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Appendix 1. Search strategy

#1	Neck OR cervical OR Cx OR spine OR spinal OR vertebra* OR cervicothoracic OR cervico-thoracic OR cervico-occipital OR cervix
#2	Fusion OR internal fixat* OR arthrodes* OR instrumentation OR stabilization OR ACDF OR anterior cervical decompression OR Anterior Cervical Discectomy
#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 OR junctional disease* OR junctional problem* OR junctional stenosis OR adjacent segment patholog*
#4	Adjacent segment degeneration OR adjacent level degeneration OR adjacent disc degeneration OR adjacent disk degeneration OR adjacent level disc degeneration OR ASDeg
#5	#3 OR #4
#6	Risk factor* OR prognostic factor* OR predictive factor* OR odds ratio* OR hazard ratio*
#7	#1 AND #2 AND #5 AND #6

Appendix 2. Assessment items of the Quality in Prognostic Studies tool

Study Participation

1. Source of target population
2. Method used to identify population
3. Recruitment period
4. Place of recruitment
5. Inclusion and exclusion criteria
6. Adequate study participation
7. Baseline characteristics
- S. Summary of study participation

Study Attrition

1. Proportion of baseline sample available for analysis
2. Attempts to collect information on participants who dropped out
3. Reasons and potential impact of subjects lost to follow-up
4. Outcome and prognostic factor information on those lost to follow-up (participants lost to follow up are adequately described for key characteristics)
5. Outcome and prognostic factor information on those lost to follow-up (there are no important differences between key characteristics and outcomes in participants who completed the study and those who did not)
- S. Summary of attrition

Prognostic Factor Measurement

1. Definition of the prognostic factor
2. Valid and reliable measurement of PF
3. Method and setting of prognostic factor measurement
4. Proportion of data on prognostic factor available for analysis
5. Method used for missing data
- S. Summary of PF measurement

Outcome Measurement

1. Definition of the outcome
2. Valid and reliable measurement of outcome
3. Method and setting of outcome measurement
- S. Summary of outcome measurement

Study Confounding

1. Important confounders were measured
2. Definition of the confounding factor
3. Valid and reliable measurement of confounders
4. Method and setting of confounding measurement
5. Method used for missing data
6. Important potential confounders were accounted for in the study design
7. Important potential confounders are accounted for in the analysis (i.e. appropriate adjustment)
- S. Summary of study confounding

Statistical Analysis and Reporting

1. Presentation of analytical strategy
2. Model development strategy (the strategy for model building is appropriate and is based on a conceptual framework or model)

3. Model development strategy (the selected statistical model is adequate for the design of the study)
4. Reporting of results
5. Summary of statistical analysis and reporting

Items in New Castle-Ottawa Quality Assessment Scale for Case-control Studies

Adequacy of case definition

1. Is the case definition adequate?
 - a. yes, with independent validation
 - b. yes, with record linkage or based on self-report
 - c. no description
2. Representativeness of the cases
 - a. consecutive or obviously representative series of cases
 - b. potential for selection biases or not stated
- 3) Selection of Controls
 - a. community controls
 - b. hospital controls
 - c. no description
- 4) Definition of Controls
 - a) no history of disease (endpoint)
 - b) no description of source

Comparability

- 1) Comparability of cases and controls
 - a) study controls for _____ (Select the most important factor)
 - b) study controls for any additional factor (This criteria could be modified to indicate specific control for a second important factor)

Exposure

- 1) Ascertainment of exposure
 - a) secure record (e.g. surgical records)
 - b) structured interview where blind to case/control status
 - c) interview not blinded to case/control status
 - d) written self-report or medical record only
 - e) no description
- 2) Same method of ascertainment for cases and controls
 - a) yes
 - b) no
- 3) Non-Response rate
 - a) same rate for both groups
 - b) non-respondents described
 - c) rate different and no designation

Appendix 3. Associations between potential risk factors and the incidence of adjacent segment disease (ASD) in the included studies involved the sensitive analysis

