	0.997*		
Pulmonary diseases	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	Yes: 3 / No: 15	Yes: 29 / No: 107	OR: 0.7 (95%CI: 0.20 to 2.7)	0.648		No evidence
Residential area	Wang S et al., 2017[30]	ASD: 21 Ctrl: 96	Chi-square test	Urban: 9 / Rural: 12	Urban: 34 / Rural: 62	OR: 1.4 (95%CI: 0.5 to 3.6)	0.523		No evidence
History of smoking	Bagheri SR et al., 2019[26]	ASD: 76 Ctrl: 554	Chi-square test	Yes: 26 / No: 50	Yes: 157 / No: 397	OR: 1.3 (95%CI: 0.8 to 2.2)	0.292		No evidence
	Wang S et al., 2017[30]	ASD: 21 Ctrl: 96	Chi-square test	Yes: 10 / No: 11	Yes: 42 / No: 54	OR: 1.2 (95%CI: 0.5 to 3.0)	0.747		
	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	Yes: 6 / No: 12	Yes: 34 / No: 102	OR: 1.5 (95%CI: 0.5 to 4.3)	0.451		
	Liang J et al., 2014[37]	ASD: 28 Ctrl: 56	Chi-square test	Yes: 8 / No: 20	Yes: 10 / No: 46	OR: 1.8 (95%CI: 0.6 to 5.4)	0.263		
Surgical									
Intraoperative blood loss (ml)	Wang H et al., 2017[29]	ASD: 15 Ctrl: 222	Independent t-test	457.9 ± 27.7	445.5 ± 30.8	MD: 12.4 (95%CI: -3.7 to 28.5)	0.130		No evidence
Number of fused segments	Bagheri SR et al., 2019[26]	ASD: 76 Ctrl: 554	Chi-square test	> 4: 57 / < 4: 19	> 4: 225 / < 4: 329	OR: 4.4 (95%CI: 2.5 to 7.6)	<0.001		Conflicting
	Wang H et al., 2017[29]	ASD: 15 Ctrl: 222	Chi-square test	2: 4 / 1: 11	2: 55 / 1: 167	OR: 1.1 (95%CI: 0.3 to 3.6)	0.870		
	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	2: 6 / 1: 12	2: 56 / 1: 80	OR: 0.7 (95%CI: 0.3 to 2.0)	0.525		
	Lee YS et al., 2015[34]	ASD: 16 Ctrl: 99	Log rank test	NA	NA	NA	NS*		
	Liang J et al., 2014[37]	ASD: 28 Ctrl: 56	Independent t-test	1.5 ± 0.7	1.6 ± 0.6	MD: -0.7 (95%CI: -0.4 to 0.2)	0.643		
Operation time (minutes)	Wang H et al., 2017[29]	ASD: 15 Ctrl: 222	Independent t-test	165.0 ± 10.3	160.1 ± 13.3	MD: 4.9 (95%CI: -2.0 to 11.8)	0.1635		No evidence
Use of allograft	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	Yes: 4 / No: 14	Yes: 38 / No: 98	OR: 0.7 (95%CI: 0.2 to 2.4)	0.610		No evidence
	Liang J et al., 2014[37]	ASD: 28 Ctrl: 56	Chi-square test	Yes: 19 / No: 9	Yes: 31 / No: 25	OR: 1.7 (95%CI: 0.7 to 4.4)	0.273		

Rigid instrumentation	Bagheri SR et al., 2019[26]	ASD: 76 Ctrl: 554	Chi-square test	Rigid: 56 / Dynamic: 20	Rigid: 375 / Dynamic: 179	OR: 1.3 (95%CI: 0.8 to 2.3)	0.293		No evidence
Use of bone morphogenetic proteins	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	Yes: 3 / No: 15	Yes: 12 / Mo: 124	OR: 2.1 (95%CI: 0.5 to 8.2)	0.300		No evidence
Radiographic									
Preoperative measures									
Adjacent disc anterolisthesis (mm)	Kaito T et al., 2010[39]	ASD: 13 Ctrl: 58	Independent t-test	0.6 ± 1.1	0.3 ± 0.9	MD: 0.3 (95%CI: -0.3 to 0.9)	0.301		No evidence
Adjacent disc translation (mm)	Kaito T et al., 2010[39]	ASD: 13 Ctrl: 58	Independent t-test	1.5 ± 1.1	0.8 ± 1.0	MD: 0.7 (95%CI: 0.1 to 1.3)	0.028		Conflicting
	Lee CS et al., 2009[40]	ASD: 26 Ctrl: 26	Logistic regression	NA	NA	OR: 0.4* (95%CI: 0.0 to 3.8)	0.29*		
Adjacent disc range of motion (degrees)	Wang H et al., 2017[29]	ASD: 15 Ctrl: 222	Independent t-test	10.4 ± 2.0	11.1 ± 2.9	MD: -0.7 (95%CI: -2.2 to 0.8)	0.359		No evidence
	Cho TK et al., 2014[36]	ASD: 10 Ctrl: 144	Independent t-test (L3-L4)	10.0 ± SD not reported	14.4 ± SD not reported	NA	0.644*		
	Kaito T et al., 2010[39]	ASD: 13 Ctrl: 58	Independent t-test	7.6 ± 3.5	6.9 ± 3.1	MD: 0.7 (95%CI: -1.2 to 2.6)	0.475		
Adjacent disc wedging (degrees)	Lee CS et al., 2009[40]	ASD: 26 Ctrl: 26	Logistic regression	NA	NA	OR: 0.6* (95%CI: 0.2 to 20.6)	0.67*		No evidence
Adjacent segment instability	Yugue I et al., 2016[32]	ASD: 44 Ctrl: 117	Log rank test	NA	NA	NA	0.690*		No evidence
	Lee CS et al., 2009[40]	ASD: 26 Ctrl: 26	Logistic regression	NA	NA	OR: 0.6* (95%CI: 0.1 to 6.5)	0.73*		
Adjacent segment rotational deformity (degrees)	Lee CS et al., 2009[40]	ASD: 26 Ctrl: 26	Logistic regression	NA	NA	OR: 0.7* (95%CI: 0.1 to 11.4)	0.14*		No evidence
C7 to central sacral vertical line (mm)	Mastsumoto T et al., 2017[28]	ASD: 20 Ctrl: 100	Independent t-test	12.2 ± 9.2	9.5 ± 7.7	MD: 2.7 (95%CI: -1.2 to 6.6)	0.169		No evidence
Epifusional segment angle (degrees)	Rothenfluh DA et al., 2015[35]	ASD: 45 Ctrl: 39	Independent t-test	8.8 ± 4.8	8.6 ± 4.1	MD: 0.2 (95%CI: -1.8 to 2.2)	0.839		No evidence
	Liang J et al., 2014[37]	ASD: 28 Ctrl: 56	Independent t-test	9.5 ± 4.7	10.1 ± 4.4	MD: -0.6 (95%CI: -2.7 to 1.5)	0.566		

