

## **Abstract**

While prolonged standing has shown to be detrimentally associated with musculoskeletal symptoms, exposure limits and underlying mechanisms are not well understood. We systematically reviewed evidence from laboratory studies on musculoskeletal symptom development during prolonged ( $\geq 20$  minutes) uninterrupted standing, quantified acute dose-response associations and described underlying mechanisms.

Peer-reviewed articles were systematically searched for. Data from included articles were tabulated, and dose-response associations were statistically pooled. A linear interpolation of pooled dose-response associations was performed to estimate the duration of prolonged standing associated with musculoskeletal symptoms with a clinically relevant intensity of  $\geq 9$  (out of 100).

We included 26 articles (from 25 studies with 591 participants), of which the majority examined associations of prolonged standing with low back and lower extremity symptoms. Evidence on other (e.g., upper limb) symptoms was limited and inconsistent. Pooled dose-response associations showed that clinically relevant levels of low back symptoms were reached after 71 minutes of prolonged standing, with this shortened to 42 minutes in those considered pain developers. Regarding standing-related low back symptoms, consistent evidence was found for postural mechanisms (i.e., trunk flexion and lumbar curvature), but not for mechanisms of muscle fatigue and/or variation in movement. Blood pooling was the most consistently reported mechanism for standing-related lower extremity symptoms.

Evidence suggests a detrimental association of prolonged standing with low back and lower extremity symptoms. To avoid musculoskeletal symptoms (without having a-priori knowledge on whether someone will develop symptoms or not), dose-response evidence

from this study suggests a recommendation to refrain from standing for prolonged periods >40 minutes. Interventions should also focus on underlying pain mechanisms.

**Key words:** Standing - Musculoskeletal symptoms – Systematic review – Exposure limit

## **Introduction**

Prolonged periods of standing are traditionally common in certain occupations, including in retail, food, healthcare, education, and manufacturing industries. It has been shown that 62% of a sample from the general Australian working population reported their work involved standing[1]; which is consistent with findings from a study in a Canadian working population[2].

A growing body of evidence suggests that prolonged sitting is associated with several adverse health outcomes[3-5]. Consequently, expert recommendations advise workers to replace periods of sitting at work with standing and other light activities such as walking[6]. There is a growing interest in workplaces implementing this advice[7], most notably through the introduction of sit/stand office workstations[8]. However, these alternatives to sitting, such as standing, may expose workers to other health consequences[9].

Adverse health outcomes of standing have been previously reported[10], and include lower extremity venous disorders[11, 12], perinatal health complications (such as preterm delivery and pre-eclampsia)[13] and musculoskeletal symptoms (e.g. self-reported pain, discomfort or complaints in any region of the musculoskeletal system). In a recent systematic review on epidemiological evidence, it was identified (albeit from limited high quality evidence from longitudinal studies) that occupational standing was detrimentally associated with low back symptoms[14]. Evidence regarding the association of excessive standing and lower extremity symptoms was inconclusive, while of the limited evidence with upper extremity symptoms, a significant association did not seem to be evident.

One key issue inadequately addressed to date is the dosage of prolonged standing that may induce musculoskeletal symptoms. The prolonged standing strain index developed by Halim and Omar[15], which was based on a review of (scientific and professional)

occupational health literature and expert (e.g., ergonomic practitioners, medical doctors and physiotherapists) opinions, states that  $\leq 1$  hour of continuous standing can be considered safe,  $>1$  hour of continuous standing is slightly unsafe and  $>1$  hour of continuous standing in combination with  $>4$  hours of standing per day as unsafe. The scientific basis of these exposure limits was, however, unclear as a systematic review of evidence on dose-response associations has not been undertaken.

Apart from the lack of understanding about exposure limits, underlying mechanisms explaining the associations of prolonged standing with musculoskeletal symptoms have not been elucidated. Such knowledge is needed for the development of interventions targeted at preventing detrimental effects of prolonged standing. Previous work has suggested mechanisms of muscle fatigue[16], static postures and lack of variation in movement[17, 18] to be possible contributors to standing-related low back symptoms. It has also been suggested that there may be different subgroups of people that do and do not develop low back symptoms during periods of prolonged standing[19-21]; often referred to as 'pain developers' and 'non-pain developers', respectively. However, factors that distinguish pain developers from non-pain developers are not well understood yet. For the association of standing and lower limb symptoms, mechanisms of muscle fatigue[22] and mechanisms from a non-musculoskeletal origin such as those of swelling[23] due to blood pooling in the lower limbs[16] have been suggested. However, a systematic overview of such mechanisms has not, as yet, been provided.

Considering the current emphasis on replacing office workplace sitting with standing, and the number of existing occupations that have traditionally been exposed to prolonged standing, a profound understanding of the health consequences of standing is needed to inform healthy work practices. Evidence-based exposure limits of standing are needed, while

an understanding of the mechanisms with regards to the association of prolonged standing and musculoskeletal symptoms is required. Our prior review of epidemiological studies examined the evidence of medium to long term dose-response relationships[14] but was not able to address acute dose-response relationships and contemporaneous potential mechanism changes. In this review we therefore aimed to: 1) systematically review the evidence on the acute associations between prolonged uninterrupted standing and non-specific musculoskeletal symptoms from controlled laboratory studies; 2) describe acute dose-response associations for standing and musculoskeletal symptoms to establish exposure limits; and, 3) tabulate potential mechanisms for these associations.

## **Methods**

### *Search strategy*

This review was a-priori registered[24] and executed according to the PRISMA statement guidelines[25]. To identify relevant publications, a comprehensive literature search was undertaken in electronic databases from database inception to 21 June 2016 using a combination of terms relevant to 'standing' and 'work-related' (Supplementary Material 1-6). No specific terms for health outcomes were used as this study is part of a larger review aimed at assessing the associations of standing with multiple health outcomes.

Two reviewers independently screened all potentially relevant titles and abstracts for eligibility, and if necessary, full-text articles were checked. Differences in judgment were resolved through a consensus procedure. Reference lists of selected articles were screened to identify additional potentially eligible articles. Studies were included if the article reported on the association of prolonged standing (defined for the purpose of this study as uninterrupted periods of standing for  $\geq 20$  minutes) with non-specific musculoskeletal

symptoms from a laboratory study; i.e., a controlled study which reported both the exposure to prolonged standing and musculoskeletal and possibly physiological outcomes (e.g., muscle activity, posture and leg circumference). We included articles published in English and in peer-reviewed journals. Reviews, editorials, letters and conference proceedings were excluded. Studies in which standing was not the main exposure variable (e.g., standing was only part of a certain condition/trial such as 'lifting during standing'), or in which standing was only used as a confounding variable, were excluded. Only articles describing a general adult population were included (e.g., excluding studies selecting workers with chronic disorders and non-adult populations). Moreover, for the purpose of this review, studies concerned with specific musculoskeletal conditions (e.g., osteoarthritis, fracture, cartilage damage) were excluded.

