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Proximal gait adaptations in individuals with knee osteoarthritis: A systematic review and meta-analysis

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ABSTRACT

Clarifying proximal gait adaptations as a strategy to reduce knee joint loading and pain for individuals with knee osteoarthritis (OA) contributes to understanding the pathogenesis of multi-articular OA changes and musculoskeletal pain in other joints. We aimed to determine whether biomechanical alterations in knee OA patients during level walking is increased upper trunk lean in the frontal and sagittal planes, and subsequent alteration in external hip adduction moment (EHAM) and external hip flexion moment (EHFM). A literature search was conducted in PubMed, PEDro, CINAHL, and Cochrane CENTRAL through May 2018. Where possible, data were combined into a meta-analysis; pooled standardized mean differences (SMD) of between knee OA patients and healthy adults were calculated using a random-effect model. In total, 32 articles (2037 participants, mean age, 63.0 years) met inclusion criteria. Individuals with knee OA had significantly increased lateral trunk lean toward the ipsilateral limb (pooled SMD: 1.18; 95% CI: 0.59, 1.77) along with significantly decreased EHAM. These subjects also displayed a non-significantly increased trunk/pelvic flexion angle and EHFM. The GRADE approach judged all measures as "*very low*." These results may indicate that biomechanical alterations accompanying knee OA are associated with increased lateral trunk lean and ensuing alterations in EHAM. Biomechanical alterations in the sagittal plane were not evident. Biomechanical adaptations might have negative sequelae, such as secondary hip abductor muscle weakness and low back pain. Thus, investigations of negative sequelae due to proximal gait adaptations are warranted.

1. Introduction

Knee osteoarthritis (OA) contributes to altered gait since individuals try to avoid knee pain, minimize joint force (Winter and Eng, 1995), and avoid feelings of joint instability (Shakoor et al., 2003). The trunk is the heaviest part of the body, and its function can affect the orientation of the ground reaction force vector and knee moment. Alteration of trunk kinematics has been identified as a possible strategy to reduce knee joint loading and knee pain for knee OA patients (Hunt et al., 2010; Linley et al., 2010). In 2013, Mills et al. conducted an extensive review and found that alteration in spatiotemporal parameters, including greater stride duration and decreased cadence are characteristic of knee OA (Mills et al., 2013b). However, they could not identify biomechanical alterations of the trunk during level walking because relatively few studies met their inclusion criteria. Thus, proximal compensatory strategies used by individuals with knee OA remains unclear.

Many previous studies focused on lateral trunk lean toward the ipsilateral limb (Hunt et al., 2008; Hunt et al., 2011; Simic et al., 2012; Takacs et al., 2014; van der Esch et al., 2011). This proximal adaption is suggested to be a dominant means patients use to avoid severe knee pain and cartilage contact stress in the knee joint. Lateral trunk lean of 4, 8, and 12° in healthy adults reduces external peak knee adduction moment (EKAM) by 7, 21, and 25%, respectively, compared to adults with a normal gait (Hunt et al., 2011). However, lateral trunk lean in individuals with knee OA was weakly related with knee pain (Hunt et al., 2008; van der

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Esch et al., 2011), and increased trunk lean did not immediately improve symptoms (Simic et al., 2012; Takacs et al., 2014). Further, the relationship between lateral trunk lean and EKAM is likely weaker in individuals with moderate to severe knee OA than in those with mild knee OA (Hunt et al., 2008). Thus, the role of proximal adaptation in the frontal plane for knee pain and EKAM in individuals with knee OA requires reconsideration.

Biomechanical alterations in the sagittal plane were not well characterized in previous studies. Sagittal plane motion of the trunk can influence the external knee flexion moment (EKFM) which contributes to greater knee joint contact stress independent of EKAM (Walter et al., 2010), progressive tibial cartilage damage (Chehab et al., 2014), and severe gait-related knee pain (O'Connell et al., 2016). It is plausible that individuals with knee OA lean their trunks anteriorly toward the ipsilateral limb, an adjustment that would successfully reduce EKFM through reduction of the moment arm. However, we are not aware of any review that explores proximal gait adaptations and considers kinematics/kinetics of both frontal and sagittal planes. Updated information concerning biomechanical alterations associated with knee OA during level walking would help clinicians and physical therapists understand proximal gait compensation behavior. This issue is important since effort to limit ipsilateral knee pain may place relatively greater loads on contralateral joints (Shakoor et al., 2002). In turn, such greater loads might affect multi-articular OA changes. Also, proximal adaptations may induce multi-articular muscle soreness (Hunt et al., 2011) and cause hip muscular weakness through decreasing electromyogenic activation (Nuesch et al., 2016; Robbins et al., 2016).

This systematic review aimed to summarize current evidence of proximal biomechanical alterations in individuals with knee OA during level walking, discuss their relevance to knee pain and knee joint moments (EKAM, EKFM), and assess potential negative sequelae of observed proximal gait alterations. We hypothesized that knee OA–associated biomechanical alterations were increased lateral trunk lean toward the ipsilateral limb in conjunction with increased trunk/pelvic flexion and resulting alterations in hip joint moments.

2. Methods

This study was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2009), PRISMA protocols (PRISMA-P) (Shamseer et al., 2015), Meta-analysis of Observational Studies in Epidemiology (MOOSE) checklist (Stroup et al., 2000), and Cochrane Handbook for Systematic Reviews of Interventions (Higgins and Green, 2011). A detailed protocol for this systematic review has not been published and registered.

2.1. Literature search and study selection

PubMed, Physiotherapy Evidence Database, Cumulative Index to Nursing and Allied Health Literature, and Cochrane Central Register of Controlled Trials were searched (Supplemental Appendix S1, Method 1).

Included studies met the following criteria: (i) were published in a peer-reviewed journal, (ii) were written in English, (iii) had a control group of age-matched healthy adults, (iv) included patients who were diagnosed with knee OA in the tibiofemoral joint, and (v) outcomes included kinematic and/or kinetic parameters in trunk and hip. Knee OA was defined radiographically or clinically using established existing criteria for OA such as American College of Rheumatology criteria (Altman et al., 1986). Since biomechanical alterations during gait occur with normal aging, this review included only studies with an age-matched control group. No restrictions on study dates, follow-up duration, disease severity, lower limb alignment, disease laterality (unilateral vs. bilateral), or knee OA type (medial vs. lateral) were used. Studies including participants who underwent total joint arthroplasty were excluded. Databases were searched through May 2018. The inclusion process is shown in Supplemental Appendix S1, Method 2.

2.2. Outcome measures, data extraction, and risk of bias assessment

The primary outcomes in this review were: (i) kinematics that describes the peak angle of the trunk and hip joint during gait; and (ii) kinetics that describes the peak hip joint moment during gait. A secondary outcome was trunk and hip joint excursions during gait. The trunk consists of the following 2 segments: upper trunk (thorax: neck to abdomen) and lower trunk (pelvis) (Van Criekinge et al., 2017). A single reviewer (HI) collected data regarding authors, years, subject population, Kellgren and Lawrence (KL) grade, knee pain intensity, walking speed, knee alignment, outcome measures, walking tasks, and funding sources using standardized data forms. Definition of upper trunk segment and lateral trunk lean angle was also extracted purely for descriptive purpose. To standardize pain outcomes across studies, all pain scales were converted to 0–100 and pain scores were recalculated as in a previous meta-analysis (Wandel et al., 2010). The same reviewer used the modified Downs and Black scale (Downs and Black, 1998) to evaluate risk of bias for each study's (Supplemental Appendix S1, Method 3).

2.3. Data analysis

Pooled estimates and 95% confidence intervals (CIs) for standardized mean differences (SMD) were calculated using the DerSimonian-Laird method (Deeks and Higgins, 2010) (Supplemental Appendix S1, Method 4). SMD were calculated using the mean between-group difference (knee OA and healthy adults) divided by the pooled standard deviation (SD). Meta-analyses were performed using Review Manager Version 5.3 (Nordic Cochrane Centre, Cochrane Collaboration, Copenhagen, Denmark). SMD effect size was interpreted using Cohen's d (Cohen, 1992) (<0.5, small; 0.5–0.8, moderate; and ≥0.8, large). Prediction intervals for each outcome variable were also estimated (Riley et al., 2011). When mean and SD values were not directly reported, they were calculated from other available data whenever possible. For significant findings are reported as exact p values (i.e., $p = 0.037$, not $p < 0.05$), we calculated SD using a RevMan calculator. Findings from principal component analysis were also extracted and summarized as non-pooled data. To address the role of increased lateral trunk lean in individuals with knee OA, post-hoc linear regression analyses were performed to examine relationships among trunk lean angle, knee pain intensity, and EKAM. Relationship among increased trunk flexion angle, knee pain, and EKFM was not assessed because few studies assessed these parameters within same trial. All other statistical analyses were performed using JMP Pro 13.0 (SAS Institute, Cary, NC, USA).

2.4. Additional methods

Additional methods are available in Supplemental Appendix S1: test for publication bias (Method 5), test for heterogeneity (Method 6), and GRADE approach (Method 7).

Table 1
Summary of included studies.