Factor	Study	Definition/ Level of exposure (n=sample size)	Prevalence/incidence of ASD	Statistics (e.g. odds ratio, mean value, mean difference)	95% Confidence intervals	Results in meta-analysis	Effect	Strength of evidence
Demographics								
Age	RASD							
	Ahn et al, 2016	The effect of age >50 y/o with reference to ≤ 50 y/o on RASD incidence (n=64)	<4 yrs	UOR >50y/o: 2.78 (p=0.048) AOR >50y/o: 2.68 (p=0.068) (unknown adjustment)	UOR: 1.01-7.63 AOR: 0.99-7.75		No effect	Moderate evidence
	Nassr et al., 2009	The correlation between age and increase in Hilibrand grading after ACDF	<4 yrs	r=0.005 (p=0.970)			No effect	
	Yu et al., 2016	The effect of age ≥50.46 y/o with reference to age <50.46 y/o for RASD incidence (n=263)	≥4 yrs	UOR: 1.82 (p=0.021)	UOR: 1.09-3.03		Risk factor	Very limited evidence
	CASD							
	Kong et al., 2017	The effect of age >60 y/o with reference to age ≤ 60y/o on CASD incidence (n=256)	≥4 yrs	UOR: 0.84 (calculated by 2*2 table) CHR: 0.916 (p=0.838)	UOR: 0.34-2.05 CHR: 0.394-2.129		No effect	Limited evidence

	Song K.J. et al., 2014	The difference of mean age between people with and without CASP (n=231)	≥4 yrs	Mean age CASD: 57.73±9.34 y/o Non-CASD: 54.09± 11.19 y/o (p=0.716)	Mean age CASD: 39.42-76.04 y/o Non-CASD: 32.16-76.02 y/o		No effect	
	CASD with second surgery							
	Wang et al., 2017	The effect of age at first ACDF with reference to age >65 y/o on CASD incidence (n=144)	≥4 yrs	UOR 51-65 y/o: 1.16 (p=0.777) UOR ≤ 50 y/o: 3.02 (p=0.045) Between ≤ 50, 51-65 and >65 y/o (p=0.037) (χ ² /z=4.361)	UOR: 0.42-3.19 UOR: 1.02-8.88		Risk factor	Very limited evidence
Sex	RASD							
	Yu et al., 2016	The effect of male with reference to female for RASD incidence (n=263)	≥4 yrs	UOR: 1.18 (p>0.05) (Calculated by 2*2 table)	UOR: 0.73-1.91		No effect	Very limited evidence
	CASD							
	Kong et al., 2017*	The effect of male with reference to female on CASD incidence (n=256)	≥4 yrs	UOR: 0.68 (calculated by 2*2 table) CHR: 0.685 (p=0.294)	UOR:0.32-1.45 CHR: 0.337-1.390	Pooled UOR for ≥4yrs occurrence: 1.20; 95% CI: 0.58 to 2.48	No effect	Limited evidence
	Song J.S. et al., 2013*	The effect of male with reference to female on CASD incidence (n=242)	≥4 yrs	UOR: 1.29 (p=0.043) (Calculated by 2*2 table)	UOR: 0.59-2.8			

	Song K.J. et al., 2014*	The effect of male with reference to female on CASD incidence (n=231)	≥4 yrs	UOR: 2.91 (<i>p</i> =0.092) (Calculated by 2*2 table)	UOR: 0.8-10.62			
	CASD with second surgery							
	Wang et al., 2017	The effect of male with reference to female on CASD incidence (n=144)	≥4 yrs	UOR: 0.83 (<i>p</i> =0.63) ($\chi^2/z=0.232$) (calculated by 2*2 table)	UOR: 0.39-1.77		No effect	Very limited evidence
Follow-up time	RASD							
	Nassr et al., 2009	The correlation between follow-up time with RASD incidence.	<4 yrs	(<i>p</i> =0.170) (<i>r</i> =0.110)			No effect	Very limited evidence
BMI	RASD							
	Ahn et al, 2016	The effect of BMI (unknown cut-off and reference group) on RASD incidence (n=64)	<4 yrs	UOR: 1.06 (<i>p</i> =0.392)	UOR: 0.93-1.22		No effect	Limited evidence
	CASD							
	Kong et al., 2017	The effect of BMI >25 kg/m ² with reference to BMI ≤ 25kg/m ² on CASD incidence (n=256)	≥4 yrs	UOR: 0.64 (calculated by 2*2 table) CHR=0.704 (<i>p</i> =0.351)	UOR: 0.29-1.40 CHR: 0.337-1.471		No effect	Very limited evidence
	CASD for second surgery							
	Wang et al., 2017	The mean difference of BMI between people	≥4 yrs	Mean BMI CASD: 24.9±4.5 kg/m ²	Mean BMI CASD: 16.08-33.72 kg/m ²		No effect	Very limited evidence