#### *Data extraction and risk of bias assessment*

Two reviewers independently assessed all selected articles for risk of bias and extracted relevant data. In cases of disagreement, consensus was reached during a meeting. Risk of bias was evaluated using an adapted version of a published methodological quality scoring system[26], based on eleven criteria for the reporting of study methods and results (Supplementary Material 7). Studies with a summary score  $\geq 0.75$  out of 1.00 were considered to be of high methodological quality[26], hence low risk of bias.

The following data from each included article were extracted: first author and year of publication, study design, sample description (i.e., number of participants, age, sex, country and other relevant specifics), standing condition (i.e., the duration of prolonged standing), other associated physiological outcomes (e.g., muscle activity, posture, spinal shrinkage, spinal load, leg circumference) and dose-response estimates. From articles reporting on

multiple conditions, only data from the prolonged standing condition were extracted. Where insufficient information was reported in the articles, authors were contacted to retrieve additional information. When dose-response information was otherwise unavailable, Digizeit software (Digizeit, Braunschweig, Germany, [www.digitizeit.de](http://www.digitizeit.de)) was used to digitize information on dose-response association from figures presented in the original articles.

### *Data-analysis*

All included articles were qualitatively described according to their extracted data and risk of bias. Study findings were stratified according to the symptom body area.

Dose-response data from individual studies were plotted and statistically pooled using Microsoft Excel (Microsoft Corporation, Redmond USA). To do so, musculoskeletal symptom outcomes were harmonized by normalizing outcomes to a 100 point scale. A linear interpolation of the pooled dose-response was performed to estimate musculoskeletal symptom intensity with a given dosage of prolonged standing. To develop evidence-based exposure limits, the dosage of prolonged standing accompanying a clinical relevant musculoskeletal symptom intensity level of 9 (out of 100)[27] was estimated. As earlier study samples have been stratified into pain developers and non-pain developers[19-21], based on whether, a-posteriori, participant's symptoms exceeded or changed by more than a given threshold amount, the abovementioned procedure were repeated for: a) all participants (combining data from pain developers and non-pain developers, and using data from articles not distinguishing these two groups), and separately for b) pain developers and c) non-pain developers.

Potential mechanisms underlying the associations of prolonged standing with musculoskeletal symptoms were tabulated.

## **Results**

### *Study selection*

The flow chart of the search and selection of literature is presented in Figure 1. The search strategy yielded, after removing duplicates, 13,702 individual articles that were screened for inclusion. A total of 509 full text articles were considered, of which 296 met the criteria of describing outcomes of standing, 140 of them reporting on musculoskeletal symptoms. A total of 17 of these articles specifically addressed the association of prolonged standing and non-specific musculoskeletal symptoms using a laboratory study design. After screening the reference lists of these articles, nine more articles were added, resulting in a total of 26 articles[16-21, 23, 28-46] (reporting from 25 studies with 591 participants) included in the current review from which risk of bias assessment and data-extraction was conducted (see Supplementary Material 8 and 9 for a summary of findings).

### *Data extraction*

All included articles described studies in which participants performed a laboratory static standing trial, while in ten studies participants[18, 20, 28, 32, 34-36, 38-40] additionally performed a light manual (e.g., clerical, assembly or precision) tasks for a prolonged period of time, averaging 107.5 (SD:40.9) minutes, ranging from 32 to 240 minutes. During these trials, musculoskeletal symptoms was self-reported, and in most of the studies, also other physiological outcomes (e.g., muscle activity, body postures or lower limbs swelling) were repeatedly objectively measured. Studied samples typically consisted of young and generally healthy participants without comorbidities such as pre-existing musculoskeletal symptoms



and/or other conditions that would prevent them from standing for a prolonged period of time. Participants also typically did not have any prior habituation to prolonged standing.

Identified articles reported musculoskeletal symptoms in the low back[17-21, 29-32, 35-43, 45] (19 articles), upper back[29] (two articles), trunk[44] (one article), neck/shoulder[44] (one article), and lower limbs[32] (one article), while various articles reported symptoms in specific areas of the lower limbs; i.e., thighs/buttocks[44], hips[29], upper legs[29], knees[29], lower legs[29, 33], ankles[29], feet[29, 32]. One article reported general symptoms (not in any specific body area)[34] while four articles measured and/or combined symptoms from various body areas[16, 23, 28, 46]. Thirteen articles assessed pain[17, 19, 21, 31, 35-43, 45], 10 articles assessed discomfort[16, 18, 20, 28, 29, 32, 33, 44, 46], one article assessed comfort[23] and one article assessed unpleasantness[34]. Musculoskeletal symptoms were assessed with self-reports using a visual analog scale (VAS) in 17 articles[17-21, 31-43], while five articles used a 0-10 scale[16, 28, 44-46], one article used a Borg scale[29] and one article used a 1-9 comfort rating scale[23].

Extracted studies showed consistent associations of prolonged standing with low back and lower extremity symptoms, with all identified studies showing symptom development (at least in a subgroup of the participants) during prolonged standing. However, inconsistent and limited study findings on other body area (e.g., upper limb) symptoms were found.

Thirteen articles categorized participants into pain developers and non-pain developers, using the following thresholds to make this categorization: one article used  $>10/100$  symptoms intensity[21], one article used a change of  $>8/100$ [43] and two articles used a change  $>10/100$  during the entire trial[19, 41], seven articles used a change  $>10/100$  from the baseline score[17, 30, 31, 35-38, 40], one article used any change in symptoms during

the standing trial[42] and one article used symptoms intensity >20/100 at any point and >10/100 overall[39]. The prevalence of pain developers reported in the included articles ranged from 28%[41] to 71%[35], with an average of 44%.

### *Risk of bias*

The average methodological quality score was 0.80 (SD:0.12) out of 1, ranging from 0.59 to 0.95, with 10 articles describing a study considered to have a high risk of bias (sum scores <0.75) (Supplementary Material 9).

### *Exposure limits for prolonged standing*

Plots for the dose-response of prolonged standing and low back and lower extremity symptoms are shown in Figures 2-4 in which results of 18 articles are presented. As two papers reported on the same study data[18, 20], only data from one article was used for data pooling[18].

Information from five articles could not be pooled because: only symptoms[29] or change in symptoms[36] at the end of the trial were reported; or, no time series on symptoms were provided[37, 41, 42]. While the association of prolonged standing and upper extremity symptoms had been evaluated in some of the studies[16, 28, 39, 44], the articles did not report on any development of symptoms during their respective trials, hence no dose-response associations could be assessed. Two articles reported general musculoskeletal symptoms (not in any specific body area)[23, 46] and were therefore also not presented in the plots.

Dose-response associations from 14 articles on the association of prolonged standing and low back symptoms, for participants not differentiated into pain developers and non-

pain developers (Figure 2), show a gradual increase in low back symptoms during prolonged standing. The pooled dose-response association is depicted by:

$$\text{Symptoms} = 0.12 * \text{standing time} + 0.66$$

According to this equation, a clinical relevant symptom intensity of  $\geq 9/100$ [27] would be achieved after 71 minutes of prolonged standing.