Author	Subject population	KL grade	Pain	Walking speed (m/s)	Knee alignment[†]
Astephen JL (2008) Canada	C: Asymptomatic subjects (N = 60; age: 50.3 ± 10.1 y; BMI: 25.5 ± 4.0 kg/m^2; 61.7%F) E1: Moderate knee OA (N = 60; age: 58.3 ± 9.3 y; BMI: 31.0 ± 5.2 kg/m^2; 33.3%F) E2: Severe knee OA (N = 60; age: 64.5 ± 7.8 y; BMI: 32.1 ± 5.5 kg/m^2; 55.0% F)	C: – E1: I–IV E2: III–IV	WOMAC pain (0–20 points) C: 0.44 ± 1.41 E1: 7.53 ± 3.94 E2: 10.6 ± 5.82	C: 1.36 ± 0.19 E1: 1.25 ± 0.22 E2: 0.92 ± 0.24	–
Bechard DJ (2014) Canada	C: Healthy adults (N = 20; age: 51.0 ± 8.0 y; BMI: 25.9 ± 3.2 kg/m^2; 40.0%F) E: Symptomatic radiographic knee OA (N = 20; age: 55.0 ± 8.0 y; BMI: 28.9 ± 3.0 kg/m^2; 60.0%F)	C: – E: II: N = 9 III: N = 10 IV: N = 1	KOOS (0–100 points) C: – E: 55.4 ± 16.4	C: 1.33 ± 0.18 E: 1.27 ± 0.16	Mechanical axis C: – E: 6.1 ± 3.2
Bejek Z (2006) Hungary	C: Healthy adults (N = 20; age: 68.8 ± 9.1 y; height: 1.7 ± 0.2 m; mass: 73.3 ± 11.4 kg; 60.0%F) E: Radiographic knee OA (N = 20; age: 69.7 ± 8.9 y; height: 1.7 ± 0.1 m; mass: 71.1 ± 11.9 kg; 60.0%F)	C: – E: III (N = 5) IV (N = 15)	HSSKS (0–100 points) C: 98.9 ± 1.1 E: 47.9 ± 13.6	–	–
Bolink SA (2012) Netherlands	C: Healthy adults (N = 30; age: 61.0 ± 5.6 y; 40.0%F) E: End stage knee OA (N = 20; age: 67.4 ± 7.7 y; 65.0%F)	C: – E: III-IV	–	C: 1.29 ± 0.19 E: 0.85 ± 0.16	–
Brandon SC (2011) Canada	C: Asymptomatic subjects (N = 44; age: 50.7 ± 10.3 y; BMI: 25.9 ± 3.7 kg/m^2) E: Moderate knee OA (N = 44; age: 59.4 ± 8.5 y; BMI: 30.4 ± 4.6 kg/m^2)	C: – E: I : N = 4 II: N = 24 III: N = 16	WOMAC pain (0–20 points) C: – E: 7.00 ± 4.00	C: 1.32 ± 0.14 E: 1.28 ± 0.17	–
Butler RJ (2011) US	C: Asymptomatic subjects (N = 15; age: 56.3 ± 10.7 y; BMI: 27.8 ± 5.7 kg/m^2) E1: Medial knee OA (N = 15; age: 66.2 ± 7.8 y; BMI: 32.2 ± 7.9 kg/m^2) E2: Lateral knee OA (N = 15; age: 65.7 ± 6.4 y; BMI: 30.4 ± 7.5 kg/m^2)	C: – E1: I: N = 5 II: N = 4 III: N = 6 E2: I: N = 3 II: N = 5 III: N = 7	–	C: 1.50 ± 0.10 E1: 1.40 ± 0.20 E2: 1.40 ± 0.30	–
Creaby MW (2012) Australia	C: Healthy adults (N = 31; age: 63.8 ± 8.0 y; BMI: 25.5 ± 3.7 kg/m^2; 64.5%F) E1: Uni-pain/uni-medial knee OA (N = 11; age: 64.5 ± 7.6 y; BMI: 31.1 ± 3.8 kg/m^2; 45.5%F) E2: Uni-pain/bi-medial knee OA (N = 22; age: 65.1 ± 9.4 y; BMI: 26.8 ± 5.0 kg/m2; 54.5%F) E3: Bi-pain/bi-medial knee OA (N = 56; age: 64.5 ± 8.0 y; BMI: 27.9 ± 4.1 kg/m2; 42.9%F)	E1: II: N = 2 III: N = 3 IV: N = 6 E2: II: N = 10 III: N = 9 IV: N = 3 E3: II: N = 17 III: N = 17 IV: N = 22	NRS pain (0–10 points) C: 0.0 ± 0.0 E1: 2.6 ± 2.6 E2: 1.8 ± 1.9 E3: 2.3 ± 2.1	C: 1.42 ± 0.18 E1: 1.15 ± 0.12 E2: 1.28 ± 0.22 E3: 1.20 ± 0.16	–
Duffell LD (2017) UK	C1: Healthy younger adults (N = 36; age: 43.9 ± 7.7 y; height: 1.7 ± 0.1 m; mass: 70.4 ± 13.2 kg; 50.0%F) C2: Healthy older adults (N = 23; age: 66.8 ± 5.6 y; height: 1.7 ± 0.1 m; mass: 68.1 ± 11.0 kg; 65.2%F) E1: Radiographic knee OA in younger adults (N = 13; age: 49.5 ± 8.6 y; height: 1.7 ± 0.1 m; mass: 78.2 ± 19.6 kg; 53.8%F) E2: Radiographic knee OA in older adults (N = 12; age: 67.6 ± 3.6 y; height: 1.7 ± 0.1 m; mass: 78.9 ± 15.1 kg; 41.7%F)	–	–	C1: 1.18 ± 0.14 C2: 1.18 ± 0.14 E1: 1.09 ± 0.12 E2: 1.02 ± 0.17	–
Esrafilian A (2013) Iran	C: Healthy adults (N = 15; age: 50.0 ± 5.0 y; height: 1.7 ± 0.1 m; mass: 60.6 ± 6.0 kg) E: Symptomatic radiographic knee OA (N = 15; age: 51.0 ± 5.6 y; height: 1.7 ± 0.1 m; mass: 58.0 ± 8.0 kg)	–	–	C: 1.02 ± 0.24 E: 0.71 ± 0.19	–
Federolf PA (2013) US	C: Healthy adults (N = 5; age: 61.0 ± 2.6 y; height: 1.7 ± 0.0 m; mass: 79.1 ± 7.3 kg) E: Radiographic knee OA (N = 5; age: 61.6 ± 2.1 y; height: 1.8 ± 0.1 m; mass: 88.5 ± 7.5 kg)	C: – E: II or III	–	–	–
Hunt MA (2010) Australia	C: Healthy adults (N = 20; age: 63.2 ± 12.4 y; height: 1.7 ± 0.1 m; mass: 69.3 ± 12.1 kg; 75.0%F) E1: Symptomatic mild medial knee OA (N = 25; age: 61.2 ± 7.7 y; height: 1.7 ± 0.1 m; mass: 73.7 ± 14.0 kg; 60.0%F) E2: Symptomatic moderate medial knee OA (N = 25; age: 63.6 ± 8.4 y; height: 1.7 ± 0.1 m; mass: 78.4 ± 14.8 kg; 44.0%F)	C: – E1: II E2: III E3: IV	WOMAC pain (0–20 points) C: – E1: 6.4 ± 3.2 E2: 6.8 ± 2.6 E3: 8.1 ± 3.1	C: 1.38 ± 0.17 E1: 1.28 ± 0.16 E2: 1.21 ± 0.17 E3: 1.17 ± 0.16	Mechanical axis C: – E1: 178.2 ± 1.5 E2:

(*continued on next page*)

Table 1 (*continued*)