		with and without CASD (n=144)		Non-CASD: 24.4±3.7 kg/m2 (<i>p</i> =0.671) (χ^2/z = 0.425)	Non-CASD: 17.15-31.65 kg/m2			
Smoking status	RASD							
	Ahn et al, 2016	The effect of smoker with reference to non-smoker on RASD incidence (n=64)	<4 yrs	UOR: 1.16 (<i>p</i> =0.790)	UOR: 0.41-3.27		No effect	Limited evidence
	CASD							
	Kong et al., 2017	The effect of smoker with reference to non-smoker on CASD incidence (n=256)	≥4 yrs	UOR: 1.12 (calculated by 2*2 table) CHR: 1.134 (<i>p</i> =0.730)	UOR: 0.52-2.41 CHR: 0.555-2.317		No effect	Very limited evidence
	CASD with second surgery							
	Wang et al., 2017	The effect of smoker with reference to non-smoker on CASD incidence (n=144)	≥4 yrs	UOR: 1.08 (<i>p</i> =0.572) (χ^2/z =0.139) (Calculated by 2*2 table)	UOR: 0.49-2.38		No effect	Very limited evidence
Alcohol	CASD							
	Kong et al., 2017	The effect of history of consuming alcohol on CASD incidence (n=256)	≥4 yrs	UOR: 0.70 (calculated by 2*2 table) CHR: 0.76 (<i>p</i> =0.475)	UOR: 0.32-1.56 CHR: 0.36-1.62		No effect	Very limited evidence
Comorbidities								
Diabetes mellitus	RASD							
	Ahn et al, 2016	The effect of DM on RASD incidence (n=64)	<4 yrs	UOR: 0.72 (<i>p</i> =0.565)	UOR: 0.23-2.23		No effect	Limited evidence
	CASD							

	Kong et al., 2017	The effect of DM on CASD incidence (n=256)	≥4 yrs	UOR: 1.30 (calculated by 2*2 table) CHR:1.466 (p=0.434)	UOR: 0.46-3.65 CHR: 0.562-3.827		No effect	Very limited evidence
	CASD with second surgery							
	Wang et al., 2017	The effect of DM on CASD incidence (n=144)	≥4 yrs	UOR: 0.76 (p=0.567) ($\chi^2/z=0.328$) (calculated by 2*2 table)	UOR: 0.30-1.94		No effect	Very limited evidence
Radiographic phenotype								
Plate to disc distance (PDD)	RASD							
	Yu et al., 2016	The effect of cephalad and caudal PDD <5 mm on RASD incidence with reference to cephalad PDD <5 mm and caudal PDD ≥5 mm or cephalad PDD ≥5 mm and caudal PDD <5 mm (n=263)	≥4 yrs Radiograph obtained 1 wk after surgery	UOR: 1.560 (p=0.013)	UOR: 1.096-2.222		Risk factor	Very limited evidence
	CASD							
	Song K.J. et al., 2014 (High risk)	The mean difference of postoperative cephalad and caudal PDD between people with and without CASD (n=231)	≥4 yrs	Cephalad PDD: CASD: 3.15±1.93mm Non-CASD: 2.57±1.54mm (p=0.153) Caudal PDD: CASD: 3.76±2.51mm Non-CASD: 3.86±2.08mm (p=0.951)	Cephalad PDD: CASD: -0.63-6.93mm Non-CASD: -0.45-5.59mm Caudal PDD: CASD: -1.16-8.68mm		No effect	Very limited evidence

					Non-CASD: -0.22-7.94mm			
	CASD with second surgery							
	Zhao et al., 2014	The effect of cephalad and caudal PDD <5mm with reference to cephalad and caudal PDD ≥5mm on CASD incidence (n=68)	<4 yrs	Cephalad UOR: 0.67 (p=0.525) Caudal UOR: 0.69 (p=0.457) (Calculated by 2*2 table)	Cephalad UOR: 0.19-2.35 Caudal UOR: 0.26-1.83		No effect	Very limited evidence
Developmental canal stenosis	CASD							
	Kong et al., 2017	The effect of developmental stenosis on CASD incidence (n=256) (Pavlov ratio less than 0.80 at C5 level)	≥4 yrs	UOR: 2.04 (calculated by 2*2 table) CHR: 1.949 (p=0.067) AHR: 3.250 (p=0.002) (adjusted for C5-C6 level involved, degeneration of adjacent segment and curve pattern of C2-C7)	UOR: 0.95-4.37 CHR: 0.954-3.980 AHR: 1.538-6.867		No effect	Very limited evidence
	CASD with second surgery							
	Zhao et al., 2014	The effect of developmental cervical canal stenosis on CASD incidence (n=68) (Pavlov ratio <0.75 is indicated as developmental canal stenosis)	<4 yrs	UOR: 2.88			Risk factor	Very limited evidence