Facet joint degeneration (Weishaupt grade)	#Mastsumoto T et al., 2017[28]	ASD: 20 Ctrl: 100	Chi-square test (L3-L4)	≥ 2: 9 / < 2: 11	≥ 2: 41 / < 2: 59	OR: 1.2 (95%CI: 0.5 to 3.1)	0.741	Pooled OR = 1.33 (0.28 to 6.42) (*P*=0.72)	Conflicting
	#Mastsumoto T et al., 2017[28]	ASD: 20 Ctrl: 100	Chi-square test (L5-S1)	≥ 2: 4 / < 2: 16	≥ 2: 34 / < 2: 66	OR: 0.5 (95%CI: 0.2 to 1.6)	0.226		
	#Heo Y et al., 2015[33]	ASD: 33 Ctrl: 345	Chi-square test (Pathria grade)	≥ 2: 13 / < 2: 20	≥ 2: 20 / < 2: 324	OR: 10.5 (95%CI: 4.6 to 24.2)	<0.001		
	Lee YS et al., 2015[34]	ASD: 16 Ctrl: 99	Log rank test	NA	NA	NA	NS*		
	#Kaito T et al., 2010[39]	ASD: 13 Ctrl: 58	Chi-square test Independent t-test	≥ 2: 5 / < 2: 8 2.2 ± 0.7	≥ 2: 34 / < 2: 24 2.6 ± 0.6	MD: -0.4 (95%CI: -0.8 to 0.0)	0.039		
	Lee CS et al., 2009[40]	ASD: 26 Ctrl: 26	Logistic regression	NA	NA	OR: 0.0* (95%CI: 0.0 to 0.1)	<0.01*		
Facet sagittalization (degrees)	Cho TK et al., 2014[36]	ASD: 10 Ctrl: 144	Independent t-test	62.6 ± SD not reported	72.3 ± SD not reported	NA	0.102*		No evidence
	Kaito T et al., 2010[39]	ASD: 13 Ctrl: 58	Independent t-test	63.0 ± 11.8	63.8 ± 17.0	MD: -0.8 (95%CI: -10.7 to 9.1)	0.873		
	Okuda S et al., 2004[41]	ASD: 4 Ctrl: 58	Independent t-test	56 ± 13	63 ± 16	MD: -7 (95%CI: -23.4 to 9.4)	0.397		
Facet tropism (degrees)	#Heo Y et al., 2015[33]	ASD: 33 Ctrl: 345	Independent t-test	8.9 ± 6.6	6.6 ± 5.6	MD: 2.3 (95%CI: 0.3 to 4.4)	0.025	Pooled MD = 2.39 (-1.34 to 6.12) (*P*=0.21)	Conflicting
	Cho TK et al., 2014[36]	ASD: 10 Ctrl: 144	Independent t-test	5.1 ± SD not reported	5.7 ± SD not reported	NA	0.707*		
	#Sakaura H et al., 2013[38]	ASD: 4 Ctrl: 36	Independent t-test	8.3 ± 6.8	5.3 ± 4.5	MD: 3.0 (95%CI: -2.0 to 8.0)	0.236		
	#Kaito T et al., 2010[39]	ASD: 13 Ctrl: 58	Independent t-test	5.8 ± 4.1	4.7 ± 4.0	MD: 1.1 (95%CI: -1.4 to 3.6)	0.375		
	#Okuda S et al., 2004[41]	ASD: 4 Ctrl: 58	Independent t-test	16 ± 9	4 ± 3	MD: 12 (95%CI: 8.3 to 15.7)	<0.001		
Lamina inclination (degrees)	#Heo Y et al., 2015[33]	ASD: 33 Ctrl: 345	Independent t-test	112.6 ± 12.8	111.3 ± 7.4	MD: 1.3 (95%CI: -1.6 to 4.2)	0.371	Pooled MD = 6.11 (-1.38 to 13.60) (*P*=0.11)	Conflicting
	Cho TK et al., 2014[36]	ASD: 10 Ctrl: 144	Independent t-test	107.5 ± SD not reported	108.9 ± SD not reported	NA	0.486*		

	#Sakaura H et al., 2013[38]	ASD: 4 Ctrl: 36	Independent t-test	134.8 ± 3.4	127.0 ± 4.7	MD: 7.8 (95%CI: 2.9 to 12.7)	0.003		
	#Kaito T et al., 2010[39]	ASD: 13 Ctrl: 58	Independent t-test	124.4 ± 5.1	123.5 ± 3.9	MD: 0.9 (95%CI: -1.6 to 3.4)	0.480		
	#Okuda S et al., 2004[41]	ASD: 4 Ctrl: 58	Independent t-test	138 ± 1	124 ± 4	MD: 14 (95%CI: 10.0 to 18.0)	<0.001		
Lumbar scoliosis (degrees)	Okuda S et al., 2004[41]	ASD: 4 Ctrl: 58	Independent t-test	7 ± 8	4 ± 6	MD: 3 (95%CI: -3.3 to 9.3)	0.347		No evidence
Lumbopelvic mismatch (degrees)	#Kim WJ et al., 2019[27]	ASD: 37 Ctrl: 40	Independent t-test	15.1 ± 12.3	12.8 ± 9.3	MD: 2.3 (95%CI: -2.6 to 7.2)	0.355	Pooled OR = 1.75 (0.76 to 4.40) (*P*=0.23)	Conflicting
	#Mastsumoto T et al., 2017[28]	ASD: 20 Ctrl: 100	Chi-square test	> 10: 15 / < 10: 5	> 10: 40 / < 10: 60	OR: 4.5 (95%CI: 1.5 to 13.4)	0.007		
	#Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Chi-square test	> 10: 7 / < 10: 9	> 10: 47 / < 10: 72	OR: 1.2 (95%CI: 0.4 to 3.4)	0.745		
	#Rothenfluh DA et al., 2015[35]	ASD: 45 Ctrl: 39	Chi-square test	> 10: 35 / < 10: 12	> 10: 8 / < 10: 29	OR: 10.6 (95%CI: 3.8 to 29.4)	<0.001		
Pelvic incidence (degrees)	#Kim WJ et al., 2019[27]	ASD: 37 Ctrl: 40	Independent t-test	54.9 ± 9.4	52.3 ± 11.3	MD: 2.6 (95%CI: -2.1 to 7.3)	0.278	Pooled MD =2.16 (-1.51 to 5.84) (*P*=0.25)	Conflicting
	#Mastsumoto T et al., 2017[28]	ASD: 20 Ctrl: 100	Independent t-test	59.7 ± 8.3	56.8 ± 9.1	MD: 2.9 (95%CI: -1.5 to 7.3)	0.190		
	#Wang S et al., 2017[30]	ASD: 21 Ctrl: 96	Independent t-test	52.9 ± 11.1	54.6 ± 9.8	MD: -1.7 (95%CI: -6.5 to 3.1)	0.491		
	#Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Independent t-test	64.6 ± 13.8	62.7 ± 15.7	MD: 1.9 (95%CI: -5.8 to 9.6)	0.626		
	#Heo Y et al., 2015[33]	ASD: 33 Ctrl: 345	Independent t-test	56.9 ± 11.0	59.4 ± 10.4	MD: -2.6 (95%CI: -6.3 to 1.2)	0.181		
	#Rothenfluh DA et al., 2015[35]	ASD: 45 Ctrl: 39	Independent t-test	60.9 ± 10.0	51.7 ± 10.4	MD: 9.2 (95%CI: 4.8 to 13.6)	<0.001		
Pelvic tilt (degrees)	#Kim WJ et al., 2019[27]	ASD: 37 Ctrl: 40	Independent t-test	23.9 ± 8.5	21.4 ± 8.8	MD: 2.5 (95%CI: -1.4 to 6.4)	0.209	Pooled MD = 2.43 (-0.02 to 4.89) (*P*=0.05)	Conflicting
	#Mastsumoto T et al., 2017[28]	ASD: 20 Ctrl: 100	Independent t-test	27.0 ± 6.2	22.9 ± 7.8	MD: 4.1 (95%CI: 0.43 to 7.77)	0.029		