Author	Subject population	KL grade	Pain	Walking speed (m/s)	Knee alignment[†]
	E3: Symptomatic severe medial knee OA (N = 25; age: 68.0 ± 6.6 y; height: 1.7 ± 0.1 m; mass: 81.7 ± 20.2 kg; 48.0%F)				176.6 ± 2.7 E3: 175.4 ± 2.6
Kierkegaard S (2015) Denmark	C: Healthy adults (N = 29; age: 66.0 ± 7.9 y; BMI: 24.8 ± 3.3 kg/m^2; 48.0%F) E: Symptomatic radiographic knee OA (N = 57; age: 65.6 ± 7.6 y; BMI: 29.1 ± 4.1 kg/m^2; 50.9%F)	–	VAS pain (0–100 mm) C: – E: 12.0 ± 23.7	C: 1.18 ± 0.19 E: 1.28 ± 0.16	–
Kiss RM (2011) Hungary	C: Healthy adults (N = 20; age: 71.9 ± 2.8 y [male], 69.4 ± 3.4 y [female]; BMI: 25.2 ± 4.1 kg/m^2 [male], 25.9 ± 2.8 kg/m^2 [female]; 60.0%F) E1: Moderate radiographic knee OA (N = 45; age: 70.1 ± 3.6 y [male], 68.4 ± 2.5 y [female]; BMI: 29.9 ± 3.4 kg/m^2 [male], 31.1 ± 5.3 kg/m^2 [female]; 46.7%F) E2: Severe radiographic knee OA (N = 45; age: 67.6 ± 3.3 y [male], 69.3 ± 4.2 y [female]; BMI: 30.1 ± 3.8 kg/m^2 [male], 29.3 ± 5.1 kg/m^2 [female]; 51.1%F)	C: – E1: III E2: IV	KOOS (0–500 points) C: 483.1 ± 25.1 (male), 477.8 ± 27.4 (female) E1: 264.2 ± 90.4 (male), 275.3 ± 78.8 (female) E2: 205.6 ± 84.7 (male), 198.4 ± 78.4 (female)	C: 1.17 ± 0.12 E1: 1.11 ± 0.14 E2: 0.98 ± 0.18	–
Levinger P (2012) Australia	C: Asymptomatic subjects (N = 28; age: 65.1 ± 11.2 y; BMI: 25.7 ± 3.9 kg/m^2; 53.0%F) E: Radiographic knee OA (N = 50; age: 66.4 ± 7.6 y; BMI: 29.6 ± 5.1 kg/m^2; 46.0%F)	–	WOMAC pain (0–500 points) C: – E: 162.0 ± 109.4	C: 1.30 ± 1.10 E: 1.20 ± 0.20	–
Linley HS (2010) Canada	C: Healthy adults (N = 40; age: 63.0 ± 10.0 y; BMI: 27.4 ± 5.5 kg/m^2; 57.5% F) E: Symptomatic medial knee OA (N = 40; age: 64.0 ± 9.0 y; BMI: 24.0 ± 3.2 kg/m^2; 57.5%F)	C: 0: N = 31 I: N = 7 II: N = 2 E: I: N = 4 II: N = 20 III: N = 9 IV: N = 7	WOMAC pain (0–20 points) C: – E: 5.55 ± 2.87	C: 1.12 ± 0.19 E: 1.00 ± 0.20	–
Liu YH (2014) Taiwan	C: Healthy adults (N = 15; age: 63.2 ± 9.9 y; height: 1.6 ± 0.1 m; mass: 60.5 ± 8.4 kg; 60.0%F) E1: Mild radiographic knee OA (N = 15; age: 63.1 ± 11.9 y; height: 1.6 ± 0.1 m; mass: 68.4 ± 10.3 kg; 60.0%F) E2: Severe radiographic knee OA (N = 15; age: 63.1 ± 8.2 y; height: 1.6 ± 0.1 m; mass: 64.0 ± 8.5 kg; 86.7%F)	C: – E1: I or II E2: III or IV	VAS pain (0–100 mm) C: – E1: 42.1 ± 15.8 E2: 45.8 ± 17.2	C: 0.89 ± 0.32 E1: 0.95 ± 0.17 E2: 0.82 ± 0.19	Mechanical axis C: – E1: 1.28 ± 3.6 E2: 5.13 ± 4.5
McKean KA (2007) Canada	C: Healthy adults (N = 42; age: 52.2 ± 10.1 y [male], 48.7 ± 10.3 y [female]; BMI: 24.7 ± 3.2 kg/m^2 [male], 24.4 ± 3.6 kg/m^2 [female]; 57.1%F) E: Knee OA (N = 39; age: 55.1 ± 13.8 y [male], 57.0 ± 11.2 y [female]; BMI: 29.7 ± 4.6 kg/m^2 [male], 31.5 ± 5.2 kg/m^2 [female]; 38.5%F)	C: – E: I–III	WOMAC pain (0–20 points) C: 0.20 ± 0.60 (male), 0.10 ± 0.40 (female) E: 7.30 ± 3.70 (male), 7.70 ± 4.00 (female)	C: 1.60 ± 0.20 (male), 1.40 ± 0.20 (female) E: 1.30 ± 0.20 (male), 1.30 ± 0.30 (female)	–
Messier SP (1992) US	C: Healthy adults (N = 15; age: 58.1 ± 2.1 y; mass: 85.8 ± 4.4 kg) E: Clinically diagnosed knee OA (N = 15; age: 58.7 ± 2.3 y; mass: 85.9 ± 4.5 kg)	C: – E: 2.2 ± 0.2	–	1.12–1.34	–
Messier SP (2005) US	C: Healthy adults (N = 10; age: 73.0 ± 1.6 y; mass: 58.3 ± 2.7 kg; 90.0%F) E: Radiographic knee OA (N = 10; age: 74.1 ± 1.5 y; mass: 65.1 ± 2.6 kg)	C: – E: II: N = 3 III: N = 5 IV: N = 2	Likert scale (1–6) C: – E: 2.48 ± 0.70	C: 1.30 ± 0.08 E: 1.10 ± 0.04	–
Metcalfe AJ[a] (2013) UK	C: Healthy adults (N = 20; age: 68.3 ± 5.9 y; BMI: 26.3 ± 3.6 kg/m^2; 50.0%F) E: Medial knee OA scheduled for UKA or TKA (N = 20; age: 69.0 ± 7.2 y; BMI: 31.1 ± 3.5 kg/m^2; 45.0%F)	C: – E: III: N = 7 IV: N = 13	WOMAC score (0–100 points) C: – E: 46.2 [31–80]	C: 1.33 ± 0.21 E: 0.97 ± 0.23	–
Mills K (2013) US	C: Healthy adults (N = 18; age: 52.5 ± 10.8 y; height: 1.7 ± 0.1 m; mass: 67.9 ± 9.6 kg; BMI: 24.3 ± 2.7 kg/m^2; 72.0%F) E1: Unilateral knee OA (N = 18; age: 53.1 ± 7.2 y; height: 1.7 ± 0.1 m; mass: 72.3 ± 10.7 kg; BMI: 25.7 ± 1.9 kg/m^2;72.0%F) E2: Bilateral knee OA (N = 18; age: 54.6 ± 7.8 y; height: 1.7 ± 0.1 m; mass: 72.4 ± 11.4 kg; BMI: 25.2 ± 2.8 kg/m^2 72.0%F)	C: – E1: II–III E2: III–III	VAS pain (0–100 mm) C: – E1: 43.3 ± 20.5 E2: 41.8 ± 19.0	C: 1.10 E1: 1.10 E2: 1.10	Mechanical axis C: 180.4 ± 3.87 E1: 181.0 ± 4.91 E2: 180.8 ± 3.44
Mundermann A (2005) US	C1: Healthy adults (N = 19; age: 61.7 ± 12.3 y; BMI: 26.1 ± 2.6 kg/m^2; 68.4% F) C2: Healthy adults (N = 23; age: 63.7 ± 9.2 y; BMI: 27.1 ± 4.0 kg/m^2; 43.5% F) E1: Less severe radiographic knee OA (N = 19; age: 65.2 ± 12.5 y; BMI: 26.9 ± 3.1 kg/m^2; 68.4%F) E2: More severe radiographic knee OA (N = 23; age: 65.0 ± 8.0 y; BMI: 27.8 ± 4.8 kg/m^2; 43.5%F)	C: – E1: II–IV E2: III–IV	VAS pain (0–100 mm) C1: – C2: – E1: 13.6 ± 8.8 E2: 17.4 ± 7.6	C1: 1.26 ± 0.23 C2: 1.25 ± 0.22 E1: 1.16 ± 0.15 E2: 1.23 ± 0.21	E2 > E1 (6.0°greater varus in E2)

Table 1 (*continued*)

