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REVIEW

The effects of inspiratory muscle training on inspiratory muscle strength, lung function and quality of life in adults with spinal cord injuries: a systematic review and Meta-analysis

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ABSTRACT

Purpose: This systematic review and meta-analysis aimed to evaluate the effectiveness of inspiratory muscle training (IMT) on respiratory muscle strength, lung function and quality of life (QOL) in adults with spinal cord injuries (SCI).

Methods: Databases were searched up to June 2022; CENTRAL, CINAHL, MEDLINE, PEDRo, and PubMed. Following PRISMA reporting guidelines, two independent reviewers selected studies and extracted data. Study quality and levels of evidence were assessed.

Results: Following selection from 624 initial search results, six randomised controlled trials were identified, comprising 124 participants. Quality of Evidence was very low to moderate. Meta-analysis showed that post intervention, IMT significantly improved maximal inspiratory pressure (MD 15.72 cmH2O, 95% CI 5.02, 26.41, $p = 0.004$) when compared with a control intervention. There was no significant benefit for physical QOL (SMD 0.12, 95% CI −1.01, 1.25, $p = 0.84$), mental QOL (SMD −0.2, 95% CI −1.72, 1.33, $p = 0.80$), maximal expiratory pressure (MD 5.19 cmH2O, 95% CI −4.16, 14.55, $p = 0.80$), or FEV1 (MD 0.26 L, 95% CI −0.19, 0.7, $p = 0.26$). Sensitivity analyses found larger effects for studies with 8 week interventions (MD 17.5 cmH2O (95% CI 3.36 to 31.66)) and spring loaded devices alone (MD 21.18 cmH2O, 95% CI 9.65 to 32.72).

Conclusion: Moderate quality evidence suggests IMT improves respiratory strength in adults with an SCI. The mental and physical QOL outcomes provided very low quality of evidence, with considerable heterogeneity between study results, leading to inconsistency. Further research is warranted to investigate medium and long-term impact of robust IMT protocols, accounting for patient motivation and adherence to IMT.

➤ IMPLICATIONS FOR REHABILITATION

- Inspiratory muscle training (IMT) significantly improves respiratory muscle strength in adults with spinal cord injuries—irrespective of time since injury, or degree of injury completeness.
- IMT is a feasible, safe, and worthwhile intervention to implement with adults with spinal cord injuries and can be utilized in a variety of settings.
- IMT interventions that are 8 weeks long and utilize a spring-loaded inspiratory threshold device may generate the largest improvements in respiratory strength.

Introduction

A traumatic spinal cord injury (SCI) refers to damage to the spinal cord, resulting in a lesion that causes impairments and/or paralysis to sensory, motor and autonomic functions below the level of injury [1]. Respiratory complications remain the most common cause of mortality following SCI, as respiratory function and airway clearance is impaired to varying degrees depending on the level and completeness of the injury [2,3,p.668]. This dysfunction has the potential to greatly affect an individual's physical and psychological well-being [1,4].

Research suggests that strengthening the respiratory muscles may improve pulmonary function during initial recovery post SCI, and lower the risk of excessive decline in lung function and cough capacity during the chronic phase [5,6]. Inspiratory muscle training (IMT) is strength training that specifically targets the respiratory muscles, to improve inspiratory muscle strength—and subsequently—respiratory function [7]. Methods such as abdominal weights [7], incentive spirometers [8], inspiratory resistance devices [5,9–14], and normocapnic hyperpnea training [15] are examples of ways researchers have attempted to strengthen the inspiratory muscles. Although these methods are diverse, similar outcome measures are used to monitor changes in respiratory function and lung volumes. The most commonly reported outcome measures are lung volumes and flows, such as maximal

inspiratory pressure, maximal expiratory pressure, forced expiratory volume in 1 s, peak expiratory flow rate, maximal voluntary ventilation, and functional outcomes such as quality of life, dyspnoea, and rate of perceived exertion [9,10]. Maximal inspiratory pressure is the most widely used measure of respiratory muscle strength [9], and may be a pre-cursor for the development of pneumonia in individuals with levels below lesion-specific reference values [16]. Considering respiratory dysfunction accounts for 28% of deaths within the first year after an SCI [17], utilizing IMT may lower an individual's risk of mortality—potentially impacting quality of life.

To date, various methodological limitations, small sample sizes and heterogeneity in participant characteristics and outcome measures have prevented various systematic reviews [4,9,10,15,18,19] from determining an overall effect of IMT on respiratory strength and quality of life. A Cochrane review by Berlowitz and Tamplin [9] synthesized nine studies performing respiratory muscle training interventions. Meta-analyses for maximal inspiratory pressure ($n = 147$) and maximal expiratory pressure ($n = 151$) found a statistically significant difference in favour of the intervention over control groups, however meta-analyses for forced expiratory volume in 1 s ($n = 97$) determined no significant difference between groups. Berlowitz and Tamplin [9] state these findings were conservative as only five randomised control trials were included in the analysis. This bias contributed to their certainty in the evidence—as maximal inspiratory pressure, maximal expiratory pressure, forced expiratory volume in 1 s and quality of life were given a Grading of Recommendations, Assessment, Development and Evaluation (GRADE) [20] of low certainty.

Berlowitz and Tamplin [9] concluded that additional research is needed to determine whether IMT has an effect on lung function, respiratory strength and any carryover effects to quality of life. They also state the need to discern an optimum method and treatment length for IMT [9]. This gap in literature contributed to the overall aim of this systematic review. Additionally, the findings from Raab et al. [16] may assist in understanding the impact IMT has at reducing respiratory complications, as a means to improve quality of life. However, whether IMT provides enough of a training effect on maximal inspiratory pressure to improve respiratory strength needs to be explored. Given this, investigating the impact of IMT on respiratory strength in adults with SCI is an important and worthwhile area of research because of the potential to improve patient care.

Therefore, the research questions for this systematic review are:

1. Does IMT improve respiratory muscle strength, lung function values and influence quality of life?
2. Is there an optimal length of intervention and resistance device for performing IMT?

Methods

Identification of studies and search strategy

A search was performed using the following databases: CENTRAL, CINAHL, MEDLINE, PEDRo, and PubMed. Searches were conducted on June 16th, 2022. See Supplemental File Appendix 1 on the eAddenda for the full search strategy and search terms. Following the database searches, grey literature concerning the Conference Proceedings Citation Index (CPCI-S), Current Controlled Trials (ISRCTN Registry), National Institute of Health Clinical Trials Database (ClinicalTrials.gov), the WHO International Clinical Trials Registry Platform and System for Information on Grey Literature

in Europe, and the Science Citation Index Expanded (SCI-E) through ISI Web of Science, as well as the reference lists of included papers were examined for additional relevant articles. Two reviewers (AW and RS) independently performed initial screening of titles and abstracts against the eligibility criteria (Box 1). After non-relevant articles were discarded, a second screening involved reading full texts and analysing whether studies met the eligibility criteria. Final decisions regarding article selection were then made.

Box 1. Inclusion criteria.

