**Web Appendix**

**Table 1. Included studies for Key Question 1.**

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| --- | --- | --- | --- | --- | --- |
| **Author (year)** | **Study design** | **Population** | **Follow-up****(% followed)** | **Definition of radiographic spinal degeneration** | **Risk** |
| **Lumbar** |
| Aono (2010) | Prospective, longitudinal, population-based studyASAP Study | N = 142\*Female: 100%Mean age (range): 54.7 (40–70) years | Mean 12.1 years (range, 8–14)(% f/u NR) | Lumbar disc degeneration = degenerative spondylolisthesis (> 5% slip)  | Incidence: 12.7% (18/142) |
| Cheung (2009) | Prospective, cross-sectional, population-based studyVolunteers of Southern Chinese origin | N = 1043Female: NRMean age (range): NR (18-55) years | Mean: NR(% f/u NR) | Lumbar disc degeneration = total score calculated by the summation of the individual Schneiderman’s grade at each level:* Score of 0 = all 5 levels are non-degenerated; score of 15 (max. score) = all 5 levels with grade 3 degeneration
* ≤ 1 = non-degenerated
* > 1 and < 4 = mild
* ≥ 4 = moderate to severe

Schneiderman’s classification:* Grade 1 – slight decrease in signal intensity in the nucleus pulposus
* Grade 2 – represents generalized hypointense nucleus
* Grade 3 – generalized hypointense nucleus with disc space narrowing
 | Prevalence at follow-up:†*18-29 years:* * Any: 42%
* Mild: 14%
* Moderate/severe: 28%

*30-39 years:* * Any: 48%
* Mild: 17%
* Moderate/severe: 31%

*40-49 years:* * Any: 70%
* Mild: 35%
* Moderate/severe: 35%

*≥50 years:* * Any: 88%
* Mild: 28%
* Moderate/severe: 60%
 |
| Hasset (2003) | Prospective, longitudinal, population-based studyChingford Study  | N = 796‡Female: 100%Mean age (±SD): 53.8 ± 6.0 years | 9 years(79%; 796/1003) | Lumbar disc degeneration = disc space narrowing and anterior vertebral osteophytes grades ≥ 1 in ≥ 1 vertebrae; using method described by Lane et al.:* Disc space narrowing: 0 = none, 1 = definite (mild) narrowing, 2 = moderate, 3 = severe (complete loss of joint space)
* Anterior vertebral osteophytes: 0 = none, 1 = small (definite), 2 = moderate, 3 = large

Progression = an increase in grade in an affected vertebra at baseline | Prevalence at 1 year* DSN: 67.6% (538/796)
* AVO: 91.3% (727/796)

Progression* DSN: 28.8% (148/514) §

Yearly rate: 3.2%* AVO: 34.7% (248/714) \*\*

Yearly rate: 3.9% |
| Kalichman (2009) | Prospective, cross-sectional, population-based studyFramingham Heart Study | N = 187††Female: 44%Mean age (±SD): 52.6 ± 10.8 years | Mean: NR(5.3%; 187/3529) | Lumbar disc degeneration = assessed using 4 different spinal degeneration features*Intervertebral disc narrowing*: normal (grade ≤ 1) and affected (grade ≥ 2)* Grade 0 = normal, disc higher than the upper disc, except for L5-S1 disc
* Grade 1 = slight, disc as high as the upper disc if it is normal;
* Grade 2 – moderate, disc narrower than the upper disc if it is normal
* Grade 3 – severe, endplates almost in contact

*Facet joint osteoarthritis*: absent (grade ≤ 1) or present (grade ≥ 2) on any side at any level* Grade 0 (normal)
* Grade 1 (mild degenerative disease) = narrowing of the joint space (< 2 mm) and/or small osteophytes and/or mild hypertrophy of the articular process
* Grade 2 (moderate degenerative disease) = narrowing of the joint space (< 1 mm) and/or moderate osteophytes and/or moderate hypertrophy of the articular process and/or mild subarticular bone erosions
* Grade 3 (severe degenerative disease) = severe narrowing of the joint space and/or large osteophytes and/or severe hypertrophy of the articular process and/or severe subarticular bone erosions and/or subchondral cysts and/or vacuum phenomenon in the joints

*Spondylolisthesis*: present (slippage of a vertebra and the spine above it relative to the vertebra below) or absent for each subject*Spinal stenosis*:* < 10 mm diameter of the spinal canal measured at the level of the intervertebral disc
* Reported as present or absent at any level
 | Prevalence at follow-up:‡‡Disc narrowing (grade ≥ 2):* Overall: 63.9% (117/187)
* Males: 64.1% (66/104)
* Females: 63.8% (51/83)
* <40 years: 21%
* 40-49 years: 52%
* 50-59 years: 68%
* ≥60 years: 81%