Stratified dose-response associations from the 10 different studies which provided data separately for pain developers (Figure 3) and non-pain developers (Supplementary Material 10) were plotted. The pooled dose-response association in the group of pain developers is depicted by:

$$\text{Symptoms} = 0.20 * \text{standing time} + 0.52$$

According to this equation, a clinical relevant symptom intensity of  $\geq 9/100$ [27] would be achieved after 42 minutes of prolonged standing in pain developers.

The pooled dose-response association in the group of non-pain developers was depicted by:

$$\text{Symptoms} = 0.02 * \text{standing time} + 0.31$$

According to this equation, a clinical relevant symptom intensity of  $\geq 9/100$ [27] would be achieved after 480 minutes (8 hours) of prolonged standing.

Finally, using data from six different articles[16, 28, 32-34, 44], the dose-response associations between prolonged standing and lower limb symptoms were plotted (Figure 4), showing an increasing pattern of lower limbs symptoms during prolonged standing. Due to the wide heterogeneity in associations (between studies), these data were not statistically pooled.

#### *Mechanisms for musculoskeletal symptoms due to prolonged standing*

Mechanisms for the development of low back and lower extremity symptoms due to prolonged standing are described in Tables 1 and 2 (from 17 and 10 studies, respectively). For low back symptoms, mechanisms at the level of the muscle, such as increased co-contraction, muscle fatigue or muscle stiffness, and a lack of muscle strength or endurance have been hypothesized to be a potential cause of low back symptoms. However, we could not find consistent evidence in supporting these mechanisms, with studies that did and did not find a significant association of these factors with either prolonged standing or the development of standing-related symptoms. We did however find consistency in evidence for mechanisms for the development of standing-related low back symptoms due to postures such as an increase in trunk flexion, axial rotation and lumbar curvature[18, 31, 42]. Evidence for a mechanism of (either too much or too little) variation in movement causing low back symptoms during standing showed a rather inconsistent picture with studies that did and did not find an association between factors like body sway, shifting of body weight and fidgeting with prolonged standing or the development of symptoms[16, 17, 29-32, 46].

For lower extremity symptoms, the mechanism of blood pooling during prolonged standing was most often reported. Consistent evidence showed that prolonged standing may cause an increase in blood flow (assessed by using Laser Doppler Flowmetry measured at the level of the skin), skin temperature and leg volume (typically assessed by measuring leg circumference), that may be associated with the development of musculoskeletal symptoms[16, 23, 28, 32-34, 45]. Evidence for mechanisms of (either too much or too little) variation in movement or muscle fatigue being the cause of standing-related lower-extremity symptoms showed a rather inconsistent picture with both studies that did and did not find an association of certain factors with prolonged standing or the development of symptoms.

## Discussion

### *Prolonged standing and musculoskeletal symptoms*

We have described the evidence on acute associations of prolonged standing and musculoskeletal symptoms from controlled laboratory studies. Prolonged standing was consistently associated with the development of low back and lower extremity symptoms in all identified studies reporting on these symptoms. There was inconsistent and limited evidence concerning risk for symptoms in other (e.g. upper extremity) areas. Our findings are broadly in line with what has been reported in earlier reviews[10, 14] showing the association of standing and musculoskeletal symptoms in epidemiological studies.

Importantly, our findings extend previous reports by quantifying the acute dose-response association between prolonged standing and low back symptoms. These findings were based on pooled dose-response associations of various studies from which data on low-back symptoms (i.e., pain and discomfort) were harmonized. In a general population (i.e. those not differentiated into pain developers and non-pain developers) it appeared that, a clinical relevant symptom intensity of  $\geq 9/100$  was evident after 71 minutes of prolonged standing, whereas such an intensity is reached after only 42 minutes in participants who develop pain. To minimize the risk of people developing musculoskeletal symptoms due to prolonged standing (without having a-priori knowledge on whether someone will develop symptoms or not), this information suggests ~40 minutes should be adopted as an exposure limit for prolonged standing. It should, however, be noted that even after a break from standing, symptoms are more likely to return in those that have developed standing-related symptoms prior to taking a break[47]. Care should thus be taken with applying the established threshold in those that have been exposed to earlier episodes of prolonged standing.

The dose-response associations of prolonged standing with lower extremity symptoms were substantially more heterogeneous than those for low back symptoms, as a result of which specific exposure limits for this body area were not determined. One possible reason for the heterogeneity could be the different areas of the lower extremity that were studied, with articles reporting lower limb symptoms in general[16, 32, 44], and symptoms in specific areas such as the feet[28, 32, 34], ankles[28] and lower legs[33].

An alternative approach to reducing the risk of developing standing-related musculoskeletal symptoms may be to distinguish pain developers from non-pain developers for more targeted intervention strategies. Specific groups of standing-related pain developers have been described[19-21], with an average prevalence of 44% in the study samples described in our review. The reliability and validity of the pain developer paradigm has been reported. Sorensen and colleagues described a number of symptoms that were reported by both standing-related pain developers and regular pain patients, thereby concluding to have found evidence for the validity of the paradigm[41]. Nelson-Wong and colleagues[37] showed high repeatability in identifying pain developing participants when tested four weeks apart. Our findings provide some guidance on identifying pain developers (Table 1). For example, pain developers showed to have a larger lumbar curvature[42] and a smaller hip range of motion[19] than non-pain developers. However, more information on the pain developer paradigm is needed to enable targeted intervention actions.

#### *Mechanisms for the association of prolonged standing with musculoskeletal symptoms*

Evidence on potential underlying mechanisms for the development of musculoskeletal symptoms due to prolonged standing was tabulated (Tables 1-2). Some consistency in the evidence for the postural mechanisms for the development of low back symptoms was

found with postures such as trunk flexion, axial rotation and lumbar curvature seemingly playing a role in the development of low back symptoms related to standing[18, 31, 42]. Such postures may induce an increase in lumbar load during prolonged standing[18], while the low back load during standing has already been shown to be higher than during sitting[48]. These elevated loads may play a role in the development of low back symptoms during prolonged standing.

For low back symptoms, mechanisms at the level of muscle, such as an increased co-contraction, muscle fatigue or stiffness, or a lack of muscle strength or endurance have been hypothesized to be a potential cause of low back symptom development. However, we only found limited, but inconsistent, evidence to support these mechanisms. Although variation in postures has often been suggested to be an important factor in the prevention of musculoskeletal symptoms[49], we identified only limited and inconsistent evidence supporting such a mechanism.