Design

- Randomised controlled trial

Participants

- Adults (>18 years old)
- Traumatic spinal cord injuries, acute or chronic
- American Spinal Injury Association (ASIA) levels A, B, C, D, incomplete or complete injuries

Intervention

- Inspiratory muscle training with a device that provides resistance on inspiration
- Intervention at least 2 weeks long, frequency of sessions at least 2 days per week
- Training can include a warm-up and cool down, but no adjunct therapies combined with inspiratory muscle training
- Based in hospital or community settings
- Duration, frequency and intensity of training must be recorded

Outcome measures

- Primary: maximal inspiratory pressure (MIP), quality of life (QOL)
- Secondary: maximal expiratory pressure (MEP), forced expiratory volume in 1 second (FEV$_1$)

Comparisons

- Inspiratory muscle training versus no training, sham intervention or usual care

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Assessment of characteristics of studies

Quality

Methodological quality of included studies was assessed using the Cochrane Risk of Bias tool, assessing each domain of bias as high, low or unclear. Criteria for making judgements about risk of bias was provided from the Cochrane Handbook for Systematic Reviews [21]. The GRADE [20] tool was used to grade the overall body of evidence gathered in this review, dictating the certainty of each outcome as high, moderate, low and very low.

Participants

Studies were included if participants were >18 years old, had suffered a traumatic spinal cord injury, at ASIA levels A, B, C, or D. Individuals could be in the acute (<3 months) or chronic

(>3 months) stage of their injury. Data was extracted regarding participants age, sex, injury type (i.e., Level and ASIA classification), and time since diagnosis.

Intervention

The experimental intervention was IMT, using an inspiratory training device (PowerBreathe®, HaB International ltd, Southam, UK; Philips Threshold® IMT, Respironics Inc, Parsippany, New Jersey; Respifit S® electronic, Eumedics GmbH, Purkersdorf, Austria; DHD Medical Products, Diemolding healthcare Division, Canatota NY) that provides resistance on inspiration. Data was extracted about the type of device used, the duration, resistance and frequency of training, as well as location where training took place. Control interventions were sham treatments, no training or usual care.

Outcome measures

The primary outcome measures were inspiratory muscle strength, and quality of life. Inspiratory muscle strength was measured via maximal inspiratory pressure, and assessed using a manometer, with values expressed in cmH_2O. Quality of life measures were the Medical Outcomes Short Form Survey (SF-36 or SF-12)—with data regarding the physical and mental health components extracted.

The secondary outcome measures were lung function, expiratory muscle strength, and likelihood of developing pneumonia. The measure for lung function was forced expiratory volume in 1 s—assessed by spirometry and expressed in litres. Expiratory muscle strength was measured via maximal expiratory pressure using a manometer and expressed in cmH_2O.

Data analysis

Two reviewers (AW and RS) used standard forms to extract data from the studies. Post-intervention data was deemed continuous, and pooled using meta-analysis. Negative values were standardised. Data was expressed as a mean difference (MD) or standardised mean difference (SMD). A 95% confidence interval (CI) was set and statistical significance at $p < 0.05$. Meta-analysis was performed with the Review Manager (RevMan 5.4.1, The Cochrane Collaboration, 2020) (RevMan) statistical software using the Generic Inverse Variance Method, with a random-effects model. A sensitivity analysis was also planned to address the secondary research question around the impact of duration of intervention and type of device. Selected studies were pooled or sub-grouped together using RevMan. Data was expressed as a mean difference, with 95% CI and statistical significance at $p < 0.05$.
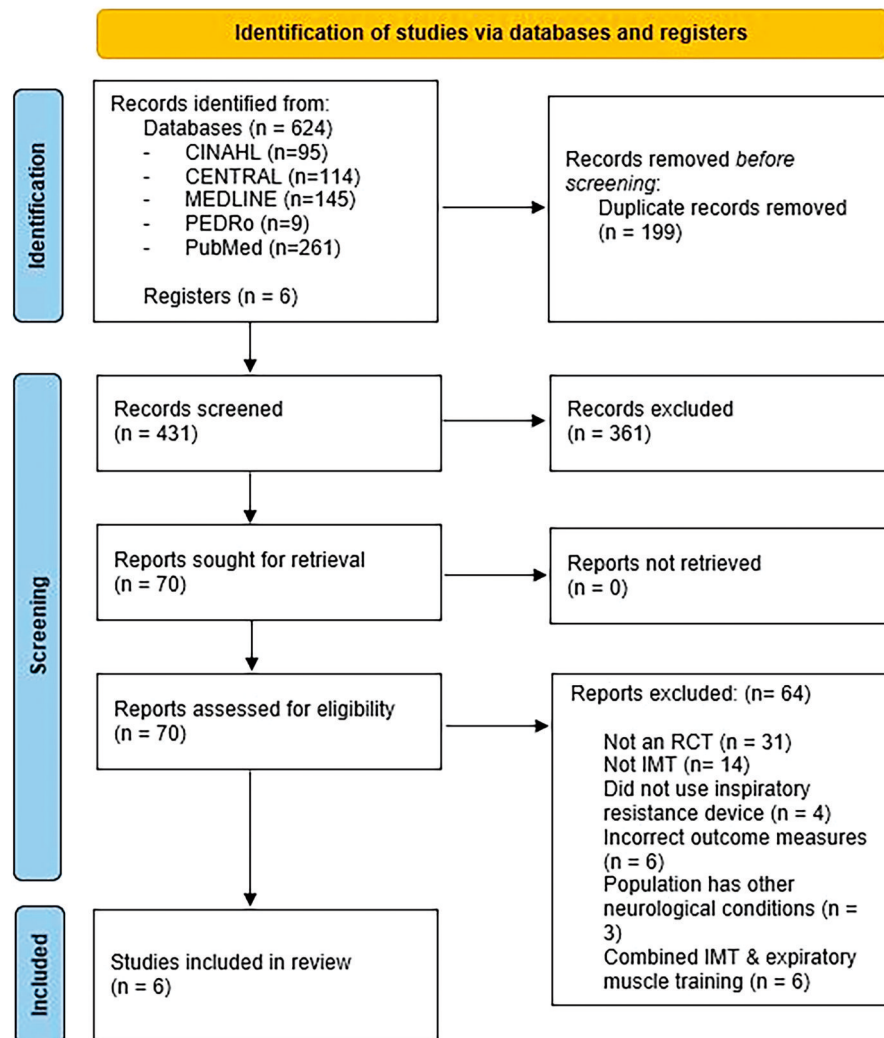

Figure 1. Flow of studies through the review.

Table 1. Summary of included studies ($n = 6$).

