Chronic pain with physical findings in the neck-shoulder girdle and exposures in the workplace: A systematic review

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Scientific evidence concerning the causal relationship between the disease "chronic pain of the neck-shoulder girdle" (cervico-brachial syndrome) and exposures in the workplace (excluding computer work): A reference document for the Danish National Board of Industrial Injuries

1. Background to the review

"Chronic neck-shoulder pain (cervicobrachial syndrome)" was accepted onto the Danish list of prescribed occupational diseases some 20 years ago, the qualifying exposure being that of "quick and repetitive precision-work with static load of the neck-shoulder area" which has been present for several (by rule of thumb, ten or more) years.

This evidence-based review was undertaken at the request of the Danish National Board of Industrial Injuries to clarify the appropriateness of the current prescription, and as necessary to identify potential alternatives by specific reference to the scientific evidence on neck-shoulder disorders and work activities. The commissioning brief imposed some delimitations and identified several intended outputs. In accordance with these guidelines:

1) The focus in terms of **disease** has been on "a chronic pain condition of the soft tissue parts of the neck and shoulder girdle" *with* associated tenderness on palpation; with or without pain radiating into one or both arms. More specific disorders were considered only as a source of diagnostic confusion, and attention was restricted to studies in which symptom reports were supported by findings on clinical examination.
2) The focus in terms of **exposure** was broad but included the following as possible causal elements:
   a) Physical risk factors: forceful exertions, repetitive work, working postures of the neck and shoulder, static work (work with little variation of posture), and precision work; where possible to consider these factors separately and in combination, including the effect of different durations and patterns of exposure, and possible dose-response relationships and/or thresholds of effect.
   b) Occupational psychosocial factors (e.g. job demands, job control, co-worker support).

Factors of personal vulnerability – e.g. sex, age, mental health were also considered.

3) The focus in terms of **attribution** was on the strength of associations between exposures and outcome, and the weight of evidence favouring causation as compared with other explanations.

Subsidiary practical questions concerned the validity of diagnosis, and the importance and background characteristics of the disorder under consideration. In respect of the former, how reproducible was the diagnosis? In respect of the latter, what is known about the natural history of the disorder, its impact and its prognosis?

Following a description of background matters, we report the findings of a systematic literature review and synthesis of evidence directed at this commissioning brief.

2. The Outcome

2.1. Neck pain in the general population

Most observations in the general population have been on neck pain, rather than neck pain with physical signs. In this section we describe the epidemiology of neck pain and conclude with a few relevant studies on neck pain with supplemental examination findings.

Prevalence

Neck pain is extremely common as judged by estimates from surveys in various settings. According to studies from Finland and Canada, two-thirds of adults experience neck pain at some time;[1,2] in an age- and sex-stratified sample of adults aged ≥25 years from the Netherlands, the 12-month period prevalence was 31%, with a point prevalence of 21% and a prevalence of chronic symptoms (current pain lasting >3 months in the past 12 months) of 14%;[3] a study from the UK estimated the prevalence of neck pain lasting >1 week in the past four weeks in adulthood to be about 14%;[4] three studies from Sweden variously estimated a prevalence of chronic neck pain (>3 or >6 months) of 14%-23%;[5-7] and a large population survey from Finland indicated a prevalence of severe longstanding neck pain of 9%-14% in adults aged ≥30 years.[1]

Prevalent neck pain, including chronic neck pain, is reported more often by older subjects,[8] with a peak sometimes described in mid-life.[1,2,8,9] At all ages, symptoms are somewhat more common in women than in men: in a Dutch study by Picavet *et al*, for example, 25% of women had current neck pain as compared with 16% of men;[3] in surveys from southern and western Sweden, 19% - 23% of women reported chronic symptoms versus 14.5% of men;[5,6] and in Finland the respective estimates for severe longstanding neck pain were 14% and 9-12%.[1]

Other reported associations with prevalent chronic neck pain include smoking,[1,2,8] obesity,[1] local injury,[1,2] low educational level,[1,2] pain at other anatomical sites,[1,2,8] poor mental health,[12,8,9] and unemployment.[2,8]

Incidence and natural history of neck pain

A few population-based cohort studies provide information on incidence, persistence, and natural history of neck pain in the community. Côté *et al* studied 1100 randomly selected adults from Saskatchewan.[10] Among those free of neck pain in the six months prior to baseline, the 12-month cumulative incidence of new symptoms was 14.6%, but disabling pain (high intensity pain and at least moderate limitation of activity) developed in only 0.6% of the cohort. Among subjects with neck pain at baseline, only a third enjoyed a complete resolution a year on; a further third reported persistence, almost 10% experienced an aggravation of symptoms, and a fifth had had recurrent episodes of discomfort.

Similar estimates have been obtained in the UK and the Netherlands. Croft *et al* found a cumulative annual incidence of neck pain lasting >1 day (in those free of neck pain in the month before baseline) of 17.9% in adults from south Manchester,[11] and a 12-month persistence rate of almost 50% in those who were initially symptomatic.[12] Luime *et al*[13] followed a cohort of 769 service workers from various industries over a two-year period. Incidence and prevalence rates remained stable in each year of follow-up - with 17% to 18% reporting new symptoms and a third reporting prevalent symptoms; however, recurrence rates were high, at 61% to 65%, suggesting that chronic neck pain is an episodic recurrent condition in which many individuals shift their status over time. In this respect neck pain appears to behave like low-back pain.

Several non-occupational risk factors for incidence and persistence have been identified by investigations. In Saskatchewan women had a generally higher incidence than men (16.9% vs. 10.0%), but disabling neck pain was more common in men (1.1% vs. 0.4%).[10] Incidence rate ratios (RR) for persistence, aggravation, and recurrence were all about 1.2 times higher in women than men. In an occupational cohort from France[14] the incidence of treated neck pain was 2-3 times higher, and that of neck pain lasting >30 days was five times higher in women than in men; in Finland, female forestry workers had a higher incidence of radiating neck pain than males,[15] and in the UK, Croft *et al* found a similar differential by gender for incidence (RR 1.3)[11] although not for persistence.[12] Age has been reported as a risk factor for persistence,[10,12] recurrence,[10] and sometimes, but not always, for incidence.[10,11,14,15] A number of other risk factors have been related to both outcomes, including previous neck injury, concurrent pain at other sites, mental distress, and poor self-assessed health.[8,11,12,14,15] Such factors tended to increase risks by about 1.5 to 2.5-fold. Some studies also suggest possible associations with obesity and smoking.[15]

A systematic review of the clinical course of non-specific neck pain pointed to a shortage of adequately powered and well-conducted studies on persistence of symptoms.[16]

Neck pain with physical signs

Information on the incidence and natural history of neck pain with signs on clinical examination is more limited still at the population level. However, a few studies provide useful observations. Hoving *et al*[17] report an investigation of persistence in Dutch primary care consulters with neck-shoulder pain present for $\geq$2 weeks and reproduced reliably by passive movement on physical examination. Around 37% of the cohort were still symptomatic after 12 months of follow-up. Factors associated with non-recovery were similar to those mentioned above, and included age, concomitant low back pain and traumatic onset. Other risk factors included female gender and adverse pattern of presenting symptoms (pain >12 weeks, unremitting pain in the two weeks prior to presentation, pain radiating below the elbow, and severe functional limitations). In Denmark, a four-year prospective study of industrial and service workers investigated risk factors for incident neck pain with palpation tenderness.[18] New onset symptoms (neck-shoulder pain) arose in 14% of participants, but the incidence of pain with associated tenderness was substantially lower, at 1.7%. Non-occupational risk factors for this last outcome included female gender (Odds Ratio (OR) 1.8, 95%CI 1.1-3.2) and high baseline levels of somatic distress, as measured by a stress profile questionnaire (OR 2.8, 95%CI 1.4-5.4). Finally, Cassou *et al*[19] studied chronic neck-shoulder pain with limitations of movement in a large cohort of industrial workers undergoing routine health surveillance assessments in France. A comparison of two examinations in 1990 and 1995 suggested a five-year incidence of 7.3% in men and 12.5% in women, and persistence rates of 35% and 47% respectively. Incidence risk increased with age in both sexes, as did the risk of persistence in women (this last pattern being less clear in men). In both sexes, depressive symptoms at baseline were moderately associated with incidence of neck-shoulder disorder (ORs 1.3 and 1.5).

2.2. Pathogenesis

The cervical spine is the most mobile and least stable part of the human spine, with seven vertebrae, five intervertebral discs, and 37 separate articulations, as well as a complex system of ligaments and muscles. Pain may arise from any of these structures.

Unfortunately, although the International Association for the Study of Pain (IASP) recognises about 60 sources of neck pain, the origin of symptoms is typically unclear.[20] The IASP defines three categories as common - ‘cervical spinal pain of unknown origin’ (neck pain in the absence of a clear diagnosis), zygapophyseal joint pain, and discogenic pain – but underlying pathology is difficult to distinguish clinically in the absence of invasive tests (e.g. discography)[21] or rare special circumstances (e.g. trauma, tumours, inflammatory arthopathy, metabolic bone disease). According to classical textbook accounts, pain that arises from deep structures around the neck (ligaments, muscles, joint, discs or bone) is poorly localised to the neck and shoulders, unless arising from irritation of nerve roots.[22] Radiation occurs most often to the occiput, nuchal muscles, and superior shoulder; and pain is characteristically altered by neck movement. However, accompanying clinical features tend to be non-specific: neck stiffness is a common accompaniment of aging and most vertebral diseases, which may or may not be associated with neck pain; numbness and tingling tends to be vague and ill-defined more often than it is segmental or dermatomal; and tenderness is poorly localised, with variable severity. Localised points of myofascial tenderness may be seen with non-specific regional neck pain but also with facet joint disease.[21]

Clinical signs tend to go with symptoms, as evidenced by various epidemiological reports. Thus, tender points are commoner in people with neck-shoulder pain than in those without[23] and increase in number with reported severity of pain;[24,25] people with neck pain tend more often to have restricted neck movement;[26,27] and those with neck pain are more likely to have positive manual neck provocation tests.[28] But tender points and restricted neck movement can also be seen in the absence of neck pain,[23,26] and in population samples the correlation between signs and symptoms tends to lie along a continuum, with no distinct clustering suggestive of different diagnostic entities.[25,26]

Moreover, correlations of symptoms and disability with suspected underlying pathology, although sometimes found, tend to be weak. Degenerative changes (e.g. loss of disc height, osteophytosis of vertebral bodies, and osteoarthritis in nearby zygapophyseal joints and other articulating surfaces) can be seen in radiographs of the cervical spine in most adults aged $\geq$30 years, whether symptomatic or not, and also exist across a continuum of severity. In the EPOZ study in Zoetermeer, radiographs of the lateral cervical spine in anteflexion were assembled for more than 5,000 adults and compared with reported symptoms.[9] Osteoarthritis of the facet joints and disc degeneration were scored independently by two observers on a five-point scale according to a standardised atlas. As in other surveys, symptoms were more common at all ages in women than in men, and peaked at around age 50 years; but by contrast, the prevalences of disc degeneration and osteoarthritis (which were much lower) were similar in both sexes and rose steadily with age. After adjustment for age, the OR for neck pain was raised 1.8-fold in men with advanced disc degeneration, and 1.5-fold in men with advanced changes of osteoarthritis, but no similar relations were found in women. In both sexes, far stronger associations were observed with measures of social inadequacy, suggesting that mental health may be a more powerful determinant of neck pain in the general population than radiological evidence of neck pathology. In other general population studies, from north-west England and North America, number of tender points has been related to measures of depression, fatigue, and sleep disturbance, as well as to female gender and report of generalised pain.[29,30]

2.3. Classification of neck pain

In the absence of reliable clinical pointers, or a clear understanding about underlying pathology and the origin of symptoms, approaches to the classification of neck pain have differed, with confusing variations in practice. It seems, for example, that the term 'cervical spondylosis' is variably applied and sometimes includes soft tissue, disc, or degenerative lesions;[21] and for some 'cervical syndrome' refers to symptomatic cervical osteoarthritis,[31] whereas others use it simply to mean chronic neck pain [Hagberg, personal communication]. Similarly, 'cervicobrachial disorder' or 'cervicobrachial syndrome' has been used at the one extreme to mean symptoms radiating from neck to upper limb and at the other, potentially, to cover all soft tissue rheumatic disorders of the upper limb and neck. Within the ICD-10 coding scheme, cervicobrachial syndrome has its own category (M53.1), but neck pain with palpation tenderness can also be represented by other categories related to fibrositis (M79.0) or cervicalgia (M54.2). And within research, the anatomical boundaries used to define the neck-shoulder area have varied across national boundaries [Viikari-Juntura, personal communication].

The main features of three popular neck pain classification schemes in occupational research are summarised in Table 1 (p52)[31,32,33] Tension neck syndrome (synonyms: tension myalgia, nuchitis, occupational cervicobrachial syndrome, fibrositis, myofascial syndrome, fibromyositis) (TNS), as defined by Waris *et al*[31] was intended to represent a non-specific regional pain syndrome, while 'cervical syndrome' was symptomatic osteoarthritis; and thoracic outlet syndrome a compression of the distal nerve roots, brachial plexus, subclavian vessels, or combined neurovascular bundle at various sites between neck and axilla due to mechanical or functional lesions. In principle, therefore, cervical syndrome and thoracic outlet syndrome are specific pathologies, and by the terms of this review, conditions to exclude. However, all diagnoses have been operationalised in terms of neck pain with a physical sign, and in the absence of investigations to demonstrate pathology; moreover, case definitions have tended to overlap, both conceptually,[34] and in actual datasets that by inference include patients satisfying several case definitions [e.g. ref 35, Table III]. No longitudinal or clinical studies have been conducted to suggest that the groups so defined differ distinctly in prognosis, or response to treatment, or objective evidence of underlying pathology – criteria that might be used to justify the application of separate diagnoses.[36]

For reasons of clarity or pragmatism, many epidemiological studies have focussed solely on symptoms of neck pain or neck-shoulder pain.[2-8,10-15] A few enquiries incorporating a physical examination employ case definitions that faithfully reflect the limitations of understanding. Thus, Andersen *et al*[18,37] and Kaergaard *et al*[38] have reported on chronic neck pain with palpation tenderness, rather than claiming to diagnose a specific pathology.

In the absence of a clear gold standard, the validity of these various approaches to diagnosis is difficult to assess. In particular, the process, although supported by physical findings, remains semi-subjective. Reliance is placed on the patient's reported experiences, outside and within the examination, as well as the examiner's judgement. There is thus potential for simple non-differential misclassification or for bias, the latter being of most concern when outcome is assessed unblinded to exposure categorisation.

Only limited reassurance can be offered on these issues. Of concern is the wide variation in outcome frequency, even when using apparently similar criteria. Thus, in some occupational surveys one-third to two-thirds of workers are classed as having neck pain with tenderness,[35,38-41] whereas in others this outcome is far less common ($\leq$10%).[42-44] In a study of slaughterhouse workers by Viikari-Juntura[32] TNS was six times less prevalent than in factory workers, and ten times less common than in scissor makers surveyed by other researchers following the same diagnostic schedule. The within- and between-observer repeatability of clinical examination findings has been measured and shown to be reasonable in a few of the core studies that inform the review (described below); a few studies that are independent of the main review suggest that physical signs in the neck-shoulder girdle can be reliably ascertained, at least under some circumstances; and in the core set the symptom component was sometimes ascertained using the Standardised Nordic Questionnaire, which is a repeatable instrument according to several accounts.[45-47] Well-designed studies have assessed outcome independent of exposure, but many have fallen short of this standard or are simply ambiguous about it.

3. The exposures under study

The physical risk factors examined in this review include frequent or rapid movements of the shoulders, arms or upper limb, including work without sufficient rest breaks; repeated neck flexion, or prolonged periods with the neck flexed at work; static loading of the neck-shoulder musculature, including work with the arms elevated above shoulder height; heavy physical work or forceful gripping; precision work; hand-transmitted vibration and lifting. The psychosocial risk factors include high mental demands, workload or pace of work; limited choice, control over work or decision latitude; job strain (the combination of high demands and low control); limited support from colleagues or managers; monotony; and work dissatisfaction.

Such factors are common across Europe in working-aged people. Thus, at interview, 31% of workers from the large 3rd European Survey on Working Conditions reported their job to involve repetitive movements for most of the time; 29% reported low control over their work pace; and >50% felt they worked to tight deadlines with little choice over working arrangements.[48] In a household survey of self-reported working conditions in the UK, 65% of respondents said that they repeated the same movements again and again; 70% worked to tight deadlines; 45% worked in awkward or tiring positions; and only 20% perceived the support of line managers to be sufficient.[49] And in a population-based case-control study from a municipality north of Stockholm (the MUSIC study), 32-58% of referents reported high demands or low decision latitude, around a third reported repetitive hand/finger movements, 37-38% reported poor general support at work, and 16-17% perceived high time pressures at work.[50] Many male referents also reported a high physical workload (24%), and working with their arms above shoulder height for ≥30 minutes/day (29%), or with vibrating tools for at least one hour/day (29%).

One difficulty in relating these general observations to the occurrence of neck disorders is the complexity of exposures; another is their overlap; and a third is how to obtain a satisfactory measure of them in studies of epidemiological scale. 'Repetition', for example, may encompass movements of the neck, the neck-shoulder girdle, the whole arm, or just the distal arm, wrist, hand, or fingers; it may be characterised in various ways – by frequency, duration, opportunity for rest breaks, range or direction of motion (exposure dose is likely to be a function of duration as well as intensity); repetition at one joint may be accompanied by static or forceful loading and repetition elsewhere; and jobs that are repetitive tend also to be monotonous, with low job control, paced demands and deadlines. Difficult choices arise as to which metrics to assess, in whom, and how; and over and above this, there is a major challenge in disentangling the separate contributions of risk factors.

Occupational health researchers have followed one of two general approaches to exposure assessment and the neck:

(1) to assess risks by a comparison of job titles, presuming one group to have more 'exposure' than another; or
(2) to ask workers to estimate their own exposures, by completing a questionnaire.

