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L'efficacia dell'allenamento della forza nei pazienti con chronic low back pain: una revisione sistematica di RCTs

Candidato:

Dott. Sante Bianchino

Relatore:

Dott. Valerio Barbari

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ABSTRACT

Introduzione. Il low back pain è un sintomo così comune che circa il 50 – 80% delle persone ne soffre almeno una volta nella vita. Tra questi soggetti si stima che circa il 30% cronicizza rappresentando un peso economico importante per le nazioni. Ad oggi i trattamenti proposti per affrontare questo disturbo sono diversi e l'esercizio sembra avere un supporto scientifico di rilievo e superiore agli altri approcci terapeutici. Ad oggi, però, non è chiaro quale tipologia di esercizio sia migliore di altre nel gestire questa problematica. Tra le diverse tipologie di esercizio, il resistance training ha ottenuto progressivamente più attenzione dalla ricerca scientifica ma, ad oggi, non è chiaro l'impatto sugli outcome dei pazienti affetti da CLBP. Lo scopo di questa revisione sistematica è di valutare l'efficacia dell'allenamento della forza nella riduzione del dolore, della disabilità e nel miglioramento della qualità della vita dei pazienti affetti da CNSLBP.

Metodi. La metodologia di esecuzione della revisione si è basata sulle linee guida del PRISMA Statement. È stata eseguita una ricerca su PubMed, PEDro e The Cochrane Library. Solo RCTs che includono soggetti > 18 anni sono stati scelti e che impostano l'allenamento su un'intensità e progressione misurata tramite scale validate. La valutazione della qualità metodologica è stata eseguita attraverso il RoB2 della Cochrane Collaboration.

Risultati. Dai 621 records ottenuti attraverso le ricerche sulle banche dati, 14 studi sono stati inclusi nella revisione e la maggior parte di essi presenta un alto rischio di bias. L'allenamento della forza ha inciso in maniera statisticamente significativa e clinicamente rilevante nel ridurre il dolore e la disabilità e migliorare la qualità della vita nei pazienti con CLBP. Inoltre vi è una moderata evidenza a favore dell'allenamento della forza vs. non intervento e usual care. Risultati controversi si hanno se confrontato con altre forme di esercizio.

Discussione e conclusioni. L'allenamento della forza sembrerebbe essere efficace, sugli outcome di interesse di questa revisione, nei pazienti con CNSLBP e tali risultati sono in linea e consistenti con altre ricerche. La qualità degli studi è mediamente bassa e non è possibile trarre conclusioni sul confronto di questo tipo di esercizio rispetto ad altri. In futuro la ricerca ha l'obiettivo di indagare se i vari tipi di esercizi possono adattarsi meglio a vari sottogruppi di pazienti. Inoltre vi è una moderata evidenza a favore dell'allenamento della forza vs. non intervento e usual care. Vi sono deboli evidenze che l'allenamento di forza sia leggermente più efficace di altre forme di esercizio ma che non sia migliore di esercizi di controllo motorio.

1) INTRODUZIONE

Il low back pain è un sintomo definito dalla localizzazione del dolore, tipicamente tra il margine inferiore dell'ultima costola e le pieghe glutee inferiori. Esso può essere associato a dolore ad una o entrambe le gambe (1). Le diagnosi correlabili a questo sintomo sono diverse e la più comune, riscontrabile nel 90% dei casi (2), è il non-specific low back pain. Questa diagnosi avviene per esclusione in seguito ad un processo di triage che mira ad escludere cause di dolore non muscolo-scheletriche e patologie specifiche muscolo-scheletriche (fratture, tumori, sindrome della cauda equina, stenosi, o altro). Il termine non-specific indica che la causa pato-anatomica del dolore non è conosciuta. Nel non-specific low back pain infatti le strutture che possono essere fonte di dolore sono diverse (dischi intervertebrali, articolazioni faccettarie, legamenti, fascia, muscoli, radici nervose e sacco durale) ma la valutazione clinica e l'imaging non possono attribuire in maniera affidabile la causa del dolore a queste strutture (3).

Il low back pain è un problema così comune che alcuni autori ritengono che il 50-80% delle persone abbia almeno un episodio di low back pain nella vita (4). Secondo il Global Burden of Disease, nel 2017, la prevalenza mondiale di low back pain standardizzata per età si stima essere del 7.5% da cui si è calcolato che in quell'anno 577 milioni di persone soffrivano di low back pain. La prevalenza inoltre è maggiore nelle femmine rispetto ai maschi e aumenta con l'età raggiungendo il picco tra gli 80 – 89 anni per poi decrescere leggermente (5). Nello stesso anno l'incidenza di low back pain si stima essere del 3,2% circa ammontando a 245,7 milioni di nuovi casi (6). Lo stesso studio fornisce alcune informazioni sul danno socio-economico del low back pain: questa condizione risulta essere la prima causa di anni vissuti con disabilità a livello mondiale e in Italia (7) e questo parametro raggiunge il suo picco in età lavorativa, ovvero tra i 45 – 49 anni (5). Inoltre, in alcuni paesi, è la prima causa che costringe i lavoratori anziani a ritirarsi precocemente dal mercato del lavoro (8).

Secondo molti esperti, nella maggior parte dei casi, un episodio acuto di low back pain si risolve completamente in 4 – 6 settimane (3), ma il tasso di ricorrenza e cronicizzazione sono alti. Nello specifico, secondo una revisione sistematica, nei soggetti che "guariscono" completamente, il rischio di soffrire di un altro episodio "activity-limiting" ad un anno dal primo è del 38,1% (9). Uno studio più recente, riguardante soggetti recatisi in pronto soccorso a causa del low back pain, denota come in media la riduzione del dolore sia repentina ma i soggetti presentano ancora

dolore a 6 mesi dall'evento. Alla baseline i soggetti presentavano un punteggio medio su una NPRS 0 – 100 di 71. Questo valore il giorno dopo diminuiva arrivando a 46,1 e dopo sei settimane a 31,8. A 12 settimane e 26 settimane i miglioramenti si attenuavano con punteggi medi rispettivamente di 24,8 e 13,5 (10). Un altro studio in soggetti care-seeking ha individuato 5 varianti cliniche del low back pain definite traiettorie; il 36% dei soggetti ha avuto rapidamente un recupero completo, il 34% un recupero più lento ma completo a 12 settimane, il 14% ha avuto un recupero incompleto a 12 settimane, l'11% aveva un dolore fluttuante e il 5% aveva un dolore persistente di intensità elevata durante le 12 settimane (11). La ragione per cui il low back pain non si risolve in molti pazienti non è ancora chiara. Numerosi fattori sono stati individuati che concorrono alla cronicizzazione e al peggioramento della prognosi. Questi sono: una maggiore disabilità, presenza di sciatica, età avanzata, scarsa salute generale, alterazione del trofismo e della composizione muscolare, errata coordinazione di alcuni muscoli (1), maggiore stress psicologico e psicosociale, caratteristiche cognitive negative, scarse relazioni sociali (personali e lavorative), maggiore richiesta fisica a lavoro e presenza di un'indennità (12).

1.1. Management del chronic low back pain (CLBP)

In termini di gestione del CLBP, sono numerosi gli approcci terapeutici che la letteratura scientifica ha investigato nel corso degli anni. Nessun trattamento può curare il low back pain persistente ma esistono alcuni interventi che possono ridurre il dolore e la disabilità e migliorare i fattori psico-sociali associati. Le linee guida più autorevoli e recenti annoverano l'esercizio tra gli interventi di prima linea per il chronic non-specific low back pain (13–17). Infatti, l'esercizio terapeutico sembra avere un costo minore, un'efficacia maggiore rispetto all'usual care e ai trattamenti manuali e rari e lievi effetti collaterali (18,19). Il razionale per cui l'esercizio sarebbe efficace nel ridurre dolore e disabilità non è a oggi del tutto chiaro e probabilmente coinvolge diversi aspetti, sia di natura biomeccanica che di natura psicologica, neurologica e sistemica. A questo proposito, una recente revisione sistematica ha riassunto i meccanismi d'azione dell'esercizio proposti da vari studi nel corso degli anni. Gli autori hanno distinto 5 principali meccanismi d'azione che possono contribuire al miglioramento dei soggetti con chronic non-specific low back pain:

- Neuro-muscolare: aumento di forza, resistenza e flessibilità dei muscoli del tronco e correzione dell'allineamento posturale;

- Psico-sociale: miglioramento di paura del dolore, stress, ansia, kinesiofobia, depressione e autoefficacia;
- Neurofisiologico: rilascio di endorfine e serotonina e influenza sui sistemi inibitori discendenti del dolore probabilmente disfunzionali;
- Cardiometabolico: perdita di peso e aumento della capacità aerobica;
- Circolatorio: flusso sanguigno maggiore che favorisce la concentrazione dei nutrienti che a loro volta accelerano i processi di guarigione; maggiore concentrazione di leucociti e macrofagi che contribuiscono all'analgesia indotta dall'esercizio (20).

Quale sia la forma nonché la posologia di esercizio più efficace però è ancora dibattuto (19,21,22). Razionali differenti hanno portato alla realizzazione di programmi di esercizi differenti per il trattamento del chronic non-specific low back pain, tra i quali annoveriamo: allenamenti per il controllo motorio, esercizi di stabilizzazione del tronco, allenamenti aerobici, allenamenti per la forza, esercizi di stretching, back school program, protocolli Mckenzie o altro. Tra questi l'allenamento della forza ha ottenuto una crescente attenzione scientifica negli ultimi 30 anni ed è stato adottato in diversi ambiti riabilitativi. Dal punto di vista muscolo-scheletrico, le evidenze dimostrano che l'allenamento della forza può ridurre il dolore e/o la disabilità e migliorare la funzione e/o la qualità di vita in diverse patologie croniche come l'artrosi di ginocchio e anca (23–25), l'artrite reumatoide (26–28), la fibromialgia (29,30), la cervicalgia (31–33) o altre. Per il trattamento del CNSLBP, alcuni autori evidenziano come questa forma di esercizio possa migliorare in particolar modo quegli impairments fisici (forza e resistenza degli estensori del tronco) (34) e quei fattori psicologici (ansia, depressione o altro) (35) in parte responsabili della disabilità dei pazienti affetti (36,37).

Ad oggi sono state pubblicate 4 revisioni sistematiche con meta-analisi che indagano il ruolo dell'allenamento della forza nel CNSLBP (21,35,38,39). Due di queste revisioni hanno analizzato il ruolo complessivo dell'esercizio fisico nel CNSLBP dividendo gli studi in sottogruppi di allenamento, e confrontando i risultati dei vari sottogruppi (35,38). Le altre due revisioni hanno valutato l'efficacia dell'allenamento della forza rispetto all'allenamento aerobico e ad un allenamento non progressivo (21,39). Dai risultati di queste quattro revisioni non emergono chiare evidenze a favore di un tipo di allenamento rispetto ad un altro. L'allenamento della forza è tra le opzioni di trattamento migliori per la gestione del CNSLBP e ha un'efficacia da lieve a moderata nel ridurre il dolore e la disabilità e nel migliorare la qualità di vita dei soggetti. Quando comparato però al Pilates, all'allenamento per il controllo motorio/stabilizzazione o all'allenamento aerobico i risultati sono controversi. Questo è principalmente dovuto alla variabilità degli interventi proposti e alle definizioni di allenamento

della forza adottate dalle suddette revisioni sebbene la network meta-analisi di Owen et al. suggerisce che differenti forme di esercizio possano avere un'efficacia diversa in base all'outcome di riferimento (35). La presente revisione, come nella revisione di Searle et al. del 2015 (38), estrae la descrizione dell'allenamento della forza dalle linee guida dell'American College of Sports Medicine: allenare la forza di uno o più muscoli o di un task motorio implica l'attuazione di uno o più esercizi contro una resistenza che aumenta nel tempo secondo determinati modelli di progressione (40,41). In aggiunta ad essa, per migliorare la generalizzabilità e applicabilità clinica dei risultati, è opportuno precisare che la progressione dei carichi degli studi inclusi deve essere eseguita secondo parametri validati (1RM, RPE, OMNI o altri). Lo scopo della presente revisione è di valutare l'efficacia dell'allenamento della forza nei soggetti con CNSLBP rispetto ad altri tipi di trattamento in termini di riduzione del dolore e della disabilità e miglioramento della qualità della vita, di valutare su quali di questi outcome risulti maggiormente efficace, di analizzare quale variabile dei programmi di allenamento sia maggiormente correlata ad outcomes migliori e di valutare la qualità degli studi condotti.

2) MATERIALI E METODI

Questa revisione sistematica è stata svolta secondo le linee guida dettate dal PRISMA statement (42).

2.1. Criteri di eleggibilità

2.1.1 Design dello studio

Sono stati selezionati solo RCTs in lingua inglese o italiana e non sono state applicate restrizioni riguardo la data di pubblicazione.

2.1.2 Partecipanti

Sono stati selezionati studi con pazienti di età maggiore o uguale a 18 anni che presentano chronic non-specific low back pain (CNSLBP), ovvero dolore non specifico localizzato tra la piega glutea inferiore e il margine costale (2) che perdura da più di 3 mesi (43), con o senza dolore radicolare o radicolopatia. Sono esclusi tutti i pazienti che presentano LBP acuto o causato da patologie specifiche (e.g. tumori, infezioni, stenosi, sindrome della cauda equina,

artrite reumatoide o altre), pazienti sottoposti a precedenti operazioni chirurgiche della colonna e che presentano comorbidità sistemiche severe (e.g. patologie cardiovascolari severe, o altre).

2.1.3 Interventi

Sono stati selezionati studi i cui partecipanti sono stati sottoposti ad un programma di esercizi per l'allenamento della forza. Il programma deve rispettare parametri validati di intensità e progressione dei carichi in modo da personalizzare e standardizzare l'allenamento della forza (e.g. 1RM, RPE, muscle failure, scala di Borg per la fatica, o altri parametri di riferimento validati che possano standardizzare la progressione dei carichi). Non sono state applicate restrizioni rispetto all'associazione dell'allenamento della forza con altri interventi. Studi i cui interventi non includono un programma di esercizi personalizzato o che non rispetti parametri validati di intensità e progressione.

2.1.4 Confronto

Qualsiasi tipo di gruppo di confronto è stato selezionato: nessun intervento, placebo, usual care, terapie passive (massoterapia, terapia manuale, terapia farmacologica, mezzi fisici o altro), terapia multidisciplinare, psicoterapia e approcci educativi (cognitive behavioural therapy, patient neuroscience education, mindfulness o altri) e altri tipi di esercizi (e.g. pilates, esercizi per il controllo motorio, stretching o altri).

2.1.5 Outcomes

Sono stati ritenuti eleggibili tutti gli studi che valutavano almeno uno degli outcome tra dolore, disabilità e qualità della vita, valutati attraverso strumenti di misura validati (patient-reported outcome measures, strumenti di misurazione oggettivi o di altra natura).

2.2. Metodi di ricerca per l'inclusione degli studi

La ricerca è stata effettuata tra Ottobre 2020 e Aprile 2021 su Pubmed, PEDro e The Cochrane Library. Le strategie di ricerca sono state adattate ai vari database utilizzando termini MeSH e gli operatori Booleani (AND, OR e NOT) ove possibile. I termini chiave utilizzati per la ricerca sono stati "Low Back Pain" e "Resistance exercise" al quale sono stati aggiunti tutti i possibili sinonimi per rendere più sensibile la ricerca. La stringa di ricerca utilizzata su pubmed è la seguente: (("Low Back Pain"[Mesh]) OR ("low back ache") OR ("back ache") OR ("back aches") OR ("backaches") OR ("backache") OR ("lower back pain") OR ("back pain")) AND

((“Resistance Training”[Mesh]) OR (“strength training”) OR (“strengthening program”) OR (“powerlifting”) OR (“weight-lifting”) OR (“weightlifting”) OR (“weight-bearing exercise”) OR (“High-Intensity Interval Training”[Mesh]) OR (“strength exercise”) OR (“strength program”) OR (“resistance exercise”) OR (“resistance program”)).

Sono state condotte ricerche manuali attraverso la consultazione della bibliografia di tutti gli RCTs inclusi in questa revisione, così come delle Linee Guida e delle precedenti revisioni riguardanti l’esercizio fisico nel CNSLBP. I riferimenti bibliografici presenti negli RCTs inclusi e di linee guida e revisioni sistematiche sono stati valutati.

2.3. Selezione degli studi ed estrazione dei dati

Inizialmente è stato fatto uno screening di titoli ed abstract degli studi, eliminando i duplicati. Successivamente sono stati analizzati i full-text degli articoli. Gli articoli completi sono stati richiesti al Servizio Bibliotecario dell’Università degli studi di Genova tramite il servizio Network Inter-Library Document Exchange (NILDE) o richiesti direttamente agli autori, se non reperibili direttamente dalle banche dati. I risultati sono stati estratti secondo il modello P.I.C.O. del presente studio e secondo le linee guida PRISMA (42). L’estrazione dei dati è stata così organizzata:

- Informazioni generali (autore, data di pubblicazione, paese in cui è stato svolto);
- Partecipanti (dimensione del campione, età, sesso, durata dei sintomi);
- Interventi/Controlli (modalità, contenuto, frequenza e durata dell’intervento);
- Outcomes e misure di esito;
- Follow-ups.

2.4. Valutazione del rischio di Bias

La valutazione del rischio di Bias degli studi è stata effettuata mediante “The Cochrane Collaboration’s Risk of Bias tool 2.0” (R.o.B.2). All’interno di questa scala di valutazione vi sono 5 domini riguardo potenziali bias: randomization process, deviations from the intended interventions, missing outcome data, measurement of the outcome e selection of the reported

results. L'interpretazione del rischio di bias per ogni dominio è guidato da preimpostate signalling questions. Tramite degli algoritmi ad ogni dominio è stato assegnato un livello di rischio di bias (high risk, low risk o some concerns) che a sua volta ha generato il rischio di bias complessivo di uno studio (44).