Study	Participants	Intervention	Outcome measures
Soumyashree and Kaur [13]	$n = 27$ Mean age: 31.7	**IMT:** Trained at 40% MIP, 15 min sessions, 5x/week for 4 weeks	MIP, MEP
	Injury type: T1-T12, ASIA A and B	**Control:** Breathing exercises	
	Diagnosis: 3 months − 1.5 years	Performed all sessions supervised at an SCI rehabilitation centre	
	M:F = 22:5		
Postma et al. [5]	$n = 40$ Mean age: 46.85	**IMT:** Received usual care and RIMT. Trained at 60% MIP, 7 sets x 2 min, then 1 min unresisted breathing 5x/week for 8 weeks	MIP, MEP, FEV_1, QOL (SF-36: physical and mental health components)
	Injury type: C5-T9, ASIA A, B, C, D	**Control:** PROM, muscle strength exercises, and functional training	
	Diagnosis: 2–4 months		
	M:F: 35:5	Performed all sessions supervised at 4 different SCI rehabilitation centres	
West et al. [14]	$n = 10$ Mean age: 29.2	**IMT:** Trained at 50–60% MIP, 30 repetitions, 2x/day, 5x/week for 6 weeks	MIP, MEP, FEV_1
	Injury type: C5-C7, ASIA A and B Diagnosis: 4–15 years	**Control:** placebo inhaler (wet air)	
	M:F: 9:1	Supervised for the first session, then performed the rest of sessions at home	
Mueller et al. [12]	$n = 16$ Mean age: 38.4	**IMT:** Trained at 80% MIP. Did 90 repetitions for 10 min sessions, 4x/week for 8 weeks	MIP, MEP, FEV_1 , QOL (SF-12: physical and mental components)
	Injury type: C5-C8, ASIA A	**Control:** Used incentive spirometer	
	Diagnosis: 6–8 months	Performed all sessions supervised at an SCI rehabilitation centre	
	M:F: 12:4		
Liaw et al. [8]	$n = 20$ Mean age: 33.7	**IMT:** Training started at the smallest inspiratory resistance setting (blue, 7 mm). Trained for 15–20min, 2x/day, 7x/week for 6 weeks. Also performed usual care	MIP, MEP, FEV_1
	Injury: C4- C7, ASIA A		
	Diagnosis: 1–4.5 months	**Control:** Usual care—PROM, mattress exercise, sitting balance, or upper limb functional training	
	M:F: 16:4	Performed all sessions supervised in inpatient hospital setting	
Derrickson et al. [11]	$n = 11$ Mean age: 27.8	**IMT:** Trained with least amount of resistance for 15 min, 2x/day, 5x/week for 7 weeks	MIP
	Injury: C4- C7, ASIA A	**Control:** Abdominal weights	
	Diagnosis: 2 days to 2.5 months	Performed all sessions supervised in inpatient hospital setting	
	M:F: 9:2		

Results

Study selection

The search yielded 624 articles from databases and grey literature sources, with 70 full-text articles assessed for eligibility after initial screening of titles and abstracts, and removal of duplicates. After reading full-text articles, 14 were excluded as they did not perform IMT, 4 did not use an inspiratory resistance device, 31 were not a randomised control trial, 6 performed both expiratory muscle training and IMT, 6 did not possess outcome measures of interest, and 3 consisted of participants who had other neurological conditions. The remaining six studies were included in this systematic review (Figure 1).

Study characteristics

The characteristics of included studies are presented in Table 1.

Participants

The six included studies had a total of 124 participants, with mean ages between 27 and 46 years old. Participants had SCI's spanning C4 to T9, with ASIA classifications A, B, C, and D. Time since diagnosis ranged from two days to 15 years. Included studies had small sample sizes, ranging between 10^{21} to 40 participants [5].

Intervention

Three studies used inspiratory training devices that provided a resistance and were spring loaded (PowerBreathe®, HaB International ltd, Southam, UK; Philips Threshold® IMT, Respironics Inc, Parsippany, New Jersey), while the other three studies used devices that were not spring loaded (Respifit S® electronic, Eumedics GmbH, Purkersdorf, Austria; DHD Medical Products, Diemolding healthcare Division, Canatota NY). Duration of IMT interventions ranged from four to eight weeks, with a training

frequency of four to seven sessions a week. Three studies trained for 15–20 min, or 30 repetitions twice a day [8,11,14], while other studies trained for 10–15 min once a day [5,12,13]. Levels of resistance participants trained at varied from 40% of their baseline maximal inspiratory pressure to 80%. Studies using the Diemolding Healthcare Division (DHD) medical products inspiratory muscle trainer (DHD Medical Products, Diemolding healthcare Division, Canatota NY) began training at the smallest resistance, which was measured as the diameter of the hole they inspired through (7 mm). Follow-up was immediately after interventions ended, excluding Postma et al. [5] who performed an additional follow-up at 16 weeks and one year post intervention.

Outcome measures

All studies measured inspiratory muscle strength using a manometer through maximal inspiratory pressure [5,8,11–14], with five studies also assessing maximal expiratory pressure [5,8,12–14]. Quality of life was assessed in two studies [5,12], using the 12-item version of the Medical Outcomes Short-form Health Survey [22], and the 36-item version of the Medical Outcomes Short-form Health Survey [23]. Both studies presented results of the physical and mental health components of the measure separately. For change in lung function, forced expiratory volume in 1 s was assessed *via* spirometry [5,8,12,14]. To determine whether IMT improved respiratory muscle strength enough to prevent the development of pneumonia, the MD generated for MIP was applied to strength discriminators for pneumonia [16].

Risk of bias

The highest source of bias was due to incomplete outcome data, as participants were lost to follow-up, or missed a large proportion of treatment sessions. Of the studies where there was incomplete outcome data [5,8,11,12], none completed an intention-to-treat analysis. However, Postma et al. [5] completed a per protocol analysis. All studies analysed outcomes they had stated *a priori*, giving a low risk for reporting bias. Two studies provided no information regarding the blinding of participants and personnel [8,11], while two others provided insufficient information to ensure participants and personnel were not aware of the experimental conditions [5,13]. Regarding detection bias, three studies did not state whether participants and personnel were blinded to outcome assessment [8,11,14], creating an unclear risk of bias. The method of allocation concealment was not described in Derrickson et al. [11] or Liaw et al. [8], and the consecutive randomisation approach used by Mueller et al. [12] is not adequate to assume participants were unaware of upcoming group allocations. Random sequence generation was implemented for all interventions, however Mueller et al. [12] did not mention their method for doing so, creating an unclear risk of bias (Figure 2).

Effect of inspiratory muscle training

Respiratory muscle strength

All six studies [5,8,11–14] totalling 124 participants reported the effect of IMT on maximal inspiratory pressure immediately post intervention. All respiratory pressures were expressed as absolute values. Compared to control (sham or no intervention), IMT significantly improved maximal inspiratory pressure by an average of 15.72 cmH$_2$O (95% CI 5.02 to 26.41) (Figure 3).

Five studies [5,8,12–14] totalling 113 participants reported the effect of IMT on maximal expiratory pressure. When compared to control, maximal expiratory pressure improved by an average of

Figure 2. Risk of bias of included studies assessed using the Cochrane Risk of Bias Tool.

5.19 cmH$_2$O (95% CI −4.16 to 14.55), however this was not statistically significant (Figure 4).

Quality of life

Two studies [5,12] provided data on 56 participants, regarding the effect of IMT on physical and mental quality of life. There was a non-significant standardised mean difference in physical quality of life of 0.12 (95% CI −1.01 to 1.25) for IMT when compared to control groups (Figure 5). IMT did not improve the mental component of quality of life compared to control groups, producing a standardised mean difference of −0.20 (95% CI −1.72 to 1.33) (Figure 6).