http://dx.doi.org/10.2106/JBJS.20.00408

	#Wang S et al., 2017[30]	ASD: 21 Ctrl: 96	Independent t-test	15.19 ± 5.56	16.19 ± 5.65	MD: -1.0 (95%CI: -3.7 to 1.7)	0.463		
	#Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Independent t-test	22.6 ± 8.9	22.1 ± 8.0	MD: 0.5 (95%CI: -3.5 to 4.5)	0.806		
	#Rothenfluh DA et al., 2015[35]	ASD: 45 Ctrl: 39	Independent t-test	22.2 ± 7.3	16.8 ± 6.8	MD: 5.4 (95%CI: 2.3 to 8.5)	<0.001		
Sacral slope (degrees)	#Bagheri SR et al., 2019[26]	ASD: 76 Ctrl: 554	Independent t-test	34.34 ± 12.8	36.14 ± 11.7	MD: -1.8 (95%CI: -4.6 to 1.0)	0.214	Pooled MD = -0.32 (-0.70 to 1.07) (*P*=0.65)	Conflicting
	#Kim WJ et al., 2019[27]	ASD: 37 Ctrl: 40	Independent t-test	31.1 ± 6.6	30.5 ± 7.1	MD: 0.6 (95%CI: -2.5 to 3.7)	0.703		
	#Mastsumoto T et al., 2017[28]	ASD: 20 Ctrl: 100	Independent t-test	32.7 ± 6.7	33.8 ± 7.2	MD: -1.1 (95%CI: -4.6 to 2.4)	0.530		
	#Wang S et al., 2017[30]	ASD: 21 Ctrl: 96	Independent t-test	37.71 ± 9.94	38.45 ± 7.8	MD: -0.74 (95%CI: -4.7 to 3.2)	0.709		
	#Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Independent t-test	42.3 ± 9.3	41.1 ± 11.7	MD: 1.2 (95%CI: -4.5 to 6.9)	0.677		
	#Rothenfluh DA et al., 2015[35]	ASD: 45 Ctrl: 39	Independent t-test	36.2 ± 8.4	34.9 ± 7.6	MD: 1.3 (95%CI: -2.2 to 4.8)	0.462		
	#Liang J et al., 2014[37]	ASD: 28 Ctrl: 56	Independent t-test	33.6 ± 10.4	34.8 ± 7.5	MD: -1.2 (95%CI: -5.2 to 2.7)	0.547		
Sagittal vertical axis (mm)	Kim WJ et al., 2019[27]	ASD: 37 Ctrl: 40	Independent t-test	2.4 ± 1.3	2.5 ± 1.1	MD: -0.1 (95%CI: -0.7 to 0.5)	0.716		Conflicting
	Mastsumoto T et al., 2017[28]	ASD: 20 Ctrl: 100	Chi-square test	> 50: 10 / < 50: 10	> 50: 21 < 50: 79	OR: 3.8 (95%CI: 1.4 to 10.2)	0.009		
Segmental lordosis (degrees)	Kim WJ et al., 2019[27]	ASD: 37 Ctrl: 40	Independent t-test	21.3 ± 9.1	22.1 ± 8.4	MD: -0.8 (95%CI: -4.8 to 3.2)	0.689		No evidence
	Mastsumoto T et al., 2017[28]	ASD: 20 Ctrl: 100	Independent t-test	11.4 ± 9.4	14.0 ± 5.8	MD: -2.6 (95%CI: -5.8 to 0.6)	0.106		
	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Independent t-test	17.1 ± 10.9	17.9 ± 11.1	MD: -0.8 (95%CI: -6.3 to 4.7)	0.774		
	Heo Y et al., 2015[33]	ASD: 33 Ctrl: 345	Independent t-test	11.9 ± 7.4	12.5 ± 6.5	MD: -0.5 (95%CI: -2.9 to 1.9)	0.666		

	Heo Y et al., 2015[33]	ASD: 33 Ctrl: 345	Independent t-test	11.9 ± 6.5	14.6 ± 7.6	MD: -2.7 (95%CI: -5.4 to 0.0)	0.051		
	Rothenfluh DA et al., 2015[35]	ASD: 45 Ctrl: 39	Independent t-test	23.6 ± 12.6	26.5 ± 11.3	MD: -2.9 (95%CI: -8.1 to 2.3)	0.273		
	Cho TK et al., 2014[36]	ASD: 10 Ctrl: 144	Independent t-test	12.4 ± SD not reported	15.2 ± SD not reported	NA	0.173*		
	Okuda S et al., 2004[41]	ASD: 4 Ctrl: 58	Independent t-test	9 ± 6	13 ± 6	MD: -4 (95%CI: -10.2 to 2.2)	0.202		
Subjacent segment angle (degrees)	Rothenfluh DA et al., 2015[35]	ASD: 45 Ctrl: 39	Independent t-test	11.9 ± 6.0	9.6 ± 6.7	MD: 2.3 (95%CI: -0.5 to 5.1)	0.101		No evidence
Thoracic kyphosis (degrees)	Mastsumoto T et al., 2017[28]	ASD: 20 Ctrl: 100	Independent t-test	24.7 ± 10.8	29.4 ± 9.8	MD: -4.7 (95%CI: -9.5 to 0.1)	0.057		No evidence
Postoperative measures									
C7 to central sacral vertical line (mm)	Mastsumoto T et al., 2017[28]	ASD: 20 Ctrl: 100	Independent t-test	12.7 ± 11.2	10.0 ± 8.8	MD: 2.7 (95%CI: -1.8 to 7.2)	0.235		No evidence
Epifusional segment angle (degrees)	Rothenfluh DA et al., 2015[35]	ASD: 45 Ctrl: 39	Independent t-test	8.6 ± 4.1	9.4 ± 3.4	MD: -0.8 (95%CI: -2.5 to 0.9)	0.338		No evidence
	Liang J et al., 2014[37]	ASD: 28 Ctrl: 56	Independent t-test	9.4 ± 5.7	8.9 ± 4.4	MD: 0.5 (95%CI: -1.7 to 2.7)	0.658		
Facet orientation (degrees)	Yugue I et al., 2016[32]	ASD: 44 Ctrl: 117	Log rank test	NA	NA	NA	0.227*		No evidence
Fusion angle (degrees)	Rothenfluh DA et al., 2015[35]	ASD: 45 Ctrl: 39	Independent t-test	22.7 ± 8.6	24.4 ± 9.3	MD: -1.7 (95%CI: -5.6 to 2.2)	0.387		No evidence
	Sakaura H et al., 2013[38]	ASD: 4 Ctrl: 36	Independent t-test	9.8 ± 7.1	12.6 ± 5.8	MD: -2.8 (95%CI: -9.1 to 3.5)	0.375		
	Kaito T et al., 2010[39]	ASD: 13 Ctrl: 58	Independent t-test	10.3 ± 6.5	10.7 ± 4.4	MD: -0.4 (95%CI: -3.4 to 2.6)	0.788		
Laminar inclination (degrees)	Yugue I et al., 2016[32]	ASD: 44 Ctrl: 117	Log rank test	NA	NA	NA	0.633*		No evidence
Sacral slope (degrees)	#Kim WJ et al., 2019[27]	ASD: 37 Ctrl: 40	Independent t-test	31.5 ± 8.1	32.1 ± 8.6	MD: -0.6 (95%CI: -4.4 to 3.2)	0.754		Conflicting