Author	Subject population	KL grade	Pain	Walking speed (m/s)	Knee alignment[†]
Naili JE[b] (2017) Sweden	C: Healthy adults (N = 25; age: 65.7 ± 9.5 y; BMI: 24.9 ± 2.9 kg/m^2; 64.0%F) E: Knee OA scheduled for TKA (N = 40; age: 65.7 ± 7.2 y; BMI: 29.3 ± 4.4 kg/m^2; 62.5%F)	C: – E: III: N = 9 IV: N = 31	VAS pain (0–100 mm) C: 0 [0–0] E: 39.0 [4.0–90.0]	C: 1.30 ± 0.18 E: 1.11 ± 0.20	–
Ogaya S (2017) Japan	C: Healthy adults (N = 14; age: 64.4 ± 11.3 y; height: 1.6 ± 0.1 m; mass: 59.4 ± 7.2 kg; 50.0%F) E: Radiographic knee OA (N = 15; age: 70.8 ± 6.8 y; height: 1.6 ± 0.1 m; mass: 67.0 ± 15.3 kg; 60.0%F)	C: – E: II: N = 1 III: N = 5 IV: N = 9	–	C: 1.11 ± 0.21 E: 0.90 ± 0.16	Knee varus angle C: 0.8 ± 3.3 E: 9.3 ± 7.6
Phinyomark A (2016) Canada	C: Healthy adults (Male: N = 18; age: 54.8 ± 10.3 y; BMI: 26.2 ± 3.6 kg/m^2; Female: N = 25; age: 52.1 ± 9.4 y; BMI: 23.9 ± 3.6 kg/m^2) E: Knee OA (Male: N = 45; age: 55.2 ± 7.5 y; BMI: 28.3 ± 4.7 kg/m^2; Female: N = 55; age: 55.3 ± 7.3 y; BMI: 27.4 ± 5.1 kg/m^2)	C: – E: II	–	C: 1.16 ± 0.05 (male); 1.16 ± 0.02 (female) E: 1.13 ± 0.05 (male); 1.15 ± 0.03 (female)	–
Sagawa Y[c] (2013) Switzerland	C: Healthy adults (N = 26; age: 66.0 ± 8.0 y; BMI: 23.4 ± 2.3 kg/m^2; 53.8%F) E: Symptomatic knee OA scheduled for TKA (N = 90; age: 68.0 ± 7.0 y; BMI: 30.4 ± 5.2 kg/m^2; 58.9%F); 4 subgroups (E1: RT, E2: RB, E3: LT, E4: LB)	C: – E: III or IV	WOMAC pain (0–100 points) C: 96.7 ± 6.85 E1: 47.8 ± 14.1 E2: 43.7 ± 19.1 E3: 45.6 ± 17.6 E4: 32.8 ± 13.8	C: 1.12 ± 0.14 E1: 1.15 ± 0.13 E2: 1.17 ± 0.13 E3: 0.84 ± 0.25 E4: 0.88 ± 0.18	Mechanical axis C: – E1: 178.7 ± 5.40 E2: 171.3 ± 6.37 E3: 181.9 ± 7.26 E4: 171.2 ± 4.59
Schmitt D (2015) US	C: Healthy adults (N = 15; age: 49.2 ± 7.1 y; height: 1.7 ± 0.2 m; mass: 67.4 ± 11.6 kg; 46.7%F) E: Radiographic knee OA (N = 20; age: 61.7 ± 6.5 y; height: 1.7 ± 0.1 m; mass: 88.4 ± 21.7 kg; 65.0%F)	–	–	C: 1.38 ± 0.22 E: 0.95 ± 0.23	–
Tanaka K (2008) Japan	C: Healthy adults (N = 5; age: 72.0 ± 10.8 y; BMI: 22.4 ± 2.4 kg/m^2; 100%F) E1: Unilateral radiographic knee OA (N = 6; age: 68.7 ± 8.1 y; BMI: 22.9 ± 2.7 kg/m^2; 100%F) E2: Bilateral radiographic knee OA (N = 6; age: 72.3 ± 3.9 y; BMI: 26.4 ± 4.9 kg/m^2; 100%F)	C: – E1: II: N = 5 III: N = 1 E2: II: N = 1 III: N = 2 IV: N = 3	–	C: 1.26 ± 0.20 E1: 1.09 ± 0.22 E2: 0.97 ± 0.23	–
Turcot K (2013) Switzerland	C: Healthy adults (N = 26; age: 66.0 ± 8.0 y; BMI: 23.5 ± 2.4 kg/m^2; 57.7%F) E1: Varus OA (N = 46; age: 68.0 ± 6.0 y; BMI: 30.7 ± 5.3 kg/m^2; 47.8%F) E2: Valgus OA (N = 14; age: 69.0 ± 8.0 y; BMI: 29.3 ± 4.3 kg/m^2; 78.6%F)	–	WOMAC pain (0–100 points) C: – E1: 40.7 ± 15.5 E2: 55.4 ± 17.7	C: 1.12 ± 0.15 E1: 1.06 ± 0.21 E2: 1.04 ± 0.20	Mechanical axis C: – E1: 171.8 ± 5.20 E2: 186.5 ± 4.10
Weidow J[d] (2006) Sweden	C: Healthy adults (N = 15; age: 69.0 [60.0–86.0] y; BMI: 26.5 [21.0–30.1] kg/m^2; 100%F) E1: Radiographic medial knee OA (N = 15; age: 70.0 [47.0–79.0] y; BMI: 29.6 [20.2–40.5] kg/m^2; 100%F) E2: Radiographic lateral knee OA (N = 15; age: 70.0 [61.0–83.0] y; BMI: 27.4 [20.2–40.5] kg/m^2; 100%F)	Ahlback grade C: – E1: 3 [1–5] E2: 1 [1–4]	–	C: 1.10 [0.8–1.7] E1: 0.90 [0.4–1.3] E2: 0.80 [0.2–1.2]	–
Zeni JA (2009) US	C: Healthy adults (N = 22; age: 59.0 ± 11.0 y; BMI: 25.1 ± 3.8 kg/m^2) E1: Moderate radiographic knee OA (N = 21; age: 63.0 ± 9.3 y; BMI: 29.2 ± 4.1 kg/m^2) E2: Severe radiographic knee OA (N = 13; age: 59.0 ± 9.8 y; BMI: 30.5 ± 5.2 kg/m^2)	C: – E1: II or III E2: IV	KOOS (0–500 points) C: 477.1 ± 26.9 E1: 286.3 ± 80.8 E2: 213.9 ± 99.3	C: 1.22 ± 0.14 E1: 1.13 ± 0.12 E2: 1.03 ± 0.26	–
Zeni JA (2011) US	C: Healthy adults (N = 15; age: 58.0 ± 9.0 y; BMI: 25.6 ± 3.5 kg/m^2) E: Knee OA (N = 30; age: 63.0 ± 7.0 y; BMI: 29.8 ± 4.2 kg/m^2)	C: – E: II–IV	KOOS (0–500 points) C: 481.0 ± 23.0 E: 270.0 ± 86.0	C: 1.24 ± 0.17 E: 1.08 ± 0.20	–

y: years; F: female; BMI: body mass index; HSSKS: Harris Hip Score Knee Score; KL grade: Kellgren Lawrence grade; KOOS; Knee Injury and Osteoarthritis Outcome Score; NRS: numeric rating scale OA: osteoarthritis; TKA: total knee arthroplasty; UKA: unicompartmental knee arthroplasty; VAS: visual analog scale; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

[a] Baseline knee pain in Metcalfe AJ 2013 was expressed as mean [lower range – upper range].

[b] Baseline knee pain in Naili JE 2017 was expressed as mean [lower range – upper range].

[c] Subgroups (right-top [RT], right-bottom [RB], left-top [LT], and left-bottom [LB]) in Sagawa Y 2013 were from the first factor plane of the multiple correspondence analysis.

[d] Values in Weidow J 2006 were expressed as mean [lower range – upper range].

[†] Knee alignment value is provided as law value (i.e., 180° is neutral alignment and value less than 180° indicates varus alignment) or corrected value (i.e., 0° is neutral alignment, and a positive value indicates varus alignment).

Table 2
Summary of study parameters.

Author	Walking Task		Device		Kinematics (Angle)									Kinematics (Joint Moment)								
					Frontal			Sagittal			Transverse			Frontal			Sagittal			Transverse		
	OGW	TW	3DMocap	Other	Upper trunk (Thorax)	Lower trunk (Pelvis)	Hip	Upper trunk (Thorax)	Lower trunk (Pelvis)	Hip	Upper trunk (Thorax)	Lower trunk (Pelvis)	Hip	Upper trunk (Thorax)	Lower trunk (Pelvis)	Hip	Upper trunk (Thorax)	Lower trunk (Pelvis)	Hip	Upper trunk (Thorax)	Lower trunk (Pelvis)	Hip
Astephen JL (2008)	X (ss)		X							●						●			●			●
Bechard DJ (2014)		X (ps)	X		●	●																
Bejek Z (2006)		X (ps)	X			●			●	●		●										
Bolink SA (2012)	X (ss)			IMU		●			●			●										
Brandon SC (2011)	X (ss)		X													●			●			
Butler RJ (2011)	X (ss)		X				●									●						
Creaby MW (2012)	X (ss)		X		●																	
Duffell LD (2017)	X (ss)						●			●						●			●			
Esrafilian A (2013)	X (ss)		X			●	●		●	●		●	●			●			●			●
Federolf PA (2013)	X (ss)		X		●	●																
Hunt MA (2010)	X (ss)		X		●	●	●									●						
Kierkegaard S (2015)		X (ss)		IMU		●			●													
Kiss RM (2011)		X (ps)	X			●			●	●		●										
Levinger P (2012)	X (ss)		X			●	●		●	●												
Linley HS (2010)	X (ss)		X		●	●																
Liu YH (2014)	X (ss)		X													●			●			●
McKean KA (2007)	X (ss)		X										●			●			●			●
Messier SP (1992)	X (ps)		X							●												
Messier SP (2005)	X (ss)		X																●			
Metcalfe AJ (2013)	X (ss)		X		●											●						
Mills K (2013)		X (ps)	X			●	●			●			●									
Mundermann A (2005)	X (ss)		X													●						
Naili JE (2017)	X (ss)		X		●	●	●	●	●	●	●	●	●			●			●			
Ogaya S (2017)	X (ss)		X							●												
Phinyomark A (2016)		X (ps)	X			●	●		●	●		●	●									

Table 2 (*continued*)

Author	Walking Task		Device		Kinematics (Angle)						Kinematics (Joint Moment)					
					Frontal			Sagittal			Transverse			Frontal			Sagittal			Transverse		
	OGW	TW	3DMocap	Other	Upper trunk (Thorax)	Lower trunk (Pelvis)	Hip	Upper trunk (Thorax)	Lower trunk (Pelvis)	Hip	Upper trunk (Thorax)	Lower trunk (Pelvis)	Hip	Upper trunk (Thorax)	Lower trunk (Pelvis)	Hip	Upper trunk (Thorax)	Lower trunk (Pelvis)	Hip	Upper trunk (Thorax)	Lower trunk (Pelvis)	Hip
Sagawa Y (2013)	X (ss)		X		●					●												
Schmitt D (2015)	X (ss)		X							●									●			
Tanaka K (2008)	X (ss)		X[a]		●																	
Turcot K (2013)	X (ss)		X		●	●	●	●	●	●	●					●						
Weidow J (2006)	X (ss)		X				●			●			●			●			●			●
Zeni JA (2009)		X (ss, ps)	X																●			
Zeni JA (2011)		X (ss, ps)	X																			

IMU: inertial measurement unit; OGW: overground walking; TW: treadmill walking; 3D mocap: 3D motion capture system; ss: self-selected speed; ps: pre-specified speed.
[a] Tanaka et al. (2008) used frame DIAS II (DKH Co., LTD., Japan).

3. Results

3.1. Study selection

The database search yielded 1666 studies (Supplemental Appendix S1, Fig. 1); thirty-two (Astephen et al., 2008; Bechard et al., 2012; Bejek et al., 2006; Bolink et al., 2012; Brandon and Deluzio, 2011; Butler et al., 2011; Creaby et al., 2012; Duffell et al., 2017; Esrafilian et al., 2013; Federolf et al., 2013; Hunt et al., 2010; Kierkegaard et al., 2015; Kiss, 2011; Levinger et al., 2012; Linley et al., 2010; Liu et al., 2014; McKean et al., 2007; Messier et al., 2005; Messier et al., 1992; Metcalfe et al., 2013; Mills et al., 2013a; Mundermann et al., 2005; Naili et al., 2017; Ogaya et al., 2017; Phinyomark et al., 2016; Sagawa et al., 2013; Schmitt et al., 2015; Tanaka et al., 2008; Turcot et al., 2013; Weidow et al., 2006; Zeni and Higginson, 2009, 2011) ultimately met the eligibility criteria and were included in the meta-analysis. Reasons for exclusion of the 144 studies that were excluded during the full-text screening process are provided in Supplemental Appendix S1, Table 1.