In the common situation of a crude comparison of job titles, all of the members of an occupational group (e.g. sewing machinist, cod trimmer) are assigned a common exposure. Thus, a degree of non-differential exposure misclassification will arise, the size of which will be influenced by true exposure variability. Moreover, where associations are found there may remain significant uncertainty as to the contributing risk factors. The direct approach of questioning workers offers the potential, cheaply and flexibly, to collect further data, including some that can only be supplied in this way (e.g. perceptions about job satisfaction). But some exposures may be hard to recall or self-estimate (e.g. cycle time, number of repetitions during a work day, cumulative exposure time), with the possibility of random measurement error (bias towards the null); and in retrospective and cross-sectional studies, those with symptoms may recall or report their exposures differently from those without (possibly leading to bias away from the null). Non-differential[51] and differential[52,53] misclassification have both been found in surveys that compared self-reports with direct observations, with some authors concluding that "the accuracy of assessments is not good for studying quantitative exposure-effect relationships"[52] or that "direct technical measurement may be preferable".[53]

Thus, in some surveys, the two broad approaches have been supplemented by direct observations in a sample (e.g video tape analysis), to corroborate and validate reports, or to characterise the main ergonomic elements of the work. Direct observational methods of exposure assessment tend to be time-consuming and difficult to apply, other than to quotas of workers doing 'representative' work. Methodological challenges therefore include representative sampling and the translation of group-assessed average levels of exposure to individuals.

Many of the core studies reported here are limited by these problems – in particular, the difficulty of characterising exposures in sufficient detail to distil the potentially causal elements and explore exposure-response relations; and the failure to translate from ergonomic observations to specific exposure assignments that were used to inform health analyses.

4. Methods

4.1. Data sources

Two primary sources of data were employed for the review:

1) During 1995 and 1997 two comprehensive reviews on work-related upper limb disorders were published: a reference text book edited by Kuorinka and Forcier[54] and a critical

review of epidemiological evidence, compiled by the National Institute of Occupational Safety and Health (NIOSH) in the US.[55] In addition, in 1999 the European Agency for Safety and Health at Work produced a review of work-related neck and upper limb musculoskeletal disorders,[56] and this was followed in 2001 by a published thesis on work-related risk factors for neck pain by Ariens.[57] We retrieved all of the unique references to neck-shoulder disorders mentioned in these four reports. For completeness we also retrieved papers listed in some of these reports under non-specific diagnostic headings (cumulative trauma disorder, repetitive strain injury (RSI) and occupational over-use syndrome).

2) We supplemented this with a systematic literature search, employing the MEDLINE, EMBASE BIDS, and Psychinfo electronic bibliographic databases.

4.2. Search strategy

The search was conducted in three stages. For the first stage, key words and medical subject headings were chosen provisionally to represent each outcome and exposure of interest, as well as words and terms representing the ingredients of a physical examination. These were combined using Boolean strings/logical operators. Titles of papers were scanned, duplicates and obviously irrelevant references eliminated, and the remaining abstracts were read independently by two researchers, JCS and KTP, to decide on the papers to be retrieved, with any differences of opinion resolved by consensus. At this point we compared the outcome of our search up to 2001 with the list of papers we knew to exist from the four earlier reports; this served both as a check on the completeness of the source reviews and as a way of helping us to refine and improve the search strategy.

For the second stage, additional search terms were added as necessary. The revised search was then run again in its entirety from the start of each database's electronic record up 3rd week of May 2006. Any further abstracts and titles were identified and processed as before, and any new papers retrieved and added to the list for review. And the references of retrieved papers were searched for additional relevant material (in a process of 'snowballing').

Some studies that incorporated a physical examination cited the origin, provenance, and measurement properties of their diagnostic methods by reference to separate methodological reports. In the third stage, we identified and retrieved these additional citations by a scrutiny of relevant papers from the first two stages.

The final search strategy is copied in Appendix 1.

4.3. Inclusion and exclusion criteria

Studies were included if:

- the case definition (outcome) included one or more symptoms *plus* one or more physical signs – neck pain or neck-shoulder girdle pain (with or without radiation to the upper limb) allied with some findings on physical examination; and
- there was an analysis of risks for such an outcome (or enough data to derive estimates of risk) by occupation or occupational exposure(s).

Tension neck syndrome, cervical syndrome, thoracic outlet syndrome and other researcher-specified diagnostic labels were eligible for inclusion provided that these criteria could be met.

A few studies defined cases according to our criteria but analysed them in combination with other disorders of the upper limb, to enhance study power. Where >50% of the analysed material fulfilled our case definition we recorded the findings under the heading of 'mixed neck-shoulder disorders'; where <50% fulfilled the case definition, or the proportion was unclear, the study was excluded.

We limited our search to primary research reports published in English. We excluded:

1) studies that *only* considered symptoms, or *only* considered signs (except to explore the general consistency of evidence);
2) studies of specific neck pathology, as defined by radiological appearance;
3) studies that considered only distal arm pain or specific pathology of the shoulder (not neck), elbow, forearm, wrist or hand;
4) studies that did not include a control group or internal comparator.

4.4. Information abstracted

For each paper that was finally reviewed we abstracted a standard set of information, comprising details of: the study populations, study design, and research setting; outcome(s) studied; confounders or effect modifiers considered; exposure contrasts; and estimates of effect (with confidence intervals).

The elements of case definition were noted in detail, as well as the labels allotted by investigators. Where given, we also recorded the provenance of proposed diagnostic schemes and any estimates of within- or between-observer repeatability, either in the reports themselves or in the references they cited as evidence in support of methods. We also noted whether the outcome was assessed blind to knowledge of exposure and vice versa.

Where counts or prevalence estimates were provided but not relative risks, we calculated odds ratios with exact 95% confidence intervals using STATA statistical software.

We also recorded/estimated effects by different durations, categories, and levels of exposure, and weighed the evidence for thresholds of effect and dose-response relationships, in as much detail as the source reports allowed.

4.5. Quality assessment

We formed a subjective judgement as to the contribution of each report to knowledge ('quality rating') taking into account its limitations of design, potential for bias or confounding, and power to detect important associations. Studies were ranked higher if they were: well-powered, employed a representative sampling frame, achieved a high effective response rate, were prospective, controlled adequately for confounding, had a clear and repeatable definition of outcome, assessed outcome blinded to exposure and vice versa, characterised exposures at least in part by objective means, and provided dose-response information.

We rated each of these qualities individually. Some of the components of our decision-making are summarised briefly below. We also formulated a final overall assessment, on a five-point scale. (This did not reflect a simple sum of each individual score but a judgement informed by them.)

Confounding and effect modification **-** The potential for important confounding is a function of the relative risk associated with a confounder, its prevalence in the population of relevance, and the likelihood that it might vary importantly according to occupational exposures. Additionally, some factors may act as effect modifiers – that is, risks may vary according to their presence or level. Based on our general understanding of musculoskeletal disease and our summary evidence on non-occupational risks for incidence and persistence of neck pain, the factors that should be allowed for in assessing confounding/effect modification are: (1) age, (2) gender and (3) mental health. Other factors that might be considered include (4) obesity, (5) smoking, and (6) past history of neck injury. We rated control of confounding as 'good' (++) if analysis and/or design allowed for all of the first three items, as 'moderate' (+) if it covered two of them, and as 'poor' if it covered only one or none of them (-). Reports that allowed for five or more of the factors highlighted, including all of the first three were scored as 'excellent' (+++) in this aspect of methodology.

Bias – Two categories of bias need to be distinguished – "inflationary" bias (bias that could cause important overestimation of relative risks) and bias towards the null (bias that could cause elevated relative risks to be underestimated).

Inflationary bias typically arises from non-independent assessment of exposures and outcomes, or from reverse causation. Thus, concern arises where blinding is insufficient, and in retrospective and cross-sectional studies that rely on self-reports of exposure. Estimates of psychosocial risk suffer the problem that pain may be a cause, rather than a consequence of low mood. (Inflationary bias can also arise in the context of an investigated cluster. Studies that make a simple comparison of job title are particularly vulnerable to this problem, although we found no reports linked to an explicit outbreak of symptoms.)

Bias towards the null is of more pressing concern where there is simple non-differential misclassification of exposure or outcome – as might arise, for example, from an unreliable protocol for assessing outcome, simple errors in the recall and self-estimation of complex exposures or a vague definition of exposure. It can also arise from the 'healthy worker' effect and the shift of affected workers to jobs with lesser exposures – a concern in cross-sectional studies and in case-control studies that fail to inquire about exposures preceding the onset of symptoms.

We scored studies separately according to the potential for each of these biases.

Sampling – We checked to see whether the sampling frame and sampling procedures were clearly stated, whether inclusion and exclusion criteria were clear, and whether we could account for all of the subjects at each stage of the account. We graded our findings on a three-point scale.

Outcome assessment – We assessed whether the case definition was explicit and relevant; whether there was empirical evidence to suggest it was repeatable; and whether assessment of outcome was blinded to exposure.

Exposure characterisation – We considered exposure assessment to be most informative (+++) where objective observations were used, in whole or part, to subcategorise individuals by level or nature of exposure (e.g. duration, intensity, cumulative dose), and these categories were then used in relevant health analyses. We considered it to provide limited additional information (++) where direct observations led to some general statement about typical exposures in workers with a given job title, but health analyses made no use of the extra detail. We noted whether exposures were ascertained blinded to outcome status.

Exposure-response information – Some studies defined exposures on a quantitative scale (e.g. number of shoulder movements per minute, % of time with the neck flexed), whereas others used ordinal measures (e.g. 'high', 'medium', or 'low' in the respondent's opinion). We rated the former more highly (+++) than the latter (++) for physical exposures, while recognising that the latter was a forced choice for estimates of psychosocial risk.

Response rates and sample size – We calculated effective response rates for the analyses of interest (focussing for the cohort studies on response at follow-up); and summed the numbers involved in each analysis. The impact of the former is likely to vary with the reason for non-response and the latter with study design (case-control studies having greater power for a given sample size than a cohort study). However, in general terms, we rated response rates of ≥85% as 'excellent' (+++), of >75-84% as 'satisfactory' (++), and of 50-74% as 'fair' (+). Studies fell into four sizes: those likely to have had 'very good' statistical power (>1000 subjects in relevant analyses), and those of 'good' (400-600+), 'reasonable' (100-399), or 'limited' (<100) sample size.

Completeness of reporting – Incomplete reporting sometimes impaired our capacity to assess overall quality. In reaching the final quality rating, we assumed that missing items did not meet the criteria set out above.

4.6. Meta-analysis

We considered the scope for meta-analysis, but as studies rarely employed the same definitions of exposure and outcome we decided that such an analysis would be inappropriate.

4.7. Rating the evidence on causal associations

Finally we rated the degree of evidence of causal association between a given exposure and a given outcome according to the template of the Scientific Committee of the Danish Society of Occupational and Environmental Medicine (Appendix 2), basing our findings on the strength, consistency, quality, and amount of evidence against specific formulations of outcome and exposure.

5. Results

Altogether the first search identified 82 potentially relevant research reports and six reviews, and all were retrieved and assessed. The second computerised literature search identified 1471 unique titles and abstracts and these were screened by JCS and KTP leading to the retrieval of a further 41 primary reports and one review. All of the retrieved papers and reviews were checked for further references of interest, and this resulted in another 13 research reports and one review being obtained and appraised.

Finally, therefore, a total of 136 primary research reports were each read independently by two observers. Among these, 115 were excluded by consensus, the main reasons being that they:

1. did not incorporate a physical examination, or did not present data for a case definition that combined symptoms with signs (n = 46);
2. did not investigate the diagnostic entity of interest, but pain or pathology at another site (n = 26) or a mixed pathology comprising <50% of cases of neck pain with physical signs (n = 8)
3. did not include a reference group, or did not provide enough information to derive estimates of occupational risk (n = 20);
4. were published in a language other than English (n = 11);
5. were relevant only to secondary questions of reliable diagnosis or natural history (n=5);
6. concerned only VDT users (n = 15).

Some papers were excluded for several of these reasons. (A list of excluded papers, with their reasons, is available on request.)

The remaining 21 reports from eight different countries were included in the review. Table 2 (p53-55) summarises their main features and our quality assessment of them. Further details of the diagnostic criteria employed are presented in Table 3 (p56-58), while risk estimates by occupational title, physical exposures, and by psychosocial work conditions follow in Tables 4 to 6 (p59-69).

Following a few general observations, we describe each of the studies in turn and comment on potential strengths and weaknesses. We conclude with a 'best evidence' synthesis and discussion, summarising them in Table 7 (p70).

5.1. General findings

Altogether 15 investigations were cross-sectional in design,[32,35,37,39-44,59-64] four were prospective[18,19,38,58] (one mostly focussing on baseline findings[38]), and two were community-based case-referent studies.[50,65] Studies ranged from the very large (n = >15,000)[19] to the very small (n = 30).[58] Most studies achieved a high response rate, but for a few[44,61,62] this could not be confirmed from the description provided.

Case definitions varied, but fell into four broad categories (Table 3). They included 16 investigations of neck pain with tenderness (11 of these using TNS as the disease label), six of neck pain with pain on neck movement (five called cervical syndrome), three of thoracic outlet syndrome (all with very few cases), and seven reports of mixed neck-shoulder disorder in which TNS or neck pain with tenderness was diagnosed in >50% of cases.[35,38,41,50,62,64,65] Several studies reported on more than one outcome. The reproducibility of diagnosis was demonstrated for four of the studies[18,35,37,38] and suggested in two others.[39,63] Blinded assessment of outcome was explicitly declared in five studies,[18,35,37,43,61] but may have occurred in several others by virtue of design or previously described methodology.[19,38,58,65]

Many physical exposures were considered in the studies, including: repetition, neck flexion, static loading, forceful work, lifting, work with the arms elevated, sitting, and hand-transmitted and whole-body vibration; while the occupational psychological exposures included control, support, demand, and perceptions of a stressful work environment. In 14 of the 21 reports, analysis was principally by a comparison of job titles; but in 11 studies physical exposures were objectively characterised to a varying extent.[18,37,39-43,61-64] Several studies offered exposure-response information by quantified level of exposure[18,37,61,62] or time worked in the job,[35,38,41] but in others only crude and sometimes composite exposure variables were used. Three studies analysed the interaction between physical exposures.[18,37,43]

Confounding was addressed in various ways (restriction, matching, stratification, regression modelling), but to a greater or lesser extent, even within reports: 15 of the 21 studies failed to fully to control for age, sex, and mental health as suggested by us on p13.

Many studies shared several limitations in common - typically, a small sample size (limited precision), limited control of confounding, lack of blinding (risk of inflationary bias), and limited exposure assessment (lack of dose-response information). Such papers tended to present only simple contingency tables (predating the advent of more sophisticated approaches to statistical analysis) and rarely considered psychosocial factors.

We rated the overall quality of information as excellent (+++++)[18,37] in only two reports, as useful but with important limitations in four reports (+++),[19,41,61,62] as moderately informative (++) in five reports,[35,38,42,43,64] and as limited in 10 reports (+).[32,39,40,44,50,58-60,63,65] (We stress that this assessment is relative to this particular study question. Some reports contain important information for other areas of inquiry.)

5.2. Description of the individual studies

Note on the organisation of text and tables. The short descriptions that follow are arranged alphabetically according to the first author's surname. Studies are also ordered alphabetically within tables, but they are grouped first, by study design in Table 2, and in Tables 3-6 according to the four broad diagnostic groupings employed by researchers.

Åkesson *et al*[59] compared 84 dental personnel with 27 age and sex-matched nurses. Details of the sampling frame and selection methods were limited. Although described as a follow-up study, analysis involved a cross-sectional comparison of workers from an earlier survey. No specific assessment of exposure was made. Dental work was assumed to involve a prolonged static workload to the neck, shoulders, and arms, as well as visually demanding precision work; but the extent of exposure was not quantified. The outcome (TNS according to the Ohlsson criteria) was assessed by a single observer with 'many years of clinical experience' who may not have been blinded to the occupations of participants; no details were given on the repeatability of diagnosis. TNS occurred more often in dental personnel than in referents with a (derived) OR of 3.2 (95% CI 0.8-18).

This study had several limitations – small size, cross-sectional sampling, lack of exposure characterisation (including the nature and level of exposure), and uncertainty about whether outcomes were assessed blinded to occupational title.

Andersen *et al*[35] conducted a survey of sewing machinists, a group whose work involved repetitive and precise movements of the upper limb as well as prolonged static loading of the neck, shoulders and arms, and sustained neck flexion. Age-matched auxiliary nurses were selected as a comparator, as they were deemed to have a similar social background but a workload that was more varied. Sewing machinists were recruited in two-stages, an initial mailing (78% response) and an invitation for follow-up examination issued to a subset of respondents still employed two years later (chosen at random within strata of employment duration); at the second stage, refusals were few but the final sample size was modest. Level of exposure was quantified only crudely, according to years in the job. However, a useful strength was the care over outcome assessment. Definitions were precisely formulated, assessments were conducted by two pre-trained observers blinded to knowledge of exposure, and the between-observer reproducibility of palpation tenderness was assessed and found to be satisfactory (kappa coefficients 0.56-0.78). Two outcomes were relevant to this report: cervicobrachial fibromyalgia (in effect neck pain with palpation tenderness) and cervical syndrome. The frequency of both rose strongly with years of employment. Thus, the odds of cervicobrachial fibromyalgia were raised 23-fold after >15 years as a sewing machinist vs. no years (nursing group). We derived these estimates from a table of frequencies and so could not adjust for age; but the data imply a much steeper gradient with time than might be accounted for by age as a confounder. An age-adjusted analysis was provided for the combined outcome 'neck-shoulder syndrome' (mainly cervicobrachial fibromyalgia, but with a significant proportion of cases with rotator cuff syndrome) and showed an even steeper gradient (OR 36.7, 95% CI 7.1-189.1, for >15 vs. 0 years of employment).

The main strengths of this paper are its care over diagnosis and blinding. Age may have confounded the findings, but seems unlikely to explain them; a healthy worker effect would, if anything, bias findings towards the null and point to an even bigger true effect. However, this well-investigated group could have been more aware of the study hypothesis than referents and more inclined to report physical discomfort; the study depends on a small group of nurses being an appropriate comparator. Exposure characterisation was limited.

Andersen *et al*[37] conducted a cross-sectional study of 3,123 workers from 19 workplaces (food processing companies, textile plants, and several other manufacturing and service companies) within the Project on Research and Intervention in Monotonous Work (PRIM) health study of 1994-5. Almost three-quarters of the target population participated. Neck-shoulder pain was scored (out of 36) according to its severity at worst and on average within the previous 3 months, its average level over the last 7 days, and its interference with daily activities during the previous 3 months. Three teams of physicians examined individuals blinded to exposure and health status. Palpation tenderness was assessed in the neck muscles, the upper trapezius border, and the supraspinatus or infraspinatus muscle. Indisputable tenderness (leading to flinch or withdrawal) was noted. The inter-rater reliability between three examiners was confirmed in a subgroup of 60 participants (kappa values, 0.45 to 0.57). Cases were defined as neck-shoulder pain with a score of ≥12 *plus* indisputable palpation tenderness. Altogether, 185 participants fulfilled these criteria.