	#Mastsumoto T et al., 2017[28]	ASD: 20 Ctrl: 100	Independent t-test	33.0 ± 7.6	34.6 ± 7.5	MD: -1.6 (95%CI: -5.3 to 2.0)	0.387	Pooled MD = -0.58 (-2.38 to 1.22) (*P*=0.53)	
	#Wang S et al., 2017[30]	ASD: 21 Ctrl: 96	Independent t-test	34.29 ± 7.8	37.1 ± 8.8	MD: -2.8 (95%CI: -6.9 to 1.3)	0.185		
	#Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Independent t-test	39.8 ± 9.1	39.8 ± 11.3	MD: 0.0 (95%CI: -4.6 to 4.6)	1.000		
	#Rothenfluh DA et al., 2015[35]	ASD: 45 Ctrl: 39	Independent t-test	37.8 ± 8.0	35.3 ± 7.7	MD: 2.5 (95%CI: -0.92 to 5.92)	0.150		
	#Liang J et al., 2014[37]	ASD: 28 Ctrl: 56	Independent t-test	31.8 ± 9.1	34.3 ± 7.0	MD: -2.5 (95%CI: -6.07 to 1.07)	0.167		
Sagittal vertical axis (mm)	Kim WJ et al., 2019[27]	ASD: 37 Ctrl: 40	Independent t-test	2.1 ± 1.8	2.3 ± 1.1	MD: -0.2 (95%CI: -0.87 to 0.47)	0.555		No evidence
	Mastsumoto T et al., 2017[28]	ASD: 20 Ctrl: 100	Chi-square test	> 50: 9 / < 50: 11	> 50: 24 / < 50: 76	OR: 2.6 (95%CI: 1.0 to 7.0)	0.060		
Segmental lordosis (degrees)	Kim WJ et al., 2019[27]	ASD: 37 Ctrl: 40	Independent t-test (L4-S1)	19.2 ± 9.4	24.8 ± 7.7	MD: -5.6 (95%CI: -9.5 to -1.7)	0.005		No evidence
	Mastsumoto T et al., 2017[28]	ASD: 20 Ctrl: 100	Independent t-test (L4-L5)	12.9 ± 6.9	12.8 ± 6.2	MD: 0.1 (95%CI: -3.0 to 3.2)	0.949		
	Zhong ZM et al., 2017[31]	ASD: 18 Ctrl: 136	Independent t-test (L4-L5)	18.4 ± 8.8	17.9 ± 9.3	MD: 0.5 (95%CI: -4.1 to 5.1)	0.830		
	Yugue I et al., 2016[32]	ASD: 44 Ctrl: 117	Log rank test (L4-L5)	NA	NA	NA	0.228*		
Adjacent spinal canal stenosis ratio on MRI	Yugue I et al., 2016[32]	ASD: 44 Ctrl: 117	Log rank test	NA	NA	NA	0.299*		No evidence
Subjacent segment angle (degrees)	Rothenfluh DA et al., 2015[35]	ASD: 45 Ctrl: 39	Independent t-test	10.9 ± 6.9	9.8 ± 6.3	MD: 1.1 (95%CI: -1.8 to 4.0)	0.450		No evidence
Fused vertebral slip (percentage)	Yugue I et al., 2016[32]	ASD: 44 Ctrl: 117	Log rank test	NA	NA	NA	0.147*		No evidence

Note. * = reported from a study; # = studies included in the meta-analysis of the risk factor with conflicting findings; 95%CI = 95% confidence interval; ASD = adjacent segment disease; ASAPSC system = American Society of Anesthesiologists Physical Status Classification system; Ctrl = control (patients without ASD); JOA = Japanese Orthopaedic Association; MD = mean difference; OR = odds ratio; NA = not available.

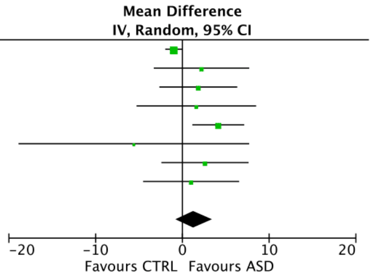
http://dx.doi.org/10.2106/JBJS.20.00408

Appendix 6. Meta-analyses of pooled risk factors for adjacent segment disease (ASD) compared to a control group without ASD (i.e. CTRL) that showed no statistical significance.

Age

	ASD			CTRL				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Bagheri, S.R. et al., 2019	61.37	4.12	76	62.37	3.9	554	28.4%	−1.00 [−1.98, −0.02]	2019
Wang, H. et al., 2017	55.3	10.5	15	53.1	10.9	222	9.8%	2.20 [−3.30, 7.70]	2017
Wang, S. et al., 2017	56.43	8.79	21	54.6	12.25	96	12.7%	1.83 [−2.66, 6.32]	2017
Zhong, Z.M. et al., 2017	59.8	14.1	18	58.2	13.4	136	7.1%	1.60 [−5.29, 8.49]	2017
Heo, Y. et al., 2015	62.79	8.22	33	58.66	9.89	345	18.8%	4.13 [1.14, 7.12]	2015
Sakaura, H. et al., 2013	53.5	12.6	4	59.1	15.1	36	2.3%	−5.60 [−18.90, 7.70]	2013
Kaito, T. et al., 2010	66	8.3	13	63.4	8.6	58	11.1%	2.60 [−2.43, 7.63]	2010
Okuda, S. et al., 2004	65	5	4	64	10	58	9.8%	1.00 [−4.53, 6.53]	2004
Total (95% CI)			**184**			**1505**	**100.0%**	**1.31 [−0.79, 3.41]**	

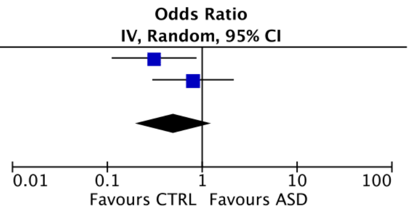
Heterogeneity: Tau^2 = 3.78; Chi^2 = 14.38, df = 7 (P = 0.04); I^2 = 51%
Test for overall effect: Z = 1.22 (P = 0.22)



Alcohol drinking

	ASD		CTRL			Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI
Wang, S. et al., 2017	6	21	54	96	48.8%	0.31 [0.11, 0.87]
Zhong, Z.M. et al., 2017	8	18	68	136	51.2%	0.80 [0.30, 2.15]
Total (95% CI)		**39**		**232**	**100.0%**	**0.50 [0.20, 1.27]**
Total events	14		122			

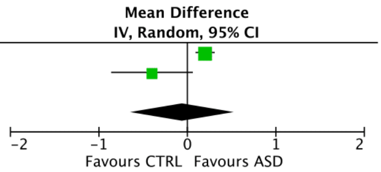
Heterogeneity: Tau^2 = 0.18; Chi^2 = 1.68, df = 1 (P = 0.19); I^2 = 41%
Test for overall effect: Z = 1.45 (P = 0.15)



Bone mineral density

	ASD			CTRL				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Wang, H. et al., 2017	−1	0.2	15	−1.2	0.3	222	57.3%	0.20 [0.09, 0.31]	2017
Wang, S. et al., 2017	−1.3	0.93	21	−0.9	1.17	96	42.7%	−0.40 [−0.86, 0.06]	2017
Total (95% CI)			**36**			**318**	**100.0%**	**−0.06 [−0.64, 0.53]**	

