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## Appendix 1

### Surgical Site Infection Definition

Infection refers to deep or organ/space as well as superficial infections that occurred within 1 year of the surgical procedure according to the Centers for Disease Control and Prevention definitions which are listed below<sup>15</sup>.

Briefly, superficial infections occurred within 30 days of the operative procedure, involved only the skin and subcutaneous tissue, and had a least one of the following: (1) purulent drainage, (2) positive culture obtained aseptically, (3) wound opened by a surgeon, or (4) a diagnosis by the surgeon or attending physician.

Complicated infections were deep infections related to the surgery that occurred within 30 days to 1 year of the procedure, involved the fascia and muscle layers, and at least one of the following: (1) purulent drainage from deep tissues, (2) a deep incision that spontaneously dehiscenced or was deliberately opened by a surgeon and was culture positive or not cultured when a fever, localized pain or tenderness was present, (3) an abscess or other evidence of infection involving the deep incision was found on direct examination during reoperation or with histopathologic or radiographic examination or (4) a diagnosis by a surgeon.

Complicated infections also included organ/space infections that involved any part of the body opened or manipulated during the operation excluding the skin incision, fascia or muscle layers, and at least one of the following: (1) purulent drainage from organ/space, (2) culture positive obtained aseptically, (3) an abscess or other evidence of infection involving the organ/space found on direct examination during reoperation or with histopathologic or radiographic examination or (4) a diagnosis by a surgeon. This included epidural infections, or discitis/osteomyelitis.

Appendix Table 1: Additional Surgeries within 2 years

Count	Subject	Infection Group	Surgical indication	Time to Additional Surgery (days)	Additional procedure
1	1	No Infection	Post-fusion adjacent level stenosis	601	Adjacent level decompression and interbody fusion
2	2	No Infection	Iatrogenic flat-back syndrome, pseudoarthrosis	378	L3 PSO, L5-S1 Revision interbody fusion, L1-S1 instrumented fusion
3	3	No Infection	Screw Malposition	3	Revision decompression & instrumentation
4	4	Infection	Deep Wound infection	16	I & D
5	5	Infection	Vertebral Osteomyelitis	180	I & D, revision decompression and instrumented fusion
6	6	No Infection	Failed Back Syndrome	512	Insertion spinal cord stimulator
7	7	Infection	Deep Wound infection	14	I & D
8	8	Infection	Deep Wound infection	20	I & D
9	9	No Infection	Persistent/Recurrent Radiculopathy	407	Revision decompression and interbody fusion
10	10	Infection	Deep Wound infection	62	I & D
11	11	Infection	Deep Wound infection	46	I & D
12	12*	Infection	Deep Wound Infection	16	I&D
13	12*	Infection	Post-fusion adjacent level stenosis	566	Adjacent level decompression and interbody fusion
14	13	Infection	Deep Wound infection	14	I & D
15	14	Infection	Deep Wound infection	19	I & D
16	15*	No Infection	Screw Malposition	7	Revision decompression & instrumentation
17	15*	No Infection	Adjacent level disc herniation	519	Discectomy
18	16	No Infection	Post-fusion adjacent level fracture	263	Adjacent level decompression and interbody fusion

19	17	Infection	Deep Wound infection	15	I & D
20	18	Infection	Deep Wound infection	9	I & D
21	19	No Infection	Screw Malposition	1	Revision decompression & instrumentation
22	20	Infection	Deep Wound infection	17	I & D
23	21	Infection	Deep Wound infection	17	I & D
24	22	Infection	Deep Wound infection	12	I & D
25	23	Infection	Deep Wound infection	27	I & D
26	24	No Infection	Pseudoarthrosis	448	Revision decompression and interbody fusion
27	25	Infection	Deep Wound infection	18	I & D
28	26	Infection	Deep Wound infection	112	I & D
29	27*	Infection	Deep Wound infection	26	I & D
30	27*	Infection	Deep Wound infection	172	I & D, revision decompression and instrumented fusion
31	27*	Infection	Post fusion adjacent level stenosis	535	Adjacent level decompression and instrumented fusion
32	28	Infection	Deep Wound infection	12	I & D
33	29	Infection	Deep Wound infection	21	I & D, revision decompression and instrumented fusion
34	30*	Infection	Deep Wound infection	20	I & D
35	30*	Infection	Deep Wound infection	7	I & D, revision decompression and instrumented fusion
36	31	No Infection	Post-fusion adjacent level stenosis	571	Adjacent level decompression and interbody fusion
37	32	Infection	Deep Wound infection	18	I & D
38	33*	Infection	Deep Wound infection	23	I & D, revision decompression and instrumented fusion