Following repeated visits to the factories, 300 repetitive work tasks (e.g. de-boning ham or poultry, sewing machine work, packing, data entering, work as a cashier, manual machine feeding) were aggregated into 103 task groups. Between 1 and 7 workers in each task group were videotaped from several angles for at least 10 working cycles or at least of 10-15 minutes. The number of shoulder movements/minute, the percentage of time in neck flexion

$>20^0$, the percentage of cycle time spent with no upper arm support or rest for >2 seconds, and force requirements (subjectively assessed on a five-point ordinal scale relative to maximum voluntary contraction) were quantified following repeated reviews of the recordings, and median values of each exposure assigned to task groups. In the final step these estimates were linked with workers' reports of the relative time spent in different activities.

Psychosocial risk factors were also assessed using the Whitehall II version of Karasek's job content questionnaire, as well as several individual characteristics (BMI, pain pressure threshold, short-form 36 (SF-36) and personality traits).

Analyses were adjusted for age, gender, psychosocial factors, past history of neck-shoulder injury, BMI and several other factors. Following this, dose-response gradients were seen by bands of repetitive shoulder movement, force requirements, neck flexion, and lack of recovery time. Prevalence ratios (PR) were raised 1.7-2.0 fold for high vs. low band comparisons. Additional analyses considered the combination of repetition with each of the other factors. (The four ergonomic exposures were significantly correlated, with coefficients ranging from 0.47 to 0.84). Risks in the top most band (high repetition with high levels of another exposure) were only a little higher than for repetition alone, with PRs of 1.9 to 2.3.

High self-reported psychosocial demands were associated with the outcome after adjusting for physical risk factors (PR 1.8), but rather weaker associations were seen with low control and low social support (PR 1.3 - 1.4).

After allowance both for physical and psychosocial workplace factors, associations were seen with female gender (PR 1.8), pain pressure threshold (PR 1.6), and neck-shoulder injury (PR 2.6); a non-significant association was seen with age, but no relation to BMI. Those in pain had worse mean SF-36 scores for several health dimensions, including vitality and mental health, and lower still when palpation tenderness was also present.

This study had numerous strong design features: a large sample; an adequate response rate; a clear sampling strategy; detailed characterisation of physical exposures with dose-response information; a clearly defined repeatable measure of outcome, assessed blinded to exposures; and thorough control of confounding. Although 25% of those invited did not take part, non-response is unlikely to explain the several dose-response gradients found. Despite painstaking efforts to measure exposures objectively, however, the final estimate depended also on individuals' reports about their relative time in different job tasks. The challenge of assessing complex time-varying exposures on an epidemiological scale is considerable:

random measurement errors would tend to obscure dose-response relationships. In theory, however, artefactual dose-response gradients might arise if those with symptoms had a greater propensity to over-estimate their exposure to certain activities (some empirical evidence suggests that report of exposures can be differential in this way[52,53]). A more exacting test is to demonstrate similar dose-response relationships prospectively.

Andersen *et al*[18] proceeded then to follow-up 3,123 workers from the PRIM baseline on three further occasions, roughly a year apart. They assessed incident neck-shoulder pain and incident neck-shoulder pain with palpation tenderness in the neck-shoulder area. An incident case was defined by a symptom score of <12 at baseline and an increase of 12 score values during follow-up; participants with indisputable palpation tenderness in the neck muscles or right upper trapezius border *and* in the right supra- or infraspinatus muscle fulfilled the additional examination criteria to become a 'clinical' case. No explicit mention was made of blinding in this report, although the complexity of exposure assignment makes this likely and blinding had previously been reported at baseline. No mention was made of the reliability of outcome assessment, although the methodology appears to be underpinned by data reported by Andersen *et al*.[37]

Baseline physical exposures were assessed according to the earlier report. At each follow-up round a screening questionnaire was completed on pain status, workplace psychosocial factors and symptoms of distress. In addition, physical workload was reassessed for new or changed job tasks. Risk of the two outcomes was calculated using a discrete survival model, with time varying measures of observed and perceived workplace factors. In all analyses a lagged function was used to link the outcomes with psychosocial and personal factors reported in the preceding round of follow-up. Risk estimates was adjusted for age, gender, psychosocial factors, level of distress, BMI, and pain pressure threshold.

Follow-up lasted almost four years and by the end the cohort had roughly halved. Dropouts were attributed mostly to young age (and labour turnover) and to some companies moving their production to Eastern Europe. No strong association was found between dropout and exposure or musculoskeletal disorders at baseline, and the prevalence of neck-shoulder pain with pressure tenderness (6.2% - 6.3%) and annual incidence (14% for symptom cases and 1.7% for clinical cases) remained stable through the study. As with the baseline report, strong exposure-response gradients were seen with all of the physical risk factors investigated, and ORs were raised by 2 to 3-fold in each high-low band comparison. Gradients were stronger for symptoms with signs than for symptoms alone. Associations with repetition were not strengthened by its combination with other risk factors, and in those with low repetition, associations with the other factors were much closer to the null. Interpretation is hampered by the high correlation between physical exposures (correlation coefficients 0.3-0.5). However, if anything, the study points to repetition as the major risk factor, and suggests that its effects in combination with other physical exposures are less than multiplicative.

Those who reported high job demands had a higher incidence of neck-shoulder pain with pressure tenderness (OR 1.7), after allowance for physical, individual, and other psychosocial risk factors; weaker non-significant associations were also seen with low job control and low social support (ORs 1.3). Finally, the authors constructed a combined physical exposure or 'physical strain' index, with workers in the highest category scoring highly on at least three of the four physical quantitative measures. The OR for becoming a clinical case was 3.2 (95% CI 1.6-6.6) in the high vs. low band comparison. In this mutually adjusted model, significant associations were also seen with high job demands (OR 2.0), female gender (OR 1.8) and high levels of distress (OR 2.8). The authors concluded that physical and psychosocial workplace factors and high personal levels of distress are predictors of incident neck-shoulder pain with pressure tenderness.

This study had numerous important strengths: a large sample; a clear sampling strategy; a prospective design; a clear outcome (probably repeatable and assessed blind to exposure); sophisticated characterisation of physical exposures, including exposures that changed over follow-up; an adequate assessment of workplace psychosocial factors and personal mental health, including changes over follow-up; a sophisticated analytic strategy with thorough control of confounding; and useful exposure-response information. Its main weakness was the substantial losses to follow-up, although some evidence was offered that this did not give rise to important selection bias. As with the baseline assessment, the method of exposure assessment, when applied to individuals, required self-reports of working patterns. Information bias could thus arise, but prospective design and the reporting of exposures before symptom onset seem to make this an implausible explanation of the findings. A challenge existed in distinguishing the separate contributions of physical risk factors that often occurred together; the evidence points most clearly to repetitive shoulder movements as a cause of neck-shoulder pain with pressure tenderness; separate smaller contributions from force, neck flexion, and limited recovery time might exist. A steeper exposure-response gradient was seen for incidence than for prevalence; however, the case definitions at baseline and follow-up were not identical, and broadly speaking, findings were consistent at the two stages. Independently, a doubling of risk was found with high job demands as defined in the job content questionnaire of Karasek. Other personal risk factors included female gender and high level of distress: assuming the multiplicative model presented in Table 5 of this report, a female worker with *high levels of distress (score >2 on the stress profile questionnaire of Setterland) might have an OR for incident neck-shoulder pain with pressure tenderness of almost 9 in comparison with a male scoring zero on the same scale.*

A study from the US by **Anderson *et al***[60] investigated members of a transit union. A stratified random sample was taken from among bus drivers and non-drivers. Exposures among drivers will have been to whole-body vibration and prolonged sitting, but the extent of these was not quantified any further. Non-drivers comprised clerks, custodians and mechanics. No refusals were encountered. All subjects were interviewed and examined by an orthopaedic physician who assessed the somewhat ill-defined outcome of 'moderate to severe neck disorder' (at least moderate neck pain affecting normal activities of daily life + restriction or pain on neck movement). The between-interviewer reliability of symptom inquiries was said to be "confirmed", but the within-observer reliability of physical signs was not assessed; nor was examination explicitly blinded to job category. No control of confounding was attempted. In crude comparison, the outcome was non-significantly more common in the bus drivers (OR 1.8, 95%CI 0.5-7.8).

This study had many limitations.

Bovenzi *et al*[61] investigated 65 male foresters and 31 male blue-collar maintenance workers (mechanics, electricians, and painters). No information was given on the sampling frame, selection methods, or response rate. The main strength of this study lies in exposure assessment. Measurements of vibration magnitude were made on the front and rear handles of three chain saws in use, individuals were asked about their frequency of daily exposures, and each person was assigned an estimated vibration dose using the formula in ISO 5349 (1986). In addition, care was taken to define the outcome criteria closely (based on Waris *et al*[31] and Viikari-Juntura[32]) and to assess outcomes blinded to exposure. On the other hand, no details were given on the reliability of diagnosis. Ergonomic assessment was limited to the use of a modified Michigan's checklist, which scored the proportion of work conditions "potentially associated with upper extremity musculoskeletal disorders"; foresters were rated at "slight excess risk". The proportion of short cycle time tasks (<30 seconds) was non-significantly more common among the referents. Forestry will have involved work with the arms elevated and forceful gripping, as well as exposure to hand-transmitted vibration, but no details were given on this. Three groups were analysed –with daily vibration exposures >7.5 m/s^2, >0 - <7.5 m/s^2, and nil (maintenance workers as a common reference category). Risk estimates were controlled for age as well as gender. The adjusted OR rose in a dose-response pattern for cervical syndrome and was raised almost 11-fold in the top band; that for TNS was raised almost four-fold for the same comparison, but not raised among workers with a lower daily vibration dose. In a simple comparison by job title the ORs for TNS and cervical syndrome were also significantly raised, by 2.1 and 6.8 respectively.

The limitations of this study included its small size, cross-sectional design, ambiguous sampling methods, and failure to consider fully exposures concurrent with vibration. Its strengths included most aspects of outcome and exposure assessment as well as its attempt to offer exposure-response data.

Cassou *et al*[19] conducted a prospective investigation (ESTEV) of workers from various industries, who attended compulsory medical examinations in 1990 and 1995 under the supervision of 400 French occupational physicians. Almost 17,000 subjects were studied, selected in age and sex strata to mimic the age-sex distribution of French employees as a whole. Cases were defined as those with chronic neck-shoulder pain (present on the day of the examination and for at least six months before, and causing functional limitation) *plus* neck or shoulder pain on passive movement. Assessments were performed by 'trained' occupational physicians, but no details were given of the steps to ensure standardisation or the reliability of diagnosis. Exposures were all self-reported and were limited in detail. For example, a subject was considered to be exposed to 'awkward work' if he reported being exposed to at least one of: awkward posture, carrying heavy loads, vibrations, or forceful operation of tools or machines; and to have 'low job control' if at least one of the following factors was reported: no means to carry out high quality work, no possibility of choosing the way in which work would be carried out, no variety of work, or no learning of new things at work. The intensity and frequency of exposure to these composite measures was not recorded.

Analyses focused separately on incidence and persistence. Both outcomes were more common in women than men and rose with age. However, not all of the findings were adjusted for age. Depressive symptoms were considered in some but not all of the analyses.

The outcome had a five-year incidence of 7.3% in men and 12.5% in women. Among workers with chronic neck-shoulder pain at baseline, around a third of men and a half of women still had the disorder at follow-up. Tables 5 and 6 present various findings on incidence of, and recovery from chronic neck pain. Exposures were assessed prior to 1990 (baseline) as well as during 1990, in case workers had changed their work because of symptoms. Associations were examined with repetitive work under time constraints, awkward work and low job control. In general, incident events were only slightly more common (PR $\leq$1.4) in those with exposures than in those without, although some associations were significant at the 5% level. Little association was seen between recovery from the outcome and awkward work, precise work, or low job control; but recovery was significantly less common in women undertaking repetitive work prior to 1990 (OR 0.5, 95% CI 0.3-0.7) and in both sexes with report of high demands (OR 0.7), and depression at baseline (OR 1.3 to 1.5).

This study had several strengths including a large sample size, a prospective design, and a high response rate. Its major limitation was the poor characterisation of exposure – self-reported without corroborating objective measures and comprising crude composite measures, not tailored specifically to ergonomic stressors of the neck-shoulder region. Confounding was weakly controlled. Only modest associations were found with repetitive work and with high self-reported job demands. However, non-differential misclassification of exposures could easily have biased estimates of association towards the null.

Ekberg *et al*[65] compared 109 'cases' (patients consulting a physician for musculoskeletal disorders of the neck, shoulder or arm and who had been on sick leave for $\leq$ 4 weeks) with 327 population controls, chosen from an insurance register. The response rate for cases was not reported; for controls it was said to be 73%, although the numbers finally analysed suggest a lower response. Subjects completed a Nordic questionnaire and were classified according to the criteria of Waris *et al* (no details were provided on the reliability of diagnosis or blinding). They also answered a questionnaire about work conditions, including: uncomfortable sitting position, physically demanding work, lifting, repetitive movements demanding precision, work with the arms lifted, high pace of work, demands on attention and the quality of work content. Among the cases, 47% had TNS and 18% had cervical syndrome or radiating neurological symptoms. Cases and controls were poorly matched on gender (80% vs. 39% female) and current smoking (62% vs. 25%). Both of these factors showed strong associations with outcome (ORs 11.4 and 3.7 respectively), but no adjustment was made for confounding. In crude analyses, very strong associations were seen with repetitive precision movements (high vs. low: OR 7.5), lifting (medium and high vs. low: OR 13.6), and ambiguity of work role (high vs. low: OR 16.5). ORs of 2.6 to 3.8 were also seen with high levels of uncomfortable sitting, rushed work pace, high demands on attention and low self-rated quality of work content.

This study had several limitations related to sampling and response rates, outcome definition and control of confounding. In addition, exposures were self-reported retrospectively and may have been differential between cases and controls, leading to information bias. Associations were seen with all of the physical exposures, rather than being specific to a few, and are large in comparison to other reports.

Hansson *et al*[62] compared 87 workers from the laminate industry (assemblers, pressers, and finishers) with 33 office and 35 industrial workers in mobile and varied work. The selection methods and response rates are unclear. The subjects (all female) completed a Nordic questionnaire and were examined and classified by a single observer (Ohlsson criteria). No information is given on the repeatability of diagnosis or on blinding. Muscle loads (*M trapezius* and *M infraspinatus*) were assessed by EMG, and wrist positions and movements measured using electrogoniometers. At interview, questions were asked about psychological demands and decision latitude. Muscle loading was similar in laminate workers and industrial controls, and higher than in office workers, while there was a gradient across the three groups for speed and frequency of wrist flexion and deviation (greatest in the laminate workers and least in the office controls). TNS was significantly more common in laminate workers than in office referents (crude OR 2.9, 95%CI 1.0 –9.4), but only slightly higher than in industrial referents (OR 1.4). Age-adjusted ORs for ‘neck disorder’ (TNS with a few cases of cervicalgia) were also higher in medium to high bands of muscle loading (ORs 1.9 and 1.5) and wrist movement (ORs 5.4 and 3.1) than in those with low exposures; additional adjustment for psychosocial factors had little effect on risk estimates.

This study was limited in terms of sample size, sampling procedures, cross-sectional design and outcome assessment. However, exposures were characterised and used in health analyses, with reasonable control of confounding.

In a study by **Hinnen *et al***,[63] cashiers using laser scanners were compared with other conventional cashiers. The sampling procedures were not fully described; however, the study excluded workers who were off sick or had had previous injuries, and so may have been prone to healthy worker selection bias. A high response rate was achieved among the remainder, who completed a self-administered questionnaire and were examined by a single physician who was not explicitly blinded to work history. The outcome studied was neck pain or neck stiffness with examination findings (painful pressure points, with or without restricted range of movement). The inter-observer reliability of the overall examination (which included shoulder movements) was described as 'satisfactory', with a Spearman rank correlation between two independent examining teams of 0.7, but the components of comparison and assessment protocol were not described. In a sub-sample, estimates were made of the number of items handled, and working postures were scored by checklist (OWAS), and subjected to movement analysis. However, these observations were not used in analyses of health outcome; rather, a simple internal comparison of cashiers was presented according to laser scan use and presence or absence of job rotation. Gender was controlled for in analysis, but other potential confounders were not. No significant associations were found with use of the laser scanner or work rotation.

This study had many limitations. In addition, despite some detailed ergonomic assessment we found it hard to achieve a firm understanding of the main ergonomic contrasts.

Kaergaard *et al*[38] studied a group of sewing machine operators, comprising a subset of the Danish PRIM study. 238 female sewing machinists completed a questionnaire and clinical examination at baseline, as did 357 women whose jobs were varied and non repetitive. Subjects were followed over a further two years, although analyses related mostly to the baseline comparison. The outcome of interest, myofascial pain syndrome, comprised neck-shoulder pain with moderate to pronounced palpation tenderness. No mention was made about the repeatability of diagnosis, although other reports by the same group imply an established repeatable methodology. Exposures were characterised only in terms of duration of employment. Additional information was collected on several personal risk factors (age, smoking, BMI, job strain, social support and a personal stress scale). The prevalence of myofascial pain syndrome was higher in sewing machine operators (15.2%) than in controls (9%) (PR 1.7, 95% CI 1.1 - 2.6). In a crude comparison, there was a U-shaped relationship with duration of employment. Multivariable analysis considered only the outcome of mixed neck-shoulder disorder (mostly TNS). In comparison with those employed for 2-10 years, PRs were raised 2.4 in those employed for ≤ 2 years and 4.4-fold in those employed for >20 years. A significant association was also found with high personal stress (PR 2.5), and non-significant associations with smoking (PR 1.6) and low social support (PR 1.7). Many dropouts were encountered over follow-up, the final material comprising 150 subjects with baseline and at least one follow-up examination. Among this group, low social support was a predictor of incident mixed neck-shoulder disorder, with an adjusted of RR of 3.7 (95% CI 1.2 - 11.3).

This study had some strengths but also some important limitations. Most analyses relevant to this review were cross-sectional, the study size was quite small, and there was limited control of confounding (other than for analyses of mixed neck-shoulder disorder). Examination was blinded to questionnaire responses, but may not have been blind to occupational title. The U-shaped relation with duration of employment raises the possibility of healthy worker selection bias (but in this event, true effects might be even larger.)