3.2. Study characteristics

Table 1 summarizes characteristics of included studies. A total of 1258 knee OA patients (mean age: 65.5 years; mean body mass: 76.8 kg) and 779 age-matched healthy adults (mean age: 58.9 years; mean body mass: 71.9 kg) were included from 32 studies from 12 different countries. Of the 25 studies that reported sex, 616 (56.3%) and 374 (58.2%) subjects were female in knee OA and control groups, respectively. Twenty-six studies reported radiographic severity of knee OA using KL grade or Ahlback grade; however, disease severity eligibility criteria differed among studies. Twenty-three studies (71.9%) (Astephen et al., 2008; Bechard et al., 2012; Bejek et al., 2006; Brandon and Deluzio, 2011; Butler et al., 2011; Creaby et al., 2012; Duffell et al., 2017; Hunt et al., 2010; Kierkegaard et al., 2015; Kiss, 2011; Levinger et al., 2012; Messier et al., 2005; Messier et al., 1992; Metcalfe et al., 2013; Mills et al., 2013a; Mundermann et al., 2005; Naili et al., 2017; Ogaya et al., 2017; Phinyomark et al., 2016; Sagawa et al., 2013; Turcot et al., 2013; Weidow et al., 2006; Zeni and Higginson, 2011) reported funding sources.

Kinematic or kinetic parameters or both were measured during over ground or treadmill walking without the use of a walking aid (Table 2). Most individuals were instructed to walk at a self-selected speed. Devices used for gait analysis to examine joint/segment kinematics were: (1) three-dimensional motion capture, and (2) inertial measurement units (IMU). Kinetics was evaluated using a force platform and three-dimensional motion capture using inverse dynamics. In the study using the IMU, the device was attached to the sacrum to evaluate pelvic range of motion during walking (Bolink et al., 2012; Kierkegaard et al., 2015). Kinematics sampling rates were 60–120 Hz. For three-dimensional motion capture, reflective marker attachment locations and trunk segment definitions varied. Definitions of lateral trunk lean angle were: (1) the angle of a line drawn from the midpoint of the anterior superior iliac spine and midpoint of the acromion with respect to a line perpendicular to the floor; (2) the angle between C7 to S1 and a vertical line, and (3) trunk segment orientation in relation to the laboratory coordinate system using a Plug-In-Gait full body system (Supplemental Appendix S1, Table 2).

Outcome measures were kinematics and kinetics of the hip joint (or both) and the proximal two segments of the upper and lower trunk (Table 2). Ten studies (31.3%) examined the kinematics of the upper trunk (thorax); most focused on frontal plane trunk motion (lateral leaning) toward the ipsilateral limb. Fourteen

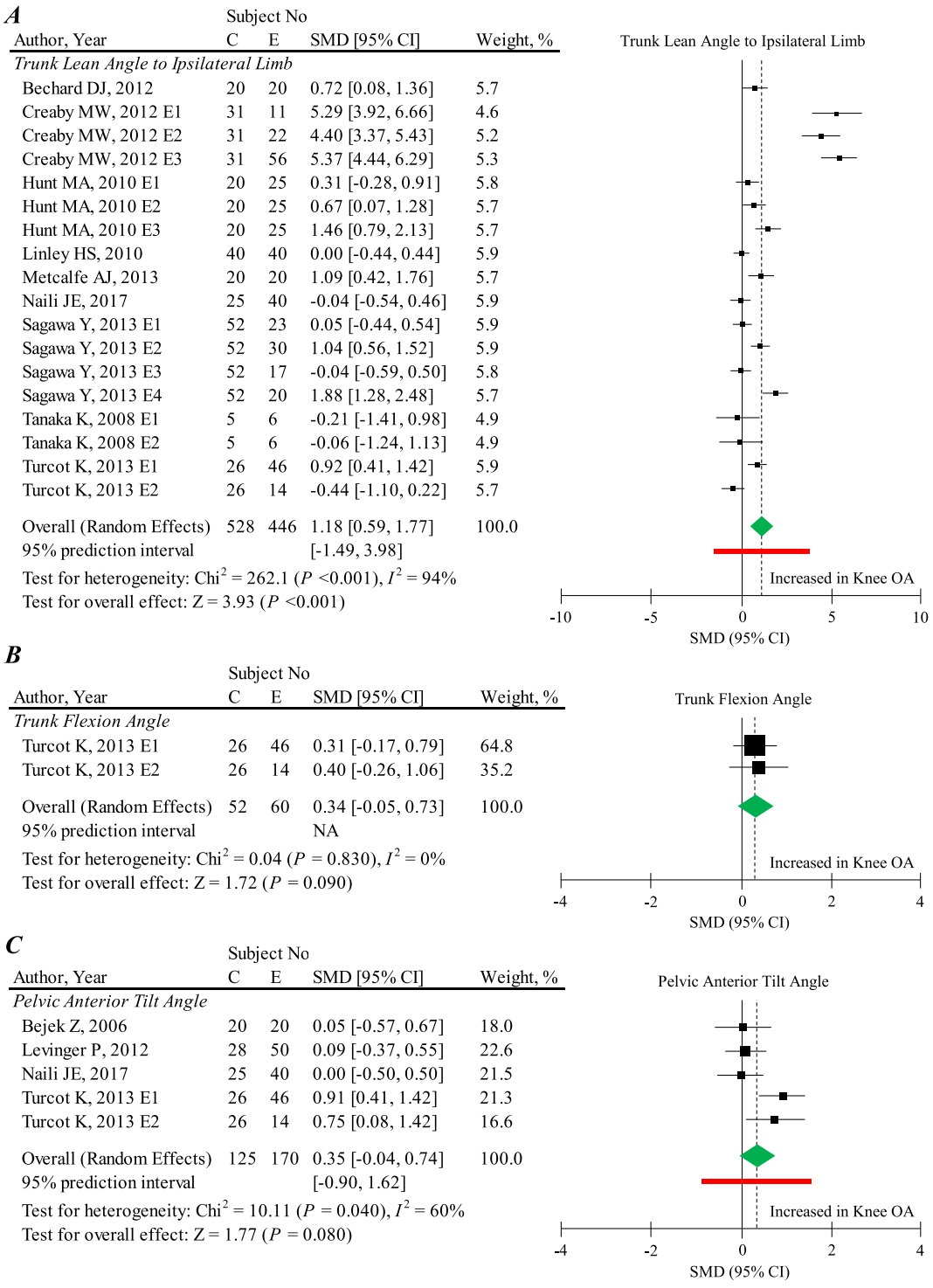

Fig. 1. SMD and 95% CI for the kinematics outcome measures. A, Trunk lean angle to ipsilateral limb. B, Trunk flexion angle. C, Pelvic anterior tilt angle. The green diamond represents the pooled effect size. The red transverse line represents the 95% prediction interval. The vertical solid line at 0 represents no difference. NA: 95% prediction interval in trunk flexion angle cannot be calculated because of the small sample size. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

(43.8%) studies examined the kinematics of the lower trunk (pelvic). Most studies evaluated kinematics in frontal and sagittal planes.

3.3. Risk of study bias

Trials had a mean Downs and Black scale score of 3.2 ± 0.7 (range, 2–4) points, indicating generally poor to moderate overall quality (Supplemental Appendix S1, Table 3). Most trials did not blind investigators who measured key outcomes. Of the 32 studies, 15 (46.9%) adequately adjusted for important confounders (i.e., age and sex).

3.4. Synthesis of results

Mean or SD values of six studies (Liu et al., 2014; Mills et al., 2013a; Mundermann et al., 2005; Ogaya et al., 2017; Schmitt