3) RISULTATI

3.1. Selezione degli studi

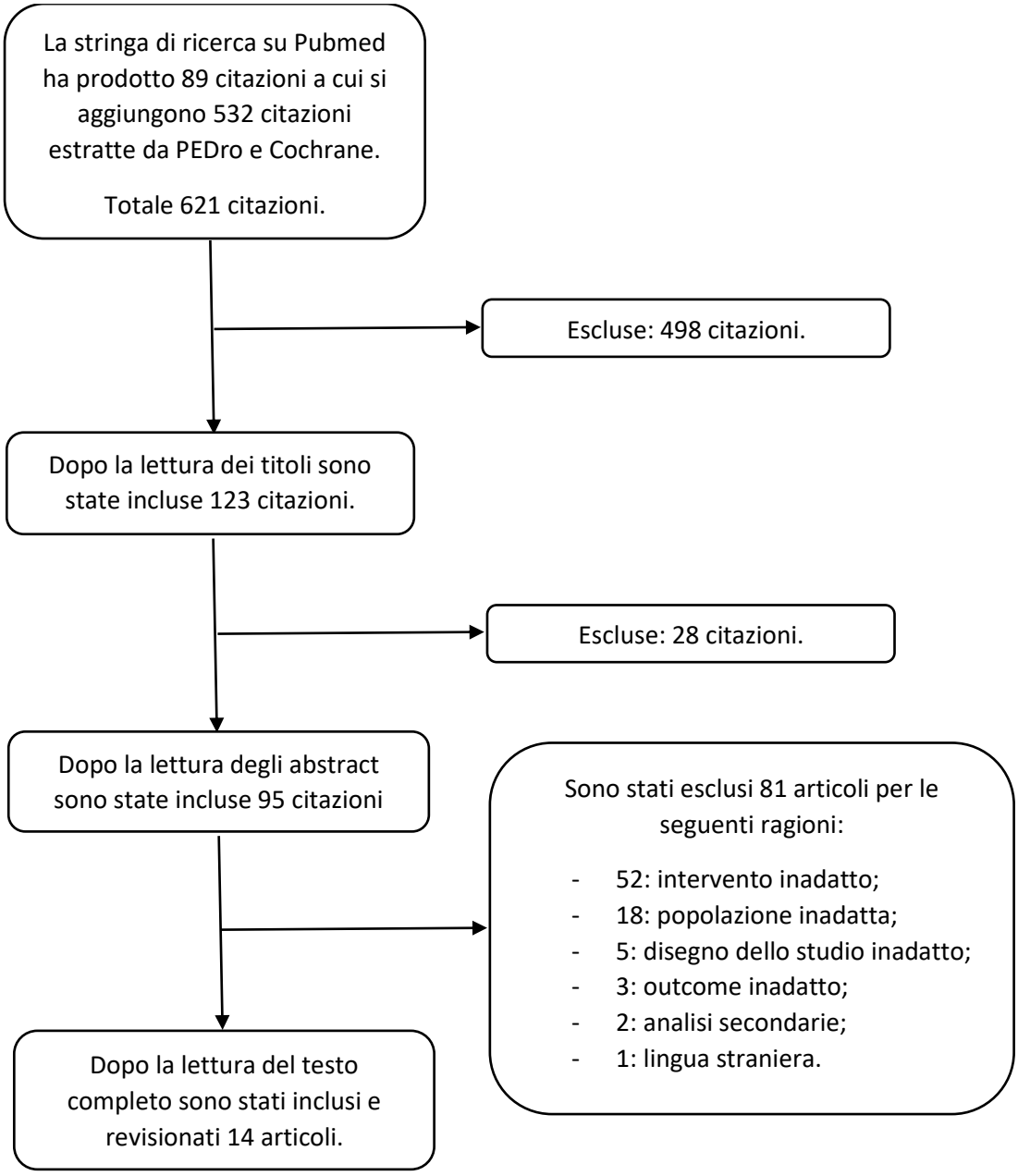

Figura 1. Diagramma di flusso della selezione degli studi.

Il processo di ricerca e selezione degli studi è schematizzato nel diagramma in Figura 1. La ricerca sui database Pubmed, PEDro e The Cochrane Library ha prodotto 643 citazioni bibliografiche. Dopo la rimozione dei duplicati ne sono rimaste 621. Di queste, 498 citazioni sono state escluse dopo la lettura dei titoli. Delle 123 citazioni rimaste, 28 sono state escluse dopo la lettura degli abstract perché non soddisfacevano i criteri di eleggibilità. Il testo integrale delle rimanenti 95 citazioni bibliografiche è stato esaminato nel dettaglio. Di queste, 81 sono state escluse per le seguenti ragioni:

- 52 adottano un intervento che non soddisfa i criteri della presente revisione;
- 18 coinvolgono una popolazione inadeguata;
- 5 adottano disegni di studio non compatibili con la presente revisione;
- 3 non valutano gli outcome necessari per la presente revisione;
- 2 sono analisi secondarie di studi inclusi nella presente revisione;
- 1 è in una lingua diversa da Inglese e Italiano.

Al termine del processo di screening 14 articoli sono stati inclusi nella presente revisione e sottoposti alla valutazione metodologica (45,46,55–58,47–54).

3.2. Caratteristiche degli studi

Le caratteristiche dei singoli studi sono sintetizzate nella tabella 1.

3.2.1 Popolazione

Il totale dei pazienti coinvolti negli RCTs inclusi ammonta a 894. Le dimensioni campionarie variano da un minimo di 19 (49) ad un massimo di 240 (52). L'età media dei soggetti è di 43,5 anni. Lo studio con la popolazione mediamente più giovane è quello di Atalay E., Akova B., et al. (57)**,** con età media di 24,9 anni; lo studio con la popolazione più anziana è quello di Madadi-Shad M., Jafarnezhadgero AA., et al. (53), con età media di 68,5 anni. Quasi tutti gli studi coinvolgono soggetti di entrambi i sessi, ad eccezione dell'articolo di Cortell-Tormo JM., Sanchez PT., et al. (49), che coinvolge solo soggetti femmine, e degli articoli di Jackson JK., Shepherd TR., et al. e Atalay E., Akova B., et al. (50,57), che includono solo soggetti maschi. Due studi (47,50) coinvolgono sportivi amatoriali: lo studio di Cai C., Yang Y., et al. include runners amatoriali mentre lo studio di Jackson JK., Shepherd TR., et al. include giocatori di hockey amatoriali. Uno studio include pazienti con CLBP e piede pronato (navicular drop

>10mm) (53). Infine tre studi attuano uno screening per fattori psico-sociali (45,47,56). Gli studi di Aasa B., Berglund L., et al. e di Verbrugghe J., Agten A., et al. includono solo pazienti con un riconoscibile pattern di dolore meccanico-nocicettivo; mentre lo studio di Cai C., Yang Y., et al. esclude soggetti con alti punteggi al Fear-Avoidance Beliefs Questionnaire.

3.2.2 Interventi

L'allenamento della forza è inteso come termine generico che può indicare qualsiasi esercizio contro una resistenza progressiva volto ad aumentare la forza di un determinato gruppo muscolare o in un determinato task motorio. Per questo motivo i programmi di allenamento nei diversi studi sono diversi tra loro in termini di posologia, intensità, tipo di esercizi e di resistenza esterna. Generalmente la durata degli interventi varia da 6 a 18 settimane e la frequenza da 1 a 4 volte a settimana. L'intensità è da moderata a alta in tutti gli studi e i parametri per la progressione dei carichi variano in base alla strumentazione usata per gli esercizi: in 3 studi (49,53,57) la progressione dei carichi è stata basata sulla OMNI Rate of Perceived Exertion (59), in altri 7 studi la progressione si fondava sulle 1, 5, 10, o 20 RM (47,48,50–52,56,58) mentre in uno studio (45) si fondava sul dolore percepito durante e il giorno successivo alla sessione di allenamento; infine in 3 studi la progressione avveniva per esaurimento muscolare (46,54,55). Questi trial hanno utilizzato la MedX Lumbar Extension Machine (LEM) in diversi programmi di rinforzo. In tutti e tre gli studi un gruppo d'intervento eseguiva una serie di estensioni lombari isotoniche alla LEM fino ad esaurimento muscolare, una volta a settimana per 12 settimane. La serie era costituita da 8 – 15 ripetizioni e una volta che il soggetto riusciva a completare una serie da 12-15 ripetizioni il carico veniva aumentato del 5%. Questo protocollo, in soggetti sani, ha dimostrato di essere efficace nell'incrementare la forza durante l'estensione lombare al pari di allenamenti a frequenza maggiore (60). Per quanto riguarda il tipo di resistenza esterna, 2 studi hanno adottato gli elastic band (49,53) e 9 trial hanno adottato manubri, bilancieri o macchinari da palestra (45,47,48,50–52,56–58). L'aderenza al programma di esercizi è stata riportata in 7 studi: 6 trial riportano un'alta aderenza al programma di esercizi (>75%) (45,49,52,55,56,58), di cui 2 studi hanno esplicitamente escluso dall'analisi soggetti con una bassa aderenza (52,55)**,** mentre un solo studio riporta un'aderenza bassa alle sessioni di allenamento supervisionate (47)**.** I gruppi di confronto degli studi inclusi sono molto eterogenei: in 5 studi ai gruppi di confronto è stato solamente imposto di non iniziare una nuova forma di allenamento (49–53), in tre studi i gruppi di confronto sono stati sottoposti ad usual care (mobilizzazioni, protocolli McKenzie, altri tipi di esercizi, interventi di ergonimia, o altro) (46,54,55) e in 6 studi ad altre forme di esercizio (45,47,48,51,56,57); infine 6 studi comparano

gruppi sottoposti ad allenamenti di forza in cui alcuni parametri (frequenza, durata, intensità o altri) variano tra i gruppi (46,52,54–56,58).

3.2.3 Misure di outcome e follow-up

Tutti gli studi esaminati hanno incluso il dolore tra le misure di outcome: 4 hanno utilizzato una Numeric Pain Rating Scale (NPRS) (47,48,56,58) e i restanti si sono avvalsi della Visual Analogue Scale (VAS). 12 degli studi inclusi hanno valutato la disabilità dei soggetti (46,48,57,58,49–56)**:** 2 hanno utilizzato il Roland Morris Disability Questionnaire (RMDQ) (48,53), mentre i restanti si sono avvalsi dell'Oswestry Disability Index (ODI). Infine 4 studi hanno valutato la qualità della vita mediante la Short Form-36 (SF-36) (49–52)**.** Tutti gli studi inclusi hanno eseguito follow-up a breve termine (< 6 mesi), uno studio ha eseguito un follow-up a medio termine (> o = 6 mesi, < 12 mesi) (47) e infine uno studio ha eseguito un follow-up a lungo termine (> o = 12 mesi) (45)**.**

3.3. Rischio di bias degli studi

Le stime del rischio di bias per i vari parametri sono riassunte nella tabella 2 mentre la valutazione dettagliata per ogni singolo studio si trova in Appendice. Il rischio di bias è stato stimato mediante "The Cochrane Collaboration's Risk of Bias tool 2.0" (R.o.B.2) e si è scelto di valutare l'effetto di "assignement to intervention" dei gruppi d'intervento. Uno studio è stato valutato a basso rischio di bias (48), 4 studi sono stati valutati a rischio non chiaro di bias (45,47,56,58) mentre i restanti sono risultati ad alto rischio di bias. Il parametro risultato con maggiore frequenza ad alto rischio di bias è stato il "Risk of Bias in the measurement of the outome" mentre il parametro risultato con maggiore frequenza a rischio non chiaro di bias è stato il "Risk of Bias in selection of the reported risult". Ai parametri "Risk of bias arising from the randomization process" e "Risk of bias due to deviations from the intended interventions" è stata data una valutazione di "some concerns" nella maggior parte degli studi, mentre al parametro "Missing outcome data" è stata data una valutazione di alto rischio di bias in metà degli studi.

Tabella 1. Tabella riassuntiva delle caratteristiche degli studi inclusi.

Informazioni generali (autore, anno, paese)	**Popolazione** (caratteristiche, dimensione, età, sesso)	**Interventi** (numero di partecipanti, volume, intensità, frequenza, durata, progressione dei carichi)	**Confronti** (numero di partecipanti, contenuto, frequenza e durata)	**Outcomes e misure di esito**
Aasa B., Berglund L., et al. 2015. Svezia.	N° 70 Età 25 < 60 F = 39 Durata sintomi: 326 settimane	N° 35; Età 42; F = 19. Entrambi i gruppi: educazione riguardo i meccanismi del dolore. Intervento: sessioni in gruppi di 5 di high load deadlift con l'ausilio di bilancieri della durata di 60min. Il programma ha durata di 8 settimane con una frequenza di 2 x sett. le prime 4 settimane e 1 x sett. le settimane 5 – 8. Il carico era selezionato da un fisioterapista in seguito all'esame fisico e gradualmente aumentato se il dolore non peggiorava alla seduta successiva. Le ripetizioni variavano in base al peso con un range da 1 a 10.	N° 35; Età 42; F = 20. Confronto: sessioni individuali di low load motor control exercises della durata di 20 – 30min. Il programma ha durata di 8 settimane con una frequenza di 2 x sett. le prime 4 settimane e 1 x sett. le settimane 5 – 8. Gli esercizi erano personalizzati e selezionati dai fisioterapisti. In aggiunta erano prescritti home exercises da eseguire in serie da 10 ripetizioni 2, 3 volte al giorno.	Dolore: VAS
Bruce-Low S., Smith D., et al. 2012. Regno Unito.	N° 72 Età 45,5 F = 30	Entrambi gli interventi hanno durata di 12 settimane. Intervento 1: N° 31; 1 serie da 8 – 12 ripetizioni con un carico pari all'80% del maximum voluntary isometric torque (MVIT) sulla Lumbar extension machine (LEM). La frequenza era di 1 x sett. e il carico veniva aumentato del 5% quando i soggetti riuscivano ad eseguire 12 ripetizioni senza arrivare ad esaurimento muscolare. Intervento 2: N° 20; come intervento 1. In aggiunta i soggetti eseguivano una serie da 105 – 140sec in più con un carico pari al 50% del MVIT a distanza di 3 giorni dalla prima.	N° 21. Tutti i gruppi continuano i loro normali trattamenti per il CNSLBP ma il gruppo di controllo non esegue le serie alla LEM.	Dolore: VAS Disabilità: ODI
Cai C., Yang Y., et al. 2017. Singapore.	N° 84 Età 21 < 45 F=42 Durata sintomi: 65,4 sett. Runners amatoriali	Tutti i gruppi: 2 sessioni di esercizi a settimana per 8 settimane + esercizi giornalieri per casa. Le sessioni avevano durata di 45min con 15 min di riscaldamento e 30min di esercizi. Tutti dovevano continuare la loro attività di corsa. Intervento 1. N°28, Età 28,9. Le sessioni supervisionate erano costituite da 3 esercizi per gli abd. d'anca e gli est. d'anca e ginocchio mediante macchine in 3 serie da 10 rip. a media intensità, basata sulle 10RM. Esercizi a casa: single-leg squat e il wall sit.	N°28, Età 26,9. Esercizi di stabilizzazione del tronco e di controllo dei muscoli trasverso dell'addome e multifido. Inizialmente i soggetti venivano istruiti a contrarre e mantenere la contrazione dei muscoli del tronco oltre i 60sec. e successivamente introducevano attività sempre più complicate da svolgere	Dolore: NPRS

		Intervento 2: N°28, Età 26,1. Le sessioni supervisionate erano costituite da esercizi per il rinforzo degli estensori del tronco inizialmente in quadrupedia e dalla 5 settimana le iperestensioni. Le serie erano 3 da 10 rip. per ogni esercizio e la progressione basata sulla %MVIC. Esercizi a casa = esercizi supervisionati ad eccezione delle iperestensioni.	mantenendo la contrazione di quei muscoli. Gli esercizi a casa erano gli stessi di quelli svolti sotto la supervisione del fisioterapista.	
Calatayud J., Guzman-Gonzalez B., et al. 2020. Spagna.	N°85 Età 18 < 75	N° 42, Età 52 Sessioni di allenamento in gruppo 3 volte a settimana per 8 sett. Le sessioni erano costituite da 3 esercizi dinamici con i theraband in successione, senza pause tra gli esercizi, e da 5 esercizi isometrici (plank e tenute addominali). 3 serie da 10 rip. per ogni esercizio dinamico e 1 serie 75sec. per ogni esercizio isometrico. La progressione degli esercizi dinamici era basata sulle 20, 15 e 10RM mentre per gli esercizi isometrici aumentava il tempo sotto tensione e diminuiva la base d'appoggio.	N°43, Età 50 2 sessioni di Back School di gruppo e supervisionate a settimana per le prime 3 settimane. Le restanti 5 settimane i soggetti dovevano eseguire gli stessi esercizi a casa. Il programma consisteva in 5 esercizi di rinforzo per il core e 5 esercizi di stretching. Erano eseguite 10 rip. per esercizio di quelli per il core e 4 ripetizioni da 10sec di quelli di stretching	Dolore: NPRS Disabilità: RMDQ
Cortell-Tormo JM., Sanchez PT., et al. 2017. Spagna.	N° 19 Età 20 < 55 F= 19 Durata sintomi: 19,6m	N° 11, Età 35,6 2 sessioni di allenamento di gruppo a settimana per 12 sett. Ogni sessione consisteva in 45/60min. di allenamento con 6/7min. di riscaldamento, 40/50min. di esercizi e 5min. di defaticamento e stretching. Il programma è stato suddiviso in 3 fasi. La fase 1 (sessioni 1-5) prevedeva un circuito di 1-2 serie di esercizi di stabilizzazione e controllo motorio con un intensità pari a 4 sulla scala OMNI. La fase 2 (sessioni 6-12) consisteva in un circuito di 2-3 serie di esercizi dinamici e isometrici con un'intensità di 6-7 sulla scala OMNI. La fase 3 (sessioni 13-24) consisteva in 3 serie da 12 rip. ad esercizio con carichi simmetrici e asimmetrici di intensità pari a 8-9 sulla OMNI.	N° 8, Età 35,6 I soggetti del gruppo di controllo dovevano continuare le loro normali attività senza iniziare un programma di esercizi.	Dolore: VAS Disabilità: ODI Qualità della vita: SF-36
Jackson JK., Shepherd TR., et al. 2011. Canada.	N° 45 Età > o = 45 F= 0 Durata sintomi: 23,1 m. Giocatori di Hockey amatoriali	Intervento 1: Middle age participants. N° 15, Età 52. Intervendo 2: Old age participants. N° 15, Età 63. Entrambi i gruppi di intervento sono stati sottoposti ad un programma di allenamento di forza di 16 settimane con 3 settimane iniziali di familiarizzazione con il programma. Il programma era svolto presso palestre scelte dai soggetti ai quali erano state fornite istruzioni sul programma e la posologia degli esercizi. Il programma prevedeva una progressione periodizzata degli esercizi basata sulle 5RM con una settimana di recupero ogni 3 settimane di allenamento e con un intensità moderata (60-70% RM) le prime 8	N° 15, Età 57 Il gruppo di controllo ha eseguito la fase di familiarizzazione con il programma di esercizi ma non ha iniziato il programma di allenamento vero e proprio. Ai soggetti è stato detto di continuare con le loro normali attività e di non iniziare una qualsiasi nuova forma di attività fisica.	Dolore: VAS Disabilità: ODI Qualità di vita: SF-36

		settimane e elevata (75-83% RM) le ultime 4 settimane. Inoltre era costituito da 3-6 serie di esercizi svolti 4 volte a settimana per gli arti superiori, inferiori e per il tronco.		
Kell RT., Asmundson GJ., 2008. Canada.	N° 27 F= 11 Durata sintomi: 27,6m	N° 9, Età 40,1, F= 3. I soggetti hanno svolto un programma periodizzato di allenamento di forza di 18 settimane con 2 settimane iniziali di familiarizzazione con gli esercizi e la settimana 3, 11 e 18 di recupero e test. Il programma era svolto in palestra 3 volte a settimana con un intensità moderata (53-72% RM) e la progressione era basata sulle 10RM.	Controllo 1: aerobic training, N° 9, Età 36,7, F= 4. I soggetti hanno svolto un programma periodizzato di allenamento aerobico (modalità a scelta del soggetto) di 18 settimane con 2 settimane iniziali di familiarizzazione con gli esercizi e la settimana 3, 11 e 18 di recupero e test. Le sessioni duravano 25-55min. ed erano svolte 3 volte a settimana con una bassa intensità (8-12 Borg RPE). Controllo 2: N° 9, Età 35,3, F= 4. Ai soggetti è stato chiesto di mantenere il loro precedente livello di attività fisica e di non iniziare alcuna nuova attività.	Dolore: VAS Disabilità: ODI Qualità di vita: SF-36.
Kell RT., Risi AD., et al. 2011. Canada.	N° 240 Età 18 < 50 F= 83 Durata sintomi: 37,2m Soggetti sedentari	Tutti i gruppi di intervento eseguono un programma di allenamento della forza periodizzato di 16 settimane con le stesse fasi e procedure di intensità e progressione previste per lo studio di Jackson JK, et al. 2011. Le differenze esistenti riguardano il volume di allenamento tra i gruppi di intervento. Intervento 1: N° 60, Età 42,8, F= 20, allenamento 2 volte a sett. Intervento 2: N° 60, Età 41,7, F= 22, allenamento 3 volte a sett. Intervento 3: N° 60, Età 42,4, F= 18, allenamento 4 volte a sett.	N° 60, Età 43,2, F= 23. Ai soggetti è stato detto di poter eseguire qualsiasi terapia volessero ad eccezione di iniziare qualsiasi nuova forma di allenamento.	Dolore: VAS Disabilità: ODI Qualità di vita: SF-36
Madadi-Shad M., Jafarnezhadgero AA., et al. 2020. Iran.	N° 36 Età 65 < 75 Soggetti con CLBP e piede pronato	N° 18, Età 68. I soggetti hanno eseguito un programma di allenamento di 16 settimane con 2 settimane iniziali di stretching degli eversori di caviglia e 14 settimane di test e allenamento. L'allenamento consisteva in 5 esercizi per il core e gli arti inferiori con 1-2 serie da 14-16 rip. per esercizio eseguiti 3 volte a settimana. La progressione dell'intensità era basata sulla OMNI.	N° 18, Età 68,9. Al gruppo di controllo era stato chiesto di non eseguire alcun tipo di esercizio.	Dolore: VAS Disabilità: RMDQ