In Finland, **Kuorinka *et al***[39] conducted a cross-sectional study of 93 factory workers performing scissor-making operations. These were compared with 163 other factory workers and 143 shop assistants whose findings were reported in a separate paper. Sampling excluded subjects with recent trauma and those off sick, although the latter included only one suspected case of occupational rheumatic disease. The outcome studied was TNS. A physiotherapist, who was not blinded to work history, completed a standardised interview and examination; diagnosis was assigned later according to the criteria of Waris *et al*, by a team of specialists. Between-observer agreement on palpable hardenings and tender points in the neck was reported to be reliable (Yule's modified coefficient of contingency: 0.73 - 0.83), but details were not given of the study leading to these estimates. Scissor-making was characterised according to the number of items handled (estimated from individual productivity records), and selected video taping and visual observations of work stations. All tasks were considered repetitive, with a cycle time ≤26 seconds, although none of the detailed aspects of job assessment were incorporated into health analyses. All but three of those studied were female; no control of other potential confounders was attempted, although comparison groups were similar in mean age. In crude (derived) analyses, ORs for TNS were raised 2.6 - 4.1 fold in scissor makers relative to other occupations, but no relation was found to the number of items handled per year.

There were many limitations including: small sample, cross-sectional sampling frame, unblinded assessment of outcome, and external reference group. Characterisation of exposure was limited in relation to health outcome.

A parallel study by **Luopajärvi *et al***[40] provided the referents for Kuorinka's study of scissor-makers. In the report by Luopajärvi *et al*, 152 female assembly packers were compared with 133 female shop assistants. The two groups had a similar mean age. Those with recent trauma and those off sick were excluded from study, but none of these appear to have had neck disorders. Among the remainder a high response rate was achieved. A pre-trained physiotherapist assessed the outcomes of TNS and cervical syndrome (Waris criteria), but no mention is made about the repeatability of the protocol or blinding. Workplaces were assessed ergonomically by an expert team, and work movements evaluated by a work study engineer and physician. At a semi-quantitative level, exposures of packers were characterised as mostly involving repetitive finger-hand movements (up to 25,000 cycles/work day), some static loading of upper limb muscles, extremes of wrist and finger movement, and lifting (average daily load 5,000 kg). However, no comparable data were collected on controls, no individual exposure assessments were made, and no analyses were presented that made use of these ergonomic observations. The OR of TNS was moderately and non-significantly elevated in assembly line packers relative to shop assistants (OR 1.6, 95%CI 0.9-2.7).

There were several limitations including: small sample, cross-sectional sampling frame, and *potentially unblinded assessment of outcome. Exposures were assessed in a semi-quantitative way but only characterised at group level*.

Nordander *et al*[42] investigated 322 fish processors and 337 other workers from the same communities (caretakers, park keepers, gardeners, maintenance workers). The sampling frame comprehensively covered all of the fish processors from 13 plants on the south east coast of Sweden. Those on long-term sick leave were also studied and high levels of response were achieved overall. TNS and cervical syndrome were confirmed (Ohlsson criteria) by a single examiner following a standardised protocol. No mention was made, however, about the repeatability of the method or about blinding.

Ergonomic assessment was based on direct observations and videotaping. Work tasks of six types (trimming cod, packing, work on herring machine etc) were classified according to 60 permutations of workload (weights handled, cycle time and degree of constrained neck posture). Women were estimated to spend 63% of their time in non-lifting jobs (<1kg) with a cycle time <10 seconds and a constrained neck posture, and a quarter of the time lifting loads of 1-10 kg in longer cycles (10-60 seconds) without neck constraint; men spent only 21% of the time in repetitious constrained neck posture work, 34% of time lifting weights ≥25 kg with cycle times of 10-60 seconds, and 26% in jobs with the minimum of all three exposures. However, no comparable assessment was made of controls and findings on the two health outcomes, although stratified by gender, were presented only at the general group level (fish processors vs. referents). They were also unadjusted for age or other confounders, although comparison groups had similar mean ages. The OR for TNS was 2.6 in men to 3.0 in women; cervical syndrome was also more common in fish processors than in referents, but the difference was confined to women (5% vs. 0%).

The main limitations were: cross-sectional sampling, potentially unblinded assessment of outcome, weak control of confounding, and the lack of analysis by level or type of exposure On the other hand, the ergonomic ingredients of fish processing were well described at group level.

A report by **Ohlsson *et al***[64] represents a further investigation of the same workforce. On this occasion 206 female fish processors were compared with 208 women of similar mean age, employed in the same localities (in day nursery and elderly care, or in offices). As before, those on long-term sick leave were included. Health and exposure assessments followed similar protocols, with the same potential strengths and weaknesses. In addition, direct observations and videotaping enabled the range, velocity and pattern of wrist movements to be assessed and a questionnaire collected information on psychosocial aspects of the work (e.g. difficulty of decision making, attentiveness required, control, stimulation, fellowship, social network, work strain, stress/worry, and self-reported muscular tension). The main tasks were packing fish (44% of time), trimming cod (32%), or filleting herrings (11%). These jobs were all characterized as highly repetitive (cycle time < 30 seconds), with constant wrist movements (hand still <1% of the time), a 'poor' standing posture, and moderate levels of physical activity. Job complexity was rated as simple with few challenges. No sub-analyses were conducted - all workers were considered to share these exposure patterns in common and were compared to controls according to job title. As in the study by Nordander *et al*,[42] TNS and cervical syndrome were diagnosed more often in the fish processors (TNS: OR of 4.7 (95%CI 1.9-12.8); cervical syndrome: 5% vs 0%). For the outcome of mixed neck-shoulder disorder (mainly TNS or cervical syndrome), strong associations were seen with self-report of high vs. low job strain (OR 6.6), as well as high vs low muscle tension (OR 4.0) and high vs low stress or worry (OR 3.2). Similar gradients were seen in controls.

This study had similar limitations to those described above for Nordander et al.

Separately, **Ohlsson *et al***[41] compared 82 female industrial workers in highly repetitive jobs (assembling fuses and electronic equipment) with 64 women in more varied work (office, supermarket and canteen workers). In addition, 79 former workers from the first group and 25 from the latter were contacted. All subjects completed a Nordic questionnaire and were examined by a single observer according to a standard protocol (Ohlsson criteria). The examiner was blinded to information on the work tasks of exposed women, but was not blinded to exposed-referent status. The outcomes of relevance were TNS and thoracic outlet syndrome (cervical syndrome was present in only one worker). Exposed subjects were classified by job category (assembly, polishing, or 'fairly mobile') and duration of employment. In addition, videotape recordings were made of representative work tasks in 74 of 82 exposed workers, and work postures and movements systematically scored by two independent observers. Estimates were made for the proportion of time with the neck flexed, or the upper arm elevated or abducted; and the number of movement changes/hour at the neck, and shoulder. Exposures were compared for the three job categories (assembly, polishing, mobile work). Half of the study group worked with their neck flexed (>30^0) for >90% of the time and with the upper arm elevated (>30^0) for >11% of the time; assembly and polishing more often involved neck flexion and neck and arm movements than mobile work, while assembly work involved more extremes of arm movement than polishing. Work rotation was less common in the study group as a whole than in the referents (26% vs. 97%), but short pauses during work were more common (71% vs. 55%).

In crude analysis, TNS was almost five times more common among the industrial workers; thoracic outlet syndrome was diagnosed in 4% of this group vs. none of the referents. Most analyses employed a definition of 'mixed neck-shoulder disorder' (80% of cases had TNS). The OR for this outcome, when adjusted for age and mental health, was similar to that in the crude analysis of TNS overall. It was also higher for assembly workers (OR 6.7) and polishers (OR 4.4) than for industrial workers whose tasks were 'fairly mobile' (OR 2.3). Risks were much higher in the first 10 years of employment (OR 9.6) than in those who had worked for ≥ 20 years (OR 3.8). These findings suggest the possibility of a healthy worker survival bias, and 'pain in the musculoskeletal system' was cited as a reason for leaving by 28% of former industrial workers (although the corresponding figure for referents was 35%). The final multivariate model was tested on the subset of 74 industrial workers who were videotaped, replacing the repetitive work factor with the videotape variables: in stepwise regression, neck flexion proved to be a highly significant variable (P = 0.005).

This study had some useful strengths, including an internal comparison of job titles supported by exposure measurements. It highlights the possibility of healthy worker survival bias.

Silverstein[43] studied 574 subjects from various industries (electronic assembly, motor appliance manufacture, investment casting, apparel, foundry and bearing manufacture). TNS was assessed using criteria modified from Waris and other authors, and explicitly defined in an appendix to this research thesis. Test-re-test reliability of diagnosis was not assessed, although the diagnosis was made blinded to exposure history. A particular strength of this study was the detailed job analysis. At least three workers in each selected job were videotaped performing the work for at least three cycles. For each subject filmed, a stopwatch was used to estimate mean cycle time. EMG recordings incorporated into the video record, were used to estimate grip forces (from previous calibration plots). Jobs were classified as of high repetition if the cycle time was <30 seconds or >50% of the cycle time involved the same kind of fundamental cycle; 'high force' was defined as an adjusted force of >6 kg. Using work histories and the job analysis, subjects were placed in one of four mutually exclusive categories: low force-low repetition, high force-low repetition, low force-high repetition and high force-high repetition. However, only 1.4% of men and 7.7% of women fulfilled the case definition of TNS. The proportions with the outcome were presented graphically for each exposure category. Our derived estimates of RR for women (Table 5) take low-repetition low-force jobs as the reference group: in comparison, only the OR for workers in high force-low repetition work were elevated (ORs 1.7-1.9), and these not significantly at the 5% level; TNS was actually less common in high-repetition high-force jobs than in the reference category.

This landmark survey has several well-known strengths including careful characterisation of exposures and outcomes. However, the outcome of TNS was uncommon and data were presented without control of confounding (other than by gender stratification). Numbers within sub-analyses were small, giving rise to wide CIs. However, (and in contrast to its findings on other upper limb disorders), this study did not suggest a strong association between physical risk factors and TNS.

Toomingas *et al*[44] investigated 71 platers (engaged in welding, plating, grinding, and hammering metal sheets), 71 vehicle assembly workers (engaged in screwing metal components) and 45 white-collar workers. Details were not given of the sampling frame, sampling procedures, or response rates. The outcome of TNS was clearly defined and ascertained by two physicians, one examining the platers and controls, and the other the assemblers. Blinding to exposure was thus incomplete. No details were given of between-observer repeatability of diagnosis. The acceleration levels of sample tools (nutrunners, impulse wrenches, screwdrivers, wrenches) were measured, and individuals completed a questionnaire about their daily exposure times, but no estimate of exposure dose was used in the analyses of interest. The groups were gender-matched but differed significantly in age. The crude (derived) OR for TNS was 4.5 (95% CI 0.6-194.1) in platers and assemblers vs. referents.

This study had several limitations in terms of sample size, outcome assessment, control of confounding and exposure characterisation. The findings are, however, consistent with those of Bovenzi et al[61] in vibration-exposed foresters.

Tornqvist *et al*[50] report a case-control study concerning subjects who sought care for neck or shoulder disorders from 70 care givers in the municipality of Norrtälje during 1994-7. Controls were selected at random from the study base using a population register. Subjects who had sought care for neck or shoulder or low back disorders in the six months prior to 1994 were excluded. The remainder completed a self-administered questionnaire, a structured interview, and a physical examination, and were classified as having TNS, cervical brachialgia, shoulder tendinitis or none of these. The criteria employed were not clearly stated, although a research abstract[66] suggests that diagnoses were repeatable between-observers. Analysis was conducted only for 'mixed neck-shoulder disorders'; among women, TNS comprised 53% of the case material. Questionnaire data were collected on repetitive hand finger movements (many times/minute ≥ 2 days/week); work with vibrating tools (≥ 60 minutes/day); and work organisation and psychosocial factors (job demands, decision latitude, job strain, time pressure, level of social support at work, quantitative work demands). Assessment was also made by structured interview of: energy expenditure in the job, work with hands above shoulder height (≥ 30 minutes/day), constrained sitting (≥ 4 hours/day), visually demanding precision work (≥4 hours/day), the opportunity for creativity, and demands relative to competence. Analysis was stratified by gender and adjusted for age and previous chronic neck-shoulder symptoms. Significant associations were found with repetition (OR 2.2, 95% CI 1.5 - 3.2), work with hands above shoulder height (OR 1.6, 95% CI 1.0 - 2.7), VDU work (OR 1.9, 95% CI 1.0 - 3.4), and job strain (OR 1.6, 95% CI 1.1 - 2.5), as well as poor support at work (OR 1.4, 95% CI 10 - 2.0). Cases were also more likely to report long working hours, non-fixed salary and lone working. The authors estimated a population attributable proportion of 18% among women for work with repetitive hand-finger movements.

The main limitations of this study are reliance on self-reported exposures, with the potential for information bias, and the failure to analyse TNS and cervical brachialgia as independent outcomes.

Veiersted *et al*[58] prospectively investigated 30 female workers during the first year of their employment in a chocolate manufacturing plant. Recruitment was confined to those who had not consulted medical services during the previous year with neck-shoulder pain, and who had no known disorder predisposing to myalgia. A questionnaire was administered about postures perceived as strenuous to the neck and shoulder muscles. At ten-week intervals over the next year subjects were reassessed by a physician. An incident case of trapezius myalgia was recorded if neck-shoulder pain lasting >2 weeks and causing work interference was linked with one tender or trigger point in the trapezius muscle. No details were given on repeatability of diagnosis and no comment about blinding. Seventeen subjects fulfilled the case definition. The hazard ratio for this outcome was increased nearly 11-fold in those who had perceived their neck-shoulder postures to be strenuous at baseline, after allowing for self-reported stress.

This small study lacked information on the reliability of outcome and blinding, and had no objective characterisation of exposure. Although self-reports about work posture were collected prior to symptom onset, those who were dissatisfied with their work environment may have had higher awareness of symptoms and been more apprehensive (tender) during examination.

Viikari-Juntura[32] assessed 113 slaughterhouse workers for TNS. She compared her estimate of prevalence with those for scissor-makers, shop assistants and factory workers, the referent data coming from the studies of Kuorinka *et al*[39] and Luopajärvi *et al*.[40] Subjects on sick leave were excluded, although none had a relevant musculoskeletal illness. A high response rate was achieved. A single observer examined all of the workers, following a closely defined pre-specified diagnostic schedule (an extension of the Waris criteria). No mention is made about the repeatability of the protocol; the study design precluded blinding. Ergonomic exposures were not characterised in detail. However, other studies from the industry suggest that the work involves forceful repetitive use of the upper limb in the cutting of some 1200 kg of veal or 3000 kg of pork/day. Slaughterhouse workers were poorly matched to referents in terms of gender. A crude comparison indicates that TNS was >5 times less common in slaughterhouse workers than in factory workers and 10 times less common than in scissor makers.

This study made an important contribution to the development of diagnostic criteria for upper limb and neck disorders, but has several limitations in the context of this review. These include a small sample size, limited exposure characterisation, and the lack of a true reference group. However, it highlights, large differences in the prevalence of neck disorders when different research groups have attempted to apply the same diagnostic criteria in different settings.

6. Discussion and evidence synthesis

Our method of investigation had some potential limitations. In particular, although we aimed to make the search thorough, it may not have been comprehensive. It did not, for example, encompass the non-peer review ('grey') literature, or publications in languages other than English (much of the interest in occupational cervicobrachial syndrome has come from Japan and Scandinavia), or an approach to authors active in the field. Moreover, defining search terms for an outcome with many synonyms and a wide variety of exposures was challenging. However, we think it unlikely that important high quality reports will have been overlooked by the strategy. Our review focussed on neck pain with physical signs rather than neck pain as a whole; as a check on the impact of this delimitation we re-ran the search omitting the filter for physical examination but applying one to retrieve higher quality prospective studies (details available on request): we found and read 10 additional cohort reports, but found only one with detailed exposure assessment (referred to below) and none that would cause us to change our appraisal of the evidence.

Among the studies we did identify, smaller ones were not clearly more positive than the larger ones, which tends to argue against significant publication bias.

A more important limitation lies in the nature of the reports that we found. According to our assessment, the evidence base on occupation and neck pain with physical signs rests substantially on two high quality investigations in the same study population, plus sundry other observations of lesser quality, almost always based on retrospective or cross-sectional observations and typically limited by poor precision and control of confounding.

The exposures of interest are complex and usually seen in combination. Analyses based on a comparison of job title (most of the reports) offer only a general indication of the nature and extent of these exposures; while those based on analysis of work activities have adopted a variety of approaches to exposure categorisation that hinders synthesis.

Approaches to case definition have also varied (at the extremes from brief to long-lasting duration of symptoms – see Table 3), but have been more homogeneous than those to exposure. An important consideration in synthesis is the extent to which studies based on a different outcome can be considered together. We think they can – in part for the reasons set out on p7, but also because the differences in practice seem quite small. The bulk of the evidence relates either to neck pain with palpation tenderness or to mixed neck-shoulder disorder (mainly TNS). Surveys with these end-points sometimes reported also on thoracic outlet syndrome (3 studies)[41,62,64] or cervical syndrome (6 studies),[35,40,42,60,61,64] but as may be seen from Table 4, such studies reached similar conclusions for these disease labels as they did for TNS.

For simplicity, therefore, we focus the evidence synthesis that follows on neck pain with palpation tenderness and mixed neck-shoulder disorder (mainly TNS), considered as a single group. Two other studies with less specific outcomes – neck-shoulder pain with examination findings[19,63] – are included in passing.

6.1. Physical risk factors

Repetition – Seven reports (six investigations) from Table 5[18,37, 41,43,50,62,65] and nine from Table 4,[32,35,38-42,62,64] (14 in total, allowing for overlaps[41,62]), concerned repetition/repetitive jobs and these outcomes. Only one of the studies offered prospective information.[18]

Relative risks $\geq$ 1.7 (P<0.05) were reported, for at least some comparisons, in 11 of the 14 studies and an RR >1.5 in one of the remaining three. Moreover, both papers with the highest quality rating (+++++) pointed to an RR $\geq$1.8, with an exposure-response relation for repetitive shoulder movements,[18,37] and both of the two rated next highest in quality (+++) were similarly positive. Another study of low quality found a strong exposure-response gradient,[65] as did an analysis based on years of employment in an exposed job;[35] two other cross-sectional studies did not show a clear relation with employment duration, but hinted instead at a healthy worker selection effect.[38,41] Repetition was sometimes defined at the shoulder,[18,37] sometimes at the wrist, hand or fingers,[40,50,62,64] and sometimes ambiguously. Positive findings were not clearly limited to one category of definition.

The evidence in favour of a causal association relies mainly on the findings at baseline and at follow-up of one high-quality investigation, but is supported by consistent observations in many smaller studies of lesser quality. Such a pattern is unlikely to arise by chance or through confounding (even though control of confounding was often suboptimal). Moreover, among the 14 studies, we rated five as low in potential for inflationary bias[18,35,37,38,43] and four of these were positive (RR$\geq$ 1.7, P<0.05).