Lung function

Lung function measured *via* forced expiratory volume in 1 s was reported in four of the studies [5,8,12,14] totalling 86 participants. IMT improved forced expiratory volume in 1 s compared to control by an average of 0.26 L (95% CI −0.19 to 0.7)—however there was not a significant difference in experimental over control groups ($p = 0.26$) (Figure 7).

Sensitivity analyses

Changes in maximal inspiratory pressure for spring-loaded and non-spring-loaded devices

Three studies [5,13,14] totalling 77 participants used a spring-loaded device (PowerBreathe®, HaB International ltd, Southam, UK; Philips Threshold® IMT, Respironics Inc, Parsippany, New Jersey) for IMT. Analysing only these studies, IMT significantly
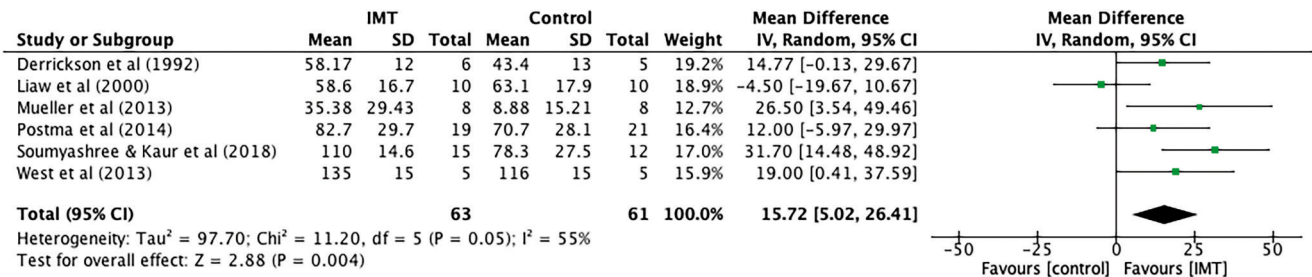
Study or Subgroup	IMT Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Derrickson et al (1992)	58.17	12	6	43.4	13	5	19.2%	14.77 [-0.13, 29.67]
Liaw et al (2000)	58.6	16.7	10	63.1	17.9	10	18.9%	-4.50 [-19.67, 10.67]
Mueller et al (2013)	35.38	29.43	8	8.88	15.21	8	12.7%	26.50 [3.54, 49.46]
Postma et al (2014)	82.7	29.7	19	70.7	28.1	21	16.4%	12.00 [-5.97, 29.97]
Soumyashree & Kaur et al (2018)	110	14.6	15	78.3	27.5	12	17.0%	31.70 [14.48, 48.92]
West et al (2013)	135	15	5	116	15	5	15.9%	19.00 [0.41, 37.59]
Total (95% CI)			63			61	100.0%	15.72 [5.02, 26.41]

Heterogeneity: Tau^2 = 97.70; Chi^2 = 11.20, df = 5 (P = 0.05); I^2 = 55%
Test for overall effect: Z = 2.88 (P = 0.004)

Figure 3. Mean difference (95% CI) in maximal inspiratory pressure (cmH$_2$O) due to inspiratory muscle training, estimated by pooling data from six studies (n = 124).

Study or Subgroup	IMT Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Liaw et al (2000)	39.7	18.8	10	40.9	8.9	10	23.9%	-1.20 [-14.09, 11.69]
Mueller et al (2013)	7.5	14.73	8	3.25	13.27	8	22.5%	4.25 [-9.49, 17.99]
Postma et al (2014)	53.5	25.7	19	61.7	27.9	21	18.4%	-8.20 [-24.81, 8.41]
Soumyashree & Kaur et al (2018)	62.6	20.5	15	49.1	17.2	12	21.8%	13.50 [-0.72, 27.72]
West et al (2013)	94	19	5	71	15	5	13.5%	23.00 [1.78, 44.22]
Total (95% CI)			57			56	100.0%	5.19 [-4.16, 14.55]

Heterogeneity: Tau^2 = 52.04; Chi^2 = 7.45, df = 4 (P = 0.11); I^2 = 46%
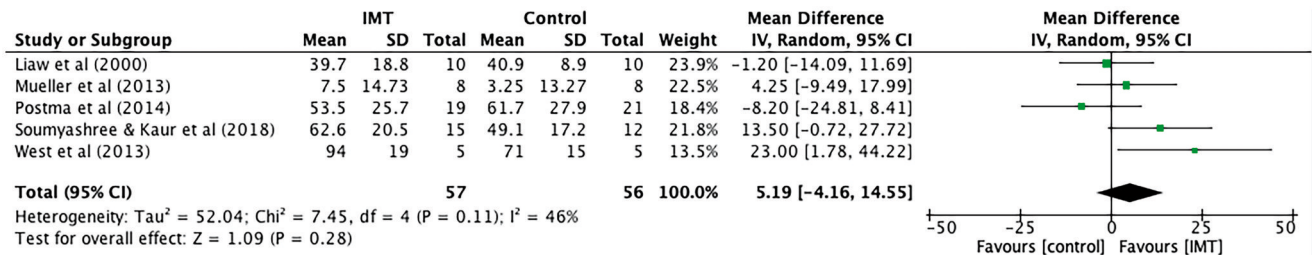Test for overall effect: Z = 1.09 (P = 0.28)

Figure 4. Mean difference (95% CI) in maximal expiratory pressure (cmH2O) due to inspiratory muscle training, estimated by pooling data from five studies (n = 113).

Study or Subgroup	IMT Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Mueller et al (2013)	1.63	4.05	8	-2.75	6.4	8	43.6%	0.77 [-0.25, 1.80]
Postma et al (2014)	58.7	21.3	19	67.3	22.4	21	56.4%	-0.39 [-1.01, 0.24]
Total (95% CI)			27			29	100.0%	0.12 [-1.01, 1.25]

Heterogeneity: Tau^2 = 0.48; Chi^2 = 3.56, df = 1 (P = 0.06); I^2 = 72%
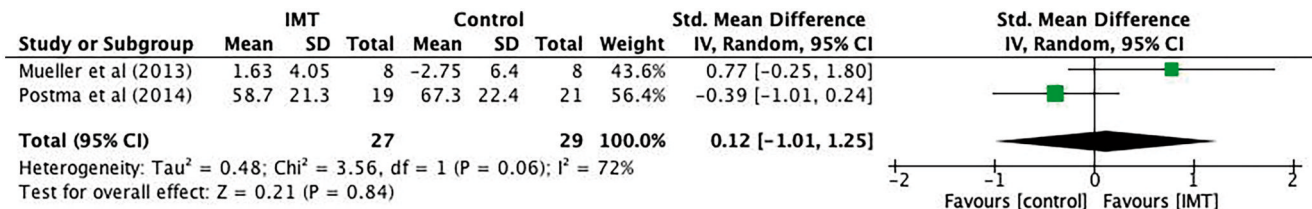Test for overall effect: Z = 0.21 (P = 0.84)