Facet joints OA (grade ≥ 2):* Overall: 64.5% (118/187)
* Males: 60.2% (62/104)
* Females: 70% (56/83)
* <40 years: 24.0%
* 40-49 years: 44.7%
* 50-59 years: 74.2%
* ≥60 years: 84.0%

Degenerative spondylolisthesis:* Overall: 13.6% (25/187)
* Males: 7.7% (8/104)
* Females: 21.3% (17/83)
* <40 years: 0%
* 40-49 years: 2.1%
* 50-59 years: 10.8%
* ≥60 years: 34.0%

Spinal stenosis:* Overall: 8.0% (15/187)
* Males: 8.7% (9/104)
* Females: 7.2% (6/83)
* <40 years: 5%
* 40-49 years: 1%
* 50-59 years: 4%
* ≥60 years: 12%
 |
| Kauppila (1997/1998) §§ | Prospective, longitudinal, population-based studyFramingham Heart Study | N = 617\*\*\*Female: 64.8%Mean age (±SD): 53.9 ± 4.7 years | 25 years(21.8%; 617/2824) | Lumbar disc degeneration = 1) presence of disc space narrowing or endplate sclerosis; using method described by Lane et al.:* Disc space narrowing: 0 = none, 1 = definite (mild) narrowing, 2 = moderate, 3 = severe (complete loss of joint space)
* Endplate sclerosis: 0 = none, 1 = present

2) degenerative spondylolisthesis (> 3% slip)Progression (lumbar disc deterioration between exams) = a decrease in disc space or appearance of endplate sclerosis | Prevalence at baseline:*Disc space narrowing** Overall: 14.4% (87/606)
* Male: 18.8% (40/213)
* Females: 12.0% (47/393)

*End-plate sclerosis** Overall: 3.5% (21/606)
* Males: 5.6% (12/213)
* Females: 2.3% (9/393)

Prevalence at follow-up*Disc space narrowing** Overall: 59.6% (361/606)
* Male: 59.6% (127/213)
* Females: 59.5% (234/393)

*End-plate sclerosis** Overall: 26.7% (162/606)
* Males: 28.2% (60/213)
* Females: 26.0% (102/393)

*Degenerative spondylolisthesis** Overall: 20.1% (123/617)
* Male: 10.6% (23/217)
* Female: 25.0% (100/400)

Cumulative incidence*Disc space narrowing** Overall: 45.2% (274/606)
* Male: 40.8% (87/213)
* Females: 47.6% (187/393)

*End-plate sclerosis** Overall: 23.3% (141/606)
* Males: 22.5% (48/213)
* Females: 23.7% (93/393)

*Degenerative spondylolisthesis** Overall: 19.7% (121/615) †††
 |
| Cervical |
| Wilder (2003) | Prospective, longitudinal, population-based studyClearwater Osteoarthritis Study | N = 2505‡‡‡Female: NRMean age: NR (≥ 40 years) | Mean 5.6 years(71.8%; 2505/3489)  | Cervical disc degeneration: OA grades 2, 3, or 4 according to the OA criteria of Kellgren and Lawrence: * Grade 0 = absent/normal
* Grade 1 = questionable osteophytes, no sclerosis, and no joint space narrowing
* Grade 2 = definite osteophytes, mild sclerosis, and possible joint space narrowing
* Grade 3 = definite joint space narrowing with moderate multiple osteophytes and moderate sclerosis
* Grade 4 = severe joint space narrowing with cysts, large osteophytes and severe sclerosis present.
 | Prevalence (at baseline)* 21.7% (543/2505)

Cumulative incidence * OA grades ≥ 2: 51.5% (1011/1962)
* OA grades ≥ 3: 15.8% (309/1962)
 |
| Wilder (2011) | Prospective, longitudinal, population-based studyClearwater Osteoarthritis Study | N = 707§§§Female: 66.8%Mean age (±SD): 66.8 ± 8.9 yearsBaseline OA score = 2: 70.4% (498/707)Baseline OA score = 3: 29.6% (209/707) | Mean (±SD): 5.8 ± 4.2 years (% f/u NR) | Cervical disc degeneration: OA grades 2, 3, or 4 according to the OA criteria of Kellgren and Lawrence: * Grade 0 = absent/normal
* Grade 1 = questionable osteophytes, no sclerosis, and no joint space narrowing
* Grade 2 = definite osteophytes, mild sclerosis, and possible joint space narrowing
* Grade 3 = definite joint space narrowing with moderate multiple osteophytes and moderate sclerosis
* Grade 4 = severe joint space narrowing with cysts, large osteophytes and severe sclerosis present.