On balance we conclude that by the criteria in Appendix 2 there is moderate evidence (++) of a causal relationship between repetition at the shoulder and neck-shoulder pain with palpation tenderness, but less conclusive evidence (+) for repetition at the hand-wrist.

Neck flexion – The two surveys by Andersen *et al*[18,37] also found an exposure-response relation with proportion of cycle time with the neck flexed >20^0 (Table 5), with RRs raised significantly (1.7 to 2.6-fold) in the highest band. Indirect support for these findings comes from four surveys of moderate quality that compared job titles – two with ergonomic observations of a constrained neck posture with neck flexion,[41,42] and three others in which this seems likely given the nature of the work[35,38,59] (Table 4). All found a more than doubling of risk (P<0.05); we rated two of these five as having a low potential for inflationary bias.

The major limitation on this interpretation is that the exposed groups in these studies are likely also to have been exposed to repetitious work (and so feature in the preceding section). Disentangling the separate contributions of repetition and neck posture is difficult. However, the analyses of Andersen *et al*[18,37] (Table 5) suggest that repetitive movement of the shoulder carries a significant risk of incident and prevalent complaints even in the absence of neck flexion; that the combination of exposures is not clearly more injurious; and that the risk estimates associated with neck flexion in the absence of repetition are only moderately and non-significantly higher (ORs 1.4 to 1.6, P>0.05).

The evidence in favour of a causal association is almost as good for neck flexion with repetition as with repetition alone. However, there is only limited evidence on neck flexion in the absence of repetition, and none that clearly excludes chance as an explanation of the findings. By the criteria of Appendix 2 we conclude that there is moderate evidence (++) of a causal relationship between the combination of neck flexion with repetition and neck shoulder *pain with palpation tenderness; there is limited evidence (+) for the exposure of neck flexion in the absence of repetition.*

Other postures and static loading – We found studies that assessed several other metrics of posture. Exposure definitions differed considerably – there being one study of EMG activity,[62] two of work with the hands above shoulder height,[50,65] and one based on self-reports of "postures strenuous to the neck and shoulders".[58] Several of these will have involved static loading of the neck-shoulder musculature, as may some of the occupational studies on sewing machinists,[35,38] dental personnel,[59] foresters,[61] and female fish processors[42,64] (although also involving repetition and constrained neck posture). The most specific investigation, of EMG activity in *M trapezius* by Hansson *et al*,[62] found ORs non-significantly raised 1.5 to 1.9-fold in a study of limited statistical power. The two case-control studies that asked about work with the arms above shoulder height reported positive associations with mixed neck-shoulder disorder (ORs 1.6[50] and 4.8[65]), but we rated both as having important potential for inflationary bias. Questions were also posed in these investigations about "constrained"[50] or "uncomfortable"[65] sitting (ORs ranged from 1.6 to 3.6), with the same potential limitation.

There is moderate evidence (++) that static loading of the neck-shoulder musculature in combination with repetition and neck flexion increases the risks of neck pain with palpation tenderness. There is suggestive but inconclusive evidence (+) that static loading of the neck-shoulder musculature makes an independent contribution, over and above repetition.

Forceful work – The high quality studies by Andersen *et al*[18,37] found an exposure-response relation with forceful gripping, assessed as the proportion of maximum voluntary contraction (Table 5). RRs were raised significantly by 2-fold in the highest band. But in the subset of workers with high grip force but low repetition of shoulder movements ORs were more modestly raised ($\leq$ 1.4-fold) and associations were not significant at the 5% level. Silverstein[43] also found an elevation of risk for work involving high force but low repetition (vs. low-force low-repetition jobs) (ORs 1.7 to 1.9), but in a considerably smaller analysis these did not achieve statistical significance. The study by Vikari-Juntutra found a much lower risk of TNS in slaughterhouse workers than various other comparison groups, although their work was described as involving forceful use of the upper limb. Finally, Andersen *et al*[35] found an exposure-response relationship to years as a sewing machinist, a job described as involving force as well as repetition and static neck postures.

T*here is only limited evidence (+) that force is a causal risk factor in the absence of repetition, and none that clearly excludes chance as an explanation of the findings.*

Other physical exposures

Precision work – We found two studies that investigated the exposure of "visually demanding precision work"[50] or "work with precise movements" (Table 5);[19] neither of these was positive. It is possible to imagine that some of the occupations in Table 4 had a requirement for precision too – including dental personnel,[59] fish processors,[42,64] and sewing machinists.[35,38] *If there is an effect on risk of neck disorders, we would expect this to arise through its requirement for a constrained neck posture and/or static loading of the neck-shoulder girdle, and so to be encompassed by the evidence statements given above.*

Rest breaks – The studies by Andersen *et al*[18,37] also analysed the proportion of the work cycle in which micropause rest breaks were absent. Where this reached or exceeded 80%, RRs for prevalent and incident outcomes were roughly doubled, there being some evidence of an exposure-response gradient (Table 5). No other studies considered this exposure. In practice, repetition and rest breaks are related; but Andersen *et al* describe subgroups in whom the high relative absence of micropauses was combined with a low repetition of shoulder movements, and here risks were only moderately and non-significantly elevated (PR 1.4). *We found insufficient evidence (0) to draw a conclusion about rest breaks separate from repetition.*

Lifting/manual handling – In two case-control studies of mixed neck-shoulder disorder inquiries were made about manual handling, with contrasting results. Tornqvist *et al* found an OR of 0.8 for manual material handling ($\geq$50 Newtons, $\geq$ 60 minutes/day), whereas Ekberg *et al* estimated a much higher risk (OR 13.6) for self-report of moderate to heavy as compared with light lifting.[65] In the study by Luopajarvi *et al*[40] assemblers were noted to carry loads averaging 5,000 kg/day and were found to have a non-significantly greater risk of TNS (OR 1.6) and a non-significantly lower risk of cervical syndrome (OR 0.3) than shop assistants. *On the basis of this review there is insufficient evidence of a causal association (0).*

High physical workload – Tornqvist *et al* also found no association between high estimated energy expenditure in women ($\geq$ 3 TWA MET) and mixed neck-shoulder disorder.[50] *On the basis of this review there is insufficient evidence of a causal association (0).*

Vibration – We found three studies related to hand-transmitted vibration (HTV). Bovenzi *et al*[61] reported significant associations between a daily vibration dose >7.5 m/s^2 and both TNS (OR 3.8) and CS (OR 10.7), with an exposure-response gradient for CS; data from Toomingas *et al*[44] imply an OR of 4.5 for TNS in platers and assemblers with exposure to HTV vs. other workers, but with very wide CIs; and a case-control study by Tornqvist *et al*[50] found no association of mixed neck-shoulder disorder with an exposure time of >60 minutes/day, albeit in women. (A stronger association was found in men, whose magnitudes of exposure may have been higher, but in this group TNS was only a minority of the analysed material.) We rated two of the studies low in quality of information, however, and all three as having some potential for inflationary bias (in two studies the selection methods were not described). Most convincing are the findings of Bovenzi *et al*; but foresters (the exposed group) were likely also to have had exposure to work that loaded the neck-shoulder girdle, and an apparent relation to estimated vibration dose could reflect the duration of neck-shoulder straining work (a component of dose estimation). *On the basis of this review there is insufficient evidence of a causal association (0).*

We found a single study on whole-body vibration and moderate to severe neck pain with physical signs; risks were non-significantly raised (OR 1.8) in a study of limited quality with potential for inflationary bias. *On the basis of this review there is insufficient evidence of a causal association (0).*

6.2. Occupational psychosocial factors

Job demands – We found four studies that assessed occupational demands against the outcome of neck pain with tenderness or mixed neck shoulder disorder,[18,37, 50, 65] and one study of chronic neck pain with physical signs.[19] In three of these studies, exposure was defined according to Karasek's job content questionnaire.[18,37, 50] In the studies by Andersen *et al*, high demands were associated similarly with the prevalence[37] and incidence[18] of neck pain with tenderness (RRs 1.8 and 2.0, P<0.05); while mixed neck-shoulder disorder was significantly associated with high demands on attention in one case-control study (OR 3.8).[65] However, findings have not been wholly consistent. In the case-control study[50] a significant association was found with high job strain (see below), but not with high demands, high time pressure, or demands relative to competence; and job demands were significantly but only moderately related to incident chronic neck disorder (OR 1.2) and recovery from chronic neck disorder (OR 0.7) in the large cohort study by Cassou *et al*.[19]

A problem of interpretation (applying to all of the psychosocial factors) is that, in the absence of an independent measure of exposure, findings may be unusually prone to common instrument bias (e.g. a general tendency to complain may manifest both in physical symptoms and negative perceptions about the work environment). There is no ready answer to this problem. None of the studies attempted an independent assessment of demands (or control or support in relation to the sections that follow); but some adjusted for distress[18,38] or depressive symptoms,[19] which could be a marker of such a tendency.

Another issue is that views about work demands could actually reflect a fast and repetitive pace of work. The cohort studies by Andersen *et al*[18] and Cassou *et al*[19] attempted to allow for occupational physical activity as a confounder. However, in doing so, they identify risks of somewhat different magnitude for somewhat different end-points.

The two studies of highest quality suggest an association between job demands and neck pain with tenderness that could be causal; but the remaining literature is contradictory and relatively small. Chance and common instrument bias may be other explanations of the positive reports. We therefore rate the evidence for a causal association as limited (+).

Control over work – Five studies considered control over work. Those by Andersen *et al* estimated RRs of 1.4 cross-sectionally[37] and 1.3 prospectively;[18] the case-control study by Tornqvist *et al*[50] reported ORs of 1.1 for low decision latitude and 1.4 for low participation in planning; and the cohort study by Cassou *et al*[19] placed risk estimates close to unity, both for new onset complaints and for recovery from complaints at the start of follow-up. Finally, a cross-sectional study of fish processors found a lower risk (OR 0.68) in those with high job control. Findings in these investigations were seldom significant at the 5% level.

A limited literature is consistent in ruling out a more than moderate association between low job control and neck disorders. The study of highest quality by Andersen et al[18] was careful to control for many confounders, including physical activities, but does not exclude chance as an explanation of the 30% increase incident risk; moreover, even a prospective design does not exclude the possibility of common instrument bias. We therefore rate the evidence for a causal association as limited (+).

Job strain – Three studies reported on job strain,[38,50,64] including two that defined strain as the combination of high demands and low control according to the Karasek model.[38,50,64] Positive associations were seen in one cross-sectional study (OR 3.0 with an exposure-response pattern)[50] and one case-control study (OR 1.6),[50] but not in the cross-sectional study by Kaergaard *et al*.[38] In the cohort study by Andersen *et al*,[18] although demand and support were independent weak predictors of incident neck pain with palpation tenderness, no significant contribution was found by adding an interaction term for the combination of the two.

On the basis that there is some evidence for an independent contribution from the component items of strain and none that suggests a negative interaction between the two, we assign the same rating for evidence of causal association as for demands and control above (+).

Support at work – Four studies considered job support, including two with a prospective element. Those by Andersen *et a*l[18,37] found risks raised by an amount similar to that for low job control, as did the case control study by Tornqvist *et al* (OR 1.3 to 1.4).[50] The study by Kaergaard *et al*,[38] which was nested within the PRIM study, was somewhat more positive. The adjusted PR for prevalent neck-shoulder disorder was 1.66 and that for incident neck-shoulder disorder was raised 3.7-fold, although based on an analysis of only 149 subjects, and with substantial losses to follow-up. Findings in the two large studies by Andersen *et al* were not significant at the 5% level.

The two studies of highest quality point to a moderate association (RR 1.3), but do not rule out chance as an explanation of the findings. The alternative evidence is scant. We therefore rate the evidence for a causal association as limited (+).

Other psychosocial factors – We found single reports concerning **job creativity**, **satisfaction** with job content, and **perceptions that work was stimulating**. These came from two case-control studies that we rated lower in quality and high in potential for inflationary bias. Poor content of work carried a higher risk of mixed neck shoulder disorder (OR 2.9), while belief that work was stimulating was associated with a lower risk (0.35), lack of job creativity being neutral (OR 1.0). None of these findings was significant at the 5% level. *There is insufficient evidence (0) to draw meaningful conclusions on these exposures*.

7. Relation to the wider literature

We are aware of several other reviews of neck pain and occupational risk factors,[54-7,67-9] although none focussed specifically on neck pain with physical signs. Many of the reports included in these reviews cover users of computers and visual display terminals (who were excluded from our commissioning brief).

Bernard *et al*[55] examined over 40 studies of neck or neck-shoulder disorders and concluded there was 'evidence' (++ by the criteria in Appendix 2) of a causal relation with highly repetitive work and forceful exertion; strong evidence (+++) concerning static contraction, prolonged static loading, or extreme working postures involving the neck-shoulder muscles (many of these reports also involved repetition); and insufficient evidence on hand-arm vibration. The criteria for ‘high’ quality in this review (participation rate >70%, included a physical examination, blinding, and some objective exposure assessment) were less stringent than ours to the extent that issues of bias, confounding, repeatability of outcome, and precision were not addressed in detail; little weight was given to quantitative dose-response information, and several studies were accepted that did not furnish risk estimates but only tests of statistical significance. A review by Ariens *et al*[67] (which predates the main PRIM reports) was more critical. Among 22 cross-sectional studies, two cohort studies and one case-referent study relevant to physical risk factors (three including an examination), they identified “some evidence” on positive relations with neck flexion (four reports), forceful use of the arm (two reports), arm posture (six reports), prolonged sitting (eight reports), twisting or bending of the trunk (six reports), and hand-arm vibration (three reports); but noted that almost all of the studies were cross-sectional and most were lowly in quality. Kuorinka *et al*[54] focussed in their review on applying the Bradford-Hill criteria of causality to research evidence on occupational exposures and TNS, concluding the strongest evidence related to repetitive work and constrained neck posture.

Occupational psychosocial risk factors were considered in another review by Ariens *et al*[68] who reported “some evidence” for a positive relationship between neck pain and high job demands, low social (co-worker) support, low job control, high and low skill discretion and low job satisfaction; inconclusive evidence was found for high job strain and low supervisor support.

Since then the Dutch researchers have published two reports on neck pain from their three-year Study on Musculoskeletal disorders, Absenteeism, Stress, and Health (SMASH).[70,71] In common with the PRIM investigators, they assessed physical workload through detailed analyses of video recordings, but took as their outcome incident symptoms, rather than symptoms with physical signs. An exposure-response relation was found with neck flexion $\geq$20,^{0} the RR being 1.6 (95%CI 0.7 – 3.8) in those with this exposure for >70% of the time as compared with <60%.[70] A significant association was also reported with sitting, but only at the extremes of exposure distribution (OR 2.3 for sitting >95% vs. <1% of the time). No association was found with neck rotation. However, neck flexion, neck rotation and low decision authority were risk factors for sickness absence due to neck pain.[71]

Broadly speaking, our conclusions are in agreement with a wider literature, despite some differences of focus. They are also plausible from an ergonomic viewpoint. While the mechanism that causes neck pain with palpation tenderness is uncertain, Kuorinka *et al* have identified several possibilities that could stem from repetitive movements of the arm, static neck posture and loading of the neck-shoulder musculature, including: overload of the Type I muscle fibres in *M trapezius*; reduced microcirculation to *M trapezius*, with pain sensitisation; ATP depletion or dysfunctional energy metabolism in contracting muscles, with activity-related pain; selective motor unit fatigue; and muscle fibre rupture (see ref 54, p91-93).

8. Conclusion and final comments

Table 7 (p70) summarises our assessment of the causal evidence in relation to neck pain with palpation tenderness. This is strongest for repetition, by itself or in combination with neck flexion or static loading of the neck-shoulder musculature (++); suggestive for static loading, neck flexion, or force in the absence of repetition (+), high job demands (+), low control of work (+), and low social support (+); and insufficient (0) for lifting/manual handling, physical workload, vibration, and certain other little studied psychosocial factors.

In trying to define a threshold at which repetition significantly increases risk, the only useful information comes from the prospective study of Andersen *et al.*[18] This represents a single study and defines repetition solely in terms of shoulder movements. (We found no good evidence that would enable an assessment of risks by duration of exposure or cumulative dose, based on time and frequency of movement.) Only in the highest category of repetition (>15 shoulder movements/minute) were risks significantly raised to the 5% level. The attributable fraction among exposed workers at this level would be 67%, assuming causal relations and assuming this to be a true unbiased estimate of risk.

Female gender and mental distress appear to be significant risk factors for the outcome, even after allowance for occupational exposures. The studies by occupational title have generally addressed gender by restriction or matching, and analyses of occupational activity have typically treated gender and mental health as confounders; thus, we found no data on the potential for effect modification by these personal risk factors.

One final issue, of relevance to interpretation but not much discussed in the literature we found, concerns the disorder under review. Some authorities[34] would question whether TNS, or neck pain with palpation tenderness, is a distinct diagnostic entity – there being no strong pathological, patho-anatomical, or epidemiological evidence to justify disease labelling (despite the theories advanced above). Moreover, evidence on the clinical course and functional impact of this outcome is strictly limited and it is not clear how often the condition persists, given the continuation or discontinuation of exposure. The best studies have shown that the diagnostic label of neck pain with palpation tenderness can be reproducible between observers at the research level, with sufficient care and training; but reproducibility may well be lower between clinicians in routine practice. In our view, the case for compensation begins with case definition and there is significant scientific doubt about the disorder as a diagnostic entity, principally because of a lack of evidence that neck pain with tenderness differs from neck pain alone in its causes and outcome.

If there is acceptance of TNS as a compensable entity then there is reasonable evidence to suggest a causal association, on the balance of probabilities, with certain repetitive movements of the upper limb and with neck flexion or static loading of the neck-shoulder musculature. A practical and challenging need would arise to identify such exposures in claimants, and this might be met by the application of nationally representative job exposure matrices or population surveys of exposure, should these exist. If there is not acceptance at present of a distinct disease entity then future research effort should be directed towards a better understanding of pathogenesis, to improve outcome classification, and a better characterisation of clinical course.

9. Summary

9.1. Background

Chronic neck pain is common in the general population, where it often runs an episodic recurrent course. Sufferers with physical signs, such as tenderness or restricted neck movement, tend to report more disability. This review was undertaken to determine the strength of scientific evidence linking chronic neck-shoulder pain with exposures in the workplace (other than in computer users). We were asked to focus on symptoms with associated tenderness on palpation. This pattern of complaints is sometimes described as 'tension neck syndrome' (TNS), or 'cervicobrachial syndrome', although terminology varies a lot and understanding of pathogenesis and natural history is limited.