Figure 5. Standardised mean difference (95% CI) in quality of life: physical component due to inspiratory muscle training, estimated by pooling data from two studies (n = 56).
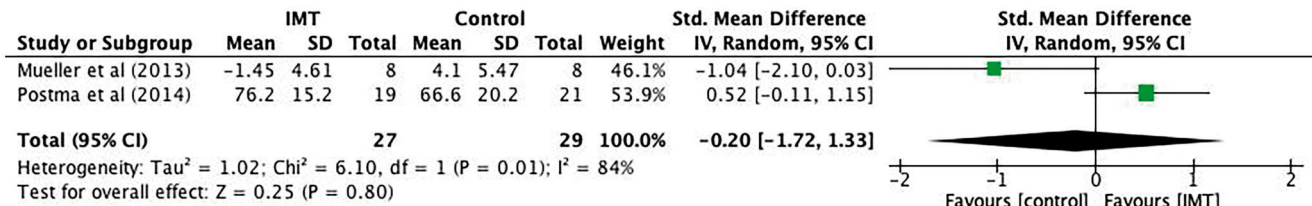
Study or Subgroup	IMT Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Mueller et al (2013)	-1.45	4.61	8	4.1	5.47	8	46.1%	-1.04 [-2.10, 0.03]
Postma et al (2014)	76.2	15.2	19	66.6	20.2	21	53.9%	0.52 [-0.11, 1.15]
Total (95% CI)			27			29	100.0%	-0.20 [-1.72, 1.33]

Heterogeneity: Tau^2 = 1.02; Chi^2 = 6.10, df = 1 (P = 0.01); I^2 = 84%
Test for overall effect: Z = 0.25 (P = 0.80)

Figure 6. Standardised mean difference (95% CI) in quality of life: mental component due to inspiratory muscle training, estimated by pooling data from two studies (n = 56).

Study or Subgroup	IMT Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Liaw et al (2000)	1.6	0.4	10	1.7	0.8	10	22.6%	-0.10 [-0.65, 0.45]
Mueller et al (2013)	0.42	0.44	8	0.21	0.32	8	27.8%	0.21 [-0.17, 0.59]
Postma et al (2014)	2.43	0.8	19	2.48	0.81	21	24.2%	-0.05 [-0.55, 0.45]
West et al (2013)	3.79	0.46	5	2.88	0.24	5	25.5%	0.91 [0.46, 1.36]
Total (95% CI)			42			44	100.0%	0.26 [-0.19, 0.70]

Heterogeneity: Tau^2 = 0.15; Chi^2 = 10.99, df = 3 (P = 0.01); I^2 = 73%
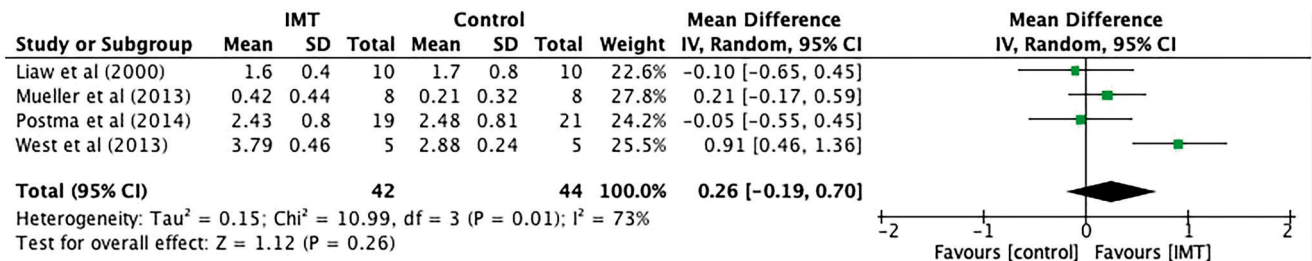Test for overall effect: Z = 1.12 (P = 0.26)

Figure 7. Mean difference (95% CI) in Forced expiratory volume in 1 s (L) due to inspiratory muscle training, estimated by pooling data from four studies (n = 86).

improved maximal inspiratory pressure compared to control groups, with an average of 21.18 cmH$_2$O (95% CI 9.65 to 32.72).

Three studies [8,11,12] totalling 47 participants used a non-spring-loaded threshold device (Respifit S® electronic, Eumedics GmbH, Purkersdorf, Austria; DHD Medical Products, Diemolding healthcare Division, Canatota NY) for IMT. IMT did not significantly improve maximal inspiratory pressure compared to control

groups, producing a MD of 10.86 cmH$_2$O (95% CI −6.22 to 27.94) (Figure 8).

Changes in maximal inspiratory pressure for six and eight week interventions

Four studies [5,8,12,14] with a sample of 86 participants performed IMT interventions which lasted six and eight weeks. When
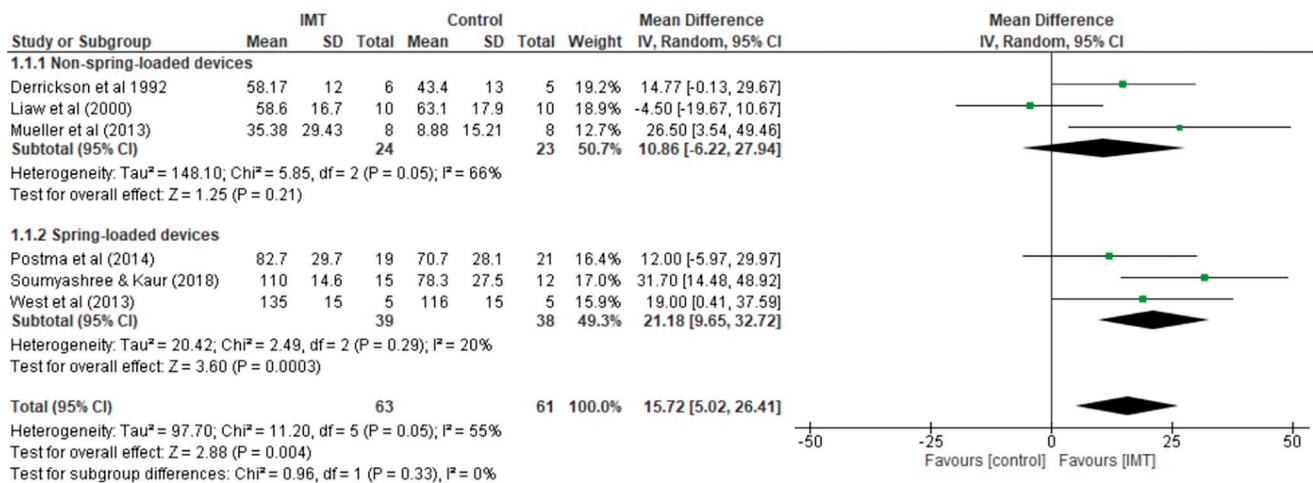
Figure 8. Mean difference (95% CI) in maximal inspiratory pressure due to inspiratory muscle training, estimated by pooling data from six studies, sub-grouped into studies utilizing non-spring-loaded and spring-loaded threshold devices (n = 124).
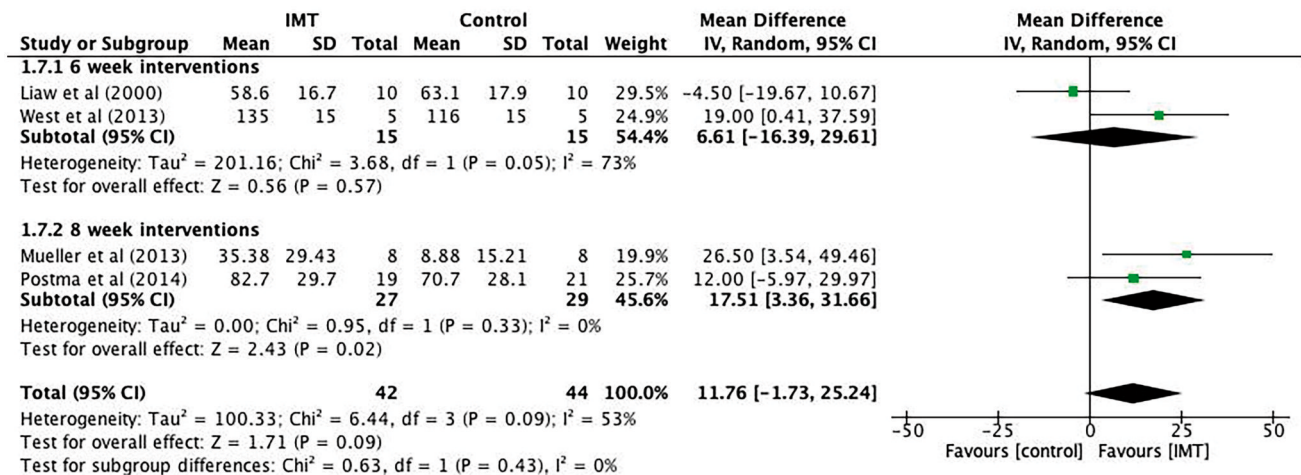