For lower extremity symptoms, although not necessarily musculoskeletal in nature, blood pooling in the lower extremities is one of the most often reported mechanisms for the adverse associations observed with prolonged standing. It has been shown previously that prolonged standing can increase intravascular hydrostatic venous pressure[50], whereas the lack of muscle pump action may contribute to venous stasis[50] and increased lower limb volume[23, 28, 45] which may put passive structures under stress, causing symptoms. Relatively consistent evidence showed that prolonged standing may cause an increase in blood flow, skin temperature and leg volume, providing funding for this mechanism. Evidence for mechanisms of variation in movement or muscle fatigue being the cause of standing-related lower-extremity symptoms was rather inconsistent, with both studies that

did and did not find an association between postural or muscle activity variables and either prolonged standing or the development of symptoms.

### *Implications for occupational health*

Based on evidence examined in this review, it can be concluded that interventions to prevent standing-related musculoskeletal symptoms should aim at reducing prolonged standing time to below the evidence-based exposure limit suggested. However, interventions impacting on underlying mechanisms could also be considered. Such interventions may, for example, be directed at postures during standing or may be targeted at preventing lower limb blood pooling.

Various interventions for the prevention of standing-related musculoskeletal symptoms have been suggested, including those based on the notion that symptom development can be altered through postural modifications[31, 51] or movement[36]. These include breaking up prolonged standing by intermittent sitting[47] (to keep prolonged bouts below exposure limits) or by movement[52], or by applying certain shoe or floor conditions[53] (to address possible underlying mechanisms. However these interventions have generally only shown moderate effects on reducing symptoms so far[47, 52, 53]. In addition to health outcomes, interventions should also consider potential impact on work productivity to ensure they are feasible and sustainable.

### *Methodological considerations*

Substantial evidence on the association of standing with musculoskeletal symptoms was found from laboratory studies, with data on physiological outcomes providing insight into possible mechanisms for the association. Although the evidence presented in this review



provides detailed information about the acute response to prolonged standing in a controlled situation, information on both the effect of long-term exposure to prolonged standing and/or responses to prolonged standing outside a laboratory setting is lacking. This includes a lack of information on, for example, more dynamic types of standing (as opposed to the predominantly static standing performed in laboratory settings), or standing that is broken up by bouts of other activities (e.g., sitting). Moreover, the described studies were typically conducted among groups of relatively healthy populations (i.e., young participants without comorbidities such as pre-existing musculoskeletal symptoms) (see information in Supplementary Material 8). As such, the current review findings cannot necessarily be extrapolated to other (more generic) populations. Some studies excluded participants from occupations that encompass substantial amounts of prolonged standing[28, 30, 31, 33]. Thus, at least for these studies, the findings from this review cannot be generalized to populations of workers that are habituated to prolonged standing. Therefore, it remains unknown whether dose-response associations differ for such populations as compared to the general population.

Regarding risk of bias, the majority of the articles in this systematic review did not control for relevant other (potentially confounding) factors. As a result of which, the role of socio-demographic (e.g., age and sex) and other (e.g., psychosocial or physical work demands) factors on the association of prolonged standing with musculoskeletal symptoms remains unknown. Moreover, most studies scored relatively low on the sample size, analytical methods used, and reporting data in sufficient detail. Such aspects should therefore deserve more attention in future work as they may underlie the lack of consistent findings for some of the aspects studied in our review.

No clear difference in dose-response associations could be obtained from studies reporting musculoskeletal pain compared to those reporting musculoskeletal discomfort (as per the dashed and solid lines in Figures 2-4). Such a difference was expected as earlier work had indicated that whilst they were strongly related, discomfort is more sensitive and develops earlier than pain in response to exposures to physical work demands[54]. This suggests participants in the various studies examined in this review perceived symptom intensity similarly regardless of whether pain or discomfort was the anchor term used.

## **Conclusion**

This systematic review on laboratory studies found convincing evidence for a detrimental association between acute prolonged standing and development of musculoskeletal symptoms in the low back and lower extremities. We have reported on underlying mechanisms for these associations. Moreover, a safe exposure limit of 40 minutes of uninterrupted standing has been suggested before people typically develop clinically relevant levels of low back symptoms. This general exposure limit needs to be considered in relation to other factors which may influence a worker's risk including prior exposure, unaccustomed to standing, older, and having comorbidities. Interventions should therefore be aimed at reducing prolonged standing time, below the provided exposure limit, or should focus on underlying pain mechanisms. Also interventions targeted at pain developers specifically should be developed.

## **Acknowledgements**

Funding sources: GNH was supported by a NHMRC Career Development Fellowship (NHMRC #108029). DD was supported by a NHMRC Senior Research Fellowship (NHMRC #1078360). LS was supported by a NHMRC Senior Research Fellowship (NHMRC #1019980). CGM was supported by a NHMRC Principal Research Fellowship (NHMRC #1103022). We are grateful for the financial assistance from the Victorian Government's OIS Program.

## **Author contribution**

PC, LW, SP and JS conducted literature screening and data extraction of all included papers. LR and DB conducted the literature search in electronic data bases. All authors (PC, LW, SP, JS, LR, DB, GH, DD and LS) analysed the data and reviewed the manuscript for important intellectual content. LS is the study guarantor.