Cervical spine OA progression: increase from OA grade 2 or 3 to any higher grade during the following period | Incidence of progression* Overall: 47.9% (339/707)

Males: 49.4% (116/235)Females: 47.2% (223/472)* Age 40–49: 41.9% (13/31)

Male: 30.0% (3/10)Females: 47.6% (10/21)* Age 50–59: 53.1% (60/113)

Male: 41.4% (12/29)Females: 57.1% (48/84)* Age 60–69: 47.9% (128/267)

Male: 46.0% (40/87)Females: 48.9% (88/180)* Age 70–79: 48.1% (126/262)

Male: 58.9% (56/95)Females: 41.9% (70/167)* Age 80+: 35.3% (12/34)

Male: 35.7% (5/14)Females: 35.0% (7/20)Progression rates (per 100 person-years of observation)* Overall:

Males: 8.9%Females: 8.0%* Age 40–49

Male: 3.7%Females: 5.6%* Age 50–59

Male: 5.3%Females: 7.6%* Age 60–69

Male: 8.2%Females: 8.0%* Age 70–79

Male: 12.5%Females: 8.6%* Age 80+

Male: 9.3%Females: 9.3% |

AP: anteroposterior; ASAP: Asahikawa observational study of Spinal Aging in Prospective; NR: not reported; OA: osteoarthritis.

\*Subset of the ASAP Study with the following inclusion criteria: 1) no degenerative spondylolisthesis at baseline radiograph, 2) baseline age of ≥ 40 years, and 3) no serious medical history and no prior spinal interventions, 4) could be followed up for > 8 years.

†Mild and moderate to severe DDD percentages not reported in text for each age group. Percentages are estimated from figure provided.

‡Reflects number of patients with paired lumbar films available for analysis at 9 years, which comprises 79% of the original sample (n = 1003).

§Of the 538 women with DSN degeneration (grade ≥ 1) at baseline, 24 had a DSN final grade of 0 in an initially affected vertebra and were therefore excluded from progression analysis, leaving 514 paired films for analysis.

\*\*Of the 727 women with AVO degeneration (grade ≥ 1) at baseline, 13 had an AVO final grade of 0 in an initially affected vertebra and were therefore excluded from progression analysis, leaving 714 paired films for analysis.

††Among a sample of 3529 participants of the Framingham study, 187 individuals were randomly enrolled in this ancillary study

‡‡Percentages are estimated from figure provided in the article or taken from previous studies by the same author in the same population in which only specific radiographic criteria were reported (facet joint OA, Kalichman et al 2008; degenerative spondylolisthesis, Kalichman et al. 2009).

§§These two studies were conducted in the same population of patients. Each study reported prevalence/incidence of degenerative spine disease but used different criteria/definitions: presence of disc space narrowing or endplate sclerosis (Kauppila 1997); degenerative spondylolisthesis (Kauppila 1998).

\*\*\*Of the 2824 original participants who had lumbar radiographs at baseline, 1558 had died by follow-up exam and 595 did not have follow-up radiographs. Of the 671 with two sets of lumbar films, 617 had technically adequate films and make up the study population.

†††Excluding 2 subjects who had spondylolisthesis at baseline.

‡‡‡Among 3489 individuals that were enrolled in the Clearwater Osteoarthritis Study, 984 were excluded from the current analyses due to the following reasons: no follow-up time recorded (n = 859); incomplete data (n = 26); and prevalent OA at all four sites (knee, hand, foot, and cervical spine; n = 99).

§§§Subjects were required to have an OA grade 2 or 3 at baseline. A total of over 3700 subjects were enrolled in the Clearwater Osteoarthritis Study at the time of this articles publication.

**Key Question 1:** Level of Evidence Summary Tables for Included Studies

*Critical appraisal for articles on prognosis – longitudinal studies*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Methodological Principle | Aono (2010) | Hasset (2003) | Kauppila (1997) | Kauppila (1998) | Wilder (2003) | Wilder (2011) |
| Study design |  |  |  |  |  |  |
| Prospective cohort study  | √ | √ | √ | √ | √ | √ |
| Retrospective cohort study |  |  |  |  |  |  |
| Case-control study |  |  |  |  |  |  |
| Cross-sectional study |  |  |  |  |  |  |
| Patients at similar point in the course of their disease or treatment | √ | √ | √ | √ | √ | √ |
| Patients followed long enough for outcomes to occur | √ | √ | √ | √ | √ | √ |
| Complete follow-up of >80% |  |  |  |  |  |  |
| Accounting for other prognostic factors\* | √ | √ | √ | √ | √ | √ |
| Evidence Level | II | II | II | II | II | II |

\*Authors must consider other factors that might influence patient outcomes

*Critical appraisal for article on prognosis- cross-sectional studies*

|  |  |  |
| --- | --- | --- |
| Methodological Principle | Cheung (2009) | Kalichman (2009) |
| Study design |  |  |
| Prospective cohort study  |  |  |
| Retrospective cohort study |  |  |
| Case-control study |  |  |
| Cross-sectional study | √ | √ |
| A representative sample of the population of interest | √ | √ |
| Exposure that precedes an outcome of interest (e.g., sex, genetic factor)  | √ | √ |
| Accounting for other prognostic factors |  | √ |
| For surveys, a return rate of > 80% |  |  |
| Evidence Level | IV | IV |