9.2. Methods

We focused on studies of chronic neck pain that included a physical examination. We searched four comprehensive reviews (a reference textbook by Taylor & Frances, a major report by NIOSH, a report published by the European Agency for Safety and Health at Work, and a doctoral research thesis), and supplemented this with a comprehensive systematic literature search of the MEDLINE, EMBASE BIDS, and Psychinfo electronic bibliographic databases from inception to the 3rd week of May 2006. For this last search we combined keywords for the outcome and exposures to various occupational risk factors, both physical (eg repetition, force, working posture, static work, vibration) and psychosocial (eg job demands, control over work, support at work). We rated each paper for its quality of information, both overall and by criteria related to study design, study power, sampling methods, response rate, potential for bias or confounding, and approaches to exposure and outcome assessment. We gave weight in particular to studies with objective quantitative estimates of exposure and those that provided dose-response information. We summarised the main features and findings of each paper and appraised each critically in commentary and in tables.

9.3. Results and conclusions

We found 21 relevant reports, of which 15 were cross-sectional in design, four were prospective, and two were community-based case-referent studies. Case definitions varied, but most studies considered the outcome of neck pain with tenderness (often called TNS) or mixed neck-shoulder disorder (comprising mostly TNS). Reproducibility of diagnosis was demonstrated for four of the studies and suggested in two others.

Most studies shared common limitations - typically a small sample size, limited control of confounding, failure to assess outcome blinded to knowledge of exposure, and limited exposure assessment. We rated the overall quality of information as excellent in only two reports; as useful but with important limitations in four reports; as moderately informative in five reports; and as limited in 10 reports.

Among the 21 studies, 14 were related to repetitive work. Relative risks (RR) ≥1.7 (P <0.05) were reported in 11 of the 14 studies. Both of the papers with the highest quality rating pointed to a RR ≥1.8 with an exposure-response relation for repetitive shoulder movements, and both of the two rated next highest in quality were similarly positive. This pattern of consistent observations is unlikely to arise by chance or through confounding and indicates moderate evidence (++) of a causal relation between repetition at the shoulder and neck-shoulder pain with palpation tenderness. The best estimate of a threshold would be >15 shoulder movements/minute, although based on a single high quality study. There is less conclusive evidence related to repetition at the hand-wrist (+).

We also found seven studies (two of high quality) on neck flexion, all suggesting a more than doubling of risk (P <0.05). However, in one high quality study that considered sustained neck flexion in the absence of repetition, risks were only moderately elevated (1.4 - 1.6-fold, P >0.05). We conclude that there is moderate evidence (++) of a causal relation between neck flexion with repetition and neck-shoulder pain with palpation tenderness, but only limited evidence (+) for the exposure of neck flexion in the absence of repetition.

We drew similar conclusions in relation to static loading of the neck-shoulder musculature, based on two high quality studies and 10 other potentially relevant reports.

On the basis of two high quality studies and three other reports we found only limited evidence (+) that force is a causal risk factor in the absence of repetition, and none that clearly excluded chance as an explanation of the findings.

We also found some reports on precision work, rest breaks, lifting/manual handling, high physical workload, hand-arm vibration, and whole-body vibration, but none with sufficient evidence of a causal association (0).

Occupational psychosocial factors were studied less often, but our review identified four studies on job demands, five studies on control over work, three on job strain, and four studies of support at work. The two studies of highest quality (which reported on all of these exposures) suggest an association with neck pain and tenderness that could be causal, but the remaining literature was contradictory and relatively small for job demands, while tending to rule out a more than moderate association (RR 1.3) with control and support. We rated the evidence on each exposure as limited and similarly for job strain (+).

An issue worth highlighting concerns the definition of the disorder investigated. Some authorities would question whether TNS, or neck pain with palpation tenderness, is a distinct diagnostic entity (there being no strong pathological, patho-anatomical, or epidemiological evidence to justify labelling it as a distinct disease). Evidence on a clinical course and functional impact of this outcome is also limited. The best studies have shown that this diagnostic label is reproducible between well-trained research observers, but reproducibility of diagnosis may well be lower in routine clinical practice. The case for compensation depends importantly on whether there is acceptance of TNS as a disease entity.

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Table 1: Criteria of three common classification schemes applied in occupational health investigations of neck pain

Disorder	Symptoms							Signs				
	Neck pain	Stiffness or fatigue in neck	Headaches radiating from neck	Neck pain radiating to upper limbs	Numbness in hands	Weakness in upper limb		>1 tender spot and/or hardening	Muscle tightness, movement	Limitation of neck movement	Radiating pain on movement	Other
TNS												
Waris[31]	Y*	Y	Y*					Y	Y			
Viikari-Juntura[32]	Y*	Y	Y*					Y				
Ohlsson[33]	Y	Y	Y					Y				
CS												
Waris[31]				Y	(Y)	(Y)				Y	Y	
Viikari-Juntura[32]				Y						Y	Y	
Ohlsson[33]				Y	Y	Y				Y	Y	
TOS												
Waris[31]				Y								Morley & Adson +ve
Viikari-Juntura[32]				Y								+ve elevated arm test
Ohlsson[33]				Y†	Y†							Morley & Roo test +ve

TNS= tension neck syndrome; CS=cervical syndrome; TOS=thoracic outlet syndrome
Y = mandatory item (Y) = optional item
* either one of these; † ulnar nerve pattern; +ve = positive

Table 2: Features of the studies included in the review

First author, year (Location)	Study populations	Exposures(s)		Outcomes(s)	Sampling methods	Response rate	Potential bias		Confounding	Blinding	Outcome			Exposure assessment		Quality rating
		Categories	Main assessment methods(s)				Inflationary	To the null			Clear	Repeatable		Objective	Dose-response data	
Cohort studies																
Andersen JH, 2003[18] Denmark	Workers from the PRIM study followed up over 4 years	Repetition Force Neck flexion Rest breaks Demands Control Support	Walk-through surveys; videotape analysis of 103 task groups; self-completed questionnaire on physical and psychosocial factors	NP + palpation tenderness	+++	+	L	L	+++	+	+++	+++		+++	+++	+++++
Cassou B, 2002[19] France	14,995 workers free of CNP and 1,804 with CNP followed up over 5 years	Repetition Posture Precise work Demands Control	Self-completed questionnaire, checked by physicians	NP + painful neck movement	+++	+++	L	H	-/++	?+	++	-		-	-	+++
Kaergaard A,* 2000[38] Denmark	E: 238 sewing machine operators NE: 357 workers in varied jobs	Static loading Repetition Neck flexion Job strain Social support	Comparison of job titles (including time in the job); self-completed questionnaire on psychosocial factors	Myofascial pain syndrome Neck-shoulder disorder	+++	-/+++	L	P	-/+++	?+	+++	+++		+	++	++
Veiersted KB, 1994[58] Norway	30 manual workers without NSP at baseline; one-year follow-up	Posture	Interviewer-administered questionnaire	NSP + palpation tenderness	++	+++	L	P	-	?+	++	-		-	-	+
Cross sectional surveys																
Åkesson I,[‡] 1999[59] Sweden	E: 84 dental personnel; NE: 27 nurses	Static loading Precise work Neck flexion	Comparison of job titles	TNS	++	+++	P	P	+	-	+++	-		+	-	+
Andersen JH, 1993[35] Denmark	E: 82 sewing machine operators NE: 25 auxiliary nurses	Repetition ForceStatic loading Neck flexion	Comparison of job titles	CBFM CS Neck-shoulder disorder	++	+++	L	P	-/+	+	+++	+++		+	+	++

First author, year (Location)	Study populations	Exposures(s)		Outcomes(s)	Sampling methods	Response rate	Potential bias		Confounding	Blinding	Outcome		Exposure assessment		Quality rating
		Categories	Main assessment methods(s)				Inflationary	To the null			Clear	Repeatable	Objective	Dose-response data	
Andersen JH, 2002[37] Denmark	3123 workers from food processing, textiles and servicing plants (PRIM study baseline)	Repetition Force Neck flexion Rest breaks Demands Control Support	Walk-through surveys; videotape analysis of 103 task groups; self-completed questionnaire on physical and psychosocial factors	NP + palpation tenderness	+++	++	L	L	+++	+	+++	+++	+++	+++	+++++
Anderson R, 1992[60] USA	E: 128 coach drivers NE: 67 controls	Whole-body vibration Sitting	Comparison of job titles	Radiating NP + pain on neck movement	+++	+++	P	P	-	-	++	-	+	-	+
Bovenzi M, 1991[61] Italy	E: 65 foresters NE: 31 maintenance workers	Vibratory tools Posture Force	Comparison of job titles; measurement of accelerations of tools; questionnaire (to estimate vibration dose)	TNS CS	?	?	P	P	+	+	+++	-	+++	+++	+++
Hansson GA, 2000[62] Sweden	E: 87 laminate workers NE: 68 office and industrial workers	Static loading Repetition	Comparison of job titles; EMG recordings; electrogoniometry; questionnaire	TNS TOS Neck-shoulder disorder	?	?	P	P	++/ +++	-	+++	-	+++	++	+++
Hinnen U, 1992[63] Switzerland	E: 46 laser scan cashiers NE: 106 conventional cashiers	Rest breaks	Comparison of job titles; production records; observation of work tasks; movement analysis	NP + exam findings	+	+++	P	L	-	-	++	++	+	-	+
Kuorinka I, 1979[39] Finland	E: 93 scissor makers NE: 143 shop assistants, 163 factory workers	Repetition	Comparison of job titles; production records; video-tape analysis; observation of work tasks	TNS	++	++	P	L	-/+	-	+++	++	+	-	+
Luopajarvi T, 1979[40] Finland	E: 152 assembly packers NE: 133 shop assistants	Repetition	Comparison of job titles; expert ergonomic assessment	TNS CS	++	+++	P	P	-/+	-	+++	-	+/++	-	+
Nordander C, 1999[42] Sweden	E: 322 fish processors NE: 337 other workers	Repetition Neck flexion Lifting	Comparison of job titles; video-tape analysis; observation of work tasks	TNS CS	+++	+++	P	P	-/+	-	+++	-	+/++	-	++
Ohlsson K, 1994[64] Sweden	E: 206 fish processors NE: 208 other workers	Repetition Posture Demands Control	Comparison of job titles; video-tape analysis; observation of work tasks; questionnaires	TNS CS TOS Neck-shoulder disorder	+++	+++	P	P	-	-	+++	-	+/++	-/++	++

First author, year (Location)	Study populations	Exposures(s)		Outcomes(s)	Sampling methods	Response rate	Potential bias		Confounding	Blinding	Outcome		Exposure assessment		Quality rating
		Categories	Main assessment methods(s)				Inflationary	To the null			Clear	Repeatable	Objective	Dose-response data	
Ohlsson K, 1995[41] Sweden	E: 82 industrial workers in repetitive jobs NE: 64 workers in varied jobs	Repetition Neck flexion Arm abduction Rest breaks	Comparison of job titles; video-tape analysis	TNS TOS Neck-shoulder disorder	++	+++	P	P	+/++	-	+++	-	++	-/++	+++
Silverstein BA, 1985[43] USA	574 workers from 6 industrial plants	Repetition Force	EMG recordings; video-tape analysis	TNS	+++	+++	L	P	-	+	+++	-	+++	-	++
Toomingas A, 1991[44] Sweden	E: 71 platers and 70 assemblers NE: 45 white-collar workers	Vibratory tools	Comparison of job titles	TNS	?	?	P	P	-	-	+++	-	+	-	+
Viikari-Junutra E, 1983[32] Finland	E: 113 slaughterhouse workers NE: shop assistants, scissor makers, factory workers (refs 39 & 40).	Repetition Force	Comparison of job titles	TNS	+++	+++	P	P	-	-	+++	-	+	-	+
Case-control studies															
Ekberg K, 1994[65] Sweden	Cases: 109 patients with neck-shoulder disorder from primary care; 327 community referents	Repetition Posture Demands Job satisfaction	Questionnaire	Neck-shoulder disorder	++	? (c) + (r)	H	P	-	?	+	-	-	+	+
Tornqvist EW, 2001[50] Sweden	Cases: 194 women seeking care for neck-shoulder problems; 623 female referents sampled from a community register (the MUSIC study)	Repetition Vibration Arm elevation Precise work Demands Support Monotony	Self-completed questionnaire; interview	Neck-shoulder disorder	+++	? (c) + (r)	H	P	+	?	+	-	-	-	+

E – Exposed; NE - Not exposed; TNS - Tension neck syndrome, CS - Cervical syndrome, TOS - Thoracic outlet syndrome; CBFM - Cervicobrachial fibromyalgia; NP - Neck pain; NSP - Neck shoulder pain; CNP – chronic neck-shoulder pain; L – low; P – possible; H – high; (c) – cases, (r) – referents. The criteria for plus notations are explained in section 4.5, p13.

* Most relevant analyses were cross-sectional; ‡ described as a cohort study, but analysis was wholly cross-sectional

Table 3: Diagnostic criteria and methods employed in the reviewed reports

Author	Diagnostic Label	Source of definition (ref)	Symptoms: Pattern of pain	Symptoms: Stiffness/fatigue	Symptoms: Radiation to head	Symptoms: Radiation to arms	Symptoms: Numbness in hands	Examination findings: Tenderness or hardenings	Examination findings: Limited neck movement	Examination findings: Pain on neck movement	Examination findings: Radiating pain, neck movement	Other/Notes
Neck pain with tenderness												
Åkesson I, 1999[59]	TNS	33	NP, Nordic questions	X	X			X				
Bovenzi M, 1991[61]	TNS	31,32	NP on most days of a month in past 2 years *and* currently	X	X			X				Straightened cervical spine
Hansson GA, 2000[62]	TNS	33	NP, Nordic questions (last 7 days)	X	X			X				
Kuorinka I,1979[39]	TNS	31	n/s	X	X			X				
Luopajarvi T, 1979[40]	TNS	31	n/s	X	X			X				
Nordander C, 1999[42]	TNS	33	NP, Nordic questions	X	X			X				
Ohlsson K, 1994[64]	TNS	33	NP, Nordic questions	X	X			X				
Ohlsson K, 1995[41]	TNS	33	NP, Nordic questions	X	X			X				
Silverstein BA, 1985[43]	TNS	31	NP/stiffness, > once a week or >20 times in the past year	X				X		X		
Toomingas A, 1991[44]	TNS	n/s	n/s					X		X		
Viikari Juntura E. 1983[32]	TNS	31,32	NSP, n/s	X	X			X				
Andersen JH, 1993[35]	CBFM	n/s	NSP - 30d in past yr *and* lasted a month at some time					X				Tenderness in 6 of 12 defined muscles
Andersen JH, 2002[37]	NSP + tenderness	25	NSP severity score: average pain & impact in last 3 months, average pain in last 7 days					X				

			Symptoms					Examination findings				
Author	**Diagnostic Label**	**Source of definition (ref)**	**Pattern of pain**	**Stiffness/fatigue**	**Radiation to head**	**Radiation to arms**	**Numbness in hands**	**Tenderness or hardenings**	**Limited neck movement**	**Pain on neck movement**	**Radiating pain, neck movement**	**Other/Notes**
Andersen JH, 2003[18]	NSP + tenderness	25,37	NSP severity score: average pain & impact in last 3 months, average pain in last 7 days					X				
Veiersted KB, 1994[58]	NSP + tenderness	n/s	NSP for >2 weeks *with* work limitation					X				
Kaergaard A, 2000[38]	MFPS	25	NSP severity score: average pain & impact in last 3 months					X				
Mixed, but mainly neck tenderness												
Andersen JH, 1993[35]	Neck-shoulder disorder	n/s	NSP - 30d in past yr *and* lasted a month at some time					X	X		X	41cases of CBFM and 14 of CS among 74 neck-shoulder diagnoses; 19 of rotator cuff.
Ekberg K, 1994[65]	Neck-shoulder disorder	31	n/s	X	X			X	X			47% TNS, 18% CS; also shoulder tendinitis
Hansson GA, 2000[62]	Neck-shoulder disorder	33	NP, Nordic questions (last 7 days)	X	X			X				Predominantly TNS; also shoulder tendonitis & acromioclavicular syndrome
Kaergaard A, 2000[38]	Neck-shoulder disorder	25	NSP severity score: average pain & impact in last 3 months, average pain in last 7 days					X				≥75% TNS; also, shoulder tendinitis
Ohlsson K, 1994[64]	Neck-shoulder disorder	33	NP, Nordic questions	X	X			X				54% TNS
Ohlsson K, 1995[41]	Neck-shoulder disorder	33	NP, Nordic questions	X	X			X				80% TNS
Tornqvist EW, 2001[50]	Neck-shoulder disorder	65	Not defined									53% TNS; also cervical brachialgia, shoulder tendinitis

Author	Diagnostic Label	Source of definition (ref)	Pattern of pain	Symptoms: Stiffness/fatigue	Symptoms: Radiation to head	Symptoms: Radiation to arms	Symptoms: Numbness in hands	Examination findings: Tenderness or hardenings	Examination findings: Limited neck movement	Examination findings: Pain on neck movement	Examination findings: Radiating pain, neck movement	Other/Notes
Radiating neck pain with pain on neck movement												
Andersen JH, 1993[35]	CS	n/s	30d in past yr + lasted a month at some time					X*	X		X*	+ve foraminal test
Bovenzi M, 1991[61]	CS	31,32	NP on most days of a month in past 2 years *and* currently			X	X		X		X	Reduced force, deltoid, triceps, biceps
Luopajarvi T, 1980[40]	CS	31	n/s			X	(X)		X		X	
Nordander C, 1999[42]	CS	33	NP, Nordic questions			X	X		X		X	
Ohlsson K, 1994[64]	CS	33	NP, Nordic questions			X	X		X		X	
Anderson R, 1992[60]	Neck disorder	n/s	intense recurrent or continuous pain			X†		X	X	X	X	Moderate to severe category
Thoracic outlet syndrome												
Hansson GA, 2000[62]	TOS	33	NP, Nordic questions (past 7 days)			X‡	X‡					+ve Morley & Roo tests
Ohlsson K, 1994[64]	TOS	33	NP, Nordic questions			X‡	X‡					+ve Morley & Roo tests
Ohlsson K, 1995[41]	TOS	33	NP, Nordic questions			X‡	X‡					+ve Morley & Roo tests
Other												
Cassou B, 2002[19]	NP + painful movement	n/s	intermitent/persistent, past 6 months *and* causing functional limitation							X		
Hinnen U, 1992[63]	NP + exam findings	n/s	daily or occasional	X				X*		X*		

TNS = tension neck syndrome; CS = cervical syndrome; TOS = thoracic outlet syndrome; NP = neck pain; NSP = neck-shoulder pain; n/s = not stated
CBFM = Cervicobrachial fibromyalgia; MFPS = Myofascial pain syndrome; X = required; (X) = optional; * = at least one of these; † commonly present; ‡ in ulnar nerve distribution