Smith B., Bissel G., et al. 2011. Regno Unito.	N° 42 Età 42,9	Entrambi i gruppi di intervento hanno eseguito un allenamento che prevedeva una serie da 8-12 rip. 1 x sett. di estensioni lombari con la LEM per 12 settimane. La progressione dei carichi si basava sull'esaurimento muscolare: quando i partecipanti riuscivano ad eseguire più di 12 rip. il carico era incrementato del 5%. Intervento 1: N° 15, allenamento con meccanismo di stabilizzazione pelvica aggiunto alla LEM. Intervento 2: N° 15, allenamento senza stabilizzazione.	N° 12 Il gruppo di controllo continuava le normali terapie che eseguiva senza poter eseguire l'esercizio alla LEM.	Dolore: VAS Disabilità: ODI
Steele J., Bruce-Low S., et al. 2013. Regno Unito.	N° 31 F= 17 Durata sintomi: 13 a.	Entrambi i gruppi di intervento hanno eseguito un allenamento che prevedeva una serie da 12-15 rip. ca., 1 x sett. di estensioni lombari con la LEM per 12 sett. La progressione si basava sull'esaurimento muscolare: quando i partecipanti riuscivano ad eseguire più di 15 rip. il carico era aumentato del 5%. Inoltre entrambi i gruppi continuavano le loro usuali terapie per il CLBP. Intervento 1: N° 12, Età 46, allenamento alla LEM con ROM in estensione completo. Intervento 2: N° 10, Età 41,9, allenamento alla LEM con ROM limitato del 50%.	N° 9, Età 41,7 Il gruppo di controllo continuava le usuali terapie per il CLBP ma non hanno eseguito l'allenamento con la LEM.	Dolore: VAS Disabilità: ODI
Verbrugghe J., Agten A., et al. 2020. Belgio.	N° 80 Età 25 < 60 F= 46 Durata sintomi: 13,5 a.	Tutti i gruppi eseguono un HIIT ad alta intensità associato agli allenamenti peculiari di ogni gruppo. La durata del programma è di 12 settimane e la durata delle sessioni è di 1,5h per 2 volte a sett. Intervento 1 (HITSTRE): N° 21, Età 46,4, F= 13. L'allenamento consisteva in 2 serie da max 12 rip. di 6 esercizi per gli arti superiori e inferiori all'80% RM. La progr. era basata sull'1RM. Intervento 2 (HITCOM): N° 19, Età 44,9, F= 13. L'allenamento consisteva nella combinazione degli allenamenti HITSTRE e HITSTAB ma le serie erano ridotte ad 1 per esercizio.	Controllo 1 (HITSTAB): N° 20, Età 42, F=8 L'allenamento consisteva in 2 serie da 10 rip. da 10sec. l'una di 6 esercizi isometrici per il core. La progr. avveniva aumentando il tempo sotto tensione o adottando posture più difficoltose. Controllo 2 (HITMOB): N°20, Età 42,7, F=8 L'allenamento consisteva in 6 esercizi per migliorare la mobilità di tronco e anche.	Dolore: NPRS Disabilità: MODI
Verbrugghe J., Agten A., et al. 2019. Belgio.	N° 38 Età 25 < 60 F= 26 Durata sintomi: 11 a.	N° 19, Età 44,3, F= 13. Tutti i gruppi sono sottoposti ad un programma di allenamento di 12 settimane con 2 sessioni di 1,5h a settimana consistente in allenamento cardiorespiratorio, esercizi di forza e per il core. L'unica differenza risiede nell'intensità degli allenamenti. L'allenamento del gruppo d'intervento è uguale al programma HITCOM dello studio di Verbrugghe J., 2020.	N° 19, Età 44, F= 13. Il programma consiste in un allenamento cardiorespiratorio ad intensità continua, 6 esercizi di forza per gli arti superiori e inferiori al 60% RM e 6 esercizi per il core di intensità minore rispetto al gruppo di intervento.	Dolore: NPRS Disabilità: MODI
Atalay E., Akova B., et al. 2017. Turchia.	N° 20 F= 0	N° 10, Età 24,7.	N° 10, Età 25.	Dolore: VAS

		Tutti i gruppi hanno svolto un programma di esercizi della durata di 6 sett. per 3 volte a sett. Il gruppo d'intervento esegue esercizi di stretching, stabilizzazione e isotonici per il core come quelli del gruppo di controllo. In aggiunta esegue esercizi di rinforzo e stretching per il torace superiore, le spalle e il collo. Mentre gli esercizi per il core hanno la stessa posologia per entrambi i gruppi gli esercizi di rinforzo per torace, spalle e collo prevedevano un'elevata intensità (pari a 8 sulla OMNI). La progressione era dunque basata sulla OMNI.	Il gruppo di controllo esegue lo stesso protocollo del gruppo d'intervento ad eccezione degli esercizi per torace, spalle e collo. I soggetti eseguivano 2 rip. da 20sec. per ogni es. di stretching, 2 serie da 6-12 rip. per ogni esercizio isometrico e isotonico per il core.	Disabilità: MODI

Tabella 3. Tabella riassuntiva del risk of bias.

Nome dello studio	Risk of bias arising from the randomization process	Risk of bias due to deviations from the intended interventions	Missing outcome data	Risk of bias in measurement of the outcome	Risk of bias in selection of the reported result	Overall risk of bias
Aasa B., Berglund L., et al. 2015	Low risk	Low risk	Some concerns	Some concerns	Some concerns	**Some concerns**
Bruce-Low S., Smith D., et al. 2012	Some concerns	Some concerns	Low risk	High risk	Some concerns	**High risk**
Cai C., Yang Y., et al. 2017	Some concerns	Low risk	Low risk	Some concerns	Some concerns	**Some concerns**
Calatayud J., Guzman-Gonzalez B., et al. 2020	Low risk	Low risk	Low risk	Some concerns	Some concerns	**Low risk**
Cortell-Tormo JM., Sanchez PT., et al. 2017	Some concerns	Some concerns	High risk	High risk	Some concerns	**High risk**
Jackson JK., Shepherd TR., et al. 2011	Some concerns	Some concerns	High risk	High risk	Some concerns	**High risk**
Kell RT., Asmundson GJ., et al. 2008	Some concerns	Some concerns	High risk	High risk	Some concerns	**High risk**
Kell RT., Risi., et al. 2011	Some concerns	Some concerns	High risk	High risk	Some concerns	**High risk**
Madadi-Shad M., Jafarnezhadgero AA., et al. 2020	Some concerns	Some concerns	Low risk	High risk	Some concerns	**High risk**
Smith B., Bissel G., et al. 2011	Some concerns	Some concerns	High risk	High risk	Some concerns	**High risk**
Steele J., Bruce-Low S., et al. 2013	Some concerns	Some concerns	High risk	High risk	Some concerns	**High risk**
Verbrugghe J., Agten A., et al. 2020	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	**Some concerns**
Verbrugghe J., Agten A., et al. 2019	Low risk	Some concerns	Low risk	Some concerns	Some concerns	**Some concerns**
Atalay E., Akova B., et al. 2017	Some concerns	Some concerns	High risk	Some concerns	Some concerns	**High risk**

3.4. Risultati degli studi

I risultati degli studi sono sintetizzati nella Tabella 3.

3.4.1 Dolore

Follow up a breve termine (< 6 mesi)

Cinque studi mettono a confronto l'allenamento di forza con gruppi che non eseguono un allenamento di forza (49–53) e tutti mostrano una differenza statisticamente significativa (p< 0,05) tra i gruppi a favore dell'allenamento di forza. In tutti gli studi i gruppi sottoposti ad un allenamento di forza migliorano significativamente nel breve periodo. Questo miglioramento è clinicamente rilevante (MCID VAS = 20mm) (61) negli studi di Cortell-Tormo JM., Sanchez PT., et al. 2017 e di Kell RT., Asmundson GJ., et al. 2008.

Tre studi mettono a confronto l'allenamento di forza mediante LEM in aggiunta ad usual care con l'usual care da solo (46,54,55) e tutti gli studi mostrano una differenza statisticamente significativa (p< 0,05) tra i gruppi, a favore dell'allenamento di forza con LEM. Nello studio di Smith B., Bissel G., et al. 2011 la significatività è ottenuta solo nel gruppo con stabilizzazione pelvica e non nel gruppo senza stabilizzazione pelvica. In tutti gli studi i gruppi sottoposti ad un allenamento di forza migliorano significativamente nel breve periodo ad eccezione del gruppo senza stabilizzazione pelvica dello studio di Smith B., Bissel G., et al. 2011. Il miglioramento risulta clinicamente rilevante (MCID VAS = 20mm) nel gruppo che si allena 2 volte a settimana dello studio di Bruce-Low S., Smith D., et al. 2012 e nel gruppo che si allena con un ROM completo dello studio di Steele J., Bruce-Low S., et al. 2013.

Tre studi mettono a confronto l'allenamento di forza con gli esercizi di controllo motorio/stabilizzazione (45,47,56) e solo nello studio di Cai C., Yang Y., et al. 2017 la differenza tra i gruppi raggiunge la significatività statistica (p< 0,05) a favore del gruppo che allena la forza negli arti inferiori ad 1 mese. In tutti gli studi i gruppi d'intervento migliorano in maniera statisticamente significativa (p< 0,05) e clinicamente rilevante (MCID VAS = 20mm; MCID NPRS = 1,7) (62) nel breve periodo.

Quattro studi mettono a confronto l'allenamento di forza con altre forme di esercizio (48,51,56,57). Gli studi che comparano l'allenamento della forza con back school o esercizi di mobilità (48,56) non rilevano alcuna differenza statisticamente significativa (p> 0,05) tra i gruppi mentre se confrontato con l'allenamento aerobico o con esercizi generici (esercizi di stabilizzazione, mobilità e rinforzo a bassa intensità) (51,57) vi è una differenza statisticamente

significativa (p< 0,05). In tutti gli studi i gruppi d'intervento migliorano in maniera statisticamente significativa e clinicamente rilevante (MCID VAS = 20mm; MCID NPRS = 1,7) nel breve periodo.

Uno studio confronta un programma di allenamento cardiorespiratorio e di forza ad alta intensità e uno stesso allenamento a moderata intensità (58) e non rileva alcuna differenza statisticamente significativa (p> 0.05) tra i gruppi. Entrambi i gruppi d'intervento migliorano in maniera statisticamente significativa (p< 0.05) e clinicamente rilevante (MCID NPRS = 1,7) a 3 mesi.

Follow up a medio termine (6 < 12 mesi)

Uno studio confronta l'allenamento della forza con esercizi di controllo motorio/stabilizzazione (47) e non rileva alcuna differenza significativa (p> 0,05) tra i gruppi a 6 mesi. Tutti i gruppi migliorano in maniera statisticamente significativa e clinicamente rilevante (MCID NPRS = 1,7).

Follow up a lungo termine (≥ 12 mesi)

Uno studio confronta l'allenamento della forza con esercizi di controllo motorio (45) e non rileva alcuna differenza significativa (p> 0,05) tra i gruppi a 12 mesi. Tutti i gruppi migliorano in maniera significativa (p< 0,05) e clinicamente rilevante (MCID VAS= 20mm).

3.4.2 Disabilità

Follow up a breve termine (< 6 mesi)

Cinque studi mettono a confronto allenamento di forza con un gruppo che non esegue un allenamento di forza (53–57) e tutti mostrano una differenza statisticamente significativa (p< 0,05) tra i gruppi a favore dell'allenamento di forza. In tutti gli studi i gruppi d'intervento migliorano significativamente (p< 0,05) nel breve periodo. Questo miglioramento è clinicamente rilevante (MCID ODI = 12,8; MCID RMDQ = 3,5) (63,64) negli studi di Madadi-Shad M., Jafarnezhadgero AA., et al. 2020, di Jackson JK., Shepherd TR., et al. 2011, di Kell RT., Asmundson GJ. et al. 2008 e nel gruppo che si allena 4 volte a settimana dello studio di Kell RT., Risi AD., et al. 2011.

Tre studi mettono a confronto l'allenamento di forza mediante LEM in aggiunta ad usual care con l'usual care da solo (46,47,58) e tutti gli studi mostrano una differenza statisticamente

significativa (p< 0,05) tra i gruppi, a favore dell'allenamento di forza con LEM. Nello studio di Smith B., Bissel G., et al. la significatività è ottenuta solo nel gruppo con stabilizzazione pelvica e non nel gruppo senza stabilizzazione pelvica. In tutti gli studi i gruppi d'intervento migliorano significativamente (p< 0,05) nel breve periodo ad eccezione del gruppo senza stabilizzazione pelvica dello studio di Smith B., Bissel G., et al. 2011. Il miglioramento risulta clinicamente rilevante (MCID ODI = 12,8) nel gruppo che si allena 1 volta a settimana dello studio di Bruce-Low S., Smith D., et al. 2012 e nel gruppo che si allena con un ROM completo dello studio di Steele J., Bruce-Low S., et al. 2013.

Uno studio mette a confronto l'allenamento di forza con gli esercizi di stabilizzazione (56) e non rileva differenze statisticamente significative tra i gruppi. Tutti i gruppi migliorano in maniera significativa ma solo il gruppo che esegue esercizi combinati di forza e stabilizzazione raggiunge l'MCID ODI = 12,8.

Quattro studi mettono a confronto l'allenamento di forza con altre forme di esercizio (48,49,52,55). Gli studi che comparano l'allenamento della forza con programmi di back school o esercizi di mobilità (48,52) non rilevano alcuna differenza statisticamente significativa (p> 0,05) tra i gruppi mentre se confrontato con l'allenamento aerobico o con esercizi generici (esercizi di stabilizzazione, mobilità e rinforzo a bassa intensità) (49,55) vi è una differenza statisticamente significativa (p< 0,05). In tutti gli studi i gruppi d'intervento migliorano in maniera statisticamente significativa. La rilevanza clinica (MCID ODI = 12,8) viene raggiunta nello studio di Kell RT., Asmundson GJ., et al. 2011, di Atalay E., Akova B., et al. 2017 e nel gruppo che esegue esercizi combinati di forza e stabilizzazione dello studio di Verbrugghe J., Agten A., et al. 2020.

Uno studio confronta un programma di allenamento combinato di forza e cardiorespiratorio ad alta intensità con uno stesso allenamento a moderata intensità (58) e rileva una differenza statisticamente significativa (p< 0.05) tra i gruppi a favore dell'allenamento ad alta intensità. Entrambi i gruppi d'intervento migliorano in maniera statisticamente significativa (p< 0.05) ma solo il gruppo che esegue un programma ad alta intensità raggiunge la rilevanza clinica (MCID ODI= 12,8).

3.4.3 Qualità di vita

Follow up a breve termine (< 6 mesi)

Quattro studi indagano l'efficacia dell'allenamento della forza rispetto ad un gruppo a cui non è concesso l'inizio di alcuna nuova attività fisica (49–52) e tutti rilevano una differenza statisticamente significativa ($p < 0.05$) tra i gruppi, a favore dell'allenamento della forza ad eccezione dello studio di Cortell-Tormo JM., Sanchez PT., et al. In tutti gli studi i gruppi sottoposti ad un allenamento di forza migliorano significativamente ($p < 0.05$) nel breve periodo ad eccezione del gruppo d'intervento dello studio di Cortell-Tormo JM., Sanchez PT., et al.

Uno studio indaga l'efficacia dell'allenamento della forza rispetto ad un allenamento aerobico e dimostra una differenza statisticamente significativa tra i gruppi, a favore dell'allenamento della forza ($p < 0.05$). Il gruppo sottoposto ad un allenamento di forza dimostra un miglioramento statisticamente significativo a 4 mesi ($p < 0.05$).

Tabella 3. Tabella riassuntiva dei risultati degli studi inclusi.