Figure 1. Flow chart depicting the literature selection procedure

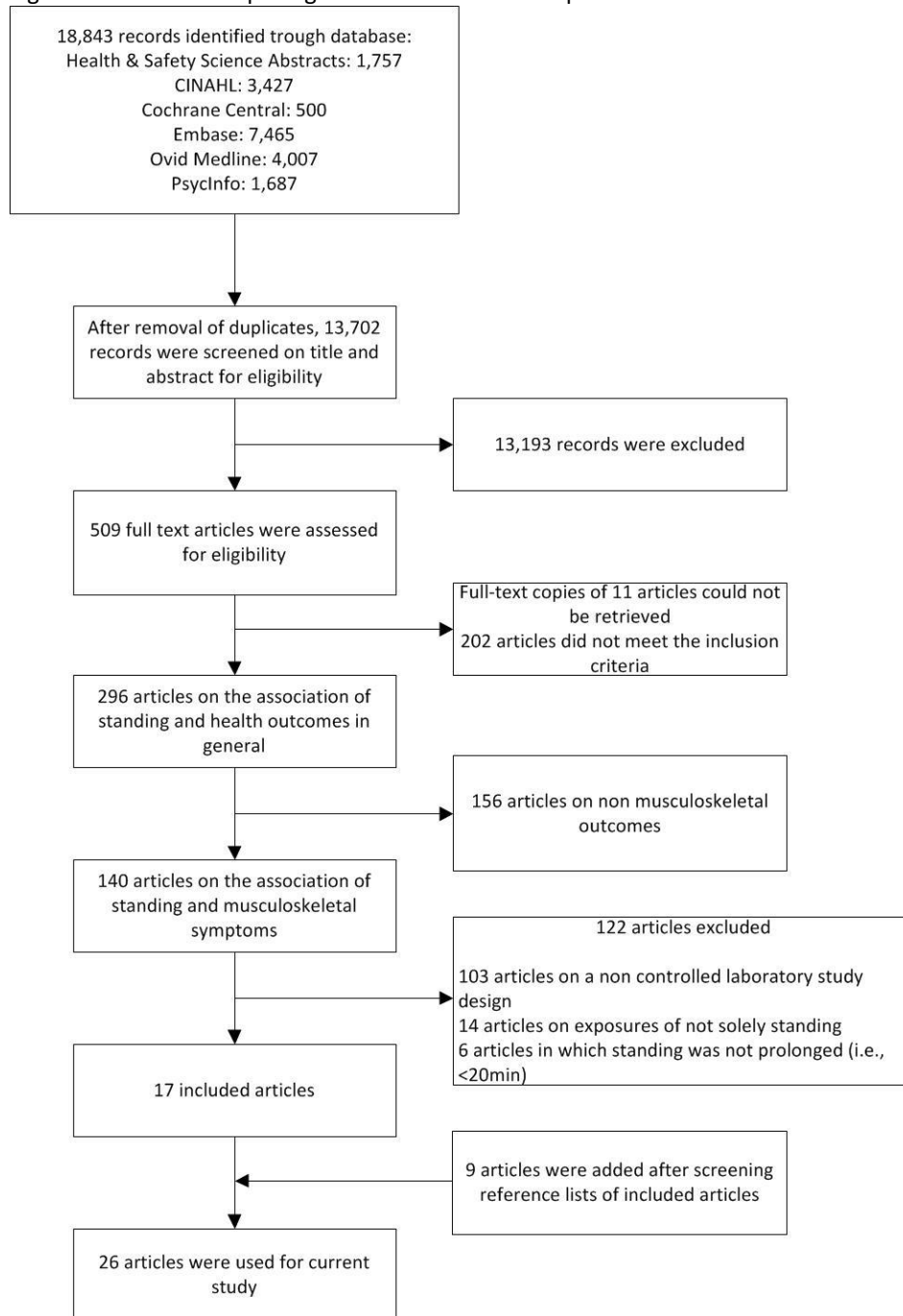


Figure 2. Dose-response of the association between prolonged standing (in minutes) and low back symptoms (i.e., pain or discomfort, on a 0 to 100 scale). Scores from articles reporting discomfort are depicting in dashed lines, while scores from articles reporting pain are depicted in solid lines. The thick grey line depicts the statistically pooled dose-response association.

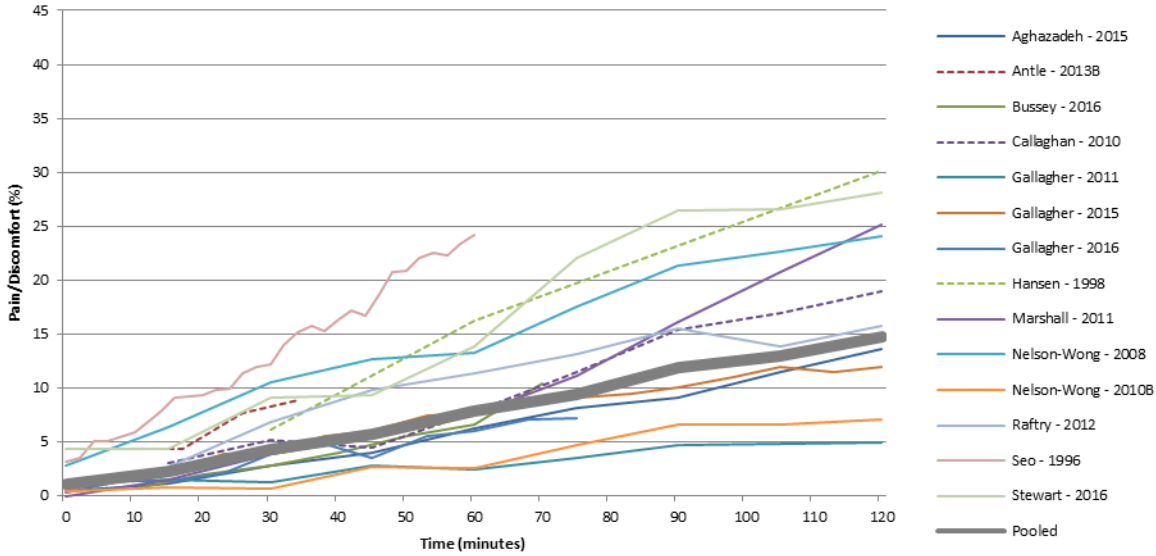


Figure 3. Dose-response of the association between prolonged standing (in minutes) and low back symptoms (i.e., pain or discomfort, on a 0 to 100 scale) in pain developers. Scores from articles reporting discomfort are depicting in dashed lines, while scores from articles reporting pain are depicted in solid lines. The thick grey line depicts the statistically pooled dose-response association.

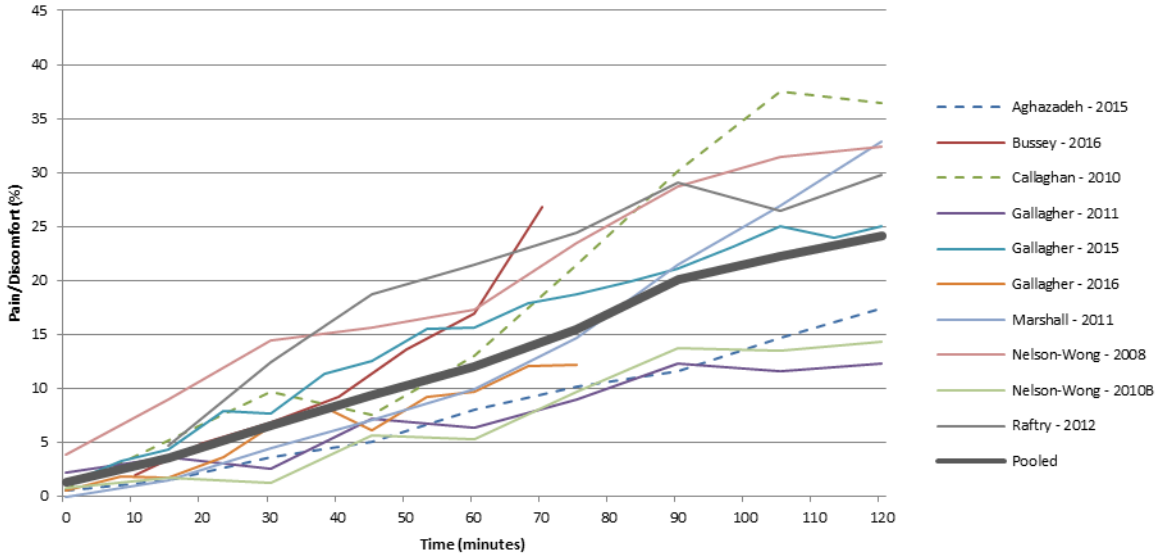


Figure 4. Dose-response of the association of prolonged standing (in minutes) and lower limb symptoms (i.e., pain or discomfort, on a 0 to 100 scale). Scores from articles reporting discomfort are depicting in dashed lines, while scores from articles reporting pain are depicted in solid lines.