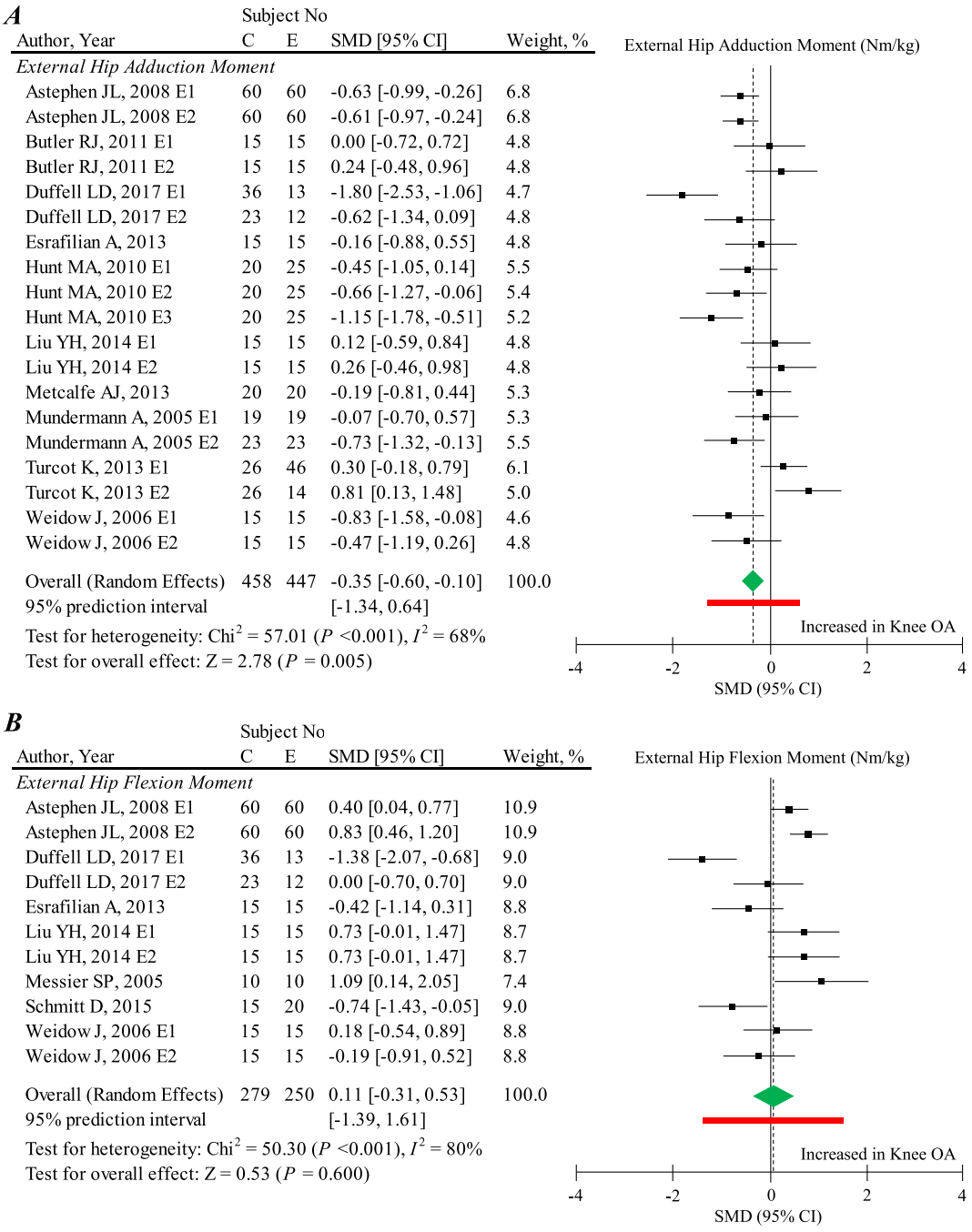

Fig. 2. SMD and 95% CI for the kinetics outcome measures. A, External hip adduction moment. B, External hip flexion moment. The green diamond represents the pooled effect size. The red transverse line represents the 95% prediction interval. The vertical solid line at 0 represents no difference. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

et al., 2015; Weidow et al., 2006) were evaluated for four complementary measures. Results of other outcome measures are provided in Supplemental Appendix S1 (forest plot, Figs. 2–6; funnel plot, Figs. 7–8). We also provide Galbraith's radial plots used to for Egger's regression test, even in outcome measures including < 10 articles (Supplemental Appendix S1, Figs. 9–11). Numerical data used in the funnel plots and publication bias tests are presented in Supplemental Appendix S1, Table 5. Results from non-pooled data are provided in Supplemental Appendix S1, Table 6.

3.4.1. Kinematics

Individuals with knee OA had significantly increased lateral trunk lean angles toward the ipsilateral limb with large effect sizes compared to healthy adults (Fig. 1A). Individuals with knee OA had non-significantly increased trunk flexion and increased pelvic anterior tilt angles compared to healthy adults (Fig. 1B, C). A meta-regression analysis examined nine study characteristics to potentially explain the significant heterogeneity in trunk lateral leaning (I^2 = 94%) and pelvic anterior tilt (I^2 = 60%) angles among studies (Supplemental Appendix S1, Table 4). Higher percentages

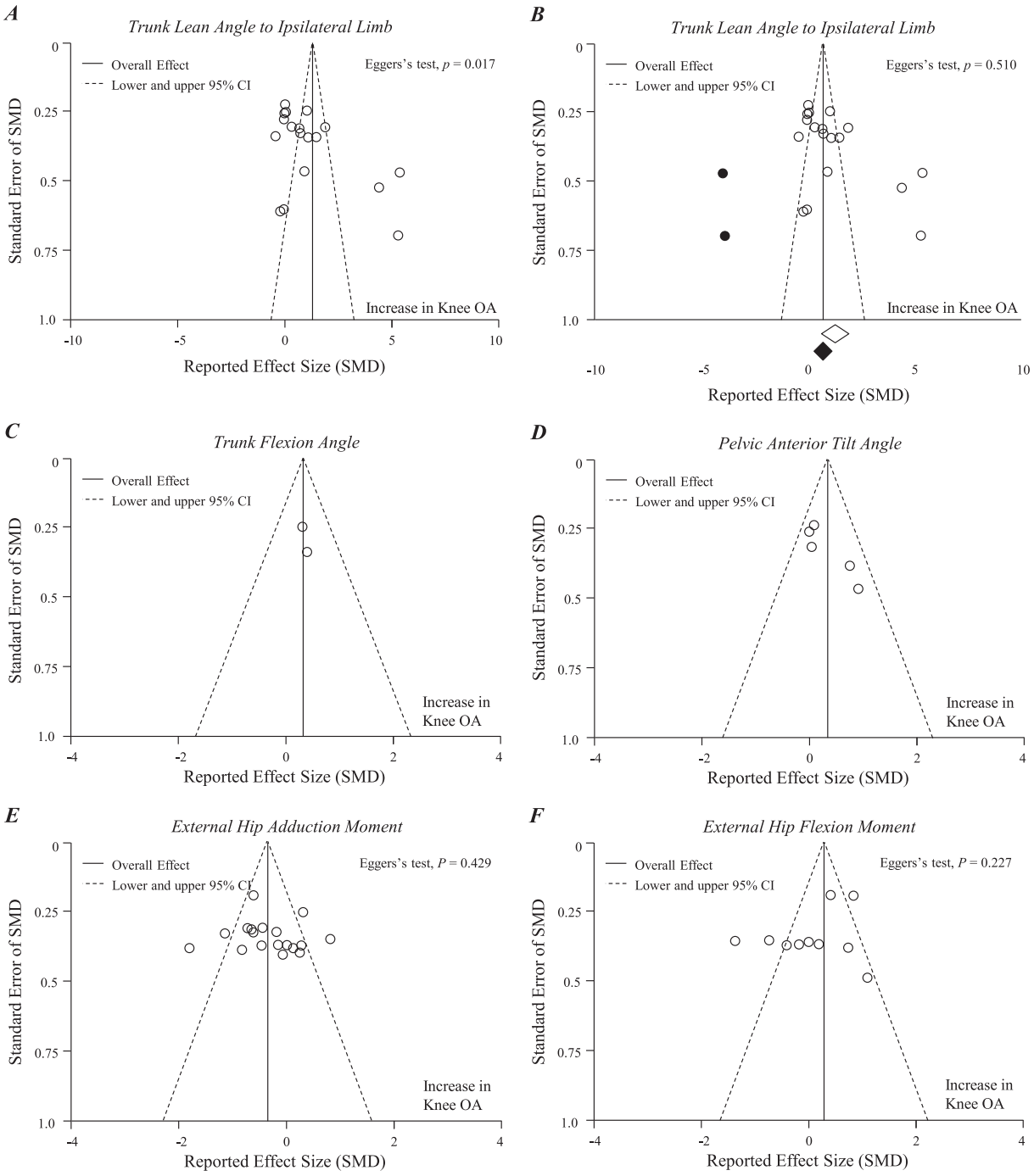

Fig. 3. Funnel plot on kinematic and kinematic outcome measures. A, Trunk lean angle to ipsilateral limb before trim-and-fill. B, Trunk lean angle to ipsilateral limb after trim-and-fill. C, Trunk flexion angle. D, Pelvic anterior tilt angle. E, External hip adduction moment. F, External hip flexion moment. The vertical dotted line represents pooled SMD. Two diagonal lines represent pseudo 95% confidence limits around the summary effect for each standard error on the vertical axis. Egger's regression test was positive for trunk lean angle ($p = 0.017$), suggesting a presence of publication bias. Using the trim-and-fill method, the intervention effect is adjusted for two possible missing articles (filled black circles) amongst published articles (open circles). The white and black diamonds represent the observed and adjusted effect size, respectively.

of female participants with severe knee pain were associated with decreased SMD for trunk lean angles, while increased Downs and Black scale score was associated with decreased SMD for pelvic anterior tilt.

3.4.2. Kinetics

Individuals with knee OA had significantly decreased external hip adduction moment (EHAM) with a small effect size (Fig. 2A). The external hip flexion moment (EHFM) was not significantly different between the 2 groups (Fig. 2B). A meta-regression analysis for explaining the high heterogeneity of EHAM ($I^2 = 68\%$) and EHFM ($I^2 = 80\%$) showed that older age was associated with increased SMD for EHFM; however, none of the variables were associated with SMD for EHAM (Supplemental Appendix S1, Table 4).

3.5. Publication bias

Asymmetry in the funnel plot was observed for trunk lean angle toward the ipsilateral limb, and the Egger's regression test was

positive for significant evidence of publication bias (Fig. 3). Using the trim-and-fill method, adjusted pooled SMD was 0.71 (95% CI, 0.28–1.15; $p = 0.001$; Fig. 3A–B). Asymmetry in the funnel plot was not observed in trunk flexion angle, pelvic anterior tilt angle, EHAM, EHFM (Fig. 3C–F) and other measures (Supplemental Appendix S1, Figs. 7–8).

3.6. Relationship between lateral trunk lean and knee Pain/EKAM

To address the role of increased lateral trunk lean as a compensatory strategy for knee pain and EKAM, we performed post-hoc linear regression analyses characterizing the relationship of trunk lean angle, knee pain, and EKAM (Fig. 4). Increased lean angle was not associated with severe knee pain ($R^2 = 0.006$; Fig. 4A). Interestingly, increased lean angle in healthy adults was associated with decreased EKAM ($R^2 = 0.850$; Fig. 4B, left panel); however in OA subjects, increased lean angle was associated with increased EKAM with high residual error ($R^2 = 0.323$). Since the relationship between trunk lean angle in OA subjects and EKAM varied widely, we further visually divided OA subjects into 3 subgroups (Fig. 4B, right panel) supported by the hierarchical cluster analysis (data not shown). Subjects in subgroup 1 who had increased trunk lean but higher EKAM had more severe varus alignment than those in subgroup 2 with increased trunk lean and an EKAM close to that of healthy adults (Fig. 4B).