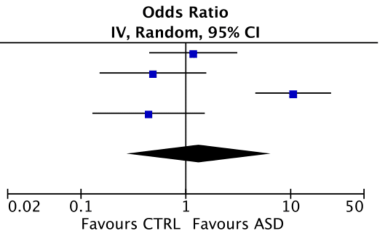
Heterogeneity: Tau^2 = 0.15; Chi^2 = 6.15, df = 1 (P = 0.01); I^2 = 84%
Test for overall effect: Z = 0.19 (P = 0.85)



Preoperative facet joint degeneration

	ASD		CTRL			Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	Year
Mastsumoto, T. et al., 2017	9	20	41	100	25.5%	1.18 [0.45, 3.10]	2017
Mastsumoto, T. et al., 2017	4	20	34	100	24.4%	0.49 [0.15, 1.57]	2017
Heo, Y. et al., 2015	13	33	20	345	26.1%	10.56 [4.60, 24.26]	2015
Kaito, T. et al., 2010	5	13	34	58	24.0%	0.44 [0.13, 1.51]	2010
Total (95% CI)		**86**		**603**	**100.0%**	**1.33 [0.28, 6.42]**	
Total events	31		129				

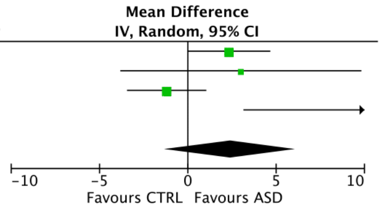
Heterogeneity: Tau^2 = 2.29; Chi^2 = 27.89, df = 3 (P < 0.00001); I^2 = 89%
Test for overall effect: Z = 0.35 (P = 0.72)



Preoperative facet tropism

	ASD			CTRL				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Heo, Y. et al., 2015	8.91	6.63	33	6.58	5.6	345	35.0%	2.33 [−0.01, 4.67]	2015
Sakaura, H. et al., 2013	8.3	6.8	4	5.3	4.5	36	17.2%	3.00 [−3.82, 9.82]	2013
Kaito, T. et al., 2010	5.8	4.1	13	7	1	58	35.4%	−1.20 [−3.44, 1.04]	2010
Okuda, S. et al., 2004	16	9	4	4	3	58	12.4%	12.00 [3.15, 20.85]	2004
Total (95% CI)			**54**			**497**	**100.0%**	**2.39 [−1.34, 6.12]**	

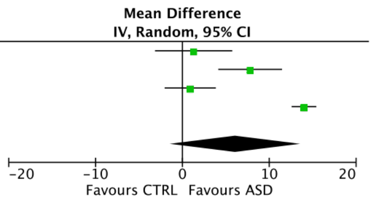
Heterogeneity: Tau^2 = 8.93; Chi^2 = 11.20, df = 3 (P = 0.01); I^2 = 73%
Test for overall effect: Z = 1.26 (P = 0.21)



Preoperative lamina inclination

	ASD			CTRL				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Heo, Y. et al., 2015	112.55	12.83	33	111.26	7.36	345	24.0%	1.29 [−3.16, 5.74]	2015
Sakaura, H. et al., 2013	134.8	3.4	4	127	4.7	36	24.7%	7.80 [4.13, 11.47]	2013
Kaito, T. et al., 2010	124.4	5.1	13	123.5	3.9	58	25.2%	0.90 [−2.05, 3.85]	2010
Okuda, S. et al., 2004	138	1	4	124	4	58	26.0%	14.00 [12.58, 15.42]	2004
Total (95% CI)			**54**			**497**	**100.0%**	**6.11 [−1.38, 13.60]**	

Heterogeneity: Tau^2 = 55.61; Chi^2 = 82.58, df = 3 (P < 0.00001); I^2 = 96%
Test for overall effect: Z = 1.60 (P = 0.11)

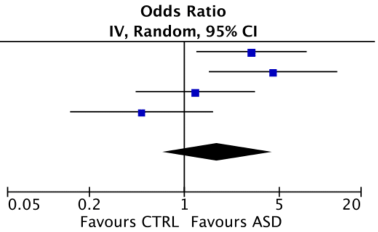


http://dx.doi.org/10.2106/JBJS.20.00408

Preoperative lumbopelvic mismatch

	ASD		CTRL			Odds Ratio	
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**IV, Random, 95% CI**	**Year**
Kim, W.J. et al., 2019	25	37	16	40	27.0%	3.13 [1.23, 7.96]	2019
Mastsumoto, T. et al., 2017	15	20	40	100	24.6%	4.50 [1.52, 13.36]	2017
Zhong, Z.M. et al., 2017	7	18	47	136	25.8%	1.21 [0.44, 3.31]	2017
Rothenfluh, D.A. et al., 2015	5	45	8	39	22.7%	0.48 [0.14, 1.63]	2015
Total (95% CI)		**120**		**315**	**100.0%**	**1.75 [0.70, 4.40]**	
Total events	52		111				

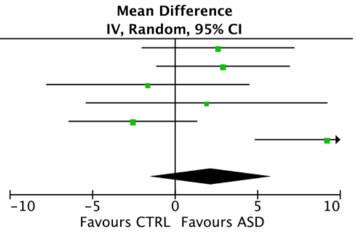
Heterogeneity: $Tau^2 = 0.59$; $Chi^2 = 9.16$, df = 3 (P = 0.03); $I^2 = 67\%$
Test for overall effect: Z = 1.19 (P = 0.23)



Preoperative pelvic incidence

	ASD			CTRL				Mean Difference	
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**	**Year**
Kim, W.J. et al., 2019	54.9	9.4	37	52.3	11.3	40	17.5%	2.60 [−2.03, 7.23]	2019
Mastsumoto, T. et al., 2017	59.7	8.3	20	56.8	9.1	100	18.7%	2.90 [−1.15, 6.95]	2017
Wang, S. et al., 2017	52.91	11.08	15	54.57	9.8	57	14.4%	−1.66 [−7.82, 4.50]	2017
Zhong, Z.M. et al., 2017	64.6	13.8	16	62.7	15.7	119	12.3%	1.90 [−5.43, 9.23]	2017
Heo, Y. et al., 2015	56.88	10.97	33	59.44	10.44	345	19.0%	−2.56 [−6.46, 1.34]	2015
Rothenfluh, D.A. et al., 2015	60.9	10	45	51.7	10.4	39	18.0%	9.20 [4.82, 13.58]	2015
Total (95% CI)			**166**			**700**	**100.0%**	**2.16 [−1.51, 5.84]**	

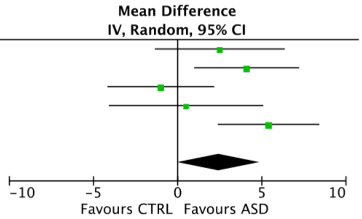
Heterogeneity: $Tau^2 = 14.50$; $Chi^2 = 17.19$, df = 5 (P = 0.004); $I^2 = 71\%$
Test for overall effect: Z = 1.15 (P = 0.25)



Preoperative pelvic tilt

	ASD			CTRL				Mean Difference	
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**	**Year**
Kim, W.J. et al., 2019	23.9	8.5	37	21.4	8.8	40	18.4%	2.50 [−1.37, 6.37]	2019
Mastsumoto, T. et al., 2017	27	6.2	20	22.9	7.8	100	21.9%	4.10 [0.98, 7.22]	2017
Wang, S. et al., 2017	15.19	5.56	15	16.19	5.65	57	21.7%	−1.00 [−4.17, 2.17]	2017
Zhong, Z.M. et al., 2017	22.6	8.9	16	22.1	8	119	15.5%	0.50 [−4.09, 5.09]	2017
Rothenfluh, D.A. et al., 2015	22.2	7.3	45	16.8	6.8	39	22.4%	5.40 [2.38, 8.42]	2015
Total (95% CI)			**133**			**355**	**100.0%**	**2.43 [−0.02, 4.89]**	