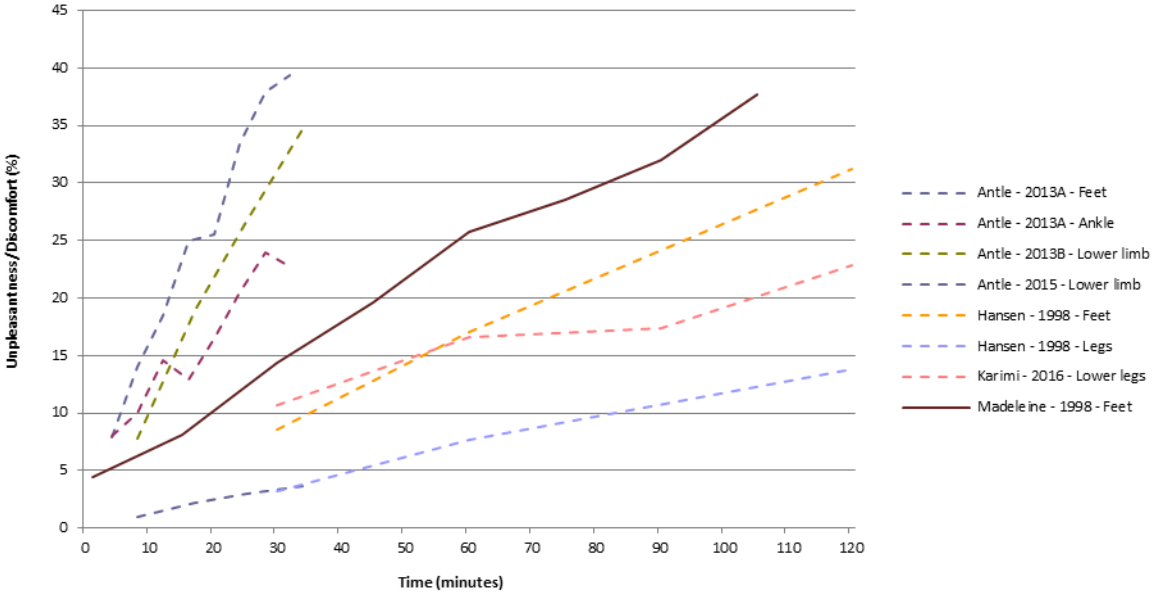


Table 1. Mechanisms for the association of prolonged standing and low back symptoms.

Possible mechanisms		Evidence in favor	Evidence against
Muscle	Co-contraction	<ul style="list-style-type: none"> <li>• Higher gluteus medius co-contraction in PD* than in NPD[19, 21, 39]</li> <li>• Higher trunk co-contraction in PD than in NPD[39]</li> <li>• Gluteus medius co-contraction decreased during prolonged standing[19]</li> </ul>	<ul style="list-style-type: none"> <li>• No change in gluteus medius co-contraction during prolonged standing[21, 35, 39]</li> <li>• No change in change in trunk muscle co-contraction during prolonged standing[35, 39]</li> <li>• No difference in trunk muscle co-contraction between PD and NPD[39]</li> </ul>
	Fatigue/ Oxygenation	<ul style="list-style-type: none"> <li>• Increase in frequency of trunk muscle activity during prolonged standing[32]</li> </ul>	<ul style="list-style-type: none"> <li>• No change in trunk muscle activity during prolonged standing[16, 18, 32, 34, 44]</li> <li>• No association of trunk muscle activity and symptoms[29]</li> <li>• No change in muscle oxygenation during prolonged standing[18, 20]</li> <li>• No association of symptoms and muscle oxygenation[20]</li> </ul>
	Strength	<ul style="list-style-type: none"> <li>• Hip abductor muscle strength reduced after prolonged standing[35]</li> </ul>	<ul style="list-style-type: none"> <li>• No difference in gluteus medius muscle strength between PD and NPD[19]</li> </ul>
	Endurance	<ul style="list-style-type: none"> <li>• Hip abductor muscle endurance reduced after prolonged standing in PD[35]</li> </ul>	<ul style="list-style-type: none"> <li>• No difference in gluteus medius muscle endurance between PD and NPD[19]</li> </ul>
	Stiffness	<ul style="list-style-type: none"> <li>• Smaller hip range of motion in PD than NPD[19]</li> </ul>	<ul style="list-style-type: none"> <li>• No difference in hamstring stiffness, stretch tolerance and extensibility between PD and NPD[40]</li> </ul>
Postural	Body sway	<ul style="list-style-type: none"> <li>• Increase in sway during prolonged standing[16, 32, 46]</li> </ul>	<ul style="list-style-type: none"> <li>• No change in sway during prolonged standing[16, 30, 34]</li> <li>• No association between the number of weight shifts and symptoms[29]</li> </ul>
	Lumbar posture	<ul style="list-style-type: none"> <li>• Increase in lumbar flexion during prolonged standing[18, 31]</li> <li>• More spinal axial rotation with symptoms[18]</li> <li>• More lumbar curvature in PD than NPD[42]</li> <li>• More lumbar curvature with symptoms[42]</li> </ul>	<ul style="list-style-type: none"> <li>• No change in asymmetrical posture during prolonged standing[17]</li> </ul>



	Posture (variation)	<ul style="list-style-type: none"> <li>• Decrease in body weight shift frequency during prolonged standing[17]</li> <li>• Decrease[17] and increase[30] in body weight shift duration during prolonged standing</li> <li>• Increase in fidget amplitude during prolonged standing[17]</li> <li>• Higher[17] and lower[30, 31] fidget frequency in PD than NPD</li> <li>• Less spinal movement in PD than NPD[30]</li> <li>• More body shifts with symptoms[18]</li> <li>• Increase in postural changes during prolonged standing[46]</li> </ul>	<ul style="list-style-type: none"> <li>• No change in body weight shift amplitude during prolonged standing[17]</li> </ul>
Loading	Lumbar load	<ul style="list-style-type: none"> <li>• Increase in lumbar load during prolonged standing[18]</li> </ul>	
Blood flow	Skin temperature	-	<ul style="list-style-type: none"> <li>• No change in skin temperature during prolonged standing[18]</li> </ul>
<p>* PD = Pain developers  NPD = Non-pain developers</p>			

Table 2. Mechanisms for the prolonged standing and lower extremity symptoms.