Figure 9. Mean difference (95% CI) in maximal inspiratory pressure due to inspiratory muscle training, estimated by pooling data from four studies, sub-grouped into six and eight week interventions (n = 86).

compared to control, six week interventions produced a non-significant effect for IMT, with an average maximal inspiratory pressure of 6.61 cmH$_2$O (95% CI −16.39 to 29.61). For eight week interventions, IMT had a significant effect over control, producing an average maximal inspiratory pressure of 17.5 cmH$_2$O (95% CI 3.36 to 31.66) (Figure 9).

Certainty of evidence

Using the GRADE assessment, the outcome maximal inspiratory pressure showed moderate quality evidence, due to risk of bias concerning blinding of participants, outcome assessment and attrition bias. Maximal expiratory pressure and forced expiratory volume in 1 s had low quality of evidence as small sample sizes and wide confidence intervals included both no effect and appreciable benefit, leading to imprecision. The mental and physical quality of life outcomes gave very low quality of evidence, as there was considerable heterogeneity between study results, leading to inconsistency (Table 2).

Discussion

The aim of this systematic review was to determine if IMT is effective at improving respiratory muscle strength, lung function and quality of life, and whether any improvements in strength

were enough to lower an individual with SCI's risk of developing pneumonia. A secondary aim was to explore whether intervention, duration or type of device impacted on effectiveness. IMT was found to have a statistically significant effect on inspiratory muscle strength. However, there was a lack of sufficient evidence to reach a clear conclusion on quality of life, maximal expiratory pressure, or forced expiratory volume in 1 s. Therefore, maximal inspiratory pressure may be a better measure of improvement for respiratory muscle strength, especially in people with lesions where the inspiratory muscles innervate (C2-T11).

The meta-analyses for maximal inspiratory pressure had the largest sample size (n = 124), and the largest effect size to favour the intervention (MD 15.72 cmH$_2$O, 95% CI 5.02–26.41). This is consistent with several other systematic reviews that examined IMT in SCI [4,9,10,19]. The sensitivity analysis comparing maximal inspiratory pressure scores for six and eight week interventions showed a significant effect favouring eight week interventions (MD 17.5 cmH$_2$O, 95% CI 3.36 to 31.66) over six week (MD 6.61 cmH$_2$O, 95% CI −16.39 to 29.61). Skeletal muscle fibre hypertrophy can occur with strength training sessions performed two to three times per week, with resistance progressively increased [24]. Participants in the eight week intervention group had more total IMT sessions than the six week, allowing them more time to

train under increasing resistance. This extra time and training sessions may explain why the Mean Difference for maximal inspiratory pressure was significantly improved compared to results for six week interventions.

To further analyse which experimental protocols were most conducive to generating improvements in maximal inspiratory pressure, a sensitivity analysis considering only IMT devices that were spring-loaded was performed. The Mean Difference improved from an original maximal inspiratory pressure of 15.72 cmH$_2$O (95% CI 5.02–26.41) to 21.18 cmH$_2$O (95% CI 9.65–32.72), with a significance of $p = 0.0003$. The statistical heterogeneity also improved from 55% to 20%. Conversely, the sensitivity analysis for maximal inspiratory pressure considering non-spring-loaded devices found a non-significant Mean Difference and greater heterogeneity between studies. These results suggest that ideal experimental conditions for IMT may involve at least eight week interventions, using spring-loaded inspiratory threshold devices

(PowerBreathe®, HaB International ltd, Southam, UK; Philips Threshold® IMT, Respironics Inc, Parsippany, New Jersey).

A 2009 update of the American Thoracic Society and the European Respiratory Society's statement on respiratory muscle testing proposes reference equations for both the mean clinically important difference (MCID) and lower limit of normal (LLN) values for maximal inspiratory and maximal expiratory pressure, according to age and sex [25]. This would assist in determining clinical relevance of our results for these outcomes. However, due to variability in weight, lesion-level and ASIA classification, there is a broad spectrum of respiratory strength and lung volumes one may expect to find clinically in individual's with SCI's. Given this, a study by Mueller et al. [26] developed regression coefficients to better determine the lesion-specific reference values for maximal inspiratory pressure in individuals with SCI's (Figure 10).

Using the regression coefficients, a 15% increase in maximal inspiratory pressure is needed for individuals with ASIA A and B

Table 2. Quality of evidence using the GRADE approach (inspiratory muscle training compared to control for adults with spinal cord injuries).

Patient or population: Adults with spinal cord injuries

Setting: Hospital and community

Intervention: Inspiratory muscle training

Comparison: Control

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control	Risk with Inspiratory muscle training				
Maximum inspiratory pressure (cmH$_2$O) follow up: range 4 weeks to 8 weeks	The mean maximum inspiratory pressure (cmH$_2$O) ranged from 43 to 78 cmH$_2$O	MD 15.72 cmH$_2$O higher (5.02 higher to 26.41 higher)	–	124 (6 RCTs)	⊕⊕⊕◯ MODERATE [a]	Inspiratory muscle training probably increases maximum inspiratory pressure (cmH$_2$O).
Maximum expiratory pressure (cmH$_2$O) follow up: range 4 weeks to 8 weeks	The mean maximum expiratory pressure (cmH$_2$O) ranged from 41 to 71 cmH$_2$O	MD 5.19 cmH$_2$O higher (4.16 lower to 14.55 higher)	–	113 (5 RCTs)	⊕⊕◯◯ LOW [a,b]	The evidence suggests that inspiratory muscle training results in little to no difference in maximum expiratory pressure (cmH$_2$O).
Forced expiratory volume in 1 s (L) follow up: range 6 weeks to 8 weeks	The mean forced expiratory volume in 1 s (L) ranged from 1.70 to 2.88 L	MD 0.26 L higher (0.19 lower to 0.7 higher)	–	86 (4 RCTs)	⊕⊕◯◯ LOW [a,b]	Inspiratory muscle training may increase/ have little to no effect on forced expiratory volume in 1 s (L) but the evidence is very uncertain.
Quality of life: physical component follow up: 8 weeks	–	SMD 0.12 higher (1.01 lower to 1.25 higher)	–	56 (2 RCTs)	⊕◯◯◯ VERY LOW [a,b,c]	The evidence is very uncertain about the effect of inspiratory muscle training on quality of life: physical component.
Quality of life: mental component follow up: 8 weeks	–	SMD 0.2 lower (1.72 lower to 1.33 higher)	–	56 (2 RCTs)	⊕◯◯◯ VERY LOW [a,b,c]	The evidence is very uncertain about the effect of inspiratory muscle training on quality of life: physical component.