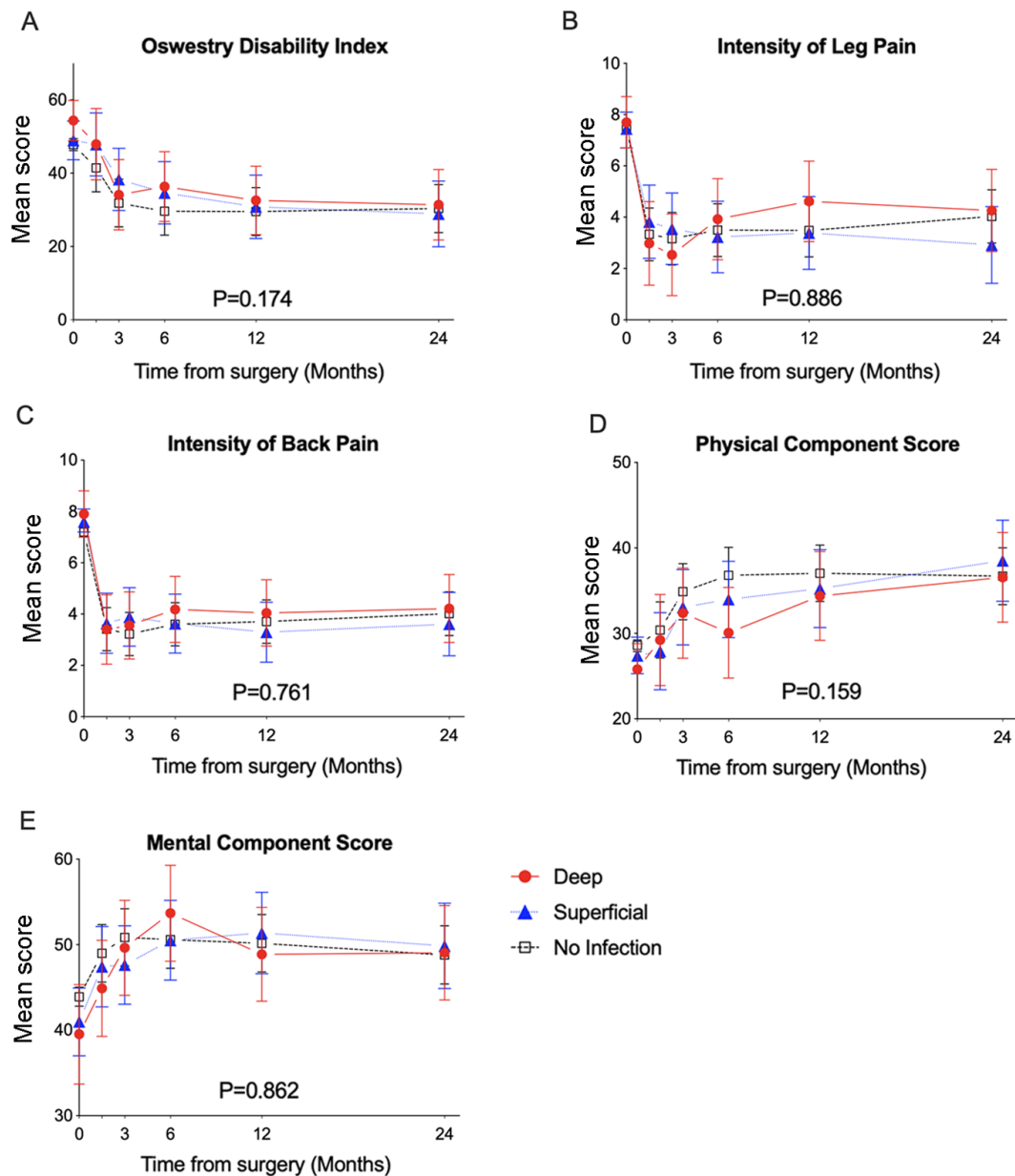
39	33*	Infection	Deep Wound infection	8	I & D
40	34	No Infection	Pseudoarthrosis	214	Revision decompression and instrumentation
41	35	No Infection	Persistent/Recurrent Radiculopathy	17	Revision decompression and instrumentation
42	36	Infection	Screw Malposition	8	I & D; Revision decompression & instrumentation
43	37	Infection	Deep Wound infection	35	I & D
44	38	Infection	Deep Wound infection	19	I & D, Interbody Fusion
45	39	Infection	Deep Wound infection	278	I & D, revision decompression and instrumented fusion
46	40*	Infection	Deep Wound infection	17	I & D, revision-instrumented fusion
47	40*	Infection	Deep Wound infection	110	I & D, revision decompression and instrumented fusion
48	41*	Infection	Deep Wound infection	11	I & D
49	41*	Infection	Post-fusion adjacent level stenosis	640	Adjacent level decompression and interbody fusion
50	42	No Infection	failure instrumented construct	68	Revision decompression and instrumentation
51	43*	Infection	CSF Leak, Deep Wound infection	5	I & D, repair dural tear
52	43*	Infection	CSF Leak, Deep Wound infection	12	I & D, repair dural tear