3.7. Quality of evidence summary

Table 3 summarizes the body of evidence using the GRADE approach. Effects estimates were downgraded in all measures because of a high risk of bias, inconsistency, imprecision, and publication bias. None of these effects estimates was upgraded. Each effect estimate scored 1 (very low) on the GRADE approach (i.e., the true effect is likely substantially different from the effect estimate) (Balshem et al., 2011).

4. Discussion

This study supports the hypothesis that significantly increased trunk lean and resulting decreased EHAM during level walking are biomechanical characteristics of knee OA patients. Knee OA subjects showed non-significantly increased trunk/pelvic flexion despite a similar EHFM, which is contrary to our hypothesis. Although evidence quality was very low according to the GRADE approach, these findings indicate that individuals with knee OA may have altered kinematics in proximal segment/joint during level walking due to leaning their trunks, particularly in the frontal plane (Fig. 5).

Biomechanical alterations associated with knee OA were an increase in lateral trunk lean, and decreased EHAM. The lower boundary of the 95% CI of SMD in trunk lateral lean was 0.59, indicating a substantial alteration magnitude. After adjustment of funnel plot asymmetry by the trim-and-fill method, the effect estimate decreased to small (<0.5). Possible sources of funnel plot asymmetry in the current meta-analysis are unknown, as factors such as poor methodological quality are also known to cause funnel plot asymmetry (Higgins and Green, 2011). Since effects estimates were highly heterogeneous, funnel plot asymmetry might be attributed to methodological differences among studies. For example, the definition of OA differed among studies and information concerning KL grade and mechanical alignment is lacking. As highlighted in the previous meta-analysis (Mills et al., 2013b), a standardized knee OA classification system encompassing radiographic, clinical, and mechanical alignment measures would facilitate inter-study comparisons. Further, different trunk segment definitions and joint angle calculation methods may contribute to funnel plot asymmetry; some studies used the acromion as a landmark, but that landmark may vary with scapula location (Bechard et al., 2012; Linley et al., 2010).

Biomechanical alteration in the sagittal plane, specifically trunk/pelvic flexion, was not significantly confirmed. These alterations were mainly reported in a single article (Turcot et al., 2013) and a lack of statistical power may explain the non-significant results. It should be also acknowledged that relationship among increased trunk flexion angle, knee pain, and EKFM was not assessed because few studies assessed these parameters within same trial. Further studies are needed to clarify whether kinematic alterations of the trunk/pelvis in the sagittal plane are a clinical hallmark associated with knee OA.

A plausible mechanism for altered trunk motion is a proximal adaptation for avoiding severe knee pain and cartilage contact stress in the knee joint. This mechanism is generally consistent with reports of experimentally induced knee pain decreasing

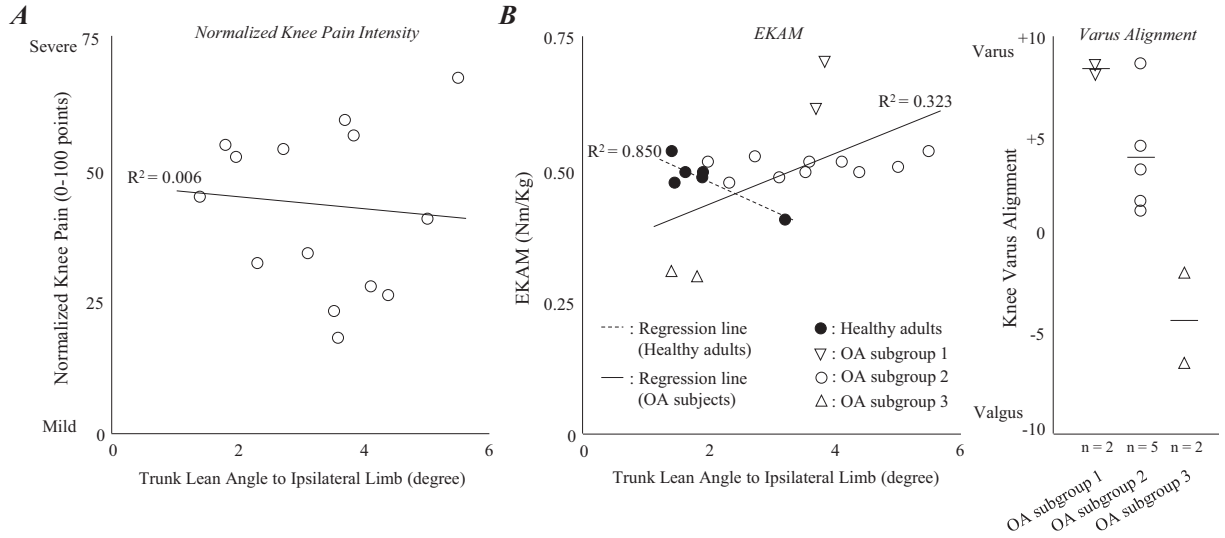

Fig. 4. Relationship between trunk lean angle toward the ipsilateral limb, knee pain intensity, and EKAM. A, Relationship between trunk lean angle in OA subjects and normalized knee pain (0–100 points; higher value indicates severe knee pain). Pearson coefficient of determination (R^2) is provided. B, Relationship between trunk lean angle in OA subjects or healthy adults and external knee adduction moment (EKAM). Pearson coefficient of determination (R^2) in each group is provided. Three OA subgroups are defined based on the magnitude of EKAM by using a hierarchical cluster analysis. Result of post-hoc subgroup analysis, illustrating the difference in knee varus alignment among three subgroups, is also provided in right panel.

Table 3
Summary of the body of evidence from GRADE's approach.

Outcome	SMD [95% CI]	Study design	Sample size	Downs and black scale score	Heterogeneity	Level of evidence (GRADE)
1. Kinematics						
1.1. Frontal plane						
1.1.1. Upper trunk						
Trunk Lean Angle to Ipsilateral Limb	1.18 [0.59, 1.77]	18 × Case-control study	Control: n = 528 OA: n = 446	3.1 ± 0.8 (3 [2–4]) points	I^2 = 94%	⊕ ⊖ ⊖ ⊖ Very Low†‡§
	0.71 [0.28, 1.15] (Trim-and-Firm)					⊕ ⊖ ⊖ ⊖ Very Low†‡
Trunk Lean Excursion	0.97 [0.09, 1.85]	6 × Case-control study	Control: n = 260 OA: n = 150	3.3 ± 1.0 (4 [2–4]) points	I^2 = 93%	⊕ ⊖ ⊖ ⊖ Very Low†‡§
Trunk Lean Angle to Contralateral Limb	0.35 [−0.11, 0.81]	5 × Case-control study	Control: n = 70 OA: n = 87	2.6 ± 0.5 (3 [2–3]) points	I^2 = 44%	⊕ ⊖ ⊖ ⊖ Very Low*‡§
1.1.2. Lower trunk						
Pelvic Obliquity Angle to Ipsilateral Limb	0.13 [−0.35, 0.61]	8 × Case-control study	Control: n = 192 OA: n = 215	2.9 ± 0.6 (3 [2–4]) points	I^2 = 82%	⊕ ⊖ ⊖ ⊖ Very Low*†‡§
Pelvic Obliquity Excursion	−0.58 [−1.68, 0.51]	6 × Case-control study	Control: n = 146 OA: n = 172	2.8 ± 1.0 (2.5 [2–4]) points	I^2 = 95%	⊕ ⊖ ⊖ ⊖ Very Low*†‡§
1.1.3. Hip joint						
Hip Adduction Angle	−0.65 [−1.23, −0.07]	13 × Case-control study	Control: n = 274 OA: n = 320	2.8 ± 0.7 (3 [2–4]) points	I^2 = 90%	⊕ ⊖ ⊖ ⊖ Very Low*†‡
Hip Adduction Excursion	−0.29 [−0.57, 0.00]	5 × Case-control study	Control: n = 97 OA: n = 105	2.0 ± 0.0 (2 [2–2]) points	I^2 = 0%	⊕ ⊖ ⊖ ⊖ Very Low*‡§
1.2. Sagittal plane						
1.2.1. Upper trunk						
Trunk Flexion Angle	0.34 (−0.05, 0.73)	2 × Case-control study	Control: n = 52 OA: n = 60	2.0 ± 0.0 (2 [2–2]) points	I^2 = 0%	⊕ ⊖ ⊖ ⊖ Very Low*‡§
Trunk Flexion Excursion	0.45 (0.05, 0.84)	2 × Case-control study	Control: n = 52 OA: n = 60	2.0 ± 0.0 (2 [2–2]) points	I^2 = 0%	⊕ ⊖ ⊖ ⊖ Very Low*‡§
1.2.2. Lower trunk						
Pelvic Anterior Tilt Angle	0.35 (−0.04, 0.74)	5 × Case-control study	Control: n = 125 OA: n = 170	2.6 ± 0.5 (3 [2–3]) points	I^2 = 60%	⊕ ⊖ ⊖ ⊖ Very Low*†‡§
Pelvic Anterior Tilt Excursion	0.42 (0.05, 0.78)	5 × Case-control study	Control: n = 116 OA: n = 152	2.6 ± 0.9 (2 [2–4]) points	I^2 = 71%	⊕ ⊖ ⊖ ⊖ Very Low*†‡§
1.2.3. Hip joint						
Hip Flexion Angle	−0.14 (−0.89, 0.60)	10 × Case-control study	Control: n = 218 OA: n = 220	2.8 ± 0.6 (3 [2–4]) points	I^2 = 92%	⊕ ⊖ ⊖ ⊖ Very Low*†‡
Hip Flexion Excursion	−0.53 (−0.96, −0.10)	11 × Case-control study	Control: n = 430 OA: n = 320	3.1 ± 0.8 (3 [2–4]) points	I^2 = 86%	⊕ ⊖ ⊖ ⊖ Very Low†‡
2. Kinetics						
2.1. Frontal plane						
External Hip Adduction Moment	−0.35 (−0.60, −0.10)	19 × Case-control study	Control: n = 458 OA: n = 447	3.1 ± 0.6 (3 [2–4]) points	I^2 = 68%	⊕ ⊖ ⊖ ⊖ Very Low†‡
2.2. Sagittal plane						
External Hip Flexion Moment	0.11 (−0.31, 0.53)	11 × Case-control study	Control: n = 279 OA: n = 250	3.0 ± 0.6 (3 [2–4]) points	I^2 = 80%	⊕ ⊖ ⊖ ⊖ Very Low†‡

GRADE: Grades of Recommendation, Assessment, Development and Evaluation; OA: osteoarthritis; SMD: standardized mean difference.
"*Very Low*" quality: very little confidence that the effects estimate and the true effect are likely to be substantially different.
* Downgraded for risk of bias (mean score of included studies was less than 3 points on the Downs and Black scale).
† Downgraded for inconsistency (results were heterogeneous across the included studies [I^2 > 50%]).
‡ Downgraded for imprecision (clinical action would depend on whether the 95% CI is in the upper or lower boundary).
§ Downgraded for publication bias (statistically significant in Egger's test or unable to determine because of a few included studies [<10 data set]).

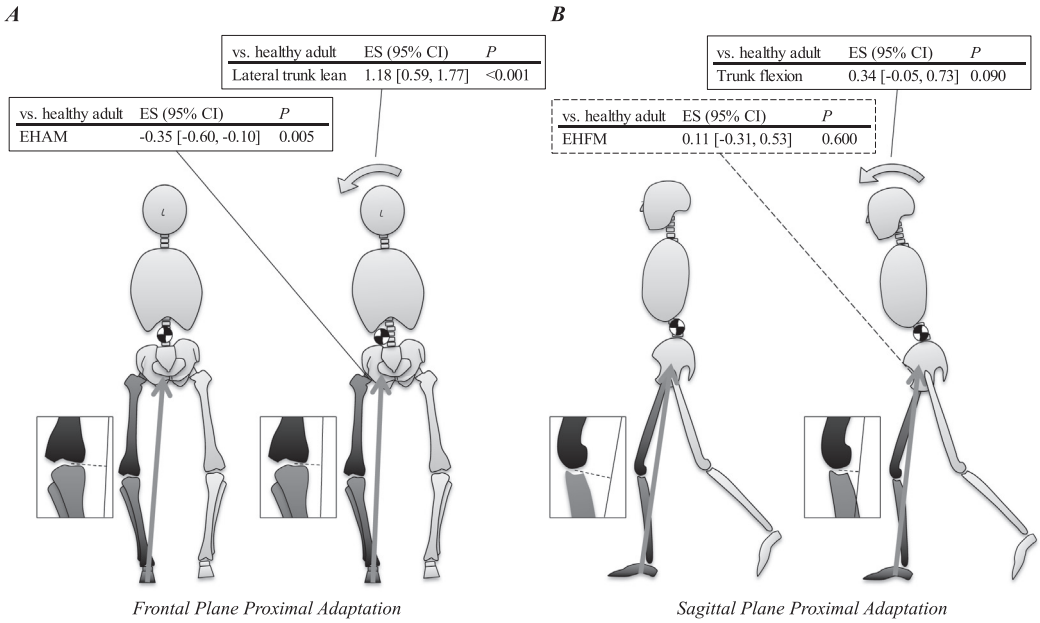

Fig. 5. Graphic abstract. Supporting our initial hypothesis, representative biomechanical alterations associated with knee OA included increased lateral trunk leaning to ipsilateral limb in conjunction with decreased external hip adduction moment (EHAM) in the frontal plane (A); and non-significantly increased trunk/pelvic flexion in sagittal plane (B); as indicated by solid black squares. Contrary to our initial hypothesis, increased external hip flexion moment (EHFM) was not confirmed, as indicated by dotted black squares. Ipsilateral (right) limb is indicated in black. Gray arrows indicate ground reaction force.

EKAM and EKFM (Henriksen et al., 2010) while knee pain relief increases EKAM and EKFM (Shrader et al., 2004). We found, however, that increased lateral trunk lean was not a significant effect modifier for milder knee pain. The weak relationship between lateral trunk motion and knee pain found in previous studies (Hunt et al., 2008; van der Esch et al., 2011) supports our findings. Increased trunk lean did not result in immediate changes in symptoms (Simic et al., 2012; Takacs et al., 2014), although EKAM decreased in a dose-response manner (Simic et al., 2012). This finding exposes a discrepancy between EKAM and knee pain intensity. Knee pain may be associated with other mechanical factors that lead to increased knee joint loading. EKFM is thought to substantially contribute to greater knee joint contact stress despite reductions in EKAM (Manal and Buchanan, 2013; Walter et al., 2010) and severe gait-related knee pain (O'Connell et al., 2016). EKFM was not well studies in the included articles.

Interestingly, increased lateral trunk lean was associated with increased EKAM, which also counters to the hypothesis mentioned above. Since a clear relationship is seen between increased lateral trunk lean angle and decreased EKAM in each study (Hunt et al., 2010; Simic et al., 2012), increased EKAM cannot be completely compensated for by increased lateral trunk lean, particularly in individuals with severe knee OA and varus alignment. The relationship between lateral trunk lean and EKAM is likely weaker in individuals with moderate to severe knee OA than in those with mild knee OA (Hunt et al., 2008). Mechanical axis has a larger impact on EKAM than on lateral trunk angle (Hunt et al., 2008). This may explain why individuals with severe knee OA have a relatively large EKAM despite the increased trunk lean angle. These findings raise the attention regarding a role of lateral trunk leaning on EKAM, an important measure of knee joint stress. The sole lateral trunk leaning strategy in individuals with severe varus alignment might be insufficient to obtain an EKAM close to that of healthy adults; this point should be considered in future observational and interventional studies.

The observed compensatory strategy may have negative sequelae as well. Displacing the trunk laterally shifts the center of gravity and allows the body to balance over the stance leg with minimal muscular support at the hip joint as indicated by decreased EHAM. The hip joint's abductor muscles have a mechanical advantage that might cause muscle weakness over time as indicated by decreased electromyogenic activation of the gluteus medius in patients with lateral trunk lean (Nuesch et al., 2016; Robbins et al., 2016). Following hip abduction muscle strength and subsequent functional limitations in those who exhibit increased lateral trunk lean are of interest.

Our findings also provide new insight into the pathogenesis of OA-related comorbidities, such as low back pain (Iijima et al., 2018; Suri et al., 2010; Wang et al., 2016; Wolfe, 1999). Increased trunk lean demands trunk muscle contraction, resulting in muscle soreness and fatigue as illustrated by increased electromyographic activity in the erector spinae after lateral trunk lean (Nuesch et al., 2016; Robbins et al., 2016). These alterations in trunk muscle activity may be important to development of low back pain. Relatively low sustained trunk muscle activation may cause muscle fatigue (van Dieen et al., 2009). Hunt et al. found that 33% of participants reported low back pain or discomfort during trunk lean (Hunt et al., 2011), although no such reports were found in individuals with knee OA during trunk lean (Gerbrands et al., 2017; Simic et al., 2012). The higher prevalence (57–66%) of low back pain in individuals with knee OA (Suri et al., 2010; Wang et al., 2016; Wolfe, 1999) may be attributed to trunk muscle activity alterations following increased lateral trunk lean.

This study has limitations. First, the effect estimate of this meta-analysis was based on cross-sectional observational studies that encountered greater bias and several more confounders than randomized controlled trials. Second, review processes, such as study selection and data extraction were performed by a single reviewer, which would yield more errors than the preferred method of independent review by two reviewers (Higgins and Green, 2011). However, to help overcome this issue, a single reviewer performed the full-text screening twice, and pursued an additional search of articles cited in original studies in addition to the standard database search. Finally, different walking tasks (treadmill and overground walking) were used among the studies, making intercomparisons difficult. Most studies using treadmills would attempt to account

for the confounding effect of walking speed by selecting gait trials at a constant speed. This approach requires OA subjects to walk faster than they normally would and changes their natural walking patterns.

In conclusion, biomechanical alterations associated with knee OA during level walking were significantly increased lateral trunk lean toward the ipsilateral limb along with non-significantly increased trunk/pelvic flexion and resultant significant alterations in EHAM. However, the body of evidence for these outcomes that are critical for clinical decision-making was ranked "*very low*" in the GRADE system. Issues include a high risk of bias, Imprecision, and heterogeneity. High heterogeneity in these outcomes was partly attributed to patients' characteristics and methodological differences in gait analyses. Observed proximal adaptations are thought to be due to avoidance of severe knee pain and cartilage contact stress. However, the sole lateral trunk lean strategy in individuals with severe varus alignment might be insufficient to obtain an EKAM close to that of healthy adults.

Conflict of interest statement

The authors did not receive financial support or other benefits from commercial sources for the work reported in this manuscript, or any other financial support that could create a potential conflict of interest or the appearance of a conflict of interest concerning the work.

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Appendix A. Supplementary material

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