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: Confidence interval; MD: Mean difference; SMD: Standardised mean difference.

GRADE Working Group grades of evidence.

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Explanations:

[a]High risk for blinding of participants, outcome assessment and attrition bias (risk of bias).

[b]Small sample size and wide confidence interval includes both no effect and appreciable benefit (imprecision).

[c]Considerable heterogeneity between study results (inconsistency.

	Pi$_{max}$ (cmH$_2$O) β [95% CI]	Pe$_{max}$ (cmH$_2$O) β [95% CI]
Constant	45.31 [62.48; 28.14]	55.72 [68.70; 42.75]
ΔHT–LT	−11.98* [−4.38; −19.59]	−7.87 [1.71; −17.45]
ΔLT–HP	10.90 [19.52; 2.28]	9.09 [17.77; 0.41]
ΔLT–LP	19.89* [30.96; 8.82]	36.18* [48.70; 23.66]
Gender	14.95* [22.87; 7.03]	19.74* [28.11; 11.37]
Age (years)	−0.60* [−0.38; −0.82]	−0.52* [−0.17; −0.87]
Height (cm)	n.s.	n.s.
Body mass (kg)	0.51* [0.73; 0.29]	n.s.
TPI (years)	n.s.	0.46* [0.75; 0.17]

*Significant influencing factor (p<0.05); n.s.: not significant.
Pi$_{max}$: maximal inspiratory pressure; Pe$_{max}$: maximal expiratory pressure; β: regression coefficient for each independent variable; CI: confidence interval; HT: high tetraplegia; LT: low tetraplegia; HP: high paraplegia; LP: low paraplegia; ΔHT–LT/ΔLT–HP/ΔLT–LP: group dummies with LT as reference; gender: 0: women; 1: men; TPI: time post-injury.

Figure 10. Regression coefficients and 95% confidence intervals to determine lesion- specific MIP and MEP values, using constants developed by Mueller et al. [26].

Table 3. Example equation to determine lesion-specific MIP value.

Participant characteristics:	Male, ASIA A, C7 lesion, 47 years old, weight 72 kg
Equation:	45.31 (constant) + −11.98 (high tetraplegia group) + 14.95 (male) + (47*-0.60) (age) + (72*0.51) (body weight)
Lesion-specific MIP:	56.8 cmH$_2$O
Improvement needed to avoid developing pneumonia:	56.8 cmH$_2$O (*15%) = 8.52 cmH$_2$O

lesions to obtain enough respiratory strength to avoid developing pneumonia [16]. For individuals with ASIA C and D lesions, a maximal inspiratory pressure of 93.5 cmH$_2$O has been identified as the discrimination between individuals with and without pneumonia [16]. An example of the equation is provided below using mean participant characteristics from Postma et al. [5], along with the MD for maximal inspiratory pressure determined in this review (Table 3).

The average pre-intervention lesion-specific maximal inspiratory pressure value is 56.8 cmH$_2$O. Therefore, an increase of 8.52 cmH$_2$O is needed to avoid developing pneumonia. Since the MD for maximal inspiratory pressure is 15.72 cmH$_2$O (95% CI 5.02–26.41), using IMT to improve maximal inspiratory pressure may decrease an individual's chances of developing pneumonia—depending on the pre-intervention lesion-specific maximal inspiratory pressure level (Table 3). This is an important clinical consideration—since pneumonia is one of the most common risk factors for mortality in SCI [2].

Results of the quality of life meta-analyses were not significant, however improvements in physical quality of life favoured the IMT group (SMD 0.12, 95% CI −1.01 to 1.25, p = 0.84). This is continuous with the results found in the systematic review by Van Houtte et al. [15], as significant improvements in respiratory strength were coupled with improvements in health-related quality of life. However this was not the same case for mental quality of life, as improvements were not mutually exclusive to the experimental group participants were in (SMD −0.2, 95% CI −1.72 to 1.33, p = 0.8). This may be attributable to several factors such as time since injury, and coping with the impact of a new disability and its effect on social participation, dependency, acceptance, social relations and completion of daily tasks [27].

Postma et al. [5] used the SF-36 version of the Medical Outcomes Short-Form Health Survey [23], while Mueller et al. [12] used the SF-12 [22] version. Both outcomes are proven reliable and valid in people with SCI [22,28,29]. However, assessment of the mental component for the SF- 36 was based on groups of individuals one and five years post SCI [29]. Since Postma et al. [5] recruited participants two to four months post SCI, this measure may not be sensitive enough to detect initial changes an SCI has on mood and emotional wellbeing.

A strategy to more accurately assess participants quality of life could be performing IMT in group sessions. This was done by Roberts et al. [30], who found patients were more motivated to complete IMT when done as a group. However, they state a focus group or patient satisfaction questionnaire needs to be undertaken to obtain qualitative feedback on factors that may influence patient's adherence and motivation to compliance with IMT long-term.

Meta-analyses for forced expiratory volume in 1 s found the mean difference crossed the line of null effect, and there was no statistically significant difference for IMT compared to control groups (MD 0.26 L, 95% CI −0.2 to 0.7, p = 0.26). Other systematic review's on IMT were inconclusive as to the effect on forced expiratory volume in 1 s [4,18], although Lemos et al. [19] did find a significant improvement in forced expiratory volume in 1 s concerning RMT interventions (through narrative synthesis). The participants had injuries spanning C2-L3—meaning some individuals did not lose innervation to their expiratory muscles. This may explain the discrepancy in results for forced expiratory volume in 1 s compared to this review.

The meta-analyses for maximal expiratory pressure did not produce a statistically significant effect for IMT, however the pooled effect favoured the intervention compared to control group (MD 5.19 cmH$_2$O, 95% CI −4.16 to 14.55). The expiratory muscles are innervated through levels T1-T12 [3,p.669], therefore IMT is unlikely to make a difference in maximal expiratory pressure as most of the individuals in the included studies had cervical spine injuries. Patients with these injuries are likely to need manual assistance to perform any forceful expiration e.g., an assisted cough [3, p.673].

In an attempt to minimize methodological bias, the GRADE approach was implemented. This took into consideration the large effect size present in each meta-analyses—allowing for more accurate recommendations to be made. Berlowitz and Tamplin [9] performed a GRADE analysis across similar outcomes, with comparable reasons for downgrading evidence. However, the recommendations for maximal inspiratory pressure differed in that this systematic review graded the quality of the evidence higher. This could be attributable to more recent randomised controlled trials that were included in this review, which gathered significant results using newer threshold training devices with a spring-loaded component.