Abbreviations: I & D = irrigation and Debridement; CSF = cerebrospinal fluid; ACDFP= Anterior Cervical Discectomy Fusion and Plate; PSO = Pedicle Subtraction Osteotomy  
\*, some subjects had more than one additional surgery

Appendix Table 2: Sensitivity analysis: comparison of patient-rated health outcomes using multiple imputation

Outcome	No Infection mean ± SE	Infection mean ± SE	Difference in Means‡	% p<0.05†
<b>ODI</b>				
1.5 months	44.4±1.8	50.1±2.6	3.9 to 7.6	99%
3 months	34.9±1.8	38.6±2.6	2.1 to 5.3	25%
6 months	33.0±1.8	36.6±2.6	2.2 to 5.4	22%
12 months	32.7±1.8	33.8±2.6	-1.0 to 2.7	0%
24 months	33.5±1.8	33.4±2.6	-2.5 to 2.0	0%
<b>Leg Pain</b>				
1.5 months	3.4±0.3	3.7±0.4	-0.01 to 0.5	0%
3 months	3.4±0.3	3.4±0.4	-0.1 to 0.5	0%
6 months	3.7 ±0.3	3.7±0.3	-0.2 to 0.4	0%
12 months	3.7±0.3	3.9±0.4	-0.1 to 0.5	0%
24 months	4.1±0.3	3.9±0.4	-0.6 to 0.2	0%
<b>Back Pain</b>				
1.5 months	3.9±0.2	4.0±0.3	-0.1 to 0.4	0%
3 months	3.8±0.2	4.1±0.3	0.8 to 5.1	0%
6 months	4.1±0.2	4.1±0.3	-0.2 to 0.2	0%
12 months	4.2±0.2	3.9±0.3	-0.6 to 0.05	0%
24 months	4.5±0.2	4.3±0.4	-0.6 to 0.1	0%
<b>PCS‡</b>				
1.5 months	30.1±0.9	28.6±1.4	-2.7 to -0.2	4%
3 months	34.5±0.9	32.6±1.4	-2.9 to -1.0	18%
6 months	36.1±1.0	33.3±1.4	-4.0 to -1.7	89%
12 months	36.5±1.0	35.5±1.4	-2.5 to 0.2	1%
24 months	36.7±0.9	37.0±1.5	-1.0 to 1.7	0%
<b>MCS‡</b>				
1.5 months	48.3±1.0	46.0±1.4	-0.3 to -1.8	46%
3 months	49.8±0.9	48.0±1.4	-2.8 to -0.6	15%
6 months	49.8±0.9	50.1 ±1.5	-1.0 to 1.5	0%
12 months	49.7±0.9	49.4±1.4	-2.4 to 1.1	1%
24 months	48.0±1.0	48.1±1.5	-1.6 to 1.5	0%

Data are mean ± SE. Abbreviations: ODI = Oswestry Disability Index; SF-12 PCS = physical component score; SF-12 MCS = mental component score. Missing data were assumed to be missing at random and were replaced with a set of plausible values derived using a multiple imputation procedure with 100 iterations taking all time points into consideration. ‡ smallest to largest mean difference out of 100 iterations. † The percentage of iterations P<0.05.



Appendix Figure 1. Subgroup analysis comparing patient-rated outcomes over time between patients that had no infection, a superficial infection or a deep infection. (A) The Oswestry Disability Index ranges from 1 to 100, with lower scores indicating less severe symptoms. (B) Intensity of leg pain and (C) intensity of back pain range from 0 to 10, with lower scores indicating less severe symptoms. (D) The SF-12 physical component score and (E) mental component score are based on normative data, with higher scores indicating better quality of life. At 0 months, the data points represent the observed means whereas the data points on the plot lines represent the estimated mean based on repeated measures mixed effects model adjusted for baseline score, infection, antibiotic, duration of antibiotics, gender, diabetes, revision, procedure, diagnosis, segmental levels operated, BMI, age, and time. Error bars denote 95% confidence interval. P-values denote the main effect for infection group.

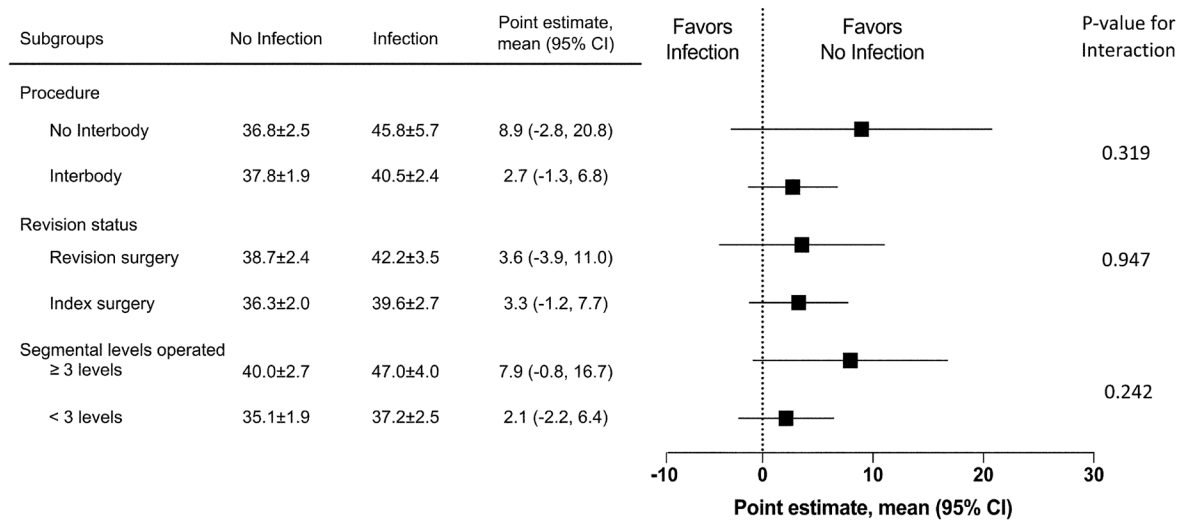


Figure 2. Forest plot of Differences in Oswestry Disability Index by Subgroup. The dashed line represents the line of no effect. Symbols show point estimates, and error bars denote 95% Confidence limits. P values indicate subgroup interactions derived from mixed-effects models.