Possible mechanisms		Evidence in favor	Evidence against
Blood pooling	Blood flow	<ul style="list-style-type: none"> <li>• Increase in blood flow at the level of the foot[16, 28, 44] and the soleus muscle[28, 44] during prolonged standing</li> <li>• More blood flow and symptoms[16, 28]</li> </ul>	<ul style="list-style-type: none"> <li>• No increase in blood flow at the level of the soleus muscle during prolonged standing[16]</li> </ul>
	Blood pressure	<ul style="list-style-type: none"> <li>• Increase in blood pressure at the level of the ankle during prolonged standing[16, 28, 44]</li> </ul>	<ul style="list-style-type: none"> <li>• No change in blood pressure at the level of the ankle during prolonged standing[44]</li> </ul>
	Skin temperature	<ul style="list-style-type: none"> <li>• Increase in lower limb skin temperature during prolonged standing[32, 34]</li> <li>• More lower limb skin temperature with symptoms[29]</li> </ul>	-
	Leg circumference/volume	<ul style="list-style-type: none"> <li>• Increase in lower leg volume during prolonged standing[23, 32-34, 45]</li> <li>• More lower leg volume and symptoms[23]</li> </ul>	<ul style="list-style-type: none"> <li>• No association of lower limb volume and symptoms[29]</li> </ul>
Muscle	Fatigue/ Oxygenation	<ul style="list-style-type: none"> <li>• Increase in tibialis and gastrocnemius muscle activity during prolonged standing[16, 33]</li> </ul>	<ul style="list-style-type: none"> <li>• No change in lower limb muscle activity during prolonged standing[16, 28, 29, 34, 44, 46]</li> <li>• No association of lower limb muscle activity and symptoms[29]</li> </ul>
Postural	Postures	<ul style="list-style-type: none"> <li>• Increase in centre of gravity changes during prolonged standing[46]</li> </ul>	<ul style="list-style-type: none"> <li>• No change in centre of pressure movement during prolonged standing[34]</li> </ul>
	Body sway	<ul style="list-style-type: none"> <li>• Increase in sway during prolonged standing[16, 32, 46]</li> <li>• More number of weight shift with symptoms[29]</li> </ul>	<ul style="list-style-type: none"> <li>• No change in sway during prolonged standing[16, 34]</li> </ul>

## Reference

1. Safe Work Australia, National hazard exposure worker surveillance: exposure to biomechanical demands, pain and fatigue symptoms and the provision of controls in Australian workplaces. 2011: Canberra, Australia.
2. Tissot, F., Messing, K., and Stock, S., Standing, sitting and associated working conditions in the Quebec population in 1998. *Ergonomics*, 2005. 48(3): 249-269.
3. Tremblay, M.S., Colley, R.C., Saunders, T.J., Healy, G.N., and Owen, N., Physiological and health implications of a sedentary lifestyle. *Applied Physiology, Nutrition, and Metabolism*, 2010. 35(6): 725-740.
4. Thorp, A.A., Owen, N., Neuhaus, M., and Dunstan, D.W., Sedentary behaviors and subsequent health outcomes in adults a systematic review of longitudinal studies, 1996-2011. *American Journal of Preventive Medicine*, 2011. 41(2): 207-215.
5. Straker, L., Coenen, P., Dunstan, D.W., Gilson, N., and Healy, G.N., Sedentary work - Evidence on an emergent work health and safety issue. 2016, Safe Work Australia: Canberra, Australia.
6. Buckley, J.P., Hedge, A., Yates, T., Copeland, R.J., Loosemore, M., Hamer, M., Bradley, G., et al., The sedentary office: a growing case for change towards better health and productivity. Expert statement commissioned by Public Health England and the Active Working Community Interest Company. *British Journal of Sports Medicine*, 2015. 49(21): 1357-1362.
7. Shrestha, N., Ijaz, S., Kukkonen-Harjula, K.T., Kumar, S., and Nwankwo, C.P., Workplace interventions for reducing sitting at work. *Cochrane Database of Systematic Reviews*, 2015. 1: CD010912.
8. Neuhaus, M., Eakin, E.G., Straker, L., Owen, N., Dunstan, D.W., Reid, N., and Healy, G.N., Reducing occupational sedentary time: a systematic review and meta-analysis of evidence on activity-permissive workstations. *Obesity Reviews*, 2014. 15(10): 822-838.
9. Callaghan, J.P., de Carvalho, D., Gallagher, K., Karakolis, T., and Nelson-Wong, E., Is standing the solution to sedentary office work? *Ergonomics in Design* 2015. 23(3): 20-24.
10. Waters, T.R. and Dick, R.B., Evidence of health risks associated with prolonged standing at work and intervention effectiveness. *Rehabilitation Nursing*, 2014. 40(3): 148-165.
11. Beebe-Dimmer, J.L., Pfeifer, J.R., Engle, J.S., and Schottenfeld, D., The epidemiology of chronic venous insufficiency and varicose veins. *Annals of Epidemiology*, 2005. 15(3): 175-184.
12. Jawien, A., The influence of environmental factors in chronic venous insufficiency. *Angiology*, 2003. 54 (Suppl 1): S19-S31.
13. Bonzini, M., Coggon, D., and Palmer, K.T., Risk of prematurity, low birthweight and pre-eclampsia in relation to working hours and physical activities: a systematic review. *Occupational and Environmental Medicine*, 2007. 64(4): 228-243.
14. Coenen, P., Willenberg, L., Parry, S., Shi, J., Maher, C., Healy, G., Dunstan, D., et al., Associations of occupational standing with musculoskeletal symptoms: a systematic review with meta-analysis. *British Journal of Sports Medicine*, 2016. 10.1136/bjsports-2016-096795.
15. Halim, I. and Omar, A.R., Development of prolonged standing strain index to quantify risk levels of standing jobs. *International Journal of Occupational Safety and Ergonomics*, 2012. 18(1): 85-96.
16. Antle, D.M. and Cote, J.N., Relationships between lower limb and trunk discomfort and vascular, muscular and kinetic outcomes during stationary standing work. *Gait & Posture*, 2013. 37(4): 615-619.
17. Gallagher, K.M., Nelson-Wong, E., and Callaghan, J.P., Do individuals who develop transient low back pain exhibit different postural changes than non-pain developers during prolonged standing? *Gait & Posture*, 2011. 34(4): 490-495.
18. Gregory, D.E. and Callaghan, J.P., Prolonged standing as a precursor for the development of low back discomfort: an investigation of possible mechanisms. *Gait & Posture*, 2008. 28(1): 86-92.