Another aspect that threatened methodological quality of this review is combining articles that are considerably heterogenous. This was found concerning devices used to deliver IMT, training protocols of studies, participant characteristics and comparison control groups. While some of these differences allowed for conclusions to be drawn concerning ideal training length or more effective device—an increase in homogeneity would have improved the certainty of this evidence. Sheel et al. [4] addressed participant heterogeneity as an "essential consideration" due to the different effect IMT will have on participants with cervical compared to thoracic injuries. Given this, Sheel et al. [4] and Van Houtte et al. [15] narratively synthesized results of their systematic reviews. Berlowitz and Tamplin [9] identified similar factors for heterogeneity, but performed a meta-analysis as they had enough

studies consisting of similar outcome measures. However, they limited subgroup analysis to outcomes with data for three or more trials, to increase internal validity. This was also performed by this systematic review, in an effort to deliver trustworthy results and minimize reporting bias. However, subgroup analysis considering intervention effect on treatment intensity and time since injury was not performed, as studies had high variability in training intensities and injury duration.

Moderate to high risk of bias was observed across the included studies. Many articles reported participants withdrew after studies had begun, and did not use an intention-to-treat analysis to account for missing outcome data. This created high-risk for attrition bias in four [5,8,11,12] of the six studies included, as they did not obtain enough participants to achieve an adequately powered sample size (of those that stipulated on this before-hand). Therefore, losing participants threatened statistical power of each study, making it difficult to detect a true difference between experimental groups that was due to the intervention itself.

Blinding of participants and personnel as well as outcome assessment was another source of bias amongst included studies. A recently published protocol concerning the use of IMT and postoperative pulmonary complications [31] is attempting to minimize blinding and allocation bias by including a low resistance and high resistance IMT group. They stated including a low resistance group is likely to blind participants with respect to their allocation, as they are likely to be unfamiliar with IMT, so are unlikely to have expectations of benefit from being in one group rather than another. Blinding and allocation bias has also been found in other systematic reviews involving IMT with participants who have asthma [32], cystic fibrosis [33] and SCI [9]. However, a systematic review analysing IMT with people who have COPD included multiple randomised controlled trials that tried to minimize allocation bias using sham inspiratory training devices [34]. It is difficult to achieve blinding in rehabilitation and inpatient settings, but the strategies highlighted above may help to mitigate these effects.

The small sample sizes and heterogeneity of participants in the included studies also limited the generalizability of results from this review, as confounding factors such as age, ASIA classification, and time since injury were not balanced across studies. However, even if studies do achieve an adequately powered sample size, participant withdrawal is highly likely due to the nature of SCI's e.g., pressure sores, early discharge, complications not related to intervention, or declining further participation. There are also limitations concerning the method for outcome assessment on individuals with SCI's. The American Thoracic Society and the European Respiratory Society have adapted guidelines for respiratory assessments involving pressure manometers and the use of spirometry [35], however discrepancy in the position participants were measured in may have attributed to statistical and clinical heterogeneity across the included studies.

In recent years, IMT has grown in popularity, bringing about changes to its design. Two of the devices used in the included studies [8,11,12] involve flow dependent resistance (Respifit S® electronic, Eumedics GmbH, Purkersdorf, Austria; DHD Medical Products, Diemolding healthcare Division, Canatota NY). A limitation to these devices is that the load is generated by airflow, i.e.; if a participant does not inspire forcefully enough, there is no training load [36]. This parameter is difficult to control for, and could have impacted the training effect on participants in these studies.

The other two devices used in the included studies [5,13,14] work *via* a one-way spring-loaded threshold valve [36]. This type

of device is advantageous, as the valve closes during inspiration and requires participants to inhale hard enough to open the valve and let air enter [36]. Therefore the inspiratory pressure remains constant, regardless of how quickly or slowly participants breathe in. A study on individuals with COPD demonstrated that inspiratory pressure load is an important variable in IMT. They found that training at higher pressure loads, using a pressure-threshold device significantly improved respiratory muscle strength, endurance and exercise tolerance compared to patients with COPD who trained at lower pressure loads [37]. A similar effect was illustrated in this systematic review, as the sensitivity analysis for spring-loaded devices (PowerBreathe®, HaB International ltd, Southam, UK; Philips Threshold® IMT, Respironics Inc, Parsippany, New Jersey) showed greater improvement in respiratory muscle strength over flow-dependent devices (Respifit S® electronic, Eumedics GmbH, Purkersdorf, Austria; DHD Medical Products, Diemolding healthcare Division, Canatota NY). This tells us that including both spring-loaded and non-spring loaded devices contributes to clinical heterogeneity, and lower estimates of treatment effect. This information will allow researchers to better understand the parameters that create a true intervention effect for IMT.

IMT has been proven effective in intensive care settings on non-SCI mechanically ventilated patients as part of their physiotherapy [38]. It's proven feasible and safe for adults with acute, complete cervical and thoracic SCI whose respiratory status was stable [7], and increases respiratory strength irrespective of time since injury, or degree of injury completeness [6]. Participants in the included studies of this systematic review handled the device independently, with little supervision, and in many different settings—as the device is small and portable. IMT can be implemented alongside regular physiotherapy, and is not time intensive—with benefits found between 10 and 20 min a day from the studies included in this review. Additionally, none of the included studies reported adverse outcomes as a result of using IMT, and those that included patient satisfaction scores reported higher levels of satisfaction and motivation [5,14]. Considering these factors, IMT should be implemented as a routine therapy for people with SCI [6].

Previous randomised controlled trials and systematic reviews have provided a strong case for IMT in SCI—however few considered evidence of carryover beyond the training period. Performing IMT as a group may help influence long-term adherence [30], however further analysis needs to be done before any conclusions are drawn. Motivation for people to continue with IMT may be based on changes in outcome measures that are perceived by them to be important, such as reductions in dyspnoea or improvements in exercise capacity, social participation and decreased hospital admissions [39]. Given this, studies which consider obtaining qualitative data from patient focus groups or semi-structured interviews would help with understanding the factors behind motivation and adherence to IMT. This data could inform the creation of guidelines for the use of IMT, so it can be implemented in various clinical settings of individuals with SCI's.

The results of this review indicate IMT can improve respiratory muscle strength in people with an SCI, no matter their level of injury or completeness. However, outcomes such as quality of life, maximal expiratory pressure, and forced expiratory volume in 1 s show no clear evidence of a benefit from IMT itself. Further evidence is therefore needed as to the benefit of IMT on these outcomes, in addition to MIP. Interventions that last eight weeks and utilize spring-loaded pressure-threshold devices are the most ideal experimental conditions, and have potential to bring about the

greatest improvements in respiratory strength. Furthermore, IMT may help decrease an individual with SCI's risk of mortality and morbidity due to respiratory complications such as pneumonia. However, these results should be interpreted with caution due to the heterogeneous nature of included studies, and small sample sizes. Although IMT is feasible and safe to implement in clinical practice, future trials are needed to determine more robust recommendations at this time.

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