Studio	**Interventi** (tipo, aderenza, drop-out)	←	**Nessuna differenza tra i gruppi**	→	**Confronti** (tipo, aderenza, drop-out)	**Outcomes**
Aasa B., Berglund L., et al. 2015. Follow up: 2 mesi, 12 mesi.	Educazione + High load deadlift Aderenza: 92% Drop-out: 20% ad 1 anno		VAS p= 0.7 (2 mesi) p= 0.5 (12 m)		Educazione + low load motor control Aderenza: 51% Drop-out: 28,6% ad 1 anno	Dolore: VAS
Bruce-Low S., Smith D., et al. 2012. Follow up: 13 sett. Drop-out: 4%	1. Usual care + LEM 1 x sett. 2. Usual care + LEM 2 x sett.	VAS e ODI (1 e 2 vs controllo) p< 0.05			Usual care	Dolore: VAS Disabilità: ODI
Cai C., Yang Y., et al. 2017. Follow up: 4 sett., 2 mesi, 3 mesi, 6 mesi	1. Lower limb exercises Aderenza: 36,9% Drop out: 10,7% a 6 mesi 2. Lumbar extensor ex. Aderenza: 33,8% Drop out: 14,2% a 6 mesi		NPRS p> 0.05 ad ogni follow up		Lumbar stabilization ex. Aderenza: 33,8% Drop out: 10,7% a 6 mesi	Dolore: NPRS
Calatayud J., Guzman-Gonzalez B., et al. 2020. Follow up: 8 sett.	Group based strength training Drop-out: 14,3%		NPRS p= 0.193 RMDQ p= 0.107		Back school program Drop-out: 30,3%	Dolore: NPRS Disabilità: RMDQ
Cortell-Tormo JM., Sanchez PT., et al. 2017. Follow up: 12 sett.	Stabilization + resistance exercises Aderenza: 95% Drop-out: 8,3%	VAS Es 1.45 (p=0.001) ODI Es 1.24 (p=0.023) SF-36 physical Es 0.82 (p=0.045)	SF-36 mental component Es 0.00 (p=0.485)		Nessuna nuova attività fisica Drop-out: 33,3%	Dolore: VAS Disabilità: ODI Qualità della vita: SF-36
Jackson JK., Shepherd TR., 2011. Follow up: 8 sett., 12 sett. Drop-out: 11.1%	1. Middle-age Periodized Resistance Training (PRT) 2. Old-age PRT	VAS, ODI, SF-36 (1 e 2 vs. controllo) p< 0.05 a 12 sett.			Nessuna nuova attività fisica	Dolore: VAS Disabilità: ODI Qualità di vita: SF-36

Kell RT., Asmundson GJ., 2008. Follow up: 8 sett., 16 sett. Drop-out: 18,2%	Periodized Resistance training	VAS, ODI, SF-36 (intervento vs. 1 e 2) p< 0.05 a 16 sett.		ODI, SF-36 mental (1 vs. 2) p< 0.05 a 16 sett.	1. Periodized Aerobic training 2. Nessuna nuova attività fisica	Dolore: VAS Disabilità: ODI Qualità di vita: SF-36
Kell RT., Risi AD., 2011. Follow up: 9 sett., 13 sett. Aderenza: 84% per il 47% dei soggetti. Drop-out: 13,8%	1. Periodized Resistance training (PRT) 2 x sett. 2. PRT 3 x sett. 3. PRT 4 x sett.	VAS, ODI, SF-36 (1,2 e 3 vs. control) p< 0.05 ad ogni follow up VAS, ODI, SF-36 (3 vs. 1 e 2) p< 0.05 a 13 sett.			Usual care	Dolore: VAS Disabilità: ODI Qualità di vita: SF-36
Madadi-Shad M., Jafarnezhadgero AA., 2020. Follow up: 14 sett. Drop-out: 0%	Ankle evertor stretching + Resistance Band Exercises	VAS Es 4.1 (p< 0.001) RMDQ Es 3 (p< 0.001)			Nessuna nuova attività fisica	Dolore: VAS Disabilità: RMDQ
Smith B., Bissel G., et al. 2011. Follow up: 12 sett.	1. LEM con STAB pelvica Drop-out: 6,3% 2. LEM no STAB Drop-out: 11,8%	VAS (1 vs. 2 e controllo) p< 0,05 Es. 0,71 ODI (1 vs. 2 e controllo) p< 0,05 Es. 1.05			Usual care Drop-out: 7,7%	Dolore: VAS Disabilità: ODI
Steele J., Bruce-Low S., et al. 2013. Follow up: 12 sett. Aderenza: > o = 75%	1. Usual care + LEM fullROM Drop-out: 16,7% 2. Usual care + LEM limROM Drop-out: 30%	VAS (1 vs. controllo) p= 0.002 ODI (1 e 2 vs. controllo) p< 0.05	VAS (2 vs. controllo) p= 0.058		Usual care Drop-out: 22,2%	Dolore: VAS Disabilità: ODI

Verbrugghe J., Agten A., et al. 2020. Follow up: 12 sett. Aderenza: 97,5%	1. HITSTRE Drop-out: 14,3% 2. HITCOM Drop-out: 5,3%		NPRS e MODI (1 vs. 2 vs. 3 vs. 4) p= 0.176 e p= 0.107		3. HITSTAB Drop-out: 10% 4. HITMOB Drop-out: 10%	Dolore: NPRS Disabilità: MODI
Verbrugghe J., Agten A., et al. 2019. Follow up: 12 sett. Aderenza: 97,5%	High intensity training Drop-out: 5,3%	MODI p< 0,05	NPRS p= 0,08		Moderate intensity training Drop-out: 10,5%	Dolore: NPRS Disabilità: MODI
Atalay E., Akova B., et al. 2017. Follow up: 45 giorni Drop-out: 0%	Conventional + upper trunk/limb exercises	VAS e MODI p< 0.01 e p< 0.001			Conventional exercises	Dolore: VAS Disabilità: MODI

4) DISCUSSIONE

L'obiettivo di questa revisione era quello di indagare l'efficacia dell'allenamento della forza nel CNSLBP eseguito secondo parametri validati di intensità e progressione dei carichi. A nostra conoscenza questa è la prima revisione che adotta criteri così dettagliati riguardo gli interventi proposti: scelta volta a garantire la selezione di interventi standardizzati e personalizzati per ottenere una migliore applicabilità clinica e generalizzabilità dei risultati. In linea generale tutti gli studi sono concordi nel provare che l'allenamento della forza, da solo o in combinazione ad altre forme di esercizio, abbia un alto impatto nel ridurre dolore, disabilità e migliorare la qualità di vita nel breve termine. Questa modalità di allenamento inoltre risulta essere maggiormente efficace rispetto al non esercizio e all'usual care mentre risultati controversi si hanno confrontandola ad altre forme di esercizio: sembrerebbe produrre maggiori benefici rispetto all'allenamento aerobico e ma ha un'efficacia simile ad esercizi per il controllo motorio, di stabilizzazione e di mobilità e ad un programma di back school. Non si possono, infine, trarre conclusioni rilevanti sull'efficacia a medio e lungo termine data la carenza di studi, sebbene i 2 studi inclusi con follow up più lunghi suggeriscono che i risultati ottenuti dall'allenamento, per quanto riguarda il dolore, possano essere mantenuti fino a 10 mesi dopo il termine dell'intervento (45,47).

I risultati di questo studio sono in linea con precedenti revisioni riguardo l'allenamento della forza nel CNSLBP, con alcune eccezioni. Alcune revisioni hanno ipotizzato che una determinata modalità di esercizio possa avere un'efficacia differente in relazione al tipo di outcome esaminato e suggeriscono che il Pilates, gli esercizi di stabilizzazione/controllo motorio e l'allenamento di forza sono le migliori forme di esercizio per il trattamento del CNSLBP (35,38). Dagli studi inclusi in questa revisione non si evincono differenze nette di efficacia in relazione agli outcome dolore, disabilità o qualità della vita ma, in accordo con i precedenti studi, gli esercizi di stabilizzazione/controllo motorio e l'allenamento di forza sembrano essere le migliori strategie e non vi sono differenze significative tra loro. Un'altra questione è evidenziata dalla revisione di Tataryn N., Simas V., et al. 2021 (39) e riguarda la durata dei programmi di allenamento. Secondo questo studio, programmi che durano 12-16 settimane hanno risultati migliori rispetto a programmi di 6-8 settimane. Sebbene questa tesi, a nostro avviso, sia principalmente frutto della differenza tra i gruppi di confronto degli studi

inclusi e non ad una differenza significativa tra i gruppi che si allenano 6-8 settimane e quelli di 12-16 settimane, i dati di alcuni RCT inclusi nella presente revisione rilevano un trend in miglioramento dalle 8 settimane in poi. In effetti allenamenti di durata maggiore potrebbero essere più efficaci in soggetti con CNSLBP poiché potrebbero migliorarne ulteriormente la qualità muscolo-tendinea. Secondo alcuni autori l'atrofia dei muscoli estensori del tronco non è solo associata, ma è anche predittiva di LBP e potrebbe contribuire al mantenimento del dolore nei soggetti con CNSLBP (65). In questo senso, allenamenti di durata inferiore alle 8 settimane potrebbero non essere sufficienti a migliorare la qualità muscolare dei soggetti in quanto gli aumenti di forza in questa fase sono causati maggiormente da modificazioni neurali piuttosto che muscolari e più tempo potrebbe essere richiesto per ottenere un evidente risultato in termini di trofismo (66). Infine, una revisione del 2018 ha analizzato studi che confrontano l'allenamento di forza e l'allenamento aerobico nel CNSLBP ma nella presente revisione, dallo screening degli RCTs, solo uno studio che confronta queste due forme di esercizio è risultato eleggibile per l'inclusione. Secondo questo studio l'allenamento di forza ha un'efficacia maggiore rispetto all'allenamento aerobico, risultato concorde con la precedente revisione. E' però opportuno precisare che sia gli studi inclusi nella revisione passata sia lo studio incluso nella presente revisione prevedono protocolli di allenamento aerobico a bassa intensità: nell'RCT incluso l'intensità a cui si allena il gruppo di controllo è pari 8-12 sulla scala Borg RPE (67). Altri autori però indicano che l'esercizio aerobico risulta essere efficace nel ridurre il dolore solo ad alte intensità (70% del consumo massimo di ossigeno), dunque studi che includono interventi a intensità più elevate sono necessari per trarre delle raccomandazioni affidabili (68).

Sebbene gli studi includano pazienti con diagnosi di CNSLBP spesso adottano ulteriori restrizioni nei criteri d'inclusione riguardo il grado di attività fisica (sedentari o sportivi amatoriali), l'età, il sesso, coesistenti condizioni cliniche (piede piatto), la dimensione del dolore (meccanico-nocicettivo), specifiche soglie di riferimento sui patient-reported outcomes (NPRS >2 e <4) e la situazione lavorativa (no lavori pesanti). Inoltre le modalità con cui viene svolto l'esercizio sono differenti tra i vari studi: variano i setting terapeutici (palestra o clinica), le resistenze utilizzate (theraband, pesi o macchinari da palestra), se è presente/assente un supervisore e la posologia dell'esercizio. Questa variabilità tra gli studi ne limita l'applicabilità clinica sebbene, in linea generale, queste differenze non sembrano avere un impatto importante sui risultati dell'intervento che si dimostra egualmente efficace nella maggioranza degli studi. Per quanto riguarda la posologia dell'allenamento della forza nel CNSLBP si ha nessuna o poche indicazioni specifiche e gli RCTs inclusi fanno per lo più riferimento a raccomandazioni

estratte da studi su soggetti sani (40,41). Oltre alla questione della durata del programma di allenamento discussa in precedenza, anche frequenza, volume, intensità, periodo di riposo, ordine e tipo di esercizi e modalità di progressione dei carichi cambiano tra gli studi e possono essere fattori determinanti l'efficacia di un programma di allenamento. Due degli studi inclusi (52,58), uno di scarsa qualità ed uno di moderata qualità, hanno confrontato allenamenti a frequenza ed intensità differente concludendo che una frequenza di allenamento di 4 volte a settimana ed un allenamento ad alta intensità (>80% RM) siano maggiormente efficaci di interventi ad intensità e frequenza minore. In aggiunta, uno studio di moderata qualità (47) indaga quali debbano essere i muscoli target dell'esercizio, includendo allenamenti per gli arti inferiori e allenamenti per i muscoli del tronco e suggerendo che risultati leggermente migliori si ottengono in chi allena gli arti inferiori. Pochi studi però sono disponibili rispetto alla variabilità che può presentare un programma di allenamento e che mettono a confronto l'efficacia di una sola variabile. Un ulteriore differenza tra gli interventi proposti nei vari studi riguarda gli interventi concomitanti all'allenamento della forza. Negli RCTs inclusi nella revisione infatti l'allenamento della forza è spesso abbinato ad esercizi di stabilizzazione/controllo motorio ma è anche stato abbinato ad interventi di PNE, all'allenamento aerobico e ad usual care. Essendo il CNSLBP una condizione che presenta diversi impairments psicofisici, la combinazione di diversi interventi potrebbe essere vincente nel migliorare le condizioni cliniche di questi pazienti. Dal punto di vista muscolo-scheletrico questi pazienti possono presentare non solo una ridotta forza, resistenza e trofismo dei muscoli del tronco, ma anche un ritardo di attivazione o un mancato rilascio di questi muscoli durante attività funzionali e questi impairments possono contribuire alla cronicizzazione o alla disabilità di questi pazienti (37,69,70). Abbinare dunque all'allenamento della forza gli esercizi per il controllo motorio potrebbe, oltre ad incrementare forza, resistenza e trofismo, ripristinare l'organizzazione neuromotoria dei muscoli del tronco, apportando un ulteriore beneficio in questi pazienti (71). Questo potrebbe essere il razionale alla base del risultato dello studio di Verbrugghe J., Agten A., et al. 2020 nel quale il gruppo che esegue una combinazione di allenamento di forza ed esercizi di stabilizzazione ottiene risultati leggermente migliori in termini di disabilità rispetto a chi esegue solo una delle 2 forme di allenamento. In aggiunta alcuni soggetti potrebbero presentare impairments psicologici quali kinesifobia e catastrofizzazione (72). In questi soggetti un approccio educativo in combinazione con l'allenamento della forza potrebbe ridurre la pericolosità percepita e l'autoefficacia nei confronti dello sforzo fisico o più in generale riguardo i movimenti della colonna vertebrale

aumentando i livelli di attività fisica dei pazienti, la compliance al programma di allenamento e i benefici dell'esercizio (68,73,74).

4.1. Considerazioni sul rischio di bias

La qualità degli studi nel complesso è stata bassa: 9 studi sono stati valutati come "high risk", 4 studi come "some concerns" e 1 studio come "low risk". Il parametro valutato come "high risk" con più frequenza è stato il "Risk of bias in measurement of the outcome", in parte a causa della natura stessa dell'intervento che delle misure di outcome considerate. Dato che i soggetti sono sia partecipanti che valutatori, in quanto gli outcome considerati sono patient-reported, è possibile che la conoscenza dell'intervento abbia influito sulla valutazione. Questa interferenza è maggiormente probabile per gli studi che confrontano gruppi di non intervento o usual care e per follow-up a breve termine. In aggiunta, i soggetti, nella quasi totalità degli studi, erano a conoscenza dell'intero design dello studio e quindi anche degli interventi di confronto. Il parametro valutato più frequentemente come "some concerns" è stato il "Risk of bias in selection of the reported result", principalmente perché la maggior parte degli studi non presentava un protocollo di studio registrato e nessuno presentava un piano d'analisi. In circa la metà degli studi il parametro "missing outcome data" è stato valutato come "high risk" in primo luogo perché molti degli studi inclusi non hanno eseguito un Intention to Treat Analysis e/o perché avevano un alto tasso di drop-out (> 20%). Infine pochi studi hanno descritto nel dettaglio la modalità di randomizzazione e solo 3 studi hanno applicato un "allocation concealment" adeguato.

5) CONCLUSIONI

L'allenamento di forza è un'ottima opzione di trattamento per i soggetti con CNSLBP. Sebbene le caratteristiche degli studi varino sia in termini di popolazione che di posologia dell'esercizio, tutti gli studi concludono che questa forma di intervento sia efficace nel migliorare gli outcome fondamentali per questi pazienti (64). Gli effetti dell'intervento infatti sembrano simili a dispetto delle varie forme di resistenza utilizzate (theraband, pesi e macchine da palestra) il che rende l'intervento applicabile in molti setting terapeutici (in palestra, presso uno studio, presso il domicilio del paziente o altri). La costante riscontrabile nei vari studi è che l'esercizio deve essere eseguito ad intensità medio-alta anche se è consigliabile nelle prime settimane adattare

l'intensità dell'allenamento al grado di attività, alla qualità muscolare e alle preferenze del soggetto. Alcuni dei protocolli di allenamento adottati negli RCTs inclusi utilizzano una resistenza medio-bassa nelle prime 2-4 settimane di allenamento per poi incrementarla gradualmente nelle settimane successive fino a raggiungere intensità elevate. Per quanto riguarda durata e frequenza dell'allenamento è opportuno ricorrere a programmi con una frequenza di almeno 2 volte a settimana e una durata di almeno 8 settimane sebbene una frequenza di 4 volte a settimana e una durata oltre le 12 settimane potrebbero apportare benefici maggiori. Un'altra questione rilevante riguarda l'abbinamento di più interventi. L'allenamento di forza, sebbene permetta di ottenere buoni risultati nel trattamento dei pazienti con CNSLBP, non è però risolutivo e può avere un'efficacia diversa a seconda della presentazione e della storia clinica del paziente, dunque affiancare uno o più tipi di intervento ad esso potrebbe apportare un ulteriore beneficio ai pazienti.

La letteratura ad oggi ha adottato criteri vaghi nello studio dell'allenamento della forza. In molti studi gli allenamenti non sono descritti con sufficiente minuziosità e troppi parametri rimangono occultati. Infatti tra i molti studi citati da precedenti revisioni riguardo l'allenamento della forza pochi sono risultati eleggibili per la presente revisione. La nostra revisione ha infatti adottato come criterio per l'inclusione degli studi l'utilizzo di una scala validata per impostare l'intensità e la progressione dell'allenamento. Questo parametro è fondamentale per rendere replicabile ma anche personalizzato l'allenamento e i prossimi studi dovranno presentare una descrizione così dettagliata degli interventi. Inoltre confrontare allenamenti di forza tra i quali differisce un solo parametro è opportuno per rilevare quale sia la posologia migliore. Come detto in precedenza il CNSLBP è una condizione che esibisce numerose presentazioni cliniche in quanto può presentare diversi impairments psicofisici. Data questa premessa potrebbe risultare che l'allenamento della forza sia più efficace per alcuni sottogruppi di pazienti rispetto ad altri o che interventi combinati soddisfino con maggior completezza le richieste di aiuto dei soggetti. A nostro avviso la ricerca futura dovrà indagare ciò che riguarda il management del CNSLBP secondo questa via, producendo una letteratura meno confusa e di maggiore qualità.

5.1. Forza e limiti dello studio

A nostra conoscenza, ad oggi questa è l'unica revisione sistematica che indaga l'efficacia dell'allenamento della forza nei soggetti con chronic low back pain per quanto riguarda dolore, disabilità e qualità della vita ed è l'unica che ha utilizzato come strumento di valutazione della

qualità degli studi la Cochrane Collaboration's Risk of Bias tool 2.0" (R.o.B.2). La peculiarità maggiore di questa revisione però risiede nei criteri di inclusione adottati. Questi risultano essere molto specifici per quanto riguarda la descrizione dell'intervento il che da un lato garantisce una migliore applicabilità clinica e generalizzabilità dei risultati ma dall'altro restringe il campo della ricerca e di conseguenza il numero degli studi inclusi. Altri limiti di questa revisione riguardano il possibile rischio di reporting bias in quanto i database sui quali è stata condotta la ricerca sono pochi e limiti derivanti dalla qualità degli studi inclusi che è generalmente scarsa.

5.2. Key points

1) L'allenamento della forza è una strategia utile per trattare i pazienti con chronic low back pain in particolare su outcome quali dolore, disabilità e qualità di vita;
2) Intensità elevata e durata e frequenza maggiori rispetto ai protocolli descritti possono apportare benefici maggiori in questo tipo di pazienti ma ulteriori studi e di maggiore qualità sono necessari per individuare la posologia migliore per il trattamento di questa condizione;
3) L'integrazione di questa forma di intervento in un approccio biopsicosociale potrebbe risultare più efficace per alcune tipologie di pazienti, in questo senso ulteriori studi sono necessari rispetto a sottogruppi specifici di pazienti.