19. Bussey, M.D., Kennedy, J.E., and Kennedy, G., Gluteus medius coactivation response in field hockey players with and without low back pain. *Physical Therapy in Sport*, 2016. 17: 24-29.
20. Callaghan, J.P., Gregory, D.E., and Durkin, J.L., Do NIRS measures relate to subjective low back discomfort during sedentary tasks? *International Journal of Industrial Ergonomics*, 2010. 40: 165-170.
21. Aghazadeh, J., Ghaderi, M., Azghani, M.R., Khalkhali, H.R., Allahyari, T., and Mohebbi, I., Anti-fatigue mats, low back pain, and electromyography: An interventional study. *International Journal of Occupational Medicine and Environmental Health*, 2015. 28(2): 347-356.
22. Balasubramanian, V., Adalarasu, K., and Regulapati, R., Comparing dynamic and stationary standing postures in an assembly task. *International Journal of Industrial Ergonomics*, 2009. 39(5): 649-654.
23. Chester, M.R., Rys, M.J., and Konz, S.A., Leg swelling, comfort and fatigue when sitting, standing, and sit/standing. *International Journal of Industrial Ergonomics*, 2002. 29(5): 289-296.
24. Coenen, P., Willenberg, L., Parry, S., Shi, J., Romero, L., Blackwood, D., Healy, G., et al., The association of prolonged standing and musculoskeletal symptoms: a systematic review of laboratory-based studies. *Prospero*, 2016: CRD42016048919.
25. Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., and Group, P., Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009. 21(339): 2535.
26. Kmet, L.M., Lee, R.C., and Cook, L.S., Standard quality assessment criteria for evaluating primary research papers from a variety of fields Alberta Heritage Foundation for Medical Research, Editor. 2004: Edmonton, Canada.
27. Kelly, A.M., Does the clinically significant difference in visual analog scale pain scores vary with gender, age, or cause of pain? *Academic Emergency Medicine*, 1998. 5(11): 1086-1090.
28. Antle, D.M., Vézina, N., Messing, K., and Côté, J.N., Development of discomfort and vascular and muscular changes during a prolonged standing task. *Occupational Ergonomics*, 2013. 11(1): 21-33.
29. Cham, R. and Redfern, M.S., Effect of flooring on standing comfort and fatigue. *Human Factors*, 2001. 43(3): 381-391.
30. Gallagher, K.M. and Callaghan, J.P., Early static standing is associated with prolonged standing induced low back pain. *Human Movement Science*, 2015. 44: 111-121.
31. Gallagher, K.M. and Callaghan, J.P., Standing on a declining surface reduces transient prolonged standing induced low back pain development. *Applied Ergonomics*, 2016. 56: 76-83.
32. Hansen, L., Winkel, J., and Jorgensen, K., Significance of mat and shoe softness during prolonged work in upright position: based on measurements of low back muscle EMG, foot volume changes, discomfort and ground force reactions. *Applied Ergonomics*, 1998. 29(3): 217-224.
33. Karimi, Z., Allahyari, T., Azghani, M.R., and Khalkhali, H., Influence of unstable footwear on lower leg muscle activity, volume change and subjective discomfort during prolonged standing. *Applied Ergonomics*, 2016. 53(Part A): 95-102.
34. Madeleine, P., Voigt, M., and Arendt-Nielsen, L., Subjective, physiological and biomechanical responses to prolonged manual work performed standing on hard and soft surfaces. *European Journal of Applied Physical and Occupational Physiology*, 1998. 77(1-2): 1-9.
35. Marshall, P.W., Patel, H., and Callaghan, J.P., Gluteus medius strength, endurance, and co-activation in the development of low back pain during prolonged standing. *Human Movement Science*, 2011. 30(1): 63-73.
36. Nelson-Wong, E. and Callaghan, J.P., Changes in muscle activation patterns and subjective low back pain ratings during prolonged standing in response to an exercise intervention. *Journal of Electromyography and Kinesiology*, 2010. 20(6): 1125-1533.

37. Nelson-Wong, E. and Callaghan, J.P., Repeatability of clinical, biomechanical, and motor control profiles in people with and without standing-induced low back pain. *Rehabilitation Research and Practice*, 2010. 2010: 289278.
38. Nelson-Wong, E. and Callaghan, J.P., Is muscle co-activation a predisposing factor for low back pain development during standing? A multifactorial approach for early identification of at-risk individuals. *Journal of Electromyography and Kinesiology*, 2010. 20(2): 256-263.
39. Nelson-Wong, E., Gregory, D.E., Winter, D.A., and Callaghan, J.P., Gluteus medius muscle activation patterns as a predictor of low back pain during standing. *Clinical Biomechanics*, 2008. 23(5): 545-553.
40. Rafferty, S.M. and Marshall, P.W., Does a 'tight' hamstring predict low back pain reporting during prolonged standing? *Journal of Electromyography and Kinesiology*, 2012. 22(3): 407-411.
41. Sorensen, C.J., Johnson, M.B., Callaghan, J.P., George, S.Z., and van Dillen, L.R., Validity of a paradigm for low back pain symptom development during prolonged standing. *Clinical Journal of Pain*, 2015. 31(7): 652-659.
42. Sorensen, C.J., Norton, B.J., Callaghan, J.P., Hwang, C.T., and van Dillen, L.R., Is lumbar lordosis related to low back pain development during prolonged standing? *Manual Therapy*, 2015. 20(4): 553-557.
43. Stewart, D.M. and Gregory, D.E., The use of intermittent trunk flexion to alleviate low back pain during prolonged standing. *Journal of Electromyography and Kinesiology*, 2016. 27: 46-51.
44. Antle, D.M., Vezina, N., and Cote, J.N., Comparing standing posture and use of a sit-stand stool: Analysis of vascular, muscular and discomfort outcomes during simulated industrial work. *International Journal of Industrial Ergonomics*, 2015. 45(98): e106.
45. Seo, A., Kakehashi, M., Tsuru, S., and Yoshinaga, F., Leg swelling during continuous standing and sitting work without restricting leg movement. *Journal of Occupational Health*, 1996. 38(4): 186-186.
46. Zhang, L., Drury, C.G., and Woolley, S., Constrained standing: Evaluating the foot/floor interface. *Ergonomics*, 1991. 34(2): 175-192.
47. Gallagher, K.M., Campbell, T., and Callaghan, J.P., The influence of a seated break on prolonged standing induced low back pain development. *Ergonomics*, 2014. 57 (4): 555-562.
48. Dolan, P., Adams, M.A., and Hutton, W.C., Commonly adopted postures and their effect on the lumbar spine. *Spine*, 1988. 13: 197-201.
49. Mathiassen, S.E., Diversity and variation in biomechanical exposure: what is it, and why would we like to know? *Applied Ergonomics*, 2006. 37(4): 419-427.
50. Tuchsén, F., Hannerz, H., Burr, H., and Krause, N., Prolonged standing at work and hospitalisation due to varicose veins: a 12 year prospective study of the Danish population. *Occupational and Environmental Medicine*, 2005. 62(12): 847-850.
51. Nelson-Wong, E. and Callaghan, J.P., The impact of a sloped surface on low back pain during prolonged standing work: a biomechanical analysis. *Applied Ergonomics*, 2010. 41(6): 787-795.
52. Lin, Y.H., Chen, C.Y., and Cho, M.H., Effectiveness of leg movement in reducing leg swelling and discomfort in lower extremities. *Applied Ergonomics*, 2012. 43(6): 1033-1037.
53. Lin, Y.H., Chen, C.Y., and Cho, M.H., Influence of shoe/floor conditions on lower leg circumference and subjective discomfort during prolonged standing. *Applied Ergonomics*, 2012. 43(5): 965-970.
54. Straker, L.M., Body discomfort assessment tool, in *The occupational ergonomics handbook*, W. Karwowski and W.S. Marras, Editors. 1999, CRC Press: Boca Raton, USA.