	Wang et al., 2017	The effect of developmental canal stenosis on CASD incidence (n=144) (For male, sagittal diameter <14mm; for female, sagittal diameter <13mm, at one level)	≥4 yrs	UOR: 2.80 (<i>p</i> =0.042)	UOR: 1.04-7.53		Risk factor	Very limited evidence
Preoperative cervical sagittal alignment	RASD							
	Ahn et al., 2016	The effect of preoperative C2-C7 sagittal Cobb angle (unknown cut-off and reference group) on RASD incidence (n=64)	<4 yrs	UOR: 1.02 (<i>p</i> =0.800)	UOP: 0.89-1.16		No effect	Limited evidence
	CASD							
	Song K.J. et al., 2014	The mean difference of preoperative cervical sagittal alignment between people with and without CASD (n=231)	≥4 yrs	Preoperative cervical sagittal alignment CASD: 15.04±10.45° Non-CASD: 17.88±13.39° (<i>p</i> =0.648)	Preoperative cervical sagittal alignment CASD: -5.44°-35.52° Non-CASD: -8.36°-44.12°		No effect	Very limited evidence
Pre-existing preoperative adjacent segment degeneration	RASD							
	Ahn et al., 2016	The effect of preoperative adjacent segment degeneration on	<4 yrs	UOR: 3.22 (<i>p</i> =0.109)	UOR: 0.77-13.51		No effect	Limited evidence

		RASD incidence (n=64)						
	CASD							
	Kong et al., 2017	The effect of mild preoperative adjacent segment degeneration for CASD incidence (n=256)	≥4 yrs	UOR: 2.22 (calculated by 2*2 table) CHR: 2.152 (<i>p</i> =0.033) AHR: 2.681 (<i>p</i> =0.011) (adjusted for C5-C6 level involved, congenital stenosis and curve pattern of C2-C7)	UOR: 1.04-4.74 CHR: 1.063-4.356 AHR: 1.259-5.709		Risk factor	Very limited evidence
Preoperative segmental height of the index level	RASD							
	Ahn et al., 2016	The effect of preoperative segmental height (unknown cut-off and reference group) on incidence of RASD (n=64)	<4 yrs	UOR: 1.00 (<i>p</i> =0.968)	UOR: 0.86-1.17		No effect	Limited evidence
Preoperative sagittal segmental alignment of fusion segment	RASD							
	Ahn et al., 2016	The effect of preoperative SSA (unknown cut-off and reference group) on RASD incidence (n=64)	<4 yrs	UOR: 1.00 (<i>p</i> =0.952)	UOR: 0.83-1.22		No effect	Limited evidence
Lower segment cervical disc degeneration	CASD with second surgery							
	Zhao et al., 2014	The difference in number of pre-operative cephalad	<4 yrs	Caudal CASD vs non-CASD Grade I: 8.8% vs 11.8%			No effect	Very limited evidence

		and caudal cervical disc degeneration (according to Miyazaki's grading system) between people with and without CASD (n=68)		Grade II: 26.5% vs 8.8% Grade III: 61.8% vs 64.7% Grade IV: 2.9% vs 14.7% ($p=0.107$)				
Preoperative cervical ROM on radiograph	CASD							
	Song K.J. et al., 2014	The mean difference of preoperative cervical ROM between people with or without CASD (n=231)	≥4 yrs	Preoperative C2-C7 ROM CASD: $42.96^{\circ} \pm 12.28^{\circ}$ Non-CASD: $41.91^{\circ} \pm 14.15^{\circ}$ ($p=0.424$)	Preoperative C2-C7 ROM CASD: $18.89^{\circ} - 67.03^{\circ}$ Non-CASD: $14.18^{\circ} - 69.64^{\circ}$		No effect	Very limited evidence
Preoperative lower segment disc bulge impingement	CASD with second surgery							
	Zhao et al., 2014	The mean difference of preoperative cephalad or caudal disc bulge impingement on CASD incidence (n=68)	<4 yrs	Lower segment CASD vs non-CASD $13.8 \pm 5.9\%$ vs $11.2 \pm 5.2\%$ ($p>0.05$, independent t-test) Lower segment CASD vs non-CASD $16.5 \pm 4.6\%$ vs $11.2 \pm 5.2\%$ ($p>0.05$, post hoc one-way ANOVA, adjusted with Bonferroni)			No effect	Very limited evidence
Preoperative lower segment disc height	RASD							
	Ahn et al., 2016	The effect of preoperative lower segment disc height (unknown cut-off and reference	<4 yrs	UOR: 1.33 ($p=0.519$)	UOR: 0.56-3.18		No effect	Limited evidence

		group) on incidence of RASD (n=64)						
Preoperative lower segment ROM	RASD							
	Ahn et al., 2016	The effect of preoperative lower segment ROM (unknown cut-off and reference group) on incidence of RASD (n=64)	<4 yrs	UOR: 1.21 (<i>p</i> =0.101)	UOR: 0.96-1.51		No effect	Limited evidence
Preoperative other-segment degeneration	RASD							
	Ahn et al., 2016	The effect of preoperative other - segment degeneration (excluding adjacent segment degeneration) on RASD incidence (n=64)	<4 yrs	UOR: 4.20 (<i>p</i> =0.017) AOR: 4.07 (<i>p</i> =0.023) (unknown adjustment)	UOR: 1.29-13.69 AOR: 1.21-13.70		Risk factor	Limited evidence
Preoperative upper segment disc bulge impingement	CASD with second surgery							
	Zhao et al., 2014	The mean difference of preoperative cephalad or caudal disc bulge impingement on CASD incidence (n=68)	<4 yrs	Upper segment CASD vs non-CASD 19.7±9.7% vs 11.8±4.8% (<i>p</i> <0.01, independent t-test) Upper segment CASD vs non-CASD 22.8±8.9% vs 11.8±4.8% (<i>p</i> <0.01, post hoc one-way ANOVA, adjusted with Bonferroni)			Risk factor	Very limited evidence
	RASD							

Preoperative upper segment disc height	Ahn et al., 2016	The effect of preoperative upper segment disc height (unknown cut-off and reference group) on incidence of RASD (n=64)	<4 yrs	UOR: 1.14 (<i>p</i> =0.675)	UOR: 0.61-2.11		No effect	Limited evidence
Preoperative upper segment ROM	RASD							
	Ahn et al., 2016	preoperative upper segment ROM (unknown cut-off and reference group) on RASD incidence (n=64)	<4 yrs	UOR: 0.99 (<i>p</i> =0.936)	UOR: 0.85-1.16		No effect	Limited evidence
Upper segment cervical disc degeneration	CASD with second surgery							
	Zhao et al., 2014	The difference in number of pre-operative cephalad and caudal cervical disc degeneration (according to Miyazaki's grading system) between people with and without CASD (n=68)	<4 yrs	Cephalad CASD vs non-CASD Grade I: 0% vs 0% Grade II: 26.5% vs 23.5% Grade III: 70.6% vs 73.5% Grade IV: 2.9% vs 2.9% (<i>p</i> =0.796)			No effect	Very limited evidence
Postoperative cervical sagittal alignment	CASD							
	Kong et al., 2017	The effect of postoperative kyphosis with reference to lordosis on CASD incidence (n=256)	≥4 yrs	UOR: 2.21 (calculated by 2*2 table) CHR: 2.961 (<i>p</i> =0.027) AHR: 1.836 (<i>p</i> =0.227)	UOR: 0.76-6.46 CHR: 1.131-7.752 AHR: 0.685-4.918		No effect	Very limited evidence

				(adjusted for C5-C6 level involved, congenital stenosis and degeneration of adjacent segment)				
	Song J.S. et al., 2013*	The mean difference of postoperative cervical sagittal alignment between people with and without CASD at C7-T1 (n=242)	≥4 yrs	Postoperative cervical sagittal alignment CASD: 16.30° Non-CASD: 18.70° (<i>p</i> =0.099)	Postoperative cervical sagittal alignment Range CASD: 1.40°-45.80° Non-CASD: 1.30°-36.80° (<i>p</i> =0.099)	Pooled mean difference for ≥4yrs occurrence: 0.22; 95% CI: -0.08 to 0.52	No effect	Limited evidence
	Song K.J. et al., 2014*	The mean difference in postoperative cervical sagittal alignment between people with and without CASD (n=231)	≥4 yrs	Postoperative cervical sagittal alignment CASD: 23.76±13.16° Non-CASD: 24.79±11.23° (<i>p</i> =0.869)	Postoperative SSA CASD: -2.03°-49.55° Non-CASD: 2.78°-46.80°			
Postoperative cervical ROM on radiograph	CASD							
	Kong et al., 2017	The effect of postoperative C2-C7 ROM >35° with reference to ≤35° for CASD incidence (n=256)	≥4 yrs	UOR: 1.03 (calculated by 2*2 table) CHR: 1.006 (<i>p</i> =0.986)	UOR: 0.48-2.20 CHR: 0.493-2.056		No effect	Conflicting evidence
	Song J.S. et al., 2013	The mean difference in postoperative C2-C7 ROM between people with and	≥4 yrs	Postoperative C2-C7 ROM CASD: 37.10° Non-CASD: 28.50° (<i>p</i> = 0.027)	Postoperative C2-C7 ROM CASD: 10.30°-68.40° Non-CASD: 4.90°-56.70°		Risk factor	