Bibliografia

1. Hartvigsen J, Hancock MJ, Kongsted A, Louw Q, Ferreira ML, Genevay S, et al. What low back pain is and why we need to pay attention [Internet]. Vol. 391, The Lancet. Lancet Publishing Group; 2018 [cited 2021 Jun 30]. p. 2356–67. Available from: https://pubmed.ncbi.nlm.nih.gov/29573870/

2. Koes BW, Van Tulder MW, Thomas S. Diagnosis and treatment of low back pain [Internet]. Vol. 332, British Medical Journal. BMJ Publishing Group; 2006 [cited 2021 Jun 30]. p. 1430–4. Available from: https://pubmed.ncbi.nlm.nih.gov/16777886/

3. Maher C, Underwood M, Buchbinder R. Non-specific low back pain [Internet]. Vol. 389, The Lancet. Lancet Publishing Group; 2017 [cited 2021 Jun 30]. p. 736–47. Available from: https://pubmed.ncbi.nlm.nih.gov/27745712/

4. Rubin DI. Epidemiology and Risk Factors for Spine Pain [Internet]. Vol. 25, Neurologic Clinics. Neurol Clin; 2007 [cited 2021 Jul 4]. p. 353–71. Available from: https://pubmed.ncbi.nlm.nih.gov/17445733/

5. Wu A, March L, Zheng X, Huang J, Wang X, Zhao J, et al. Global low back pain prevalence and years lived with disability from 1990 to 2017: estimates from the Global Burden of Disease Study 2017. Ann Transl Med [Internet]. 2020 Mar [cited 2021 Jul 4];8(6):299–299. Available from: https://pubmed.ncbi.nlm.nih.gov/32355743/

6. Jin Z, Wang D, Zhang H, Liang J, Feng X, Zhao J, et al. Incidence trend of five common musculoskeletal disorders from 1990 to 2017 at the global, regional and national level: Results from the global burden of disease study 2017. Ann Rheum Dis [Internet]. 2020 Aug 1 [cited 2021 Jul 4];79(8):1014–22. Available from: https://pubmed.ncbi.nlm.nih.gov/32414807/

7. Monasta L, Abbafati C, Logroscino G, Remuzzi G, Perico N, Bikbov B, et al. Italy's health performance, 1990–2017: findings from the Global Burden of Disease Study 2017. Lancet Public Heal [Internet]. 2019 Dec 1 [cited 2021 Jul 4];4(12):e645–57. Available from: https://pubmed.ncbi.nlm.nih.gov/31759893/

8. Schofield DJ, Shrestha RN, Passey ME, Earnest A, Fletcher SL. Chronic disease and labour force participation among older Australians. Med J Aust [Internet]. 2008 Oct 20 [cited 2021 Jul 4];189(8):447–50. Available from: https://pubmed.ncbi.nlm.nih.gov/18928439/

9. Da Silva T, Mills K, Brown BT, Herbert RD, Maher CG, Hancock MJ. Risk of recurrence of low back pain: A systematic review [Internet]. Vol. 47, Journal of Orthopaedic and Sports Physical Therapy. Movement Science Media; 2017 [cited 2021 Jul 4]. p. 305–13. Available from: https://pubmed.ncbi.nlm.nih.gov/28355981/

10. Coombs DM, Machado GC, Richards B, Oliveira CB, Herbert RD, Maher CG. Clinical course of patients with low back pain following an emergency department presentation: a systematic review and meta-analysis. Emerg Med J [Internet]. 2020 Sep 11 [cited 2021 Jul 4];emermed-2019-209294. Available from: https://pubmed.ncbi.nlm.nih.gov/32917748/

11. Downie AS, Hancock MJ, Rzewuska M, Williams CM, Lin CWC, Maher CG. Trajectories of acute low back pain: A latent class growth analysis. Pain [Internet]. 2016 Jan 1 [cited 2021 Jul 4];157(1):225–34. Available from: https://pubmed.ncbi.nlm.nih.gov/26397929/

12. Hayden JA, Chou R, Hogg-Johnson S, Bombardier C. Systematic reviews of low back pain prognosis had variable methods and results-guidance for future prognosis reviews [Internet]. Vol. 62, Journal of Clinical Epidemiology. Elsevier USA; 2009 [cited 2021 Jul 4]. Available from: https://pubmed.ncbi.nlm.nih.gov/19136234/

13. Qaseem A, Wilt TJ, McLean RM, Forciea MA. Noninvasive treatments for acute, subacute, and chronic low back pain: A clinical practice guideline from the American College of Physicians [Internet]. Vol. 166, Annals of Internal Medicine. American College of Physicians; 2017 [cited 2021 Jul 4]. p. 514–30. Available from: https://pubmed.ncbi.nlm.nih.gov/28192789/

14. Wong JJ, Côté P, Sutton DA, Randhawa K, Yu H, Varatharajan S, et al. Clinical practice guidelines for the noninvasive management of low back pain: A systematic review by the Ontario Protocol for Traffic Injury Management (OPTIMa) Collaboration [Internet]. Vol. 21, European Journal of Pain (United Kingdom). Blackwell Publishing Ltd; 2017 [cited 2021 Jul 4]. p. 201–16. Available from: https://pubmed.ncbi.nlm.nih.gov/27712027/

15. De Medicina Fisica E Reabilitacao AB. Lombalgia inespecífica crônica: reabilitação. Rev Assoc Med Bras [Internet]. 2013 Nov [cited 2021 Jul 4];59(6):536–53. Available from: https://pubmed.ncbi.nlm.nih.gov/24239032/

16. Delitto A, George SZ, Van Dillen LR, Whitman JM, Sowa G, Shekelle P, et al. Low back pain. J Orthop Sports Phys Ther [Internet]. 2012 [cited 2021 Jul 4];42(4). Available from: https://pubmed.ncbi.nlm.nih.gov/22466247/

17. Chou R, Qaseem A, Snow V, Casey D, Cross TJ, Shekelle P, et al. Diagnosis and treatment of low back pain: A joint clinical practice guideline from the American College of Physicians and the American Pain Society [Internet]. Vol. 147, Annals of Internal Medicine. American College of Physicians; 2007 [cited 2021 Jul 4]. p. 478–91. Available from: https://pubmed.ncbi.nlm.nih.gov/17909209/

18. Miyamoto GC, Lin CWC, Cabral CMN, Van Dongen JM, Van Tulder MW. Cost-effectiveness of exercise therapy in the treatment of non-specific neck pain and low back pain: A systematic review with meta-analysis [Internet]. Vol. 53, British Journal of Sports Medicine. BMJ Publishing Group; 2019 [cited 2021 Jul 5]. p. 172–81. Available from: https://pubmed.ncbi.nlm.nih.gov/29678893/

19. Saragiotto BT, Maher CG, Yamato TP, Costa LOP, Menezes Costa LC, Ostelo RWJG, et al. Motor control exercise for chronic non-specific low-back pain [Internet]. Vol. 2016, Cochrane Database of Systematic Reviews. John Wiley and Sons Ltd; 2016 [cited 2021 Jul 5]. Available from: https://pubmed.ncbi.nlm.nih.gov/26742533/

20. Wun A, Kollias P, Jeong H, Rizzo RR, Cashin AG, Bagg MK, et al. Why is exercise prescribed for people with chronic low back pain? A review of the mechanisms of benefit proposed by clinical trialists [Internet]. Vol. 51, Musculoskeletal Science and Practice. Elsevier Ltd; 2021 [cited 2021 Jul 5]. Available from: https://pubmed.ncbi.nlm.nih.gov/33254007/

21. Wewege MA, Booth J, Parmenter BJ. Aerobic vs. resistance exercise for chronic non-specific low back pain: A systematic review and meta-analysis. J Back Musculoskelet Rehabil [Internet]. 2018 [cited 2021 Jul 5];31(5):889–99. Available from: https://pubmed.ncbi.nlm.nih.gov/29889056/

22. Gomes-Neto M, Lopes JM, Conceição CS, Araujo A, Brasileiro A, Sousa C, et al. Stabilization exercise compared to general exercises or manual therapy for the management of low back pain: A systematic review and meta-analysis [Internet]. Vol. 23, Physical Therapy in Sport. Churchill Livingstone; 2017 [cited 2021 Jul 5]. p. 136–42. Available from: https://pubmed.ncbi.nlm.nih.gov/27707631/

23. N L, CJ L. Strength training in older adults: the benefits for osteoarthritis. Clin Geriatr Med [Internet]. 2010 Aug [cited 2021 Jul 7];26(3):445–59. Available from: https://pubmed.ncbi.nlm.nih.gov/20699165/

24. JP R, MM L-C, L T, C N, I B, L B, et al. High-intensity versus low-intensity physical activity or exercise in people with hip or knee osteoarthritis. Cochrane database Syst Rev [Internet]. 2015 Oct 29 [cited 2021 Jul 7];2015(10). Available from: https://pubmed.ncbi.nlm.nih.gov/26513223/

25. M F, S M, AR H, M V der E, M S, KL B. Exercise for osteoarthritis of the knee: a Cochrane systematic review. Br J Sports Med [Internet]. 2015 Dec 1 [cited 2021 Jul 7];49(24):1554–7. Available from: https://pubmed.ncbi.nlm.nih.gov/26405113/

26. E H, FJ van der G, TP VV, J S, EC V den E. Dynamic exercise programs (aerobic capacity and/or muscle strength training) in patients with rheumatoid arthritis. Cochrane database Syst Rev [Internet]. 2009 [cited 2021 Jul 7];2009(4). Available from: https://pubmed.ncbi.nlm.nih.gov/19821388/

27. A B, M V, M G, R J, P G. Efficacy of resistance exercises in rheumatoid arthritis: meta-analysis of randomized controlled trials. Rheumatology (Oxford) [Internet]. 2012 Mar [cited 2021 Jul 7];51(3):519–27. Available from: https://pubmed.ncbi.nlm.nih.gov/22120463/

28. H H, A X, C G, Z W, X W. The effect of physical exercise on rheumatoid arthritis: An overview of systematic reviews and meta-analysis. J Adv Nurs [Internet]. 2021 Feb 1 [cited 2021 Jul 7];77(2):506–22. Available from: https://pubmed.ncbi.nlm.nih.gov/33176012/

29. A A, R de AKS, SM S, LA PT, G TV. A systematic review of the effects of strength training in patients with fibromyalgia: clinical outcomes and design considerations. Adv Rheumatol (London, England) [Internet]. 2018 Oct 22 [cited 2021 Jul 7];58(1):36. Available from: https://pubmed.ncbi.nlm.nih.gov/30657077/

30. A W, H B, W B, C D, P H, P H, et al. [Physiotherapy, occupational therapy and physical therapy in fibromyalgia syndrome : Updated guidelines 2017 and overview of systematic review articles]. Schmerz [Internet]. 2017 Jun 1 [cited 2021 Jul 7];31(3):255–65. Available from: https://pubmed.ncbi.nlm.nih.gov/28493223/

31. VM I, O V, PJ M, MS F. Resistance training vs general physical exercise in multidisciplinary rehabilitation of chronic neck pain: A randomized controlled trial. J Rehabil Med [Internet]. 2018 [cited 2021 Jul 7];50(8):743–50. Available from: https://pubmed.ncbi.nlm.nih.gov/30132009/

32. A G, TM K, JP P, S B, P L, T C, et al. Exercises for mechanical neck disorders. Cochrane database Syst Rev [Internet]. 2015 Jan 28 [cited 2021 Jul 7];1(6). Available from:

https://pubmed.ncbi.nlm.nih.gov/25629215/

33. M F, R B. Systematic Review and Meta-Analysis Suggest Strength Training and Workplace Modifications May Reduce Neck Pain in Office Workers. Pain Pract [Internet]. 2021 Jan 1 [cited 2021 Jul 7];21(1):100–31. Available from: https://pubmed.ncbi.nlm.nih.gov/32657531/

34. EG C, JM R-S. Resistance Training as a Tool for Preventing and Treating Musculoskeletal Disorders. Sports Med [Internet]. 2016 Sep 1 [cited 2021 Jul 11];46(9):1239–48. Available from: https://pubmed.ncbi.nlm.nih.gov/26914266/

35. PJ O, CT M, NL M, SJJM V, SD T, H B, et al. Which specific modes of exercise training are most effective for treating low back pain? Network meta-analysis. Br J Sports Med [Internet]. 2020 Nov 1 [cited 2021 Jul 11];54(21):1279–87. Available from: https://pubmed.ncbi.nlm.nih.gov/31666220/

36. SD T, CT M, PJ O, UH M, H B, B F, et al. Domains of Chronic Low Back Pain and Assessing Treatment Effectiveness: A Clinical Perspective. Pain Pract [Internet]. 2020 Feb 1 [cited 2021 Jul 11];20(2):211–25. Available from: https://pubmed.ncbi.nlm.nih.gov/31610090/

37. JD D, J A, C S-P, M P, M D. Neuromuscular adaptations predict functional disability independently of clinical pain and psychological factors in patients with chronic non-specific low back pain. J Electromyogr Kinesiol [Internet]. 2014 [cited 2021 Jul 11];24(4):550–7. Available from: https://pubmed.ncbi.nlm.nih.gov/24837629/

38. A S, M S, A H, V C. Exercise interventions for the treatment of chronic low back pain: a systematic review and meta-analysis of randomised controlled trials. Clin Rehabil [Internet]. 2015 Dec 1 [cited 2021 Jul 15];29(12):1155–67. Available from: https://pubmed.ncbi.nlm.nih.gov/25681408/

39. N T, V S, T C, J F, JWL K. Posterior-Chain Resistance Training Compared to General Exercise and Walking Programmes for the Treatment of Chronic Low Back Pain in the General Population: A Systematic Review and Meta-Analysis. Sport Med - open [Internet]. 2021 Dec 1 [cited 2021 Jul 16];7(1). Available from: https://pubmed.ncbi.nlm.nih.gov/33683497/

40. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. Med Sci Sports Exerc [Internet]. 2009 Mar [cited 2021 Jul 17];41(3):687–708. Available from: https://pubmed.ncbi.nlm.nih.gov/19204579/

41. CE G, B B, MR D, BA F, MJ L, IM L, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. Med Sci Sports Exerc [Internet]. 2011 Jul [cited 2021 Jul 17];43(7):1334–59. Available from: https://pubmed.ncbi.nlm.nih.gov/21694556/

42. A L, DG A, J T, C M, PC G, JP I, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ [Internet]. 2009 [cited 2021 Jul 15];339. Available from: https://pubmed.ncbi.nlm.nih.gov/19622552/

43. RD T, W R, A B, Q A, MI B, R B, et al. A classification of chronic pain for ICD-11. Pain [Internet]. 2015 [cited 2021 Jul 15];156(6):1003–7. Available from: https://pubmed.ncbi.nlm.nih.gov/25844555/

44. JAC S, J S, MJ P, RG E, NS B, I B, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ [Internet]. 2019 [cited 2021 Jul 15];366. Available from: https://pubmed.ncbi.nlm.nih.gov/31462531/

45. B A, L B, P M, U A. Individualized low-load motor control exercises and education versus a high-load lifting exercise and education to improve activity, pain intensity, and physical performance in patients with low back pain: a randomized controlled trial. J Orthop Sports Phys Ther [Internet]. 2015 Feb 1 [cited 2021 Jul 15];45(2):77–85. Available from: https://pubmed.ncbi.nlm.nih.gov/25641309/

46. S B-L, D S, S B, J F, G B, L W. One lumbar extension training session per week is sufficient for strength gains and reductions in pain in patients with chronic low back pain ergonomics. Ergonomics [Internet]. 2012 Apr [cited 2021 Jul 15];55(4):500–7. Available from: https://pubmed.ncbi.nlm.nih.gov/22397454/

47. C C, Y Y, PW K. Comparison of Lower Limb and Back Exercises for Runners with Chronic Low Back Pain. Med Sci Sports Exerc [Internet]. 2017 Dec 1 [cited 2021 Jul 15];49(12):2374–84. Available from: https://pubmed.ncbi.nlm.nih.gov/28767525/

48. J C, B G-G, LL A, C C-M, MT M, R R, et al. Effectiveness of a Group-Based Progressive Strength Training in Primary Care to Improve the Recurrence of Low Back Pain Exacerbations and Function: A Randomised Trial. Int J Environ Res Public Health [Internet]. 2020 Nov 2 [cited 2021 Jul 15];17(22):1–14. Available from:

https://pubmed.ncbi.nlm.nih.gov/33187076/

49. JM C-T, PT S, I C-M, J T-M, C M-L, S L-B, et al. Effects of functional resistance training on fitness and quality of life in females with chronic nonspecific low-back pain. J Back Musculoskelet Rehabil [Internet]. 2018 [cited 2021 Jul 15];31(1):95–105. Available from: https://pubmed.ncbi.nlm.nih.gov/28826168/

50. JK J, TR S, RT K. The influence of periodized resistance training on recreationally active males with chronic nonspecific low back pain. J strength Cond Res [Internet]. 2011 Jan [cited 2021 Jul 15];25(1):242–51. Available from: https://pubmed.ncbi.nlm.nih.gov/20093971/

51. RT K, GJ A. A comparison of two forms of periodized exercise rehabilitation programs in the management of chronic nonspecific low-back pain. J strength Cond Res [Internet]. 2009 Mar [cited 2021 Jul 15];23(2):513–23. Available from: https://pubmed.ncbi.nlm.nih.gov/19209082/

52. RT K, AD R, JM B. The response of persons with chronic nonspecific low back pain to three different volumes of periodized musculoskeletal rehabilitation. J strength Cond Res [Internet]. 2011 Apr [cited 2021 Jul 15];25(4):1052–64. Available from: https://pubmed.ncbi.nlm.nih.gov/20647943/

53. M M-S, AA J, H S, VC D. Effect of a corrective exercise program on gait kinetics and muscle activities in older adults with both low back pain and pronated feet: A double-blind, randomized controlled trial. Gait Posture [Internet]. 2020 Feb 1 [cited 2021 Jul 15];76:339–45. Available from: https://pubmed.ncbi.nlm.nih.gov/31896537/

54. D S, G B, S B-L, C W. The effect of lumbar extension training with and without pelvic stabilization on lumbar strength and low back pain. J Back Musculoskelet Rehabil [Internet]. 2011 [cited 2021 Jul 15];24(4):241–9. Available from: https://pubmed.ncbi.nlm.nih.gov/22142713/

55. J S, S B-L, D S, D J, N O. A randomized controlled trial of limited range of motion lumbar extension exercise in chronic low back pain. Spine (Phila Pa 1976) [Internet]. 2013 Jul 1 [cited 2021 Jul 15];38(15):1245–52. Available from: https://pubmed.ncbi.nlm.nih.gov/23514876/

56. J V, A A, S S, D H, C D, BO E, et al. High Intensity Training to Treat Chronic Nonspecific Low Back Pain: Effectiveness of Various Exercise Modes. J Clin Med [Internet]. 2020 Jul 27 [cited 2021 Jul 15];9(8):2401. Available from: https://pubmed.ncbi.nlm.nih.gov/32727108/

57. E A, B A, H G, U S. Effect of Upper-Extremity Strengthening Exercises on the Lumbar Strength, Disability and Pain of Patients with Chronic Low Back Pain: A Randomized Controlled Study. J Sports Sci Med [Internet]. 2017 Dec 1 [cited 2021 Jul 18];16(4):595–603. Available from: https://pubmed.ncbi.nlm.nih.gov/29238262/

58. J V, A A, S S, D H, C D, B OE, et al. Exercise Intensity Matters in Chronic Nonspecific Low Back Pain Rehabilitation. Med Sci Sports Exerc [Internet]. 2019 Dec 1 [cited 2021 Jul 18];51(12):2434–42. Available from: https://pubmed.ncbi.nlm.nih.gov/31269004/

59. KM L, RJ R. Construct validity of the OMNI resistance exercise scale. J strength Cond Res [Internet]. 2006 May [cited 2021 Jul 28];20(2):252–6. Available from: https://pubmed.ncbi.nlm.nih.gov/16686549/

60. JE G, ML P, D F, SH L, DM C, R V, et al. Effect of training frequency and specificity on isometric lumbar extension strength. Spine (Phila Pa 1976) [Internet]. 1990 [cited 2021 Jul 28];15(6):504–9. Available from: https://pubmed.ncbi.nlm.nih.gov/2144914/