Table 4: Risk estimates by job title and diagnostic category

Author (year) (ref)	Diagnosis	Nos in analysis	Exposure comparisons	Measure of risk	Point estimate (95% CI)	Confounders considered
Neck pain with tenderness						
Åkesson, 1999[59]	TNS	54	Dentists vs nurses	OR	4.0 (0.8 - 25.6)	a, s
		56	Hygienists vs nurses		2.1 (0.4 - 12.2)	
		55	Dental assistants vs nurses		2.2 (0.4 - 14.9)	
		84	All dental personnel vs nurses		3.2 (0.8 - 18)	
Bovenzi, 1991[61]	TNS	96	Forestry vs maintenance workers	OR	2.1 P<0.03	a, s
Hansson, 2000[62]	TNS	122	Laminate vs industrial workers	OR	1.4 (0.6-3.8)	s
		120	Laminate vs office work		2.9 (1.0 –9.4)	
		155	Laminate vs industrial and office workers		1.9 (0.9 - 4.1)	
Kuorinka,1979[39]	TNS	236	Scissor makers vs shop workers	OR	4.1 (2.3 - 7.4)	(a), s
		256	Scissor makers vs factory workers		2.6 (1.5 - 4.6)	
Luopajarvi, 1979[40]	TNS	285	Assembly line packers vs shop assistants	OR	1.6 (0.9 - 2.7)	(a), s
Nordander, 1999[42]	TNS	414	Fish processors vs controls (women)	OR	3.0 (1.6 - 6.1)	(a), s
		245	Fish processors vs controls (men)		2.6 (0.8 - 9.8)	
		659	Fish processors vs controls (all)		2.9 (1.7 - 5.3)	
Ohlsson, 1994[64]	TNS	414	Fish processors vs controls (women)	OR	3.0 (1.6 - 6.1)	(a), s
Ohlsson, 1995[41]	TNS	146	Industrial workers vs controls	OR	4.7 (1.9 -12.8)	(a), s
Toomingas, 1991[44]	TNS	186	Platers & assemblers vs controls	OR	4.5 (0.6 - 194.1)	s
Viikari Juntura, 1983[32]	TNS	265	Slaughterhouse workers vs factory workers	OR	0.1 (<0.1 - 0.2)	-
		206	Slaughterhouse workers vs scissor makers		<0.1 (<0.1 - 0.1)	
		256	Slaughterhouse workers vs shop assistants		0.1 (<0.1 - 0.4)	
Andersen, 1993[35]	Cervicobrachial fibromyalgia		Sewing operators vs nursing aides:			a, s
		46	0-7 vs. 0 years	OR	2.7 (0.3 - 32.5)	
		50	8-15 vs.0 years		9.0 (1.6 - 91.5)	
		61	15+ vs. 0 years		23.0 (4.3 - 220.1) X^2 for trend P< 0.001	
Kaergaard, 2000[38]	Myofascial pain syndrome	238	Years as a sewing operator (vs controls):			(a), s
			>10-20 vs <=10 yrs	OR	0.6 (0.2 - 1.4)	
			>20 vs <=10yrs		3.7 (1.8 - 7.6)	

Author (year) (ref)	Diagnosis	Nos in analysis	Exposure comparisons	Measure of risk	Point estimate (95% CI)		Confounders considered
			Sewing operators vs mixed controls	PR	1.7	(1.1 - 2.6)	
Mixed, but mainly neck pain with tenderness							
Andersen, 1993[35]	Neck-shoulder disorder	107	Years as a sewing operator (vs controls):				
			0 – 7 vs. 0 years	OR	3.17	(0.62 - 16.12)	
			8 – 15 vs. 0 years		11.16	(2.38 - 52.25)	a, s, sm, lei
			>15 vs. 0 years		36.74	(7.14 - 189.1)	
Kaergaard, 2000[38]	Neck-shoulder disorder	243	Internal comparison, years as a sewing operator:				
			<=2 vs 2-10 years	PR	2.44	(0.72 - 8.23)	a, s, mh, sm, bmi, inj, other*
			10-20 vs 2-10 years		1.80	(0.62 - 5.26)	
			>20 vs 2-10 years		4.44	(1.54 - 12.78)	
Ohlsson, 1995[41]	Neck-shoulder disorder	146	Internal comparison, years a an industrial worker:				
			<10 vs 0 years	OR	9.6	(2.8 - 3 3)	
			10-19 vs 0 years		4.4	(1.5 - 13)	
			>=20 vs 0 years		3.8	(1.4 - 10)	a, s, mh
		77	Mobile workers vs controls		2.3	(0.6 - 9)	
		106	Assembly workers vs controls		6.7	(2.7 - 17)	
		91	Polishers vs controls		4.4	(1.5 - 13)	
Ohlsson, 1994[64]	Neck-shoulder disorder	414	Fish processors vs controls (women)	OR	3.2	(2.0 - 5.3)	(a), s
Radiating neck pain with pain on neck movement							
Andersen, 1993[35]	CS		Internal comparison, years as a sewing operator:				
		46	0-7 vs. 0 years		4.8 v. 0%		s
		50	8-15 vs.0 years		12.0% vs. 0%		
		61	>15 vs. 0 years		27.8% vs. 0%		
					X^2 for trend, P< 0.001		
Bovenzi, 1991[61]	CS	96	Forestry vs maintenance workers	OR	6.8	P=0.06	a, s
Luopajarvi, 1979[40]	CS	285	Assembly line packers vs shop assistants	OR	0.3	(0 - 3.6)	(a), s
Nordander, 1999[42]	CS	414	Fish processors vs controls (women)		5 vs 0%		
		245	Fish processors vs controls (men)		0 vs 1%		(a), s
		659	Fish processors vs controls (all)	OR	11.9	(1.7 - 513)	

Author (year) (ref)	Diagnosis	Nos in analysis	Exposure comparisons	Measure of risk	Point estimate (95% CI)	Confounders considered
Ohlsson, 1994[64]	CS	414	Fish processors vs controls (women)		5 vs 0% P<0.001 CI lower=3.0	(a), s
Anderson, 1992[60]	Moderate to severe neck disorder	195	Coach drivers vs controls	OR	1.8 (0.5 - 7.8)	-
Thoracic outlet syndrome						
Hansson, 2000[62]	TOS	155	Laminate s vs industrial and office workers		1.1 vs 0% P=0.38	s
Ohlsson, 1994[64]	TOS	414	Fish processors vs controls (women)	OR	2.1 (0.4 - 12.8)	(a), s
Ohlsson, 1995[41]	TOS	146	Industrial workers vs controls		4.0 vs 0% P=0.12	(a), s
Other						
Hinnen, 1992[63]	NP + exam findings	154	Non vs scanner checkout workers	OR	0.7 (0.3 - 2.0)	s
	NP + exam findings		No job rotation vs job rotation, checkout workers		1.1 (0.4 - 3.4)	
	NP + exam findings		No chute vs chute at checkout		1.2 (0.5 - 3.3)	

TNS – tension neck syndrome; CS – cervical syndrome; TOS – thoracic outlet syndrome; NP – neck pain
a – age; (a) – similar mean age; s – sex; mh – mental health; sm – smoking; bmi – body mass index; inj – past history of neck injury; lei – leisure time exercise

* also, job strain and social support

Table 5: Risks by physical occupational activity

Exposure(s) Author(s)	Outcome(s)	Exposure contrast(s)	Nos. in analysis	Effect measure	Point estimate (95% CI)	Confounders considered
REPETITION						
Neck pain with tenderness						
Andersen JH, 2002[37]	Prevalent NSP + palpation tenderness	*vs non-repetitive reference group:*				a, s, mh, bmi, inj, msd, leis
		Low: 1-15 shoulder movements/minute	2725	PR	1.3 (0.8 - 2.1)	
		High: 16-40 shoulder movements/minute			1.8 (1.1 - 2.9)	
Andersen JH, 2003[18]	Incident NSP + palpation tenderness	*vs non-repetitive reference group:*				
		Low: 1-15 shoulder movements/minute	4700	OR	1.3 (0.7 - 2.6)	a, s, mh, bmi, msd, leis, ppt
		High: 16-40 shoulder movements/minute			3.0 (1.5 - 5.8)	
Silverstein BA, 1985[43]	TNS	*Final exposure classification (women):*				
		High-repetition(HR)-low force (LF) vs LRLF	161	OR	0.8 (0.2 - 3.5)	s
		Initial exposure classification (women):				
		High-repetition(HR)-low force (LF) vs LRLF	169		0.8 (0.2 - 3.1)	
Mixed, but mostly neck pain with tenderness						
Ekberg K, 1994[65]	Neck-shoulder disorder	Repetitive precision movements (vs low):				
		Medium	436	OR	2.7 (1.1 - 6.4)*	-
		High			7.5 (2.4 - 23)*	
Hansson GA, 2000[62]	Neck-shoulder disorder	Wrist movements (vs low):				
		Medium		OR	5.4 (1.3 - 22)	a,s
		High			3.1 (0.7 - 13)	
Ohlsson K, 1995[41]	Neck-shoulder disorder	Repetitive work vs none	146	OR	4.6 (1.9 - 12)	a,s,mh
Tornqvist EW, 2001[50]	Neck-shoulder disorder	Repetitive hand/finger movements, many times/minute, >2 days/week	817	OR	2.2 (1.5 - 3.2)	a,s, inj
Other						
Cassou B, 2002[19]	Incident chronic neck pain + signs	*Repetitive work vs not:*				
		In 1990 (men)	8952	OR	0.9 (0.7 - 1.2)	a, s, mh, sm, msd, leis
		Before 1990 (men)			1.3 (1.0 - 1.7)	
		In 1990 (women)	6043	OR	1.3 (1.0 - 1.6)	
		Before 1990 (women)			1.2 (1.0 - 1.5)	
	Recovery from chronic neck pain	In 1990 (women)	1056	OR	0.8 (0.5 - 1.3)	a, s, msd, leis
		Before 1990 (women)			0.5 (0.3 - 0.7)	

Exposure(s) Author(s)	Outcome(s)	Exposure contrast(s)	Nos. in analysis	Effect measure	Point estimate (95% CI))	Confounders considered
FORCEFUL WORK						
Neck pain with tenderness						
Andersen JH, 2002[37]	Prevalent NSP + palpation tenderness	*vs non-repetitive reference group:*				
		Low (<10% of MCV)	2756	PR	1.3 (0.8 - 2.0)	a, s, mh, bmi, inj, msd, leis
		High (>=10% of MCV)			2.0 (1.2 - 3.3)	
Andersen JH, 2003[18]	Incident NSP + palpation tenderness	*vs non-repetitive reference group:*				
		Low (<10% of MCV)	4706	PR	1.9 (1.0 - 3.6)	a, s, mh, bmi, msd, leis, ppt
		High (>=10% of MCV)			2.0 (1.0 - 4.2)	
Silverstein BA, 1985[43]	TNS	*Final exposure classification (women):*				s
		Low-repetition(LR)-high force (HF) vs LRLF	113	OR	1.7 (0.4 - 7.4)	
		Initial exposure classification (women):				
		Low-repetition(LR)-high force (HF) vs LRLF	116	OR	1.9 (0.5 - 7.4)	
POSTURE/STATIC LOADING						
Neck pain with tenderness						
Andersen JH, 2002[37]	Prevalent NSP + palpation tenderness	% of cycle time with neck flexed >20^0:				
		>0-<66% vs reference	2756	PR	1.3 (0.8 - 2.1)	a, s, mh, bmi, inj, msd, leis
		>=66% vs reference			1.7 (1.1 - 2.8)	
Andersen JH, 2003[18]	Incident NSP + palpation tenderness	% of cycle time with neck flexed >20^0:				
		>0-<66% vs reference	4704	PR	1.4 (0.7 - 2.9)	a, s, mh, bmi, msd, leis, ppt
		>=66% vs reference			2.6 (1.3 - 5.1)	
Veiersted KB, 1994[58]	Incident NP + palpation tenderness	Postures strenuous to the neck & shoulders (Y/N)	30	HR	7.2 (2.1 - 25.3)	s, mh
Mixed, but mostly neck pain with tenderness						
Ekberg K, 1994[65]	Neck-shoulder disorder	Lifted arms:				
		Medium	436	OR	2.4 (0.80 - 7.1)*	-
		High			4.8 (1.3 - 18)*	
		Uncomfortable sitting (high vs low)	436	OR	3.6 (1.4 - 9.3)*	-

Exposure(s) Author(s)	Outcome(s)	Exposure contrast(s)	Nos. in analysis	Effect measure	Point estimate (95% CI)	Confounders considered
Hansson GA, 2000[62]	Neck-shoulder disorder	Muscle loading (*M trapezius*) (vs. low):				
		Medium	84	OR	1.9 (0.6 - 6.3)	a, s
		High			1.5 (0.4 - 5.2)	
		Muscle loading (*M infraspinatus*) (vs. low):				
		Medium	82	OR	0.7 (0.2 – 2.4)	
		High			0.9 (0.2 - 3.3)	
Tornqvist EW, 2001[50]	Neck-shoulder disorder	Constrained sitting ≥ 4 hours/day (Y vs. N)	817	OR	1.5 (0.7 - 2.9)	a, s, inj
		Work with hands above shoulder (>30 mins/dy)			1.6 (1.0 - 2.7)	
Other						
		Awkward work, (vs never exposed):				
Cassou B, 2002[19]	Incident chronic neck pain	In 1990 (men)	9028	OR	1.4 (1.2-1.5)	s
		Before 1990 (men)			1.4 (1.2 -1.6)	
		In 1990 (women)	6100	OR	1.3 (1.1 - 1.4)	
		Before 1990 (women)			1.1 (1.0 - 1.2)	
	Recovery from chronic neck pain	In 1990 (men)	759	OR	0.8 (0.6 - 1.0)	s
		Before 1990 (men)			0.6 (0.5 - 0.8)	
		In 1990 (women)	1063	OR	0.9 (0.8 - 1.1)	
		Before 1990 (women)			0.7 (0.6 - 0.9)	
REST BREAKS						
Neck pain with tenderness						
Andersen JH, 2002[37]	Prevalent NSP + palpation tenderness	% of time without micropause rest breaks:				
		<80% vs reference	2756	PR	1.3 (0.8 - 2.1)	a, s, mh, bmi, inj, msd, leis
		>=80% vs reference			1.8 (1.1 - 2.9)	
Andersen JH, 2003[18]	Incident NSP + palpation tenderness	% of time without micropause rest breaks:				
		<80% vs reference	4614	PR	1.0 (0.4 - 2.9)	a, s, mh, bmi, msd, leis, ppt
		>=80% vs reference			2.1 (1.1 - 3.9)	

Exposure(s) Author(s)	Outcome(s)	Exposure contrast(s)	Nos. in analysis	Effect measure	Point estimate (95% CI)	Confounders considered
PRECISION WORK						
Mixed, but mostly neck pain with tenderness						
Tornqvist EW, 2001[50]	Neck-shoulder disorder	Visually demanding precision work (≥ 4hrs/day)	817	OR	0.5 (0.0 -7.8)	
Other						
Cassou B, 2002[19]	Incident chronic neck pain	Work with precise movements (Y vs N), men	9028	OR	1.1 (0.9 - 1.2)	s
		Work with precise movements (Y vs N), women	6100		1.3 (1.1 - 1.4)	
	Recovery from neck pain	Work with precise movements (Y vs N), men	759	OR	0.9 (0.7 - 1.1)	s
		Work with precise movements (Y vs N), women	1063		1.1 (1.0 - 1.4)	
REPETITION *and* FORCE						
Neck pain with tenderness						
Andersen JH, 2002[37]	Prevalent NSP + palpation tenderness	*vs. reference group:*				
		Low repetition, low force	2725	PR	1.2 (0.7 - 2)	a, s, mh, bmi, inj, msd, leis
		High repetition, low force			1.4 (0.7 - 2.9)	
		Low repetition, high force			1.4 (0.8 - 2.4)	
		High repetition, high force			2.3 (1.4 - 4.0)	
Andersen JH, 2003[18]	Incident NSP + palpation tenderness	*vs. reference group:*				
		Low repetition, low force	4700	PR	1.3 (0.6 - 2.7)	a, s, mh, bmi, msd, leis, ppt
		High repetition, low force			3.3 (1.6 - 6.9)	
		Low repetition, high force			1.3 (0.4 - 3.7)	
		High repetition, high force			2.6 (1.2 - 5.9)	
Silverstein BA, 1985[43]	TNS	*Final exposure classification (women):*				
		High-repetition(HR)-high force (HF) vs LRLF	135	OR	0.5 (0.1 - 2.6)	s
		Initial exposure classification (women):				
		High-repetition(HR)-high force (HF) vs LRLF	142	OR	0.3 (<0.1 - 1.8)	

Exposure(s) Author(s)	Outcome(s)	Exposure contrast(s)	Nos. in analysis	Effect measure	Point estimate (95% CI)	Confounders considered
REPETITION *and* POSTURE						
Neck pain with tenderness						
Andersen JH, 2002[37]	Prevalent NSP + palpation tenderness	*vs. reference group:*				
		Low repetition, low % time neck flexed	2725	PR	1.2 (0.7 - 2.1)	a, s, mh, bmi, inj, msd, leis
		High repetition, low % time neck flexed			1.4 (0.7 - 2.9)	
		Low repetition, high % time neck flexed			1.4 (0.8 - 2.6)	
		High repetition, high % time neck flexed			1.9 (1.1 - 3.1)	
Andersen JH, 2003[18]	Incident NSP + palpation tenderness	*vs. reference group:*				
		Low repetition, low % time neck flexed	4698	PR	1.2 (0.6 - 2.5)	a, s, mh, bmi, msd, leis, ppt
		High repetition, low % time neck flexed			2.5 (1.0 - 6.0)	
		Low repetition, high % time neck flexed			1.6 (0.6 - 4.1)	
		High repetition, high % time neck flexed			3.2 (1.6 - 6.4)	
REPETITION *and* REST BREAKS						
Neck pain with tenderness						
Andersen JH, 2002[37]	Prevalent NSP + palpation tenderness	vs. reference group				
		Low repetition, low % time with micropauses	2725	PR	1.2 (0.7 - 2.1)	a, s, mh, bmi, inj, msd, leis
		High repetition, low % time with micropauses		PR	1.1 (0.5 - 2.5)	
		Low repetition, high % time with micropauses		PR	1.4 (0.7 - 2.6)	
		High repetition, high % time with micropauses		PR	1.9 (1.2 - 3.2)	
Andersen JH, 2003[18]	Incident NSP + palpation tenderness	vs. reference group				
		Low repetition, low % time with micropauses	4608	PR	1.0 (0.3 - 3.1)	a, s, mh, bmi, msd, leis, ppt
		High repetition, low % time with micropauses		PR	1.5 (0.2 - 11.9)	
		Low repetition, high % time with micropauses		PR	1.4 (0.7 - 2.9)	
		High repetition, high % time with micropauses		PR	3.1 (1.6 - 6.0)	

Exposure(s) Author(s)	Outcome(s)	Exposure contrast(s)	Nos. in analysis	Effect measure	Point estimate (95% CI)	Confounders considered
VIBRATION						
Neck pain with tenderness						
Bovenzi M, 1991[61]	TNS	Daily vibration dose: >0-7.5 vs. 0 m/s^2 >7.5 vs. 0 m/s^2	96	OR	 0.9 P>0.05 3.8 P<0.03	a, s
Mixed, but mostly neck pain with tenderness						
Tornqvist EW, 2001[50]	Neck-shoulder disorder	Work with vibrating tools (≥ 60 mins/day)	817	OR	0.9 (0.4 - 2.2)	a, s, inj
Neck pain with pain on neck movement						
Bovenzi M, 1991[61]	CS	>0-7.5 vs. 0 m/s^2 >7.5 vs. 0 m/s^2	96	OR	2.8 P>0.05 10.7 P<0.005	a, s
OTHER						
Mixed, but mostly neck pain with tenderness						
Ekberg K, 1994[65]	Neck-shoulder disorder	Lifting (High and medium vs. low)	436	OR	13.6 (4.8 - 39)*	-
Tornqvist EW, 2001[50]	Neck-shoulder disorder	Manual material handling (≥ 50 N, ≥ 60 mins/day) High energy expenditure (≥ 3 TWA MET) (Y vs N)	817	OR	0.8 (0.3 - 2.0) 1.0 (0.6 - 1.9)	a, s, inj

TNS – tension neck syndrome; CS – cervical syndrome; TOS – thoracic outlet syndrome; NSP – neck-shoulder pain

a – age, s – sex, mh – mental health, sm – smoking, bmi – body mass index, inj – past injury to neck-shoulder, msd – rheumatic disease, leis – leisure physical activity, ppt – pain pressure threshold; MCV – maximum voluntary contraction; MET – metabolic equivalent; * 90% CI

Table 6: Neck pain with physical signs and psychosocial factors in the work environment

Author(s)	Outcome(s)	Exposure contrast(s)	Nos in analysis	Effect measure	Point estimate (95% CI)	Confounders considered
JOB DEMANDS						
Neck pain with tenderness						
Andersen JH, 2002[37]	NSP + palpation tenderness	High vs low job demands	2937	PR	1.8 (1.2 - 2.7)	a,s, inj, bmi, lei, msd
Andersen JH, 2003[18]	Incident NSP + palpation tenderness	High vs low job demands	4685	PR	2.0 (1.2 - 3.3)	a,s, inj, bmi, lei, mh, other‡
Mixed, but mostly neck pain with tenderness						
Ekberg K, 1994[65]	Neck-shoulder disorder	High vs low demands on attention	436	OR	3.8 (1.4 - 11)*	-
Tornqvist EW, 2001[50]	Neck-shoulder disorder	High demands (Y vs N)	817	RR	1.3 (0.9 - 1.5)	
		High time pressure (Y vs N)			1.2 (0.8 - 1.9)	
		High quantitative demands (Y vs N)			0.8 (0.4 - 1.7)	
		High demands to competence (Y vs N)			0.8 (0.5 - 1.2)	
		Low demands to competence (Y vs N)			1.1 (0.7 - 1.8)	
Other						
Cassou B, 2002[19]	Incident chronic neck pain	High vs low job demands (men)	8952	OR	1.2 (1.0 - 1.4)	a,s, mh, sm, lei, msd, other†
		High vs low job demands (women)	6043		1.2 (1.0 - 1.4)	
	Recovery from neck pain	High vs low job demands (men)	748	OR	0.7 (0.5 - 0.9)	a, s, mh, msd, other†
		High vs low job demands (women)	1056		0.7 (0.6 - 0.9)	
CONTROL OVER WORK						
Neck pain with tenderness						
Andersen JH, 2002[37]	Prevalent NSP + palpation tenderness	Low vs high job control	2940	PR	1.4 (1.0 - 1.9)	a,s, inj, bmi, lei, msd
Andersen JH, 2003[18]	Incident NSP + palpation tenderness	Low vs high job control	4677	PR	1.3 (0.8 - 2.1)	a,s, inj, bmi, lei, mh, other‡
Mixed, but mostly neck pain with tenderness						
Ohlsson K, 1994[64]	Neck-shoulder disorder	High vs low control	206	OR	0.68 (0.27 - 1.27)	a, s
Tornqvist EW, 2001	Neck-shoulder disorder	Low decision latitude	817	OR	1.1 (0.8 - 1.6)	a, s, inj
		Low participation in planning			1.4 (0.6 - 2.9)	
Other						
Cassou B, 2002[19]	Incident chronic neck pain	Low vs high job control (men)	9028	OR	1.0 (0.9 -1.2)	s

Author(s)	Outcome(s)	Exposure contrast(s)	Nos in analysis	Effect measure	Point estimate (95% CI)	Confounders considered
		Low vs high job control (women)	6100		0.9 (0.8 - 1.0)	
	Recovery from neck pain	Low vs high job control (men)	759	OR	0.9 (0.7 – 1.1)	s
		Low vs high job control (women)	1063		1.0 (0.8 - 1.2)	
SUPPORT AT WORK						
Neck pain with tenderness						
Andersen JH, 2002[37]	Prevalent NSP + palpation tenderness	High vs low social support	2937	PR	1.3 (0.9 - 1.8)	a,s, inj, bmi, lei, msd
Andersen JH, 2003[18]	Incident NSP + palpation tenderness	High vs low social support	4430	PR	1.3 (0.8 - 2.1)	a,s, inj, bmi, lei, mh, other†
Mixed, but mostly neck pain with tenderness						
Kaergaard A,2000[38]	Prevalent neck-shoulder disorder	High vs low social support	238	PR	1.66 (0.86 - 3.23)	a, s, sm, bmi, mh
	Incident neck-shoulder disorder	High vs low social support	149	PR	3.72 (1.22 - 11.30)	a, s, mh, job strain
Tornqvist EW, 2001[50]	Neck-shoulder disorder	Poor general support at work	817	RR	1.4 (1.0 - 2.0)	a, s, inj
JOB STRAIN						
Mixed, but mostly neck pain with tenderness						
Kaergaard A, 2000[38]	Neck-shoulder disorder	High vs low job strain	239	PR	0.88 (0.45 - 1.71)	a, s, sm, bmi, mh
		Fish processors				
Ohlsson K, 1994[64]	Neck-shoulder disorder	Medium vs low work strain	206	OR	2.9 (1.1 - 7.6)	a, s
		High vs low work strain			6.6 (2.6 - 17)	
		Controls				
		Medium vs low work strain	208	OR	1.2 (0.45 - 3.2)	a, s
		High vs low work strain			3.0 (1.1 - 8.7)	
Tornqvist EW, 2001[50]	Neck-shoulder disorder	Job strain			1.6 (1.1 - 2.5)	a, s, inj
WORK CONTENT						
Mixed, but mostly neck pain with tenderness						
Ekberg K, 1994[65]	Neck-shoulder disorder	Work content (poor vs. good)	436	OR	2.6 (0.71 - 9.4)*	-
Tornqvist EW, 2001[50]	Neck-shoulder disorder	Job profile - high routine, low creativity	817	OR	1.0 (0.6 - 1.5)	a, s, inj

a – age, s – sex, mh – mental health, sm – smoking, bmi – body mass index, inj – past injury to neck-shoulder, msd – rheumatic disease, leis – leisure physical activity; NSP – neck-shoulder pain * 90% CI; ‡ – other physical and psychosocial risk factors; † – other physical risk factors

Table 7: Summary of conclusions in relation to neck pain with palpation tenderness (Tension Neck Syndrome and/or mixed neck-shoulder disorders with a preponderance of Tension Neck Syndrome)

Exposure(s)	Degree of evidence supporting causal association*
Physical	
Repetition at the shoulder	++
Repetition at the wrist-hand	+
Repetition of the shoulder with neck flexion	++
Neck flexion in the absence of shoulder repetition	+
Repetition with static loading of neck-shoulder muscles and neck flexion	++
Static loading of neck-shoulder muscles in the absence of repetition	+
Forceful work	+
Precision	0
Rest breaks (independent of repetition)	0
Lifting/manual handling	0
High physical workload	0
Hand-arm vibration	0
Whole-body vibration	0
Psychosocial	
Job demands	+
Control over work	+
Support at work	+
Job strain	+
Job creativity	0
Job satisfaction	0

* For criteria, see Appendix 2. (Exposures and exposure combinations that do not appear in this table were not studied in the reviewed papers.)

Appendix 1: Search strategy

The search below was performed in Ovid MEDLINE (from 1966 to May week 3, 2006). Owing to small differences in indexing terms between databases, small refinements were made when the search was separately run in BIDS Embase and Psychinfo. References were imported into Refman and duplicates eliminated.

A. EXPOSURE(S)

1 computer mouse.mp.
2 (control and support and demand).mp.
3 (cumulative trauma$ or cumulative injur$).mp.
4 Karasek.mp.
5 exertion of force.mp.
6 (neck extension or shoulder extension or arm extension).mp.
7 extreme posture$.mp.
8 awkward posture$.mp.
9 (neck flexion or shoulder flexion or arm flexion).mp.
10 forceful exertion.mp.
11 forceful work.mp.
12 (forceful grip or power grip or precision grip).mp.
13 job satisfaction.mp. or exp Job Satisfaction/
14 job strain.mp.
15 (keyboard or keypad).mp.
16 exp Lifting/ or lifting.mp.
17 exp Occupations/ or occupation$.mp.
18 overuse.mp.
19 exp Stress, Psychological/ or perceived psychological stress.mp.
20 personality attribute$.mp.
21 personality trait$.mp.
22 personality type$.mp.
23 (physical load$ or physical workload or paced workload or paced work).mp.
24 cumulative strain.mp.
25 (neck posture or shoulder posture or arm posture or upper limb posture).mp.
26 precis$ work.mp.
27 psychosocial.mp.
28 pulling.mp.
29 pushing.mp.
30 perceived exertion.mp
31 constrained posture.mp.
32 (repetiti$ strain$ or repetiti$ activit$ or repetiti$ action$ or repetiti$ task$ or repetiti$ work or repetiti$ job$).mp.
33 (head rotation or neck rotation or shoulder rotation or arm rotation).mp.
34 skill discretion.mp. [mp=title, original title, abstract, name of substance word, subject heading word]
35 (static posture or static loading or static force or static position or static work).mp.
36 typing speed.mp.
37 exp Computer Terminals/ or VDU.mp.
38 DSE.mp.
39 (hand-arm vibration or hand arm vibration or hand transmitted vibration or hand-transmitted vibration or vibrating tool$ or hand-powered tool$).mp.
40 visual display terminal.mp.

41 visual display unit.mp.
42 work-related.mp.
43 work pace.mp.
44 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43
45 assembly line packer$.mp.
46 assembly line worker$.mp.
47 automobile assembler$.mp.
48 boarding worker$.mp.
49 bricklayer$.mp.
50 call centre worker$.mp.
51 call centre operator$.mp.
52 car assembler$.mp.
53 carpenter$.mp.
54 cash register operator$.mp.
55 chocolate worker$.mp.
56 clerical worker$.mp.
57 computer user$.mp.
58 construction worker$.mp.
59 data processing.mp.
60 data processor$.mp.
61 data entry operator$.mp.
62 dental hygienist$.mp.
63 dentist$.mp.
64 docker$.mp.
65 electrical equipment assembler$.mp.
66 electrician$.mp.
67 electronic worker$.mp.
68 farm worker$.mp.
69 farmers$.mp.
70 film rolling worker$.mp.
71 fish filleter$.mp.
72 fish worker$.mp.
73 folding worker$.mp.
74 folding operat$.mp.
75 food process$.mp.
76 fruit picker$.mp.
77 furniture mover$.mp.
78 garment worker$.mp.
79 grocery checker$.mp.
80 grocery store checker$.mp.
81 home care worker$.mp.
82 keyboard worker$.mp.
83 keyboard operat$.mp.
84 knitting worker$.mp.
85 knitting operat$.mp.
86 laundry operat$.mp.
87 laundry worker$.mp.
88 machine operat$.mp.
89 meat cutter$.mp.
90 meat process$.mp.
91 meat wrapper$.mp.
92 meat operat$.mp.
93 musician$.mp.

94 newspaper employee$.mp.
95 newspaper worker$.mp.
96 newspaper operat$.mp.
97 nurse$.mp.
98 office worker$.mp.
99 orchard worker$.mp.
100 packaging operat$.mp.
101 packer$.mp.
102 plate worker$.mp.
103 postal clerk$.mp.
104 postal sorter$.mp.
105 poultry processor$.mp.
106 poultry worker$.mp.
107 poultry operat$.mp.
108 riveter$.mp.
109 rock blaster$.mp.
110 scissor maker$.mp.
111 secretar$.mp.
112 secretarial worker$.mp.
113 semiconductor worker$.mp.
114 sewing machine operat$.mp.
115 shipyard welder$.mp.
116 sign language interpreter$.mp.
117 slaughterhouse worker$.mp.
118 supermarket cashier$.mp.
119 telecommunication$ worker$.mp.
120 telephonist$.mp.
121 teleservice operat$.mp.
122 textile worker$.mp.
123 typist$.mp.
124 VDT user$.mp.
125 VDU user$.mp.
126 45 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 73 or 74 or 75 or 76 or 77 or 78 or 80 or 81 or 82 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 104 or 105 or 106 or 107 or 108 or 110 or 111 or 112 or 113 or 114 or 115 or 116 or 117 or 118 or 119 or 121 or 122 or 123 or 124 or 125
127 44 or 126

B. OUTCOME(S)

128 cervical syndrome.mp.
129 cervicobrachial disorder$.mp.
130 cervicobrachial fibromyalgia.mp.
131 cervicobrachial pain.mp.
132 cumulative trauma disorder$.mp. or exp Cumulative Trauma Disorders/
133 (musculoskeletal and neck).mp.
134 (musculoskeletal and neck-shoulder).mp.
135 (musculoskeletal and shoulder).mp.
136 neck discomfort.mp
137 neck myalgia.mp.
138 neck pain.mp. or exp Neck Pain/
139 neck symptom$.mp

140 neck tenderness.mp.
141 neck-shoulder myalgia.mp.
142 neck-shoulder pain.mp.
143 neck-shoulder tenderness.mp.
144 shoulder disorder$.mp.
145 shoulder girdle pain$.mp.
146 shoulder muscle fatigue.mp.
147 shoulder myalgia.mp.
148 shoulder pain.mp. or exp Shoulder Pain/
149 shoulder tenderness.mp.
150 tension neck syndrome.mp.
151 thoracic outlet syndrome.mp. or exp Thoracic Outlet Syndrome/
152 trapezius myalgia.mp.
153 (upper extremity and neck).mp.
154 (upper extremity and neck-shoulder).mp.
155 (upper extremity and shoulder).mp.
156 (upper limb and neck).mp.
157 (upper limb and neck-shoulder).mp.
158 (upper limb and shoulder).mp.
159 (WRULD and shoulder).mp.
160 (work-related upper limb disorder$ and shoulder).mp.
161 (WRULD and neck).mp.
162 (work-related upper limb disorder$ and neck).mp.
163 (WRULD and neck-shoulder).mp.
164 (work-related upper limb disorder$ and neck-shoulder).mp.
165 128 or 129 or 130 or 131 or 132 or 133 or 134 or 135 or 136 or 137 or 138 or 139 or 141 or 142 or 143 or 144 or 145 or 146 or 147 or 148 or 149 or 150 or 151 or 152 or 153 or 154 or 155 or 156 or 157 or 158 or 159 or 160 or 161 or 162 or 163 or 164

C. FILTERS FOR PHYSICAL EXAMINATION

166 physical examination.mp. or exp Physical Examination/
167 examination.mp.
168 physical signs.mp.
169 objective assessment.mp.
170 functional assessment.mp.
171 palpation.mp. or exp Palpation/
172 palpatory findings.mp.
173 palpable muscle tightness.mp.
174 tenderness.mp.
175 passive neck movement$.mp.
176 resisted neck movement$.mp.
177 range of movement$.mp.
178 neck angle$.mp.
179 neck posture$.mp.
180 neck flexion.mp.
181 neck extension.mp.
182 goniomet$.mp.
183 foraminal test.mp.
184 nerve root sign$.mp.
185 neck compression test$.mp.
186 shoulder abduction test$.mp.
187 166 or 167 or 168 or 169 or 170 or 171 or 173 or 174 or 176 or 177 or 178 or 179 or 180 or 181 or 183 or 184 or 185 or 186

188 165 and 187

EXPOSURE + OUTCOME

189 127 and 165

EXPOSURE + OUTCOME + PHYSICAL EXAMINATION

190 127 and 188

D. EPIDEMIOLGICAL FILTERS

191 risk$.mp.
192 rate$.mp.
193 exp Odds Ratio/ or odds.mp.
194 incidence.mp. or Incidence/
195 prevalence.mp. or Prevalence/
196 ratio$.mp.
197 exp Epidemiology/ or epidemiology.mp.
198 epidemiolo$.mp.
199 191 or 192 or 193 or 194 or 195 or 196 or 197 or 198

EXPOSURE + OUTCOME + PHYSICAL EXAMINATION + EPIDEMIOLGICAL FILTER

200 190 and 199

Appendix 2: Framework of the Scientific Committee of the Danish Society of Occupational and Environmental Medicine for assessing the evidence on causal associations

Strong evidence of a causal association (+++): A causal relationship is very likely. A positive relationship between exposure to the risk factor and the outcome has been observed in several epidemiological studies. It can be ruled out with reasonable confidence that this relationship is explained by chance, bias or confounding.
Moderate evidence of a causal association (++): A causal relationship is likely. A positive relationship between exposure to the risk factor and the outcome has been observed in several epidemiological studies. It cannot be ruled out with reasonable confidence that this relationship can be explained by chance, bias or confounding, although this is not a very likely explanation.
Limited evidence of a causal association (+): A causal relationship is uncertain. A positive relationship between exposure to the risk factor and the outcome has been observed in several epidemiological studies. It is not unlikely that this relationship can be explained by chance, bias or confounding.
Insufficient evidence of a causal association (0): The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of a causal association.
Evidence suggesting lack of a causal association (-): Several studies of sufficient quality, consistency and statistical power indicate that the specific risk factor is not causally related to the specific outcome.