		without CASD (n=242)						
Postoperative sagittal segmental alignment of fusion segment	CASD							
	Kong et al., 2017	The effect of postoperative SSA ≤4° with reference to >4° on CASD incidence (n=256)	≥4 yrs	UOR: 1.55 (calculated by 2*2 table) CHR: 1.561 (p=0.218)	UOR: 0.73-3.29 CHR: 0.769-3.169		No effect	Very limited evidence
Spinal canal stenosis	CASD							
	Song J.S. et al., 2013*	The mean difference in postoperative spinal canal diameter and Pavlov ratio between people with and without CASD (n=242)	≥4 yrs	Postoperative spinal canal diameter CASD: 11.2 mm Non-CASD: 15.4 mm (p=0.001) Pavlov ratio CASD: 0.52 Non-CASD: 0.82 (p=0.001) (cut off=0.70)	Postoperative spinal canal diameter Range CASD: 9.8-13.5mm Non-CASD: 12.8-17.5 mm Pavlov ratio Range CASD: 0.41-0.74 Non-CASD: 0.66-0.99	Pooled mean difference for ≥4yrs occurrence: 0.34; 95% CI: -0.27 to 0.95 (Appendix 4)	No effect	Limited evidence
	Song K.J. et al., 2014*	The mean difference of postoperative spinal canal diameter between people with and without CASD (n=242)	≥4 yrs	Postoperative spinal canal diameter CASD: 15.34±1.33mm Non-CASD: 15.07±1.59mm (p=0.993)	Postoperative spinal canal diameter CASD: 12.73-17.95mm Non-CASD: 11.95-18.19mm			
Subsidence	RASD							
	Ahn et al., 2016	The effect of subsidence with reference to no subsidence on	<4 yrs	UOR: 0.72 (p=0.565)	UOR: 0.23-2.23		No effect	Very limited evidence

		RASD incidence (n=64)						
Postoperative cervical arc chord distance	RASD							
	Yu et al., 2016	The effect of postoperative arc chord distance ≥6.75 mm with reference to <6.75 mm	≥4 yrs	UOR: 0.55 (<i>p</i> =0.019)	UOR: 0.33-0.90		Protective factor	Very limited evidence
Postoperative lower segment disc height	RASD							
	Yu et al., 2016	The mean difference of postoperative lower segment disc height between RASD and non-RASD group (n=64)	≥4 yrs Radiograph obtained 1 wk after surgery	RASD: 5.50±1.24mm Non RASD: 5.68±1.25mm (<i>p</i> >0.05)	RASD: 3.07-7.93mm Non RASD: 3.23- 8.13mm		No effect	Very limited evidence
Postoperative lower segment ROM	CASD							
	Song K.J. et al., 2014	The mean difference of postoperative lower adjacent level ROM ration between people with and without CASD (n=231)	≥4 yrs	Postoperative LSROM CASD: 16.37±14.40% Non-CASD: 12.18±14.26% (<i>p</i> =0.376)	Postoperative LSROM CASD: -11.85- 44.59% Non-CASD: -15.77- 40.13%		No effect	Very limited evidence
Postoperative non-union	RASD							
	Ahn et al., 2016	The effect of non- union (Bridwell grade I and II; >2mm motion of the PEEK cage on	<4 yrs	UOR: 1.30 (<i>p</i> =0.720)	UOR: 0.31-5.35		No effect	Limited evidence

		flexion/extension X-ray) with reference to union (Bridwell grade III and IV; and <2mm motion of the PEEK on flexion/extension X-ray) on RASD incidence (n=64)						
Postoperative upper segment disc height	RASD							
	Yu et al., 2016	The mean difference of postoperative upper segment disc height between RASD and non-RASD group (n=64)	≥4 yrs Radiograph obtained 1 wk after surgery	RASD: 5.39±1.12mm Non RASD: 5.56±1.17mm (<i>p</i> >0.05)	RASD: 3.19-7.59mm Non RASD: 3.27-7.85mm		No effect	Very limited evidence
Postoperative upper segment ROM	CASD							
	Song K.J. et al., 2014	The mean difference of postoperative upper adjacent level ROM ration between people with and without CASD (n=231)	≥4 yrs	Postoperative USROM CASD: 28.46±15.42% Non-CASD: 35.36±32.06% (<i>p</i> =0.384)	Postoperative USROM CASD: -1.76-58.68% Non-CASD: -27.48%-98.20%		No effect	Very limited evidence
T1 slope	CASD							
	Kong et al., 2017	The effect of postoperative T1 slope >20° with reference to ≤20°	≥4 yrs	UOR: 0.94 (calculated by 2*2 table) CHR: 0.873 (<i>p</i> =0.712)	UOR: 0.44-2.04 CHR: 0.423-1.801		No effect	Very limited evidence

		on CASD incidence (n=256)						
Surgical method								
Level of operation	CASD with second surgery							
	Wang et al., 2017	The association of the level of ACDF on second surgery with CASD incidence (n=144)	≥4 yrs	CASD vs non-CASD C3-C4: 5 vs 10 C4-C5: 7 vs 23 C5-C6: 13 vs 36 C6-C7: 11 vs 39 (p=0.825) ($\chi^2/z=0.901$) UOR (calculated by 2*2 table) C4-C5 (with reference to C3-C4): 0.61 C4-C5 (with reference to C5-C6): 0.84 C4-C5 (with reference to C6-C7): 1.08 C5-C6 (with reference to C3-C4): 0.72 C5-C6 (with reference to C6-C7): C6-C7 (with reference to C3-C4): 0.56	C4-C5 (with reference to C3-C4) UOR: 0.16-2.39 C4-C5 (with reference to C5-C6) UOR: 0.29- 2.42 C4-C5 (with reference to C6-C7) UOR: 0.37-3.17 C5-C6 (with reference to C3-C4) UOR: 0.21-2.51 C5-C6 (with reference to C6-C7) UOR: 0.51-3.22 C6-C7 (with reference to C3-C4) UOR: 0.56-2.00		No effect	Very limited evidence
Number of fused segments	RASD							
	Nassr et al., 2009*	The effect of multi-level fusion with reference to single	<4 yrs	UOR: 1.94 (p=0.143) (Calculated by 2*2 table)	UOR: 0.78-4.84		No effects	Very limited evidence

		level fusion on RASD incidence (n=87)						
	Komura et al., 2012	The effect of fusion across >3 disc level with reference to ≤3 disc level on RASD incidence (n=102)	≥4 yrs	UOR: 0.48 (p=0.083) (Calculated by 2*2 table)	UOR: 0.21-1.11		No effect	Limited evidence
	Yu et al., 2016*	The effect of multi-level fusion with reference to single level fusion on RASD incidence at C7-T1 (n=263)	≥4 yrs	UOR: 1.19 (p>0.05) (Calculated by 2*2 table)	UOR: 0.73-1.95		No effect	
CASD								
	Komura et al., 2012	The effect of fusion across >3 disc levels with reference to ≤3 disc levels on RASD incidence (n=102)	≥4 yrs	UOR: 0.09 (p=0.0024) (Calculated by 2*2 table)	UOR: 0.01-0.76		Protective factor	Very limited evidence Conflicting evidence
	Song J.S. et al., 2013*	The effect of multi-level fusion with reference to single level fusion on CASD incidence (n=242)	≥4 yrs	UOR: 0.63 (Calculated by 2*2 table) Number of CASD: Single level fusion: 9 (10.92%) Two-level fusion: 12 (12.12%) Three-level fusion: 10 (22.22%) Four level fusion: 2 (18.18%) (p=0.091)	UOR: 0.28-1.42	Pooled UOR for ≥4yrs occurrence: 0.55; 95% CI: 0.28 to 1.10)	No effect	Limited evidence

	Song K.J. et al., 2014*	The effect of multi-level fusion with reference to single level fusion on CASD incidence (n=231)	≥4 yrs	UOR: 0.40 (Calculated by 2*2 table) Number of CASD: Single level fusion: 3 (3.49%) Two-level fusion: 11 (9.40%) Three-level fusion: 0 (0%) Four level fusion: 1 (50%%) (<i>p</i> =0.301)	UOR: 0.11-1.46			
C5-C6 involvement in fusion	CASD							
	Kong et al., 2017	The effect of C5-C6 involvement on CASD incidence (n=256)	≥4 yrs	UOR: 2.06 (calculated by 2*2 table) CHR: 2.032 (<i>p</i> =0.084) AHR: 2.014 (<i>p</i> =0.196) (adjusted for congenital stenosis, degeneration of adjacent segment and curve pattern of C2-C7)	UOR: 0.88-4.81 CHR: 0.908-4.544 AHR: 0.696-5.825		No effect	Very limited evidence
C5-C6 and C6-C7 involvement as adjacent segments	RASD							
	Komura et al., 2012	The effect of C5-C6 and C6-C7 involvement as adjacent segments on RASD incidence (n=102)	≥4 yrs	UOR: 2.38 (<i>p</i> =0.048) (Calculated by 2*2 table)	UOR: 1.00-5.88		No effect	Very limited evidence
	CASD							
	Komura et al., 2012*	The effect of C5-C6 and C6-C7 involvement as	≥4 yrs	UOR: 5.83 (<i>p</i> =0.0074) (Calculated by 2*2 table)	UOR: 1.61-21.17		Risk factor	Very limited evidence