61. AF M, F B, F P, C C. Pain measurement in patients with low back pain. Nat Clin Pract Rheumatol [Internet]. 2007 Nov [cited 2021 Aug 1];3(11):610–8. Available from: https://pubmed.ncbi.nlm.nih.gov/17968331/

62. JT F, JP Y, L L, JL W, MR P. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. Pain [Internet]. 2001 [cited 2021 Aug 1];94(2):149–58. Available from: https://pubmed.ncbi.nlm.nih.gov/11690728/

63. LG J, C H, OP N, K S, JI B, I R, et al. Comparison of the SF6D, the EQ5D, and the oswestry disability index in patients with chronic low back pain and degenerative disc disease. BMC Musculoskelet Disord [Internet]. 2013 [cited 2021 Aug 3];14. Available from: https://pubmed.ncbi.nlm.nih.gov/23622053/

64. RW O, HC de V. Clinically important outcomes in low back pain. Best Pract Res Clin Rheumatol [Internet]. 2005 Aug [cited 2021 Aug 3];19(4):593–607. Available from: https://pubmed.ncbi.nlm.nih.gov/15949778/

65. TA R, FM C, TS J, WL P, SM H, J F, et al. Are the size and composition of the paraspinal muscles associated with low back pain? A systematic review. Spine J [Internet]. 2017 Nov 1 [cited 2021 Aug 14];17(11):1729–48. Available from: https://pubmed.ncbi.nlm.nih.gov/28756299/

66. DC H, S E, K B. Adaptations to Endurance and Strength Training. Cold Spring Harb

Perspect Med [Internet]. 2018 Jun 1 [cited 2021 Aug 14];8(6). Available from: https://pubmed.ncbi.nlm.nih.gov/28490537/

67. Williams N. The Borg Rating of Perceived Exertion (RPE) scale. Occup Med (Chic Ill). 2017 Jul 1;67(5):404–5.

68. D R, J N, E K, T W, MI H, K K, et al. Exercise-Induced Hypoalgesia in Pain-Free and Chronic Pain Populations: State of the Art and Future Directions. J pain [Internet]. 2019 Nov 1 [cited 2021 Aug 16];20(11):1249–66. Available from: https://pubmed.ncbi.nlm.nih.gov/30904519/

69. PW H, CA R. Delayed postural contraction of transversus abdominis in low back pain associated with movement of the lower limb. J Spinal Disord [Internet]. 1998 [cited 2021 Aug 19];11(1):46–56. Available from: https://pubmed.ncbi.nlm.nih.gov/9493770/

70. PH F, ML F, CG M, K R, RD H, PW H. Changes in recruitment of transversus abdominis correlate with disability in people with chronic low back pain. Br J Sports Med [Internet]. 2010 Dec [cited 2021 Aug 19];44(16):1166–72. Available from: https://pubmed.ncbi.nlm.nih.gov/19474006/

71. H T, PW H. Persistence of improvements in postural strategies following motor control training in people with recurrent low back pain. J Electromyogr Kinesiol [Internet]. 2008 Aug [cited 2021 Aug 19];18(4):559–67. Available from: https://pubmed.ncbi.nlm.nih.gov/17336546/

72. MK N, SJ L, PJ W, CJ M. Early identification and management of psychological risk factors ("yellow flags") in patients with low back pain: a reappraisal. Phys Ther [Internet]. 2011 May [cited 2021 Aug 19];91(5):737–53. Available from: https://pubmed.ncbi.nlm.nih.gov/21451099/

73. V B, L S, A C, M T. Effectiveness of communicative and educative strategies in chronic low back pain patients: A systematic review. Patient Educ Couns [Internet]. 2020 May 1 [cited 2021 Aug 19];103(5):908–29. Available from: https://pubmed.ncbi.nlm.nih.gov/31839351/

74. RMA van E, IPJ H, MLG J, J K, RJEM S. Effectiveness of Primary Care Interventions Using a Biopsychosocial Approach in Chronic Low Back Pain: A Systematic Review. Pain Pract [Internet]. 2019 Feb 1 [cited 2021 Aug 19];19(2):224–41. Available from: https://pubmed.ncbi.nlm.nih.gov/30290052/

APPENDICE

Revised Cochrane risk-of-bias tool for randomized trials (RoB 2)
TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne on behalf of the RoB2 Development Group

Version of 22 August 2019

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.

Study details	
Reference	1: Aasa B, Berglund L, Michaelson P, Aasa U. Individualized low-load motor control exercises and education versus a high-load lifting exercise and education to improve activity, pain intensity, and physical performance in patients with low back pain: a randomized controlled trial. J Orthop Sports Phys Ther. 2015 Feb;45(2):77-85, B1-4
Study design	

X Individually-randomized parallel-group trial

☐ Cluster-randomized parallel-group trial

☐ Individually randomized cross-over (or other matched) trial

For the purposes of this assessment, the interventions being compared are defined as

Experimental:	High intensity lifting exercise	Comparator:	Low-load motor control exercise

Specify which outcome is being assessed for risk of bias | Pain

Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed. | Table 2

Is the review team's aim for this result…?

X to assess the effect of *assignment to intervention* (the 'intention-to-treat' effect)

☐ to assess the effect of *adhering to intervention* (the 'per-protocol' effect)

If the aim is to assess the effect of *adhering to intervention*, select the deviations from intended intervention that should be addressed (at least one must be checked):

☐ occurrence of non-protocol interventions

☐ failures in implementing the intervention that could have affected the outcome

☐ non-adherence to their assigned intervention by trial participants

Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)

X Journal article(s) with results of the trial

X Trial protocol

☐ Statistical analysis plan (SAP)

☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)

☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)

☐ "Grey literature" (e.g. unpublished thesis)

☐ Conference abstract(s) about the trial

☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)

☐ Research ethics application

☐ Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)

☐ Personal communication with trialist

☐ Personal communication with the sponsor

Risk of bias assessment

Responses underlined in green are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?	Ref.: "The randomization was performed by a person who had not been in contact with any of the participants." "The randomization was stratified for sex and age […] into 4 groups. Within each group, separate randomization was performed by applying a computer-generated procedure of "n out of N."""	Y / PY / PN / N / NI **Y**
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		Y / PY / PN / N / NI **PY**
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	Table 1	Y / PY / PN / N / NI **NI**
Risk-of-bias judgement		Low / High / Some concerns **Low risk**
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?		NA / Y / PY / PN / N / NI **PN**
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?		NA / Y / PY / PN / N / NI
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?		NA / Y / PY / PN / N / NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Ref: "Linear mixed-model analysis was chosen because it uses all the available information in data in a repeated-measures design and is robust in handling missing data."	Y / PY / PN / N / NI **Y**
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?		NA / Y / PY / PN / N / NI **Low risk**
Risk-of-bias judgement		Low / High / Some concerns

Optional: What is the predicted direction of bias due to deviations from intended interventions?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Figure 2. 24% lost to 12mo follow-up.	Y / PY / PN / N / NI **N**
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	Ref: "Linear mixed-model analysis was chosen because it uses all the available information in data in a repeated-measures design and is robust in handling missing data."	NA / Y / PY / PN / N **PY**
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?		NA / Y / PY / PN / N / NI
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		NA / Y / PY / PN / N / NI
Risk-of-bias judgement	Nonostante il modello usato per analizzare I dati mancanti è ritenuto efficace per ridurre il risk of bias, c'è evidenza che alcuni dati mancanti dipendono dalla natura dell'intervento e dal valore dell'outcome.	Low / High / Some concerns **Some concerns**

Optional: What is the predicted direction of bias due to missing outcome data?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?	Media del dolore (VAS) nella settimana precedente. (Dworkin RH, Turk DC, 2005)	Y / PY / PN / N / NI **N**
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	Table 2	Y / PY / PN / N / NI **N**
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?		NA / Y / PY / PN / N / NI **Y**
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Caratteristiche che riducono il r.o.b.: I 2 gruppi sono 2 gruppi d'intervento; Il valutatore che può aver assistito i soggetti nel compilare il Prom è in cieco; Sono trascorsi 10 mesi dalla fine dell'intervento e l'ultimo follow-up	NA / Y / PY / PN / N / NI **PY**
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI

		PN
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias in measurement of the outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 5: Risk of bias in selection of the reported result

Signalling questions	**Comments**	**Response options**
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	Vedi protocollo NCT01061632. Questo prevedeva un follow-up a 6 mesi che non è stato riportato.	Y / PY / PN / N / NI **PN**
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?		Y / PY / PN / N / NI **NI**

5.3 ... multiple eligible analyses of the data?	Nelle tabelle dei risultati sono presenti tutte le analisi dichiarate nella sezione Metodi.	Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias due to selection of the reported result?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall risk of bias

Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the overall predicted direction of bias for this outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Study details

Reference	Cai C, Yang Y, Kong PW. Comparison of Lower Limb and Back Exercises for Runners with Chronic Low Back Pain. Med Sci Sports Exerc. 2017 Dec;49(12):2374-2384

Study design

X Individually-randomized parallel-group trial

☐ Cluster-randomized parallel-group trial

☐ Individually randomized cross-over (or other matched) trial

For the purposes of this assessment, the interventions being compared are defined as

Experimental:	LL strength training	Comparator:	LE training/Lumbar stabilization

Specify which outcome is being assessed for risk of bias	Pain
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.	Table 2

Is the review team's aim for this result…?

X to assess the effect of *assignment to intervention* (the 'intention-to-treat' effect)

☐ to assess the effect of *adhering to intervention* (the 'per-protocol' effect)

If the aim is to assess the effect of *adhering to intervention*, select the deviations from intended intervention that should be addressed (at least one must be checked):

☐ occurrence of non-protocol interventions

☐ failures in implementing the intervention that could have affected the outcome

☐ non-adherence to their assigned intervention by trial participants

Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)

X Journal article(s) with results of the trial

☐ Trial protocol

☐ Statistical analysis plan (SAP)

☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)

☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)

☐ "Grey literature" (e.g. unpublished thesis)

☐ Conference abstract(s) about the trial

☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)

☐ Research ethics application

☐ Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)

☐ Personal communication with trialist

☐ Personal communication with the sponsor

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?	Ref: "Using a block randomization table, participants were evenly allocated into one of the three treatment groups (n = 28 per group with even sex distribution): 1) LL exercises, 2) LE exercises, and 3) LS exercises."	Y / PY / PN / N / NI **PY**
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		Y / PY / PN / N / NI **NI**
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	Table 1	Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?		NA / Y / PY / PN / N / NI **PN**
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?		NA / Y / PY / PN / N / NI
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?		NA / Y / PY / PN / N / NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?		Y / PY / PN / N / NI **Y**
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?		NA / Y / PY / PN / N / NI
Risk-of-bias judgement		Low / High / Some concerns

		Low risk
Optional: What is the predicted direction of bias due to deviations from intended interventions?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 3: Missing outcome data

Signalling questions	**Comments**	**Response options**
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Figure 1. 12% drop-out	Y / PY / PN / N / NI **N**
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	Ref: "Given GEE's capability of handling outcomes with missing data and various correlations between time points (32), we could include all 84 participants' data in the analysis."	NA / Y / PY / PN / N **PY**
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?		NA / Y / PY / PN / N / NI
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		NA / Y / PY / PN / N / NI
Risk-of-bias judgement		Low / High / Some concerns

		Low risk
Optional: What is the predicted direction of bias due to missing outcome data?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	**Comments**	**Response options**
4.1 Was the method of measuring the outcome inappropriate?	Ref: "Participants were asked to rate their running-induced pain using NPRS (0–10) according to the average rating during the past 1 wk."	Y / PY / PN / N / NI **N**
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		Y / PY / PN / N / NI **N**
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?		NA / Y / PY / PN / N / NI **Y**
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Caratteristiche che riducono il r.o.b.:	NA / Y / PY / PN / N / NI **PY**

4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	i 3 gruppi sono gruppi d'intervento; ad ogni follow-up I partecipanti erano ignari dei risultati dei follow-up precedent; I valutatori che assistevano i soggetti erano ignari del trattamento che I soggetti avevano ricevuto.	NA / Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias in measurement of the outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 5: Risk of bias in selection of the reported result

Signalling questions	**Comments**	**Response options**
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?		Y / PY / PN / N / NI **NI**
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?		Y / PY / PN / N / NI **PN**

5.3 ... multiple eligible analyses of the data?	Nella sezione Risultati e nella tabella 2 sono presentati tutte le analisi dichiarate nella sezione Metodi.	Y / PY / PN / N / NI **N**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias due to selection of the reported result?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall risk of bias

Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the overall predicted direction of bias for this outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Study details

Reference	Bruce-Low S, Smith D, Burnet S, Fisher J, Bissell G, Webster L. One lumbar extension training session per week is sufficient for strength gains and reductions in pain in patients with chronic low back pain ergonomics. Ergonomics. 2012;55(4):500-7

Study design

X Individually-randomized parallel-group trial

☐ Cluster-randomized parallel-group trial

☐ Individually randomized cross-over (or other matched) trial

For the purposes of this assessment, the interventions being compared are defined as

Experimental :	One LET x week	Comparator :	Two LET x week/ control

Specify which outcome is being assessed for risk of bias	Pain/Disability
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.	Table 2

Is the review team's aim for this result…?

X to assess the effect of *assignment to intervention* (the 'intention-to-treat' effect)

☐ to assess the effect of *adhering to intervention* (the 'per-protocol' effect)

If the aim is to assess the effect of *adhering to intervention*, select the deviations from intended intervention that should be addressed (at least one must be checked):

☐ occurrence of non-protocol interventions

☐ failures in implementing the intervention that could have affected the outcome

☐ non-adherence to their assigned intervention by trial participants

Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)

X Journal article(s) with results of the trial

☐ Trial protocol

☐ Statistical analysis plan (SAP)

☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)

☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)

☐ "Grey literature" (e.g. unpublished thesis)

☐ Conference abstract(s) about the trial

☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)

☐ Research ethics application

☐ Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)

☐	Personal communication with trialist
☐	Personal communication with the sponsor

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?	Ref: "A modified randomised control trial design, as defined by Dvir (2007), was adopted."	Y / PY / PN / N / NI **NI**
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		Y / PY / PN / N / NI **NI**
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		Y / PY / PN / N / NI **NI**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?		NA / Y / PY / PN / N / NI **PN**
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?		NA / Y / PY / PN / N / NI
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?		NA / Y / PY / PN / N / NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?		Y / PY / PN / N / NI **NI**
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?		NA / Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns

		Some concerns
Optional: What is the predicted direction of bias due to deviations from intended interventions?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 3: Missing outcome data

Signalling questions	**Comments**	**Response options**
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Ref: "Following approval by the relevant ethics committees, 75 non-specific CLBP patients were assessed for eligibility and of these 72 completed the intervention […].Non-completion of training intervention due to relocation from the area n=3"	Y / PY / PN / N / NI **PY**
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?		NA / Y / PY / PN / N
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?		NA / Y / PY / PN / N / NI
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		NA / Y / PY / PN / N / NI
Risk-of-bias judgement		Low / High / Some concerns **Low risk**

Optional: What is the predicted direction of bias due to missing outcome data?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?	E' stata utilizzata la VAS per il dolore e la ODI per la disabilità.	Y / PY / PN / N / NI **Y**
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	Ref: "The intervention consisted of a 12 week training programme which was then followed by post testing (maximal lumbar isometric strength, ROM, modified-modified Schober's flexion test and completion of the ODI and the VAS)." Non è specificato nel dettaglio quando è stato effettuato il follow-up.	Y / PY / PN / N / NI **NI**
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?		NA / Y / PY / PN / N / NI **Y**
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Le aspettative tra il gruppo di controllo (usual care) e I gruppi di intervento potrebbero influenzare la misurazione dell'outcome ma tra I gruppi d'intervento questa influenza potrebbe essere ridotta.	NA / Y / PY / PN / N / NI **PY**
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI

		NI
Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the predicted direction of bias in measurement of the outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 5: Risk of bias in selection of the reported result

Signalling questions	**Comments**	**Response options**
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?		Y / PY / PN / N / NI **NI**
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?		Y / PY / PN / N / NI **NI**

5.3 ... multiple eligible analyses of the data?	Nei risultati sono presenti le analisi dichiarate nella sezione Metodi. Non sono presenti però I dati dei soggetti alla baseline.	Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias due to selection of the reported result?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall risk of bias

Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the overall predicted direction of bias for this outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Study details

Reference	Calatayud J, Guzmán-González B, Andersen LL, Cruz-Montecinos C, Morell MT, Roldán R, Ezzatvar Y, Casaña J. Effectiveness of a Group-Based Progressive Strength Training in Primary Care to Improve the Recurrence of Low Back Pain Exacerbations and Function: A Randomised Trial. Int J Environ Res Public Health. 2020 Nov 11;17(22):8326

Study design

X Individually-randomized parallel-group trial

☐ Cluster-randomized parallel-group trial

☐ Individually randomized cross-over (or other matched) trial

For the purposes of this assessment, the interventions being compared are defined as

Experimental:	Strength training	Comparator:	Back-School training

Specify which outcome is being assessed for risk of bias	Pain/Disability
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.	Table 3

Is the review team's aim for this result…?