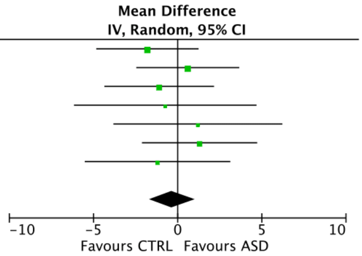
Heterogeneity: $Tau^2 = 4.63$; $Chi^2 = 9.95$, df = 4 (P = 0.04); $I^2 = 60\%$
Test for overall effect: Z = 1.94 (P = 0.05)



Preoperative sacral slope

	ASD			CTRL				Mean Difference	
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**	**Year**
Bagheri, S.R. et al., 2019	34.34	12.8	76	36.14	11.7	554	20.8%	−1.80 [−4.84, 1.24]	2019
Kim, W.J. et al., 2019	31.1	6.6	37	30.5	7.1	40	20.5%	0.60 [−2.46, 3.66]	2019
Mastsumoto, T. et al., 2017	32.7	6.7	20	33.8	7.2	100	18.1%	−1.10 [−4.36, 2.16]	2017
Wang, S. et al., 2017	37.71	9.94	15	38.45	7.8	57	6.5%	−0.74 [−6.16, 4.68]	2017
Zhong, Z.M. et al., 2017	42.3	9.3	16	41.1	11.7	119	7.6%	1.20 [−3.82, 6.22]	2017
Rothenfluh, D.A. et al., 2015	36.2	8.4	45	34.9	7.6	39	16.4%	1.30 [−2.12, 4.72]	2015
Liang, J. et al., 2014	33.6	10.4	28	34.8	7.5	56	10.2%	−1.20 [−5.52, 3.12]	2014
Total (95% CI)			**237**			**965**	**100.0%**	**−0.32 [−1.70, 1.07]**	

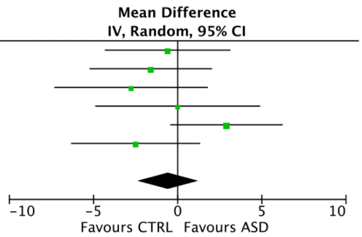
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.87$, df = 6 (P = 0.82); $I^2 = 0\%$
Test for overall effect: Z = 0.45 (P = 0.65)



Postoperative sacral slope

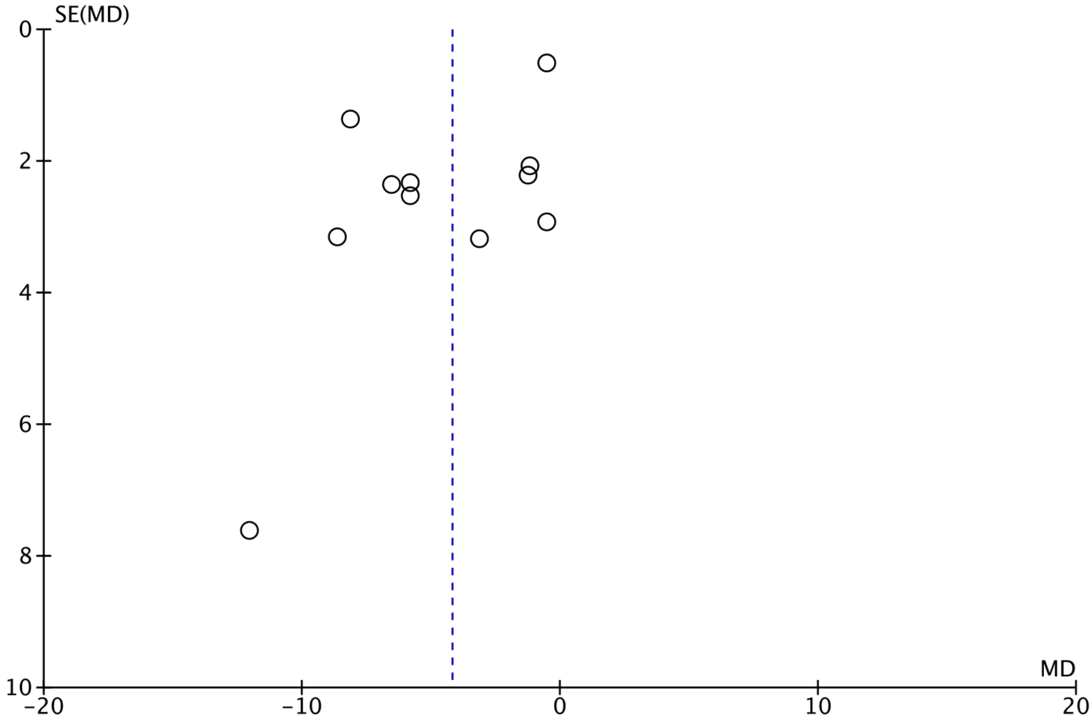
	ASD			CTRL				Mean Difference	
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**	**Year**
Kim, W.J. et al., 2019	31.5	8.1	37	32.1	8.6	40	18.0%	−0.60 [−4.33, 3.13]	2019
Mastsumoto, T. et al., 2017	33	7.6	20	34.6	7.5	100	18.7%	−1.60 [−5.24, 2.04]	2017
Wang, S. et al., 2017	34.29	7.81	15	37.06	8.78	57	13.1%	−2.77 [−7.33, 1.79]	2017
Zhong, Z.M. et al., 2017	39.8	9.1	16	39.8	11.3	119	11.6%	0.00 [−4.90, 4.90]	2017
Rothenfluh, D.A. et al., 2015	37.8	8	45	34.9	7.6	39	21.3%	2.90 [−0.44, 6.24]	2015
Liang, J. et al., 2014	31.8	9.1	28	34.3	7	56	17.3%	−2.50 [−6.34, 1.34]	2014
Total (95% CI)			**161**			**411**	**100.0%**	**−0.58 [−2.39, 1.22]**	

Heterogeneity: $Tau^2 = 1.10$; $Chi^2 = 6.37$, df = 5 (P = 0.27); $I^2 = 21\%$
Test for overall effect: Z = 0.63 (P = 0.53)



http://dx.doi.org/10.2106/JBJS.20.00408

Appendix 7. The funnel plot for assessing publication bias of studies evaluating preoperative lumbar lordosis as a risk factor for adjacent segment disease following lumbar fusion.