		adjacent segments on CASD incidence (n=102)						
Needle localization	RASD							
	Nassr et al., 2009	The effect of incorrect intraoperative needle localization (1 level above the operative level) with a 22-gauge spinal needle on RASD incidence (n=87)	<4 yrs	UOR: 3.20	UOR: 1.02-10.05		Risk factor	Very limited evidence
Intervertebral fusion devices	RASD							
	Wang et al., 2014	The effect of Zero-P implant with reference to cage and plate on RASD incidence (n=242)	<4 yrs	UOR: 0.60 (p=0.330) (Calculated by 2*2 table)	UOR: 0.29-1.24		No effect	Very limited evidence
	CASD							
	Kong et al., 2017	The effect of internal fixation with plate on CASD incidence (n=256)	≥4 yrs	UOR: 1.41 (calculated by 2*2 table) CHR: 1.206 (p=0.0798)	UOR: 0.31-6.37 CHR: 0.287-5.067		No effect	Very limited evidence
	Song J.S. et al., 2013	The effect of intervertebral fusion devices on CASD incidence (n=242) A: autogenous bone graft	≥4 yrs Group A period up time was significantly longer (p=0.02).	A with reference to B UOR: 5.66 (α<0.001) A with reference to C UOR: 10.39 (α=0.015) B with reference to C UOR: 1.84	A with reference to B UOR: 2.06-15.51 A with reference to C UOR: 4.05-26.68 B with reference to C UOR: 0.59-5.72		Risk factor	Very limited evidence

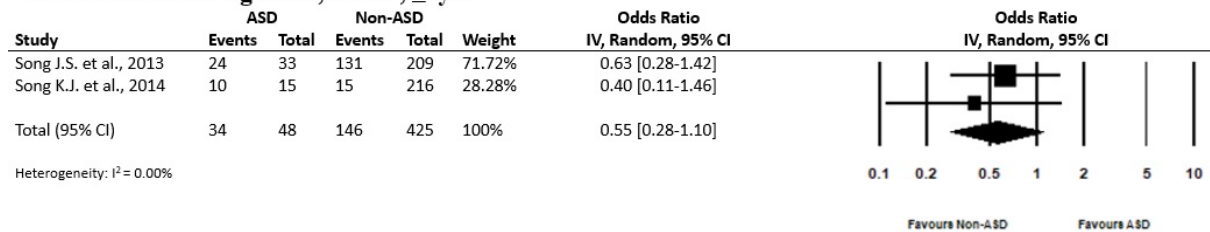
		B: autogenous bone graft and plate C: cage and plate		($\alpha=0.615$) (Calculated by 2*2 table)				
Other potential risk factors								
Preoperative myelopathy	CASD							
	Kong et al., 2017	The effect of preoperative myelopathy with reference to myeloradiculopathy on CASD incidence (n=89)	≥4 yrs	UOR: 1.98 (calculated by 2*2 table) CHR: 1.101 ($p=0.849$)	UOR: 0.59-6.60 CHR: 0.408-2.969		No effect	Very limited evidence
Preoperative radiculopathy	CASD							
	Kong et al., 2017	The effect of preoperative radiculopathy with reference to myeloradiculopathy on CASD incidence (n=214)	≥4 yrs	UOR: 1.01 (calculated by 2*2 table) CHR: 1.770 ($p=0.179$)	UOR: 0.36-2.89 CHR: 0.769-4.073		No effect	Very limited evidence
Preoperative radiculopathy and myelopathy	CASD							
	Song K.J. et al., 2014	The effect of preoperative radiculopathy and myelopathy on CASD incidence (n=231)	≥4 yrs	Radiculopathy CASD vs non CASD: 10 vs 164 Myelopathy CASD vs non-CASD: 5 vs 52 ($p=0.421$)			No effect	Very limited evidence

Abbreviation: AHR = adjusted hazard ratio; AOR = adjusted odds ratio; BMI = body mass index; CHR = crude hazard ratio; DH = disc height; DM = diabetes mellitus; PDD = plate to disc distance; PLL = posterior longitudinal ligament; ROM = range of motion; SACS = segmental alignment of cervical spine; SSA = sagittal segmental alignment; UOR = unadjusted odds ratio; y/o = years old; yrs = years

* pooled for meta-analysis

Appendix 4

Number of fused segments, CASD, ≥4yrs



The risk of multi-level fusion on CASD at ≥4years postoperative follow-up