X to assess the effect of *assignment to intervention* (the 'intention-to-treat' effect)

☐ to assess the effect of *adhering to intervention* (the 'per-protocol' effect)

If the aim is to assess the effect of *adhering to intervention*, select the deviations from intended intervention that should be addressed (at least one must be checked):

☐ occurrence of non-protocol interventions

☐ failures in implementing the intervention that could have affected the outcome

☐ non-adherence to their assigned intervention by trial participants

Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)

X Journal article(s) with results of the trial

X Trial protocol

☐ Statistical analysis plan (SAP)

☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)

☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)

☐ "Grey literature" (e.g. unpublished thesis)

☐ Conference abstract(s) about the trial

☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)

☐ Research ethics application

☐ Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)

☐ Personal communication with trialist

☐	Personal communication with the sponsor

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?	Ref: "Participants were stratified by age and successively randomized during the study period to either intervention (progressive training) or control (usual Back-School program) following simple randomization procedures (computerized random numbers). The allocation sequence was performed by a second person and concealed from the main researcher supervising the training sessions."	Y / PY / PN / N / NI **Y**
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		Y / PY / PN / N / NI **PY**
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		Y / PY / PN / N / NI **NI**
Risk-of-bias judgement		Low / High / Some concerns **Low risk**
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?		NA / Y / PY / PN / N / NI **PN**
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?		NA / Y / PY / PN / N / NI
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?		NA / Y / PY / PN / N / NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?		Y / PY / PN / N / NI **Y**
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?		NA / Y / PY / PN / N / NI
Risk-of-bias judgement		Low / High / Some concerns

		Low risk
Optional: What is the predicted direction of bias due to deviations from intended interventions?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 3: Missing outcome data

Signalling questions	**Comments**	**Response options**
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Figure 3. 22% drop-out.	Y / PY / PN / N / NI **N**
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	Ref: "Analyses were performed […] according to the intention-to-treat principle, including all participants regardless of loss to follow-up. Analyses were adjusted for the baseline level of the outcome. The estimation method was restricted maximum likelihood (REML) with degrees of freedom based on the Kenward-Roger approximation."	NA / Y / PY / PN / N **PY**
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?		NA / Y / PY / PN / N / NI
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		NA / Y / PY / PN / N / NI

Risk-of-bias judgement	Il modello usato per analizzare I dati mancanti è ritenuto efficace per ridurre il risk of bias. Nonostante ciò bisogna considerare che non abbiamo informazioni sufficienti riguardo le ragioni dei drop-out e che potrebbero essere correlate alla natura dell'intervento.	Low / High / Some concerns **Low risk**
Optional: What is the predicted direction of bias due to missing outcome data?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	**Comments**	**Response options**
4.1 Was the method of measuring the outcome inappropriate?	Ref: "An 11-point numerical rating scale, where 0 = "no pain" and 10 = "the worst possible pain", was used to assess the subject's perception of LBP intensity during the last week." Ref: "The Roland-Morris Questionnaire was used to assess physical disability due to LBP"	Y / PY / PN / N / NI **N**
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		Y / PY / PN / N / NI **N**
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?		NA / Y / PY / PN / N / NI **Y**

4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	I fattori che riducono il r.o.b. sono: l'adozione di interventi attivi per I gruppi; pur essendo un PROM, colui che assiste alla valutazione è definito, nel protocollo, cieco rispetto agli interventi;	NA / Y / PY / PN / N / NI **PY**
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias in measurement of the outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 5: Risk of bias in selection of the reported result

Signalling questions	**Comments**	**Response options**
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	Vedi protocollo: NCT03172962. Sia la durata dell'intervento che dei follow-up ha subito una variazione da 12 a 8 settimane. Inoltre non vi è una descrizione dettagliata del piano di analisi.	Y / PY / PN / N / **NI** **NI**

Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?		Y / PY / PN / N / NI **PN**
5.3 ... multiple eligible analyses of the data?	Nella sezione Risultati e nella tabella 3 sono presenti tutte le analisi descritte nella sezione Metodi.	Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias due to selection of the reported result?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall risk of bias

Risk-of-bias judgement		Low / High / Some concerns **Low risk**

Optional: What is the overall predicted direction of bias for this outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Study details

Reference	Madadi-Shad M, Jafarnezhadgero AA, Sheikhalizade H, Dionisio VC. Effect of a corrective exercise program on gait kinetics and muscle activities in older adults with both low back pain and pronated feet: A double-blind, randomized controlled trial. Gait Posture. 2020 Feb;76:339-345

Study design

X Individually-randomized parallel-group trial

☐ Cluster-randomized parallel-group trial

☐ Individually randomized cross-over (or other matched) trial

For the purposes of this assessment, the interventions being compared are defined as

Experimental:	Corrective exercise	Comparator:	control

Specify which outcome is being assessed for risk of bias	Pain/Disability

Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.

Table 4

Is the review team's aim for this result…?

X to assess the effect of *assignment to intervention* (the 'intention-to-treat' effect)

☐ to assess the effect of *adhering to intervention* (the 'per-protocol' effect)

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☐ occurrence of non-protocol interventions

☐ failures in implementing the intervention that could have affected the outcome

☐ non-adherence to their assigned intervention by trial participants

Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)

X Journal article(s) with results of the trial

☐ Trial protocol

☐ Statistical analysis plan (SAP)

☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)

☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)

☐	"Grey literature" (e.g. unpublished thesis)
☐	Conference abstract(s) about the trial
☐	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
☐	Research ethics application
☐	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
☐	Personal communication with trialist
☐	Personal communication with the sponsor

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?	Ref: "All eligible participants were randomly allocated into two equalsized groups, including an experimental (EG) and a control group (CG). The block randomization method was used to allocate study participants into EG and CG."	Y / PY / PN / N / NI **PY**
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		Y / PY / PN / N / NI **NI**
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	Table 2	Y / PY / PN / N / NI **PN**

Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)

Signalling questions	**Comments**	**Response options**
2.1. Were participants aware of their assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?		NA / Y / PY / PN / N / NI **NI**
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?		NA / Y / PY / PN / N / NI
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?		NA / Y / PY / PN / N / NI

2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?		Y / PY / PN / N / NI **NI**
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?		NA / Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias due to deviations from intended interventions?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Fig. 1. Nessun drop-out.	Y / PY / PN / N / NI **Y**
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?		NA / Y / PY / PN / N

3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?		NA / Y / PY / PN / N / NI
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		NA / Y / PY / PN / N / NI
Risk-of-bias judgement		Low / High / Some concerns **Low risk**
Optional: What is the predicted direction of bias due to missing outcome data?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?	Dolore = VAS Disabilità = RMDQ	Y / PY / PN / N / NI **N**
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	Il Gruppo d'intervento è stato valutato a circa 17 settimane dalla baseline mentre il Gruppo di controllo è stato valutato dopo 14 settimane dalla baseline.	Y / PY / PN / N / NI **PY**

4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?		NA / Y / PY / PN / N / NI
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI
Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the predicted direction of bias in measurement of the outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?		Y / PY / PN / N / NI **NI**

Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?		Y / PY / PN / N / NI **PN**
5.3 ... multiple eligible analyses of the data?	Nella sezione Risultati e nella tabella 3 sono presenti le analisi descritte nella sezione Metodi.	Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias due to selection of the reported result?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall risk of bias

Risk-of-bias judgement		Low / High / Some concerns **High risk**

Optional: What is the overall predicted direction of bias for this outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Study details

Reference	Smith D, Bissell G, Bruce-Low S, Wakefield C. The effect of lumbar extension training with and without pelvic stabilization on lumbar strength and low back pain. J Back Musculoskelet Rehabil. 2011;24(4):241-9

Study design

X Individually-randomized parallel-group trial

☐ Cluster-randomized parallel-group trial

☐ Individually randomized cross-over (or other matched) trial

For the purposes of this assessment, the interventions being compared are defined as

Experimental:	STAB	Comparator:	NOSTAB/control

Specify which outcome is being assessed for risk of bias	Pain/Disability

Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.

Table 2

Is the review team's aim for this result…?

X to assess the effect of *assignment to intervention* (the 'intention-to-treat' effect)

☐ to assess the effect of *adhering to intervention* (the 'per-protocol' effect)

If the aim is to assess the effect of *adhering to intervention*, select the deviations from intended intervention that should be addressed (at least one must be checked):

☐ occurrence of non-protocol interventions

☐ failures in implementing the intervention that could have affected the outcome

☐ non-adherence to their assigned intervention by trial participants

Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)

X Journal article(s) with results of the trial

☐ Trial protocol

☐ Statistical analysis plan (SAP)

☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)

☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)

☐	"Grey literature" (e.g. unpublished thesis)
☐	Conference abstract(s) about the trial
☐	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
☐	Research ethics application
☐	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
☐	Personal communication with trialist
☐	Personal communication with the sponsor

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?	Ref: "Participants were randomly allocated to one of three groups: Lumbar extension training with pelvic stabilization (STAB), lumbar extension trainingwithout stabilization (NO-STAB), and control."	Y / PY / PN / N / NI **PY**
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		Y / PY / PN / N / NI **NI**
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		Y / PY / PN / N / NI **NI**

Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)

Signalling questions	**Comments**	**Response options**
2.1. Were participants aware of their assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?		NA / Y / PY / PN / N / NI **PN**
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?		NA / Y / PY / PN / N / NI
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?		NA / Y / PY / PN / N / NI

2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?		Y / PY / PN / N / NI **NI**
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?		NA / Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias due to deviations from intended interventions?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Figure 1. 9% Drop-out.	Y / PY / PN / N / NI **N**
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	Nessuna informazione riguardo I dati dei drop-out.	NA / Y / PY / PN / N **PY**

3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?		NA / Y / PY / PN / N / NI **NI**
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		NA / Y / PY / PN / N / NI **NI**
Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the predicted direction of bias due to missing outcome data?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?	Dolore = VAS Disabilità = ODI	Y / PY / PN / N / NI **Y**
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		Y / PY / PN / N / NI

		N
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?		NA / Y / PY / PN / N / NI **Y**
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Dato che erano presenti 2 gruppi di intervento e un Gruppo di controllo è possibile che I risultati siano stati influenzati dalla conoscenza dell'intervento ricevuto.	NA / Y / PY / PN / N / NI **PY**
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI **PY**
Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the predicted direction of bias in measurement of the outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 5: Risk of bias in selection of the reported result

Signalling questions	**Comments**	**Response options**
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before		Y / PY / PN / N / NI

unblinded outcome data were available for analysis?		**NI**
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?		Y / PY / PN / N / NI **PN**
5.3 ... multiple eligible analyses of the data?	Nella tabelle 2 e 3 e nella sezione Risultati sono presenti le analisi descritte nella sezione Metodi.	Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias due to selection of the reported result?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall risk of bias

Risk-of-bias judgement		Low / High / Some concerns

		High risk
Optional: What is the overall predicted direction of bias for this outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Study details

Reference	Steele J, Bruce-Low S, Smith D, Jessop D, Osborne N. A randomized controlled trial of limited range of motion lumbar extension exercise in chronic low back pain. Spine (Phila Pa 1976). 2013 Jul 1;38(15):1245-52

Study design

X Individually-randomized parallel-group trial

☐ Cluster-randomized parallel-group trial

☐ Individually randomized cross-over (or other matched) trial

For the purposes of this assessment, the interventions being compared are defined as

Experimental :	LimROM strength training	Comparator :	FullROM/control

Specify which outcome is being assessed for risk of bias

Pain/Disability

Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.

Table 3

Is the review team's aim for this result…?

X to assess the effect of *assignment to intervention* (the 'intention-to-treat' effect)

☐ to assess the effect of *adhering to intervention* (the 'per-protocol' effect)

If the aim is to assess the effect of *adhering to intervention*, select the deviations from intended intervention that should be addressed (at least one must be checked):

☐ occurrence of non-protocol interventions

☐ failures in implementing the intervention that could have affected the outcome

☐ non-adherence to their assigned intervention by trial participants

Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)

X Journal article(s) with results of the trial

☐	Trial protocol
☐	Statistical analysis plan (SAP)
☐	Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
☐	Company-owned trial registry record (e.g. GSK Clinical Study Register record)
☐	"Grey literature" (e.g. unpublished thesis)
☐	Conference abstract(s) about the trial
☐	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
☐	Research ethics application
☐	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
☐	Personal communication with trialist
☐	Personal communication with the sponsor

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?	Ref: "31 participants were randomized using an online randomization program (Research Randomizer vs . 3.0) to a full ROM training group (FullROM; n = 12), a limited ROM training group (training using the mid 50% of their ROM; LimROM; n = 10), or a control group (n = 9) who did not train."	Y / PY / PN / N / NI **Y**
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		Y / PY / PN / N / NI **NI**

1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	Table 1	Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)

Signalling questions	**Comments**	**Response options**
2.1. Were participants aware of their assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?		NA / Y / PY / PN / N / NI **NI**

2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?		NA / Y / PY / PN / N / NI **PN**
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?		NA / Y / PY / PN / N / NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?		Y / PY / PN / N / NI **NI**
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?		NA / Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias due to deviations from intended interventions?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 3: Missing outcome data

Signalling questions	**Comments**	**Response options**

3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Figure 2. 23% drop-out or not analysed.	Y / PY / PN / N / NI **N**
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?		NA / Y / PY / PN / N **N**
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	Figure 2. Non ci sono informazioni sulla natura dei drop-out.	NA / Y / PY / PN / N / NI **PY**
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		NA / Y / PY / PN / N / NI **NI**
Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the predicted direction of bias due to missing outcome data?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?	Dolore = VAS Disabilità = ODI	Y / PY / PN / N / NI **Y**
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		Y / PY / PN / N / NI **PN**
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?		NA / Y / PY / PN / N / NI **Y**
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Dato che erano presenti 2 gruppi di intervento e un Gruppo di controllo è possibile che I risultati siano stati influenzati dalla conoscenza dell'intervento ricevuto.	NA / Y / PY / PN / N / NI **PY**
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI **PY**
Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the predicted direction of bias in measurement of the outcome?		NA / Favours experimental / Favours comparator /

		Towards null /Away from null / Unpredictable

Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?		Y / PY / PN / N / NI **NI**
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?		Y / PY / PN / N / NI **PN**
5.3 ... multiple eligible analyses of the data?	Nella tabella 3 e nella sezione Risultati sono presenti le analisi descritte nella sezione Metodi.	Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**

Optional: What is the predicted direction of bias due to selection of the reported result?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall risk of bias

Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the overall predicted direction of bias for this outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Study details	
Reference	Verbrugghe J, Agten A, Stevens S, Hansen D, Demoulin C, Eijnde BO, Vandenabeele F, Timmermans A. High Intensity Training to Treat Chronic Nonspecific Low Back Pain: Effectiveness of Various Exercise Modes. J Clin Med. 2020 Jul 27;9(8):2401
Study design	

X Individually-randomized parallel-group trial

☐ Cluster-randomized parallel-group trial

☐ Individually randomized cross-over (or other matched) trial

For the purposes of this assessment, the interventions being compared are defined as

Experimental:	HITCOM/HITSTRE	Comparator:	HITSTAB/HITMOB

Specify which outcome is being assessed for risk of bias	Pain/Disability
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.	Table 2

Is the review team's aim for this result…?

X to assess the effect of *assignment to intervention* (the 'intention-to-treat' effect)

☐ to assess the effect of *adhering to intervention* (the 'per-protocol' effect)

If the aim is to assess the effect of *adhering to intervention*, select the deviations from intended intervention that should be addressed (at least one must be checked):

☐ occurrence of non-protocol interventions

☐ failures in implementing the intervention that could have affected the outcome

☐ non-adherence to their assigned intervention by trial participants

Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)

X Journal article(s) with results of the trial

X Trial protocol

☐ Statistical analysis plan (SAP)

☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)

☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)

☐ "Grey literature" (e.g. unpublished thesis)

☐ Conference abstract(s) about the trial

☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)

☐ Research ethics application

☐ Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)

☐ Personal communication with trialist

☐ Personal communication with the sponsor

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?	Ref: "A permuted block randomization with a block size of four was used to foresee equal group division (1:1 allocation ratio). To ensure concealment of	<u>Y / PY</u> / PN / N / NI

	allocation, a research assistant not involved in the study picked a sealed opaque envelope containing the allocated group for each participant."	**PY**
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		Y / PY / PN / N / NI **PY**
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	Table 1.	Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Low risk**
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)

Signalling questions	**Comments**	**Response options**
2.1. Were participants aware of their assigned intervention during the trial?		Y / PY / PN / N / NI **Y**

2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?		NA / Y / PY / PN / N / NI **NI**
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?		NA / Y / PY / PN / N / NI
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?		NA / Y / PY / PN / N / NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?		Y / PY / PN / N / NI **NI**
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?		NA / Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**

Optional: What is the predicted direction of bias due to deviations from intended interventions?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Figure 1. 8% drop-out.	Y / PY / PN / N / NI **N**
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	Ref: "For dropouts, an intention-to-treat analysis (ITT) was followed, using a last-observation-carried-forward approach (LOCF) [39], only if a MID measurement was performed. If no MID measurement was performed (dropout before 12 sessions of therapy), the participant was seen as missing data and was not used for further analysis. […] None of the dropouts performed a MID measurement needed for an ITT."	NA / Y / PY / PN / N **PN**
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	Figure 1. Ref: "Six dropouts (8% of all participants) were noted. One person did not start the therapy sessions after the baseline assessment, due to practical issues. Five persons dropped out during the therapy protocols, of which three did so due to long-term sickness not related to low back pain, and two due to practical issues concerning the execution of two weekly training sessions."	NA / Y / PY / PN / N / NI **PN**
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		NA / Y / PY / PN / N / NI
Risk-of-bias judgement	Nello studio sono dichiarati 6 drop-out con relative giustificazioni. I soggetti analizzati sono però 8 in meno rispetto ai randomizzati.	Low / High / Some concerns

		Some concerns
Optional: What is the predicted direction of bias due to missing outcome data?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	**Comments**	**Response options**
4.1 Was the method of measuring the outcome inappropriate?	Dolore = NPRS Disabilità = MODI	Y / PY / PN / N / NI **PN**
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		Y / PY / PN / N / NI **PN**
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?		NA / Y / PY / PN / N / NI **Y**
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Ref: "To limit performance bias of the participants, the study was described to the participants as "a comparison between different modes of exercise therapy treatments", and participants were informed that equal progression was expected in each group."	NA / Y / PY / PN / N / NI **PY**

4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias in measurement of the outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 5: Risk of bias in selection of the reported result

Signalling questions	**Comments**	**Response options**
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?		Y / PY / PN / N / NI **NI**
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?		Y / PY / PN / N / NI **PN**

5.3 ... multiple eligible analyses of the data?	Nella tabella 2 e nella sezione Risultati sono presenti le analisi descritte nella sezione Metodi.	Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias due to selection of the reported result?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall risk of bias

Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the overall predicted direction of bias for this outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Study details

Reference	Cortell-Tormo JM, Sánchez PT, Chulvi-Medrano I, Tortosa-Martínez J, Manchado-López C, Llana-Belloch S, Pérez-Soriano P. Effects of functional resistance training on fitness and quality of life in females with chronic nonspecific low-back pain. J Back Musculoskelet Rehabil. 2018 Feb 6;31(1):95-105

Study design

X Individually-randomized parallel-group trial

☐ Cluster-randomized parallel-group trial

☐ Individually randomized cross-over (or other matched) trial

For the purposes of this assessment, the interventions being compared are defined as

Experimental:	FRT	Comparator:	Control

Specify which outcome is being assessed for risk of bias	Pain/Disability/Q.o.l.
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.	Table 2

Is the review team's aim for this result…?

X to assess the effect of *assignment to intervention* (the 'intention-to-treat' effect)

☐ to assess the effect of *adhering to intervention* (the 'per-protocol' effect)

If the aim is to assess the effect of *adhering to intervention*, select the deviations from intended intervention that should be addressed (at least one must be checked):

☐ occurrence of non-protocol interventions

☐ failures in implementing the intervention that could have affected the outcome

☐ non-adherence to their assigned intervention by trial participants

Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)

X Journal article(s) with results of the trial

☐ Trial protocol

☐ Statistical analysis plan (SAP)

☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)

☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)

☐ "Grey literature" (e.g. unpublished thesis)

☐ Conference abstract(s) about the trial

☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)

☐ Research ethics application

☐ Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)

☐ Personal communication with trialist

☐	Personal communication with the sponsor

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?	Ref: "The subjects were randomly assigned to either an exercise group (EG) or a control group (CG) using a randomized number sheet."	Y / PY / PN / N / NI **NI**
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		Y / PY / PN / N / NI **NI**
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	Table 1	Y / PY / PN / N / NI **N**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?		NA / Y / PY / PN / N / NI **PN**
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?		NA / Y / PY / PN / N / NI
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?		NA / Y / PY / PN / N / NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?		Y / PY / PN / N / NI **PN**
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?		NA / Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns

		Some concerns
Optional: What is the predicted direction of bias due to deviations from intended interventions?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 3: Missing outcome data

Signalling questions	**Comments**	**Response options**
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Figure 1. 21% drop-out.	Y / PY / PN / N / NI **N**
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	Ref: "Eleven patients in the EG attended more than 95% of the sessions, and 8 patients in the CG fully completed the measurement protocol. Their results were included in the analysis."	NA / Y / PY / PN / N **N**
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	1 drop-out nel gruppo sperimentale vs. 4 nel Gruppo di controllo	NA / Y / PY / PN / N / NI **NI**
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		NA / Y / PY / PN / N / NI **PY**

Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the predicted direction of bias due to missing outcome data?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	**Comments**	**Response options**
4.1 Was the method of measuring the outcome inappropriate?	Dolore = VAS Disabilità = ODI Qol = SF-36	Y / PY / PN / N / NI **N**
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		Y / PY / PN / N / NI **N**
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?		NA / Y / PY / PN / N / NI **Y**
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Non è descritto alcun fattore che potrebbe ridurre il r.o.b.	NA / Y / PY / PN / N / NI **PY**

4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI **PY**
Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the predicted direction of bias in measurement of the outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 5: Risk of bias in selection of the reported result

Signalling questions	**Comments**	**Response options**
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?		Y / PY / PN / N / NI **NI**
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?		Y / PY / PN / N / NI **PN**

5.3 ... multiple eligible analyses of the data?	Nelle tabelle 2 e 3 sono presenti le analisi descritte nella sezione Metodi.	Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias due to selection of the reported result?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall risk of bias

Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the overall predicted direction of bias for this outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Study details

Reference	Jackson JK, Shepherd TR, Kell RT. The influence of periodized resistance training on recreationally active males with chronic nonspecific low back pain. J Strength Cond Res. 2011 Jan;25(1):242-51

Study design

X Individually-randomized parallel-group trial

☐ Cluster-randomized parallel-group trial

☐ Individually randomized cross-over (or other matched) trial

For the purposes of this assessment, the interventions being compared are defined as

Experimental:	Middle age	Comparator:	Old age

Specify which outcome is being assessed for risk of bias	Pain/Disability/Q.o.l.
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.	Table 5

Is the review team's aim for this result…?