Heterogeneity: $Tau^2 = 11.12$

References

1. Bono CM, Lee CK. Critical analysis of trends in fusion for degenerative disc disease over the past 20 years: influence of technique on fusion rate and clinical outcome. *Spine.* 2004;29(4):455-463.
2. Rajaee SS, Bae HW, Kanim LEA, Delamarter RB. Spinal fusion in the United States: analysis of trends from 1998 to 2008. *Spine.* 2012;37(1):67-76.
3. Martin BI, Mirza SK, Spina N, Spiker WR, Lawrence B, Brodke DS. Trends in Lumbar Fusion Procedure Rates and Associated Hospital Costs for Degenerative Spinal Diseases in the United States, 2004 to 2015. *Spine.* 2019;44(5):369-376.
4. Yoshihara H, Yoneoka D. National trends in the surgical treatment for lumbar degenerative disc disease: United States, 2000 to 2009. *Spine J.* 2015;15(2):265-271.
5. Irmola TM, Hakkinen A, Jarvenpaa S, Marttinen I, Vihtonen K, Neva M. Reoperation Rates Following Instrumented Lumbar Spine Fusion. *Spine.* 2018;43(4):295-301.
6. Anderson PA, Andersson GBJ, Arnold PM, et al. Terminology. *Spine.* 2012;37(22 Suppl):S8-9.
7. Feng Y, Egan B, Wang J. Genetic Factors in Intervertebral Disc Degeneration. *Genes Dis.* 2016;3(3):178-185.
8. Kim HJ, Kang KT, Chun HJ, Lee CK, Chang BS, Yeom JS. The influence of intrinsic disc degeneration of the adjacent segments on its stress distribution after one-level lumbar fusion. *Eur Spine J.* 2015;24(4):827-837.
9. Zhang C, Berven SH, Fortin M, Weber MH. Adjacent Segment Degeneration Versus Disease After Lumbar Spine Fusion for Degenerative Pathology: A Systematic Review With Meta-Analysis of the Literature. *Clinical spine surgery.* 2016;29(1):21-29.
10. Tobert DG, Antoci V, Patel SP, Saadat E, Bono CM. Adjacent Segment Disease in the Cervical and Lumbar Spine. *Clinical spine surgery.* 2017;30(3):94-101.
11. Chosa E, Goto K, Totoribe K, Tajima N. Analysis of the effect of lumbar spine fusion on the superior adjacent intervertebral disk in the presence of disk degeneration, using the three-dimensional finite element method. *Journal of spinal disorders and techniques.* 2004;17(2):134-139.
12. Lee CK, Langrana NA. Lumbosacral spinal fusion. A biomechanical study. *Spine.* 1984;9(6):574-581.
13. Weinhoffer SL, Guyer RD, Herbert M, Griffith SL. Intradiscal pressure measurements above an instrumented fusion. A cadaveric study. *Spine.* 1995;20(5):526-531.
14. Lee CH, Hyun SJ, Kim KJ, Jahng TA, Yoon SH, Kim HJ. The efficacy of lumbar hybrid stabilization using the DIAM to delay adjacent segment degeneration: an intervention comparison study with a minimum 2-year follow-up. *Neurosurgery.* 2013;73(2 Suppl Operative):ons224-232.
15. Virk SS, Niedermeier S, Yu E, Khan SN. Adjacent segment disease. *Orthopedics.* 2014;37(8):547-555.
16. Park P, Garton HJ, Gala VC, Hoff JT, McGillicuddy JE. Adjacent segment disease after lumbar or lumbosacral fusion: review of the literature. *Spine.* 2004;29(17):1938-1944.
17. Saavedra-Pozo FM, Deusdara AM, Benzel EC. Adjacent segment disease perspective and review of the literature. *The Ochsner journal.* 2014;14(1):78-83.
18. Trivedi NN, Wilson SM, Puchi LA, Lebl DR. Evidence-Based Analysis of Adjacent Segment Degeneration and Disease After LIF: A Narrative Review. *Global spine journal.* 2018;8(1):95-102.

19. Hashimoto K, Aizawa T, Kanno H, Itoi E. Adjacent segment degeneration after fusion spinal surgery-a systematic review. *International orthopaedics.* 2019;43(4):987-993.
20. Burch MB, Wiegers NW, Patil S, Nourbakhsh A. Incidence and risk factors of reoperation in patients with adjacent segment disease: A meta-analysis. *J Craniovertebr Junction Spine.* 2020;11(1):9-16.
21. Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Published 2008. Accessed on December 20, 2020.
22. Luchini C, Stubbs B, Solmi M, Veronese N. Assessing the quality of studies in meta-analyses: Advantages and limitations of the Newcastle Ottawa Scale. *World J Meta-Anal.* 2017;5(4):80-84.
23. Lo CK, Mertz D, Loeb M. Newcastle-Ottawa Scale: comparing reviewers' to authors' assessments. *BMC Med Res Methodol.* 2014;14(45).
24. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *Bmj.* 1997;315(7109):629-634.
25. van Tulder M, Furlan A, Bombardier C, Bouter L. Updated method guidelines for systematic reviews in the cochrane collaboration back review group. *Spine.* 2003;28(12):1290-1299.
26. Bagheri SR, Alimohammadi E, Froushani AZ, Abdi A. Adjacent segment disease after posterior lumbar instrumentation surgery for degenerative disease: Incidence and risk factors. *Journal of Orthopaedic Surgery.* 2019;27(2):1-6.
27. Kim WJ, Ma CH, Kim SH, et al. Prevention of Adjacent Segmental Disease after Fusion in Degenerative Spinal Disorder: Correlation between Segmental Lumbar Lordosis Ratio and Pelvic Incidence-Lumbar Lordosis Mismatch for a Minimum 5-Year Follow-up. *Asian Spine J.* 2019;13(4):654-662.
28. Matsumoto T, Okuda S, Maeno T, et al. Spinopelvic sagittal imbalance as a risk factor for adjacent-segment disease after single-segment posterior lumbar interbody fusion. *J Neurosurg Spine.* 2017;26(4):435-440.
29. Wang H, Ma L, Yang D, et al. Incidence and risk factors of adjacent segment disease following posterior decompression and instrumented fusion for degenerative lumbar disorders. *Medicine.* 2017;96(5):e6032.
30. Wang S, Niu J, Song D, et al. Analysis of the spino-pelvic parameters for symptomatic adjacent segment degeneration after posterior lumbar interbody fusion. *International Journal of Clinical and Experimental Medicine.* 2017;10(8):12454-12460.
31. Zhong ZM, Deviren V, Tay B, Burch S, Berven SH. Adjacent segment disease after instrumented fusion for adult lumbar spondylolisthesis: Incidence and risk factors. *Clinical neurology and neurosurgery.* 2017;156:29-34.
32. Yugue I, Okada S, Masuda M, Ueta T, Maeda T, Shiba K. Risk factors for adjacent segment pathology requiring additional surgery after single-level spinal fusion: impact of pre-existing spinal stenosis demonstrated by preoperative myelography. *Eur Spine J.* 2016;25(5):1542-1549.
33. Heo Y, Park JH, Seong HY, et al. Symptomatic adjacent segment degeneration at the L3-4 level after fusion surgery at the L4-5 level: evaluation of the risk factors and 10-year incidence. *Eur Spine J.* 2015;24(11):2474-2480.

34. Lee YS, Kim YB, Park SW. Survival rates and risk factors for cephalad and L5-s1 adjacent segment degeneration after L5 floating lumbar fusion : a minimum 2-year follow-up. *Journal of Korean Neurosurgical Society.* 2015;57(2):108-113.
35. Rothenfluh DA, Mueller DA, Rothenfluh E, Min K. Pelvic incidence-lumbar lordosis mismatch predisposes to adjacent segment disease after lumbar spinal fusion. *Eur Spine J.* 2015;24(6):1251-1258.
36. Cho TK, Lim JH, Kim SH, et al. Preoperative predictable factors for the occurrence of adjacent segment degeneration requiring second operation after spinal fusion at isolated L4-L5 level. *Journal of neurological surgery Part A, Central European neurosurgery.* 2014;75(4):270-275.
37. Liang J, Dong Y, Zhao H. Risk factors for predicting symptomatic adjacent segment degeneration requiring surgery in patients after posterior lumbar fusion. *Journal of orthopaedic surgery and research.* 2014;9(97).
38. Sakaura H, Yamashita T, Miwa T, Ohzono K, Ohwada T. Symptomatic adjacent segment pathology after posterior lumbar interbody fusion for adult low-grade isthmic spondylolisthesis. *Global spine journal.* 2013;3(4):219-224.
39. Kaito T, Hosono N, Mukai Y, Makino T, Fuji T, Yonenobu K. Induction of early degeneration of the adjacent segment after posterior lumbar interbody fusion by excessive distraction of lumbar disc space. *J Neurosurg Spine.* 2010;12(6):671-679.
40. Lee CS, Hwang CJ, Lee SW, et al. Risk factors for adjacent segment disease after lumbar fusion. *Eur Spine J.* 2009;18(11):1637-1643.
41. Okuda S, Iwasaki M, Miyauchi A, Aono H, Morita M, Yamamoto T. Risk factors for adjacent segment degeneration after PLIF. *Spine.* 2004;29(14):1535-1540.
42. Adams MA, Dolan P. Recent advances in lumbar spinal mechanics and their clinical significance. *Clin Biomech.* 1995;10(1):3-19.
43. Ranger T, Newell N, Grant CA, Barker PJ, Pearcy MJ. Role of the Middle Lumbar Fascia on Spinal Mechanics: A Human Biomechanical Assessment. *Spine.* 2017;42(8):E459-465.
44. Babu R, Park JG, Mehta AI, et al. Comparison of superior-level facet joint violations during open and percutaneous pedicle screw placement. *Neurosurgery.* 2012;71(5):962-970.
45. Bible JE, Biswas D, Miller CP, Whang PG, Grauer JN. Normal functional range of motion of the lumbar spine during 15 activities of daily living. *Journal of spinal disorders and techniques.* 2010;23(2):106-112.
46. Zhang Q, Xu YF, Tian W, et al. Comparison of Superior-Level Facet Joint Violations Between Robot-Assisted Percutaneous Pedicle Screw Placement and Conventional Open Fluoroscopic-Guided Pedicle Screw Placement. *Orthopaedic surgery.* 2019;11(5):850-856.
47. Iyer S, Christiansen BA, Roberts BJ, Valentine MJ, Manoharan RK, Bouxsein ML. A biomechanical model for estimating loads on thoracic and lumbar vertebrae. *Clin Biomech.* 2010;25(9):853-858.
48. Roussouly P, Pinheiro-Franco JL. Biomechanical analysis of the spino-pelvic organization and adaptation in pathology. *Eur Spine J.* 2011;20 Suppl 5(Suppl 5):609-618.
49. Zehra U, Cheung JPY, Bow C, et al. Spinopelvic alignment predicts disc calcification, displacement, and Modic changes: Evidence of an evolutionary etiology for clinically-relevant spinal phenotypes. *JOR Spine.* 2020;3(1):e1083.

50. Xia YP, Xu TT, Shen QF, Zhang XL, Jiang H, Tian R. Radiographic predictors of residual low back pain after laminectomy for lumbar canal stenosis: a minimum of 6-year follow-up. *Chin J Traumatol.* 2008;11(3):135-140.
51. Lin RM, Jou IM, Yu CY. Lumbar lordosis: normal adults. *J Formos Med Assoc.* 1992;91(3):329-333.
52. Makhni MC, Shillingford JN, Laratta JL, Hyun SJ, Kim YJ. Restoration of Sagittal Balance in Spinal Deformity Surgery. *Journal of Korean Neurosurgical Society.* 2018;61(2):167-179.
53. Urban JP, Roberts S. Degeneration of the intervertebral disc. *Arthritis Res Ther.* 2003;5(3):120-130.
54. Schulte TL, Leistra F, Bullmann V, et al. Disc height reduction in adjacent segments and clinical outcome 10 years after lumbar 360 degrees fusion. *Eur Spine J.* 2007;16(12):2152-2158.
55. Berlemann U, Gries NC, Moore RJ. The relationship between height, shape and histological changes in early degeneration of the lower lumbar discs. *Eur Spine J.* 1998;7(3):212-217.
56. Kong LD, Zhang YZ, Wang F, Kong FL, Ding WY, Shen Y. Radiographic Restoration of Sagittal Spinopelvic Alignment After Posterior Lumbar Interbody Fusion in Degenerative Spondylolisthesis. *Clinical spine surgery.* 2016;29(2):E87-92.
57. Leveque JA, Segebarth B, Schroerlucke SR, et al. A Multicenter Radiographic Evaluation of the Rates of Preoperative and Postoperative Malalignment in Degenerative Spinal Fusions. *Spine (Phila Pa 1976).* 2018;43(13):E782-e789.
58. Kettler A, Wilke HJ. Review of existing grading systems for cervical or lumbar disc and facet joint degeneration. *Eur Spine J.* 2006;15(6):705-718.
59. Michael AP, Weber MW, Delfino KR, Ganapathy V. Adjacent-segment disease following two-level axial lumbar interbody fusion. *J Neurosurg Spine.* 2019;31:209-216.
60. Dekutoski MB, Schendel MJ, Ogilvie JW, Olsewski JM, Wallace LJ, Lewis JL. Comparison of in vivo and in vitro adjacent segment motion after lumbar fusion. *Spine.* 1994;19(15):1745-1751.
61. Huec JC, Faundez A, Dominguez D, Hoffmeyer P, Aunoble S. Evidence showing the relationship between sagittal balance and clinical outcomes in surgical treatment of degenerative spinal diseases: a literature review. *International orthopaedics.* 2015;39(1):87-95.
62. Lafage V, Schwab F, Patel A, Hawkinson N, Farcy JP. Pelvic tilt and truncal inclination: two key radiographic parameters in the setting of adults with spinal deformity. *Spine.* 2009;34(17):E599-606.
63. Le Huec JC, Charosky S, Barrey C, Rigal J, Aunoble S. Sagittal imbalance cascade for simple degenerative spine and consequences: algorithm of decision for appropriate treatment. *Eur Spine J.* 2011;20 Suppl 5(Suppl 5):699-703.
64. Senteler M, Weisse B, Snedeker JG, Rothenfluh DA. Pelvic incidence-lumbar lordosis mismatch results in increased segmental joint loads in the unfused and fused lumbar spine. *Eur Spine J.* 2014;23(7):1384-1393.
65. Schwab F, Patel A, Ungar B, Farcy JP, Lafage V. Adult spinal deformity-postoperative standing imbalance: how much can you tolerate? An overview of key parameters in assessing alignment and planning corrective surgery. *Spine.* 2010;35(25):2224-2231.
66. Diebo BG, Varghese JJ, Lafage R, Schwab FJ, Lafage V. Sagittal alignment of the spine: What do you need to know? *Clinical neurology and neurosurgery.* 2015;139:295-301.

67. Kim JY, Ryu DS, Paik HK, et al. Paraspinal muscle, facet joint, and disc problems: risk factors for adjacent segment degeneration after lumbar fusion. *Spine J.* 2016;16(7):867-875.
68. Wong AYL, Harada G, Lee R, et al. Preoperative paraspinal neck muscle characteristics predict early onset adjacent segment degeneration in anterior cervical fusion patients: A machine-learning modeling analysis. *J Orthop Res.* 2020.