X to assess the effect of *assignment to intervention* (the 'intention-to-treat' effect)

☐ to assess the effect of *adhering to intervention* (the 'per-protocol' effect)

If the aim is to assess the effect of *adhering to intervention*, select the deviations from intended intervention that should be addressed (at least one must be checked):

☐ occurrence of non-protocol interventions

☐ failures in implementing the intervention that could have affected the outcome

☐ non-adherence to their assigned intervention by trial participants

Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)

X Journal article(s) with results of the trial

☐ Trial protocol

☐ Statistical analysis plan (SAP)

☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)

☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)

☐ "Grey literature" (e.g. unpublished thesis)

☐ Conference abstract(s) about the trial

☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)

☐ Research ethics application

☐	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
☐	Personal communication with trialist
☐	Personal communication with the sponsor

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?	Ref: "Following baseline testing the 45 male subjects were randomly assigned to 1 of 3 groups based on age."	Y / PY / PN / N / NI **PY**
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		Y / PY / PN / N / NI **NI**
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		Y / PY / PN / N / NI **NI**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?		NA / Y / PY / PN / N / NI **NI**
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?		NA / Y / PY / PN / N / NI **PN**
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?		NA / Y / PY / PN / N / NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?		Y / PY / PN / N / NI **PN**
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the		NA / Y / PY / PN / N / NI

failure to analyse participants in the group to which they were randomized?		**Some concerns**
Risk-of-bias judgement		Low / High / Some concerns
Optional: What is the predicted direction of bias due to deviations from intended interventions?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Ref: "Five subjects dropped out for various reasons (e.g., other time commitments)." 11% drop out	Y / PY / PN / N / NI **N**
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?		NA / Y / PY / PN / N **PN**
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	Ref: "There were negative side effects (e.g., increased back pain) from participation in the study. Five subjects dropped out for various reasons (e.g., other time commitments); these subjects' data have been excluded from analysis."	NA / Y / PY / PN / N / NI **PY**
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		NA / Y / PY / PN / N / NI **PY**

Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the predicted direction of bias due to missing outcome data?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	**Comments**	**Response options**
4.1 Was the method of measuring the outcome inappropriate?	Dolore = VAS Disabilità = ODI Qol = SF-36	Y / PY / PN / N / NI **N**
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		Y / PY / PN / N / NI **N**
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?		NA / Y / PY / PN / N / NI **Y**
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Dato che erano presenti 2 gruppi di intervento e un Gruppo di controllo è possibile che I risultati siano stati influenzati dalla conoscenza dell'intervento ricevuto.	NA / Y / PY / PN / N / NI **PY**

4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI **PY**
Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the predicted direction of bias in measurement of the outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 5: Risk of bias in selection of the reported result

Signalling questions	**Comments**	**Response options**
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?		Y / PY / PN / N / NI **NI**
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?		Y / PY / PN / N / NI **PN**

5.3 ... multiple eligible analyses of the data?	Nella tabella 5 e nella sezione risultati sono presenti le analisi descritte nella sezione Metodi.	Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias due to selection of the reported result?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall risk of bias

Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the overall predicted direction of bias for this outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Study details

Reference	Kell RT, Asmundson GJ. A comparison of two forms of periodized exercise rehabilitation programs in the management of chronic nonspecific low-back pain. J Strength Cond Res. 2009 Mar;23(2):513-23

Study design

X Individually-randomized parallel-group trial

☐ Cluster-randomized parallel-group trial

☐ Individually randomized cross-over (or other matched) trial

For the purposes of this assessment, the interventions being compared are defined as

Experimental:	Resistance training	Comparator:	Aerobic T/Control

Specify which outcome is being assessed for risk of bias	Pain/Disability/Q.o.l.
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.	Table 6

Is the review team's aim for this result…?

X to assess the effect of *assignment to intervention* (the 'intention-to-treat' effect)

☐ to assess the effect of *adhering to intervention* (the 'per-protocol' effect)

If the aim is to assess the effect of *adhering to intervention*, select the deviations from intended intervention that should be addressed (at least one must be checked):

☐ occurrence of non-protocol interventions

☐ failures in implementing the intervention that could have affected the outcome

☐ non-adherence to their assigned intervention by trial participants

Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)

X Journal article(s) with results of the trial

☐ Trial protocol

☐ Statistical analysis plan (SAP)

☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)

☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)

☐ "Grey literature" (e.g. unpublished thesis)

☐ Conference abstract(s) about the trial

☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)

☐ Research ethics application

☐ Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)

☐ Personal communication with trialist

☐	Personal communication with the sponsor

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?	Ref: "The subjects were tested at baseline (pretraining) and then randomly assigned to 1 of 3 groups (RT, AT, or C)."	Y / PY / PN / N / NI **NI**
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		Y / PY / PN / N / NI **NI**
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	Table 6	Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?		NA / Y / PY / PN / N / NI **NI**
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?		NA / Y / PY / PN / N / NI
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?		NA / Y / PY / PN / N / NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?		Y / PY / PN / N / NI **PN**
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?		NA / Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns

		Some concerns
Optional: What is the predicted direction of bias due to deviations from intended interventions?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 3: Missing outcome data

Signalling questions	**Comments**	**Response options**
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Ref: "Initially, there were 33 subjects in the study, but 6 subjects dropped out, leaving 27 who completed the 16-week study."	Y / PY / PN / N / NI **N**
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?		NA / Y / PY / PN / N **N**
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?		NA / Y / PY / PN / N / NI **PY**
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		NA / Y / PY / PN / N / NI **NI**

Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the predicted direction of bias due to missing outcome data?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	**Comments**	**Response options**
4.1 Was the method of measuring the outcome inappropriate?	Dolore = VAS Disabilità = ODI Qol = SF-36	Y / PY / PN / N / NI **N**
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	Il Gruppo di controllo è stato valutato in 2 occasioni (0-16 settimane) mentre I gruppi di intervento in 3 occasioni (0-8-16 settimane). Questo non è stato considerato rilevante per il r.o.b.	Y / PY / PN / N / NI **N**
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?		NA / Y / PY / PN / N / NI **Y**
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Dato che erano presenti 2 gruppi di intervento e un Gruppo di controllo è possibile che I risultati siano stati influenzati dalla conoscenza dell'intervento ricevuto.	NA / Y / PY / PN / N / NI **PY**

4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI **PY**
Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the predicted direction of bias in measurement of the outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 5: Risk of bias in selection of the reported result

Signalling questions	**Comments**	**Response options**
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?		Y / PY / PN / N / NI **NI**
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?		Y / PY / PN / N / NI **PN**

5.3 ... multiple eligible analyses of the data?	Nella figura 3, nella tabella 6 e nella sezione Risultati sono presenti le analisi descritte nella sezione Metodi.	Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias due to selection of the reported result?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall risk of bias

Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the overall predicted direction of bias for this outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Study details

Reference	Kell RT, Risi AD, Barden JM. The response of persons with chronic nonspecific low back pain to three different volumes of periodized musculoskeletal rehabilitation. J Strength Cond Res. 2011 Apr;25(4):1052-64

Study design

X Individually-randomized parallel-group trial

☐ Cluster-randomized parallel-group trial

☐ Individually randomized cross-over (or other matched) trial

For the purposes of this assessment, the interventions being compared are defined as

Experimental:	4D strength training	Comparator:	3D/2D/ control

Specify which outcome is being assessed for risk of bias	Pain/Disability/Q.o.l.
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.	Table 6

Is the review team's aim for this result…?

X to assess the effect of *assignment to intervention* (the 'intention-to-treat' effect)

☐ to assess the effect of *adhering to intervention* (the 'per-protocol' effect)

If the aim is to assess the effect of *adhering to intervention*, select the deviations from intended intervention that should be addressed (at least one must be checked):

☐ occurrence of non-protocol interventions

☐ failures in implementing the intervention that could have affected the outcome

☐ non-adherence to their assigned intervention by trial participants

Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)

X Journal article(s) with results of the trial

☐ Trial protocol

☐ Statistical analysis plan (SAP)

☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)

☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)

☐ "Grey literature" (e.g. unpublished thesis)

☐ Conference abstract(s) about the trial

☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)

☐ Research ethics application

☐ Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)

☐ Personal communication with trialist

☐	Personal communication with the sponsor

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?	Ref: "Immediately after the baseline testing, the subjects were age, sex, strength (i.e., bench press and leg press) and pain matched and randomly assigned to 1 of 4 groups."	Y / PY / PN / N / NI **PY**
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		Y / PY / PN / N / NI **NI**
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		Y / PY / PN / N / NI **NI**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?		NA / Y / PY / PN / N / NI **NI**
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?		NA / Y / PY / PN / N / NI
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?		NA / Y / PY / PN / N / NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?		Y / PY / PN / N / NI **PN**
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?		NA / Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns

		Some concerns
Optional: What is the predicted direction of bias due to deviations from intended interventions?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 3: Missing outcome data

Signalling questions	**Comments**	**Response options**
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Ref: "Thirty-three subjects dropped out of the study before completion; their data were not included in the results."	Y / PY / PN / N / NI **N**
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	Vedi 3.1	NA / Y / PY / PN / N **N**
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	Ref: "Dropout rate was determined by the subjects contacting the researcher and indicating that they either no longer wished to participate or missing one testing session."	NA / Y / PY / PN / N / NI **NI**
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		NA / Y / PY / PN / N / NI **NI**

Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the predicted direction of bias due to missing outcome data?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	**Comments**	**Response options**
4.1 Was the method of measuring the outcome inappropriate?	Dolore = VAS Disabilità = ODI Qol = SF-36	Y / PY / PN / N / NI **N**
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		Y / PY / PN / N / NI **PN**
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?		NA / Y / PY / PN / N / NI **Y**
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Dato che erano presenti 3 gruppi di intervento e un Gruppo di controllo è possibile che I risultati siano stati influenzati dalla conoscenza dell'intervento ricevuto.	NA / Y / PY / PN / N / NI **PY**

4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI **PY**
Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the predicted direction of bias in measurement of the outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 5: Risk of bias in selection of the reported result

Signalling questions	**Comments**	**Response options**
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?		Y / PY / PN / N / NI **NI**
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?		Y / PY / PN / N / NI **PN**

5.3 ... multiple eligible analyses of the data?	Nella tabella 6 e nella sezione Risultati sono presenti le analisi descritte nella sezione Metodi.	Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias due to selection of the reported result?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall risk of bias

Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the overall predicted direction of bias for this outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Study details

Reference	Verbrugghe J, Agten A, Stevens S, Hansen D, Demoulin C, O Eijnde B, Vandenabeele F, Timmermans A. Exercise Intensity Matters in Chronic Nonspecific Low Back Pain Rehabilitation. Med Sci Sports Exerc. 2019 Dec;51(12):2434-2442. doi: 10.1249/MSS.0000000000002078. PMID: 31269004.

Study design

X Individually-randomized parallel-group trial

☐ Cluster-randomized parallel-group trial

☐ Individually randomized cross-over (or other matched) trial

For the purposes of this assessment, the interventions being compared are defined as

Experimental: High intensity training Comparator: Moderate intensity training

Specify which outcome is being assessed for risk of bias	Disabilità e dolore
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.	Tabella 2

Is the review team's aim for this result…?

X to assess the effect of *assignment to intervention* (the 'intention-to-treat' effect)

☐ to assess the effect of *adhering to intervention* (the 'per-protocol' effect)

If the aim is to assess the effect of *adhering to intervention*, select the deviations from intended intervention that should be addressed (at least one must be checked):

☐ occurrence of non-protocol interventions

☐ failures in implementing the intervention that could have affected the outcome

☐ non-adherence to their assigned intervention by trial participants

Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)

X Journal article(s) with results of the trial

Trial protocol

☐ Statistical analysis plan (SAP)

☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)

☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)

☐ "Grey literature" (e.g. unpublished thesis)

☐ Conference abstract(s) about the trial

☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)

☐ Research ethics application

☐ Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)

☐	Personal communication with trialist
☐	Personal communication with the sponsor

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?	Ref: "Participants were randomly assigned into an experimental group performing HIT or a control group performing moderate-intensity training (MIT). […] To ensure concealment of allocation, a research assistant not involved in the study picked a sealed, opaque, sequentially numbered envelope containing the allocated group for each participant."	Y / PY / PN / N / NI **NI**
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		Y / PY / PN / N / NI **Y**
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	Tabelle 1 e 2	Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns Low risk
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	Ref: "Given the nature of the ET, it was not possible to blind participants and caregivers for group assignment. To limit performance bias of the participants, the study was described to the participants as "a comparison between different modes of ET treatments," and participants were informed that equal progression could be expected in each group."	Y / PY / PN / N / NI **PY**
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?		Y / PY / PN / N / NI **PY**
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?		NA / Y / PY / PN / N / NI **NI**
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?		NA / Y / PY / PN / N / NI
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?		NA / Y / PY / PN / N / NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Ref: "For drop outs, an intention to treat analysis was followed, using a last observation carried forward approach if a MID measurement was performed."	Y / PY / PN / N / NI **PY**
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?		NA / Y / PY / PN / N / NI

Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias due to deviations from intended interventions?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 3: Missing outcome data

Signalling questions	**Comments**	**Response options**
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Il tasso di drop-out è del 5%	Y / PY / PN / N / NI **Y**
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?		NA / Y / PY / PN / N
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?		NA / Y / PY / PN / N / NI
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		NA / Y / PY / PN / N / NI
Risk-of-bias judgement		Low / High / Some concerns **Low risk**

Optional: What is the predicted direction of bias due to missing outcome data?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?	Disabilità = MODI Dolore = NPRS	Y / PY / PN / N / NI **N**
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	Ref: "Primary and secondary outcome measures were collected at baseline ("PRE") and at the end of the training program ("POST")."	Y / PY / PN / N / NI **PN**
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?		NA / Y / PY / PN / N / NI **Y**
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Ref: "the study was described to the participants as "a comparison between different modes of ET treatments," and participants were informed that equal progression could be expected in each group."	NA / Y / PY / PN / N / NI **PY**
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI **PN**

Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias in measurement of the outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 5: Risk of bias in selection of the reported result

Signalling questions	**Comments**	**Response options**
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	Non vi sono piani di analisi pre-specificati e il protocollo citato nei metodi sembra riguardare un altro studio.	Y / PY / PN / N / NI **NI**
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?		Y / PY / PN / N / NI **PN**
5.3 ... multiple eligible analyses of the data?	Le analisi presenti nella tabella 2 sono quelle descritte nei metodi.	Y / PY / PN / N / NI **PN**

Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias due to selection of the reported result?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall risk of bias

Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the overall predicted direction of bias for this outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Study details

Reference	Atalay E, Akova B, Gür H, Sekir U. Effect of Upper-Extremity Strengthening Exercises on the Lumbar Strength, Disability and Pain of Patients with Chronic Low Back Pain: A Randomized Controlled Study. J Sports Sci Med. 2017 Dec 1;16(4):595-603. PMID: 29238262; PMCID: PMC5721192.

Study design

X Individually-randomized parallel-group trial

☐ Cluster-randomized parallel-group trial

☐ Individually randomized cross-over (or other matched) trial

For the purposes of this assessment, the interventions being compared are defined as

Experimental: Upper-extremity exercise Comparator: General exercise

Specify which outcome is being assessed for risk of bias	Dolore /disabilità
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.	Figure 6 e 7

Is the review team's aim for this result…?

X to assess the effect of *assignment to intervention* (the 'intention-to-treat' effect)

☐ to assess the effect of *adhering to intervention* (the 'per-protocol' effect)

If the aim is to assess the effect of *adhering to intervention*, select the deviations from intended intervention that should be addressed (at least one must be checked):

☐ occurrence of non-protocol interventions

☐ failures in implementing the intervention that could have affected the outcome

☐ non-adherence to their assigned intervention by trial participants

Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)

X Journal article(s) with results of the trial

Trial protocol

☐ Statistical analysis plan (SAP)

☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)

☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)

☐ "Grey literature" (e.g. unpublished thesis)

☐ Conference abstract(s) about the trial

☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)

☐ Research ethics application

☐ Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)

☐ Personal communication with trialist

☐ Personal communication with the sponsor

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?	Ref: "The patients were categorized into two groups via draw lot (Oaks, 2012)."	Y / PY / PN / N / NI **NI**
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		Y / PY / PN / N / NI **NI**
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		Y / PY / PN / N / NI **NI**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?		Y / PY / PN / N / NI **Y**
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?		NA / Y / PY / PN / N / NI **NI**
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?		NA / Y / PY / PN / N / NI
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?		NA / Y / PY / PN / N / NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?		Y / PY / PN / N / NI **NI**
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?		NA / Y / PY / PN / N / NI **PN**
Risk-of-bias judgement		Low / High / Some concerns **Some concerns**

Optional: What is the predicted direction of bias due to deviations from intended interventions?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?		Y / PY / PN / N / NI **NI**
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?		NA / Y / PY / PN / N **PN**
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?		NA / Y / PY / PN / N / NI **NI**
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		NA / Y / PY / PN / N / NI **NI**
Risk-of-bias judgement		Low / High / Some concerns **High risk**

Optional: What is the predicted direction of bias due to missing outcome data?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?	Dolore = VAS Disabilità = MODI	Y / PY / PN / N / NI **N**
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	Figura 1	Y / PY / PN / N / NI **N**
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?		NA / Y / PY / PN / N / NI **Y**
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI **PY**
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI **PN**

Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias in measurement of the outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 5: Risk of bias in selection of the reported result

Signalling questions	**Comments**	**Response options**
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	Nello studio non è presente nè un protocollo nè un piano di analisi preimpostato.	Y / PY / PN / N / NI **NI**
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?		Y / PY / PN / N / NI **N**
5.3 ... multiple eligible analyses of the data?		Y / PY / PN / N / NI **NI**

Risk-of-bias judgement		Low / High / Some concerns **Some concerns**
Optional: What is the predicted direction of bias due to selection of the reported result?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall risk of bias

Risk-of-bias judgement		Low / High / Some concerns **High risk**
Optional: What is the overall predicted direction of bias for this outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable