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Quality based critical review of the epidemiological literature on carpal tunnel syndrome and occupation

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Authors: Sandra I. Sulsky, MPH, Ph. D,
Martha A. Mastroberti, M.S. and
Michael D. Schmidt, M.S.
Environ International Corporation, Health Science Institute
www.environhsi.com

Editorial coordinators: Annette Nold, Frank Bochmann

Editor: Hauptverband der gewerblichen Berufsgenossenschaften (HVBG)
Berufsgenossenschaftliches Institut für Arbeitsschutz – BGIA
Alte Heerstr. 111, D-53754 Sankt Augustin
Telefon: +49 / 02241 / 231 – 01
Telefax: +49 / 02241 / 231 – 1333
Internet: www.hvbg.de
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Abstract

Carpal tunnel syndrome (CTS) is a disorder of the hand wrist caused by mechanical entrapment or inflammation of the median nerve. Accepted risk factors include age, gender, hormonal changes, and metabolic diseases. The association between CTS and physical activities, including work exposures, is less clear. 334 articles published between 1997 and 2003 were reviewed. This report summarizes results from 34 occupational epidemiological studies that met specific quality criteria. A small number of studies defined repetitive work and CTS in a consistent enough manner to conclude that the evidence supports a modest positive association between repetitive work activities and risk of CTS. Three studies reported an effect of forceful work activities on CTS risk. However, since exposure and outcome definitions were not comparable, no firm conclusions regarding this relationship may be drawn. There is insufficient epidemiological evidence to either support or refute an association between other work activities and CTS. Overall, the quality of research regarding the association between occupation and CTS has improved since 1997. However, the lack of a "gold standard" medical diagnostic technique represents a major hurdle yet to be overcome. Any future investigation or literature review must address the fact that the prevalence, incidence and risk factors for CTS depend strongly on the case definition used.

Qualitätsbasierter kritischer Review der epidemiologischen Literatur: Karpaltunnelsyndrom und Beruf

Kurzfassung

Das Karpaltunnelsyndrom (KTS) ist eine Erkrankung im Handgelenk, die durch eine Kompression oder Entzündung des *Nervus medianus* (Mittelhandnerv) entsteht. Zu den gesicherten Risikofaktoren zählen Alter, Geschlecht, hormonelle Veränderungen und Stoffwechselerkrankungen. Der Zusammenhang zwischen KTS und körperlichen Aktivitäten, einschließlich Belastungen am Arbeitsplatz, ist hingegen weniger klar. Die vorliegende Studie soll zur Klärung beitragen. Es wurden 334 Aufsätze aus den Publikationsjahren 1997 bis 2003 ausgewertet. In diesem Report werden die Ergebnisse und Zusammenfassungen aus 34 arbeitsepidemiologischen Studien, die spezifische Qualitätskriterien erfüllten, dargestellt. Bei einer geringen Anzahl von Studien wurden repetitive Arbeiten und KTS einheitlich definiert. Die Ergebnisse weisen auf einen schwachen Zusammenhang zwischen repetitiven Tätigkeiten und einem KTS-Risiko hin. Bei drei Studien wurde das Arbeiten mit Kraftaufwand als Einflussfaktor auf das KTS-Risiko genannt. Da die Definitionen von Belastung und Wirkung nicht vergleichbar waren, können keine gesicherten Evidenzen für diesen Zusammenhang abgeleitet werden.
Es liegen keine abgesicherten Evidenzen aus der Epidemiologie vor, um auf einen Zusammenhang zwischen weiteren Arbeitstätigkeiten und KTS zu schließen. Insgesamt hat sich die Qualität der Forschung, die sich mit dem Zusammenhang zwischen beruflicher Tätigkeit und KTS beschäftigt, seit 1997 verbessert. Es gibt jedoch immer noch keinen „gold standard“ für die medizinische Diagnostik. Dieses Problem sollte noch gelöst werden. Zukünftige Untersuchungen bzw. Literaturauswertungen sollten berücksichtigen, dass die Prävalenz bzw. die Inzidenz und die Risikofaktoren für KTS in starkem Maße von der verwendeten Falldefinition abhängen.

Compte rendu critique de la littérature épidémiologique sélectionnée selon des critères de qualité : syndrome du canal carpien et profession

Résumé

Le syndrome du canal carpien (SCC) est causé par une compression, une infection ou une inflammation du nerf médian dans le poignet. Les facteurs de risque avérés sont, entre autres, l'âge, le sexe, les modifications hormonales et les troubles du métabolisme. En revanche, le lien entre SCC et activités corporelles, y compris sur le lieu de travail, n'a pas encore été établi. 334 études publiées entre 1997 et 2003 ont été exploitées. Dans ce compte rendu sont présentés les résultats et les résumés de 34 études épidémiologiques qui satisfaisaient à des critères de qualité spécifiques. Dans un petit nombre d'études, travaux répétitifs et SCC étaient définis de la même manière. Les résultats accréditent l'hypothèse d'un faible lien entre activités répétitives et risque de SCC. Dans trois études, le travail avec efforts physiques était cité comme facteur d'influence sur le risque de SCC. Cependant, comme les définitions des termes charge physique et effet n'étaient pas comparables, il n'est pas possible de tirer des conclusions indubitables sur cette relation. Du point de vue épidémiologique, il n'existe pas de conclusions incontestables permettant d'établir un lien entre d'autres activités professionnelles et le SCC. La qualité des études, qui ont trait à la relation entre activité professionnelle et SCC, s'est globalement améliorée depuis 1997. Cependant, il n'existe toujours pas de règle universelle pour le diagnostic médical. Ce problème reste à résoudre. À l'avenir, les études et les comptes rendus d'ouvrages devraient tenir compte du fait que la prévalence ou l'incidence et les facteurs de risque pour le SCC dépendent, dans une large mesure, de la définition de cas utilisée.

Reseña crítica, basada en la calidad, de la literatura epidemiológica: Síndrome del Túnel Carpiano y profesión

Resumen

El Síndrome del Túnel Carpiano (STC) es una lesión de la muñeca, originada por compresión o inflamación del nervus medianus (nervio mediano). Factores de riesgo comprobados son la edad, el sexo, las alteraciones hormonales y los trastornos metabólicos. En cambio, la relación entre STC y actividades físicas, incluyendo cargas de origen laboral, aún no está comprobada. La reseña abarca 334 ensayos publicados entre 1997 y 2003. El Report presenta los resultados y resúmenes de 34 estudios epidemiológicos, que cumplen criterios específicos de calidad. Un número reducido de estudios define trabajos repetitivos y STC de manera uniforme. Los resultados indican una débil relación entre actividades repetitivas y un riesgo de STC. Tres estudios indican esfuerzos laborales como factor que influye en el riesgo de STC. Pero, debido a que las definiciones de carga y efecto no son comparables, no se pueden derivar evidencias aseguradas para dicha relación. No existen evidencias aseguradas desde la epidemiología, que permitan deducir una relación entre ulteriores actividades laborales y el STC. Pero, se puede constatar que la calidad de la investigación, que se dedica a estudiar las relaciones entre actividades laborales y el STC, mejoró desde hace 1997. Sin embargo, todavía no existe un „gold standard" para el diagnóstico médico. Queda pendiente encontrarle solución a esta problemática. Futuras investigaciones o bien evaluaciones de la literatura deberán tener en cuenta, que la prevalencia o bien la incidencia y los factores de riesgo para el STC dependen, en gran medida, de la definición aplicada.

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Contents

1 Introduction

The number of cases of carpal tunnel syndrome (CTS) has increased rapidly since the early 1980s in industrialized countries around the world. These increases occurred coincidentally with several factors; including increased use of personal computers in the home and at work, increased mechanization of industrial work settings, and the designation of CTS as a work-related condition by some governments [1 to 3].

The designation of CTS as "work-related" stems from its frequent association with certain work activities, and the observation of increased prevalence within certain occupations and industries. Due to its apparent association with certain physical activities, CTS is usually considered a type of "cumulative trauma disorder" (CTD) or "repetitive strain injury" (RSI) [1; 3]. However, the general concept of RSI has been challenged at times, based on the theory that repetitive use of a body part should lead only to conditioning, as is seen with exercise [1; 3].

Even if the existence of RSI is accepted, there is some controversy over whether or not CTS should be included under its rubric, since the connection between symptoms and physical activities is uncertain [3; 4]. A large body of scientific literature has accumulated addressing the question of the work-relatedness of CTS, and a number of detailed reviews have been published. The current review summarizes results from studies published between 1997 and 2003 that met specific quality criteria. These results are summarized and used to evaluate current evidence for and against an association between occupational activities and CTS.

1.1 Background

Carpal tunnel syndrome (CTS) is a disorder caused by mechanical entrapment or inflammation of the median nerve [3; 5]. In addition to physical activities and work exposures, a number of systemic conditions have been associated with occurrence of CTS. These include the presence of underlying connective tissue disease, such as rheumatoid arthritis, acromegaly, pregnancy, use of estrogenic hormones, thyroid disease, and obesity. The prevalence of CTS is thought to peak around age 45 years, and to be as much as three times higher among women compared to men [1; 3].

Diagnosis of CTS is difficult, since no clear "gold standard" technique exists. Symptoms are widely used as diagnostic criteria in clinical practice and in epidemiological surveillance. Symptoms used in case finding include numbness and pain along the median nerve, weakness of the thenar muscle, and pain in the hand, wrist or forearm that is especially problematic at night [1; 3]. Nerve conduction (NC) tests may be the most objective available diagnostic tool for CTS, but their results do not correspond well with perceived symptoms. In addition, NC tests tend to find a higher prevalence of cases than symptom-based definitions. This contrasts with screening for other health conditions, in which symptom-based definitions are generally more inclusive than objective tests [6].

All currently used diagnostic methods are subject to error [3; 7]. Clinical diagnostic tools such as Phalen's test and Tinel's sign depend on the subjective judgement of the practitioner. Symptom lists depend on the ability of the patient to be an accurate reporter. NC is reduced in the absence of pathology if the temperature in the testing room is low enough to cause vasoconstriction [3]. The validity of NC test results is also compromised by the anthropometry of the subject, including hand size, wrist architecture, and body composition (cited in [8]). In addition, investigators may choose from a variety of NC tests, including various measurements on either the sensory or the motor nerve. Each requires the definition of a different standard against which to judge the individual findings; and there may be different associations between disease status, exposure, and each type of NC test.

Given the difficulties in diagnosing CTS, it is not surprising that *Homan* et al. [8] found little overlap among the results of six different case-finding techniques. In their research, diagnostic agreement ranged from Kappa = 0.00 for the combination of current symptoms, nocturnal symptoms, and positive physical exam findings compared to NC test results to Kappa = 0.13 for patient-reported symptoms using a hand diagram compared to NC test results.[1]

It is also unsurprising that the predictive value of any particular surveillance definition of CTS is uncertain. In cross-sectional and case-control studies, a substantial proportion of participants with NC delays were found to be symptom-free, while a nearly equal proportion with physical symptoms suggestive of CTS demonstrated normal nerve conductivity [6; 9 to 13]. *Werner* et al. [14] reported results from a prospective study demonstrating that asymptomatic, active employees with abnormal median NC were no more likely to develop CTS symptoms after 17 months than those with normal NC test results. In contrast, other investigators have observed that specific symptoms predict abnormal NC and recommend their use in epidemiological surveillance [5].

Homan et al. [8] recommended that, among the poor choices, the combination of NC testing and symptom reports offered the best option for case finding. This is compatible with an expert consensus panel recommendation to use the combination of abnormal NC and symptoms for epidemiological classification of CTS [7]. Similarly, the U.S. National Institute for Occupational Safety and Health (NIOSH) recommended a surveillance definition of CTS consisting of abnormal NC and either symptoms or clinical findings consistent with median nerve entrapment [1].

1.1.1 Occurrence of CTS

General population prevalence estimates of CTS have ranged from three per 1,000 in U.S. men to 68 per 1,000 among women in the Netherlands. The highest estimate was obtained by identifying cases through a combination of symptom reports and NC tests; the lowest prevalence was based on prior physician diagnosis of CTS [6].

The estimated prevalence of CTS in occupational cohorts similarly depends on the case finding technique. Based on reported work absences, five to ten cases per

[1] The Kappa statistic is a measure of correlation between categorical variables that is corrected for agreement by chance.

10,000 employed persons per year miss work due to CTS in the U.S. [5]. Using NC alone, *Nathan* et al. (reported in [6]) found CTS in 39 % of participants, and 20 % had both NC slowing and clinical symptoms consistent with CTS. At the other end of the spectrum, a questionnaire-based study yielded an estimated prevalence of 0.6 %, and the 1988 National Health Interview Survey found 0.5 % of employed adults in the U.S. to have CTS based on physician diagnosis and physical examination results [6].

The incidence of work-related RSI generally, and CTS in particular, increased dramatically in the U.S. after a NIOSH consensus panel released its report defining these conditions as related to occupation. In 1981 there were 23,000 cases of RSI reported by the U.S. Bureau of Labor Statistics, accounting for 18 % of all occupational illnesses that year. In 1991, the figure rose to 224,000 cases of RSI, or 61 % of all occupational illnesses. As reported in [6], increases in insurance claims for occupational CTS in specific U.S. states showed a similar trend. Between 1983 and 1988, workers' compensation claims for CTS in Wisconsin rose 462 % (from 432 to 2,429); in California, reports to the state occupational surveillance system rose 743 % over the same interval; and in Connecticut, the number of claims for all RSI increased ten-fold between 1979 and 1983. Similar patterns of increases were noted in Australia, Canada, Norway, Sweden, and Japan after RSI was defined as work-related in those countries [1 to 3]. At least some of the increased incidence might be due to increased awareness of CTS among the general public and physicians following the classification of RSI as work-related [2].

1.1.2 Occupational exposures correlated with CTS

Occupational exposures that have been associated with CTS in epidemiological studies include use of vibrating tools, work in cold temperatures, repetitive high-force motions, and prolonged activity in postures requiring wrist flexion [1; 3; 5]. The best studies take particular care with the assessment of occupational exposure. Frequently this is in the form of time and motion studies which provide individual assessments of the force, posture, frequency, etc. for each person and job task. Such time-motion studies are extremely costly and time consuming, but are the least likely to result in misclassification of exposure.

Various industries and jobs have been identified as conferring high risk of CTS on employees. These include meat processing, assembly work, machine operation, and computer keyboard work [15]. "Industry" and "job" are thus used as surrogate measures of exposure to various presumed high-risk occupational activities. Basing exposure assessment on industry or job title can lead to misclassification to the extent that there is variability in jobs and tasks required within industry and within job title. Inter-individual variability in performance of work tasks must also be considered when assessing exposure based on task.

The state of knowledge in 1997 with respect to occupational exposures and CTS was summarized in the NIOSH report "Musculoskeletal disorders and workplace factors" [5]. Of the 30 studies reviewed, only six achieved the minimum quality standard set forth by the NIOSH review panel, and all six employed the cross-sectional study design. The panel's quality assessment was based on four characteristics of study design or conduct: participation rate of at least 70 %, use of objective criteria for case ascertainment, investigators blinded to health or exposure status during data collection, and adequate assessment of exposures to the wrist.

The panel found strong evidence in favour of a positive association between risk of CTS and work that is both repetitive and forceful, with adjusted odds ratios (OR) in four studies ranging from about two to about 16. The highest OR resulted from the largest study with the most detailed exposure assessment. CTS cases were defined based on the combination of physical exam findings and symptom reports. The panel found adequate evidence for an independent effect of repetitive work, based on five studies with adjusted ORs ranging from 1.5 to 6.7. The highest estimate for this exposure was reported in the smallest study, in which force and repetition were not evaluated separately. Cases were defined using a combination of symptom reports and NC tests.

The NIOSH panel also reported some evidence for a positive association between vibration and risk of CTS. However, this conclusion was based on information in only two studies meeting minimal quality criteria, combined with information from two case reports. Of the two studies, one did not separate the effects of vibration from other occupational exposures. The second study of vibration reported an adjusted OR of 10.9 for employees using vibrating tools at work, compared to their unexposed counterparts; however, a variety of CTS case definitions based on NC tests in several different nerves was used.

The current report examines evidence for occupational risk factors for CTS based on studies published between 1997 and 2003. It is organized by case definition, since different definitions serve different purposes, including clinical case finding, surveillance, and screening. Each definition also has different implications. For example, symptoms may be of the most importance to affected individuals, and are likely to have more impact on work life than would impaired nerve conduction in the absence of symptoms. Finally, each CTS case definition is likely to identify a different number of cases in the same population.

2 Methods

A total of 665 unique papers were identified and provided by the Berufsgenossenschaftliches Institut für Arbeitsschutz – BGIA (Sankt Augustin, Germany) or Applied Epidemiology, Inc. (AEI, Amherst, MA, USA). Two hundred and fifty were screened and excluded due to lack of peer review or failure to meet the additional inclusion criteria

- provided by BGIA or identified by AEI,
- epidemiological study of occupation and carpal tunnel syndrome,
- published between 1997 and 2003,
- English or German language.

Eighty-one papers contained information on non-occupational risk factors for CTS, population incidence or prevalence estimates, or described methodological issues in diagnosis/case ascertainment or exposure assessment. Of these, 54 were read carefully and 27 were only screened for classification purposes. A total of 34 of the 334 papers described occupational exposures and their relationship with CTS. All 34 were reviewed by at least two epidemiologists. Data extracted from each occupational study are

- author(s)
- year of publication
- journal
- publication language
- purpose of study

- location of study population
- first date of follow-up (if cohort)
- last date of follow-up (if cohort)
- industry sector(s)

- study design (cohort, case-control, cross-sectional)
- minimum duration of employment

- ❒ type of analysis/statistical methods
- ❒ case ascertainment method (nerve conduction test, Phalen's, Tinel's, symptom reporting, etc.)
- ❒ exposure assessment methods
- ❒ exposure definition
- ❒ exposure metrics
  - likelihood of exposure
  - exposure intensity ranking
  - duration of exposure
  - timing of exposure
- ❒ results reported by
  - gender
  - levels of exposure/tasks
  - latency
  - different comparison groups
- ❒ selection bias potential
- ❒ information bias potential
  - investigator blinded?
- ❒ confounding bias potential
- ❒ confounding factors controlled
- ❒ comprehensiveness of follow-up (per cent missing or unknown)
- ❒ types of comparisons used (control groups, reference populations, etc.)
- ❒ participation rates (cases and controls).

Specific quality criteria used to identify the methodologically strongest and most relevant occupational studies are shown in Table 1 (see page 64). The study characteristics we considered in the quality rating were:

- clarity and relevance of the stated study objectives,
- clarity of description of study methods,
- their appropriateness with respect to the objectives, and
- their ability to minimize selection and information bias.

The outcome definition was evaluated for its specificity and the investigators' ability to measure it accurately and directly. Exposure assessments were considered to be of highest quality if they occurred during etiologically relevant time periods and were measured at the individual versus the group level, since individual level measurements are less likely than group level assessments to introduce misclassification of exposure. Studies that assessed potential confounding by known risk factors for CTS, and appropriately controlled for identified confounding, were considered to be of better quality than studies that did not consider the potential for confounding. Quality ratings were improved when the authors considered alternative explanations for their findings and assessed the potential for and likely magnitude of uncontrolled biases.

The final quality ratings were based primarily on study design and analysis methods. Papers rated "Adequate" were free of major bias; residual confounding was unlikely to have substantially influenced the results; there was reasonably complete ascertainment of cases and adequate exposure assessment. "Limited" studies were free of major bias, but residual confounding might have influenced the results; there was reasonably complete ascertainment of cases and reasonable exposure assessment methods were used. "Inadequate" studies were judged likely to be substantially influenced by major bias, or residual confounding was likely to have influenced the results, or the study outcome was not specifically CTS.

3 Results

The two epidemiologist reviewers agreed on the quality rating of 24 of the 34 occupational papers. Ten required adjudication by a third reviewer, and three of these disputed papers required discussion to reach consensus.

Table 2 (see page 65) describes the basic characteristics of all 34 occupational papers reviewed. Details of study design, exposure assessment, and covariate data collected for all studies are shown in Tables 3, 4 and 5 (see page 68, 72 and 77), respectively. The information in these Tables is meant to support the overall quality ratings for each occupational paper, which were as follows (Table 6, see page 80):

- inadequate quality: 7,
- limited quality: 16, and
- adequate for inclusion in the synthesis of evidence regarding the potential association between occupation and CTS: 11.

The following section provides a qualitative description of the 11 occupational studies that were rated adequate to include in the synthesis, as well as the 16 studies that were of limited quality. The latter were included because they provide information that can be used to add or subtract from the weight of evidence offered by the 11 better studies; but their problems with study design, analysis, and bias outweigh the usefulness of their specific effect estimates. Therefore, only the 11 adequate studies appear in the synthesis.

Most of the investigators reporting on the relation between occupational exposures and CTS used more than one diagnostic method to identify cases in their studies. Because no reliable screening test exists for detecting early cases or predicting future cases of CTS, and because the number of cases identified depends so strongly on the diagnostic method employed, we have organized the following qualitative descriptions by case definition, rather than according to exposure. Within each section, the adequate papers are discussed first, in chronological order. The limited papers are then presented chronologically.

3.1 CTS identified by combination definitions: eight adequate studies

Studies in this section identified CTS using at least two of the following:

- self-reported symptoms consistent with median nerve compression,
- clinical exam findings possibly including positive Phalen's test or Tinel's sign,
- prior physician diagnosis,
- prior carpal tunnel release surgery,
- nerve conduction test results.

Specific case definitions for each study are shown in Table 3 (see page 68).

Eight adequate studies used combination definitions to identify CTS. *Roquelaure* et al. [16] conducted a case-control study in three manufacturing facilities in western France between 1993 and 1994. Potential cases were employees whose plant medical records carried any physician note dated 1990 to 1992 that indicated the presence of symptoms consistent with CTS, positive Phalen's sign or Tinel's test, history of carpal tunnel release surgery, and/or abnormal NC tests. Individuals with CTS or other musculoskeletal diagnoses recorded prior to 1990 were excluded from the study to avoid introducing bias due to factors associated with recovery or ability to tolerate disease. Controls were matched on age (within one year), gender, and worksite, and were required to be free of CTS and musculoskeletal disorders of the upper extremity from 1984 to 1992. Any individual (potential case or control) with diagnosed malignancy, rheumatic disease, thyroid dysfunction, or diabetes was excluded from the study.

The main strength of this investigation was its detailed, individual-level exposure assessment. Job task analyses were carried out for each of the 65 cases and 65 controls who participated, and details of work rotation, tools, materials, and work pace were also collected. Although the power of the final multivariable logistic regression model was compromised by the relatively small number of cases, five occupational factors were statistically significantly positively associated with odds of CTS after controlling for age, gender, plant, household chores more than 1 hour per day, frequency of specific hand motions, indicators of wrist, elbow and trunk posture and, for women, parity greater than 3. Odds ratios (OR) and 95 % confidence intervals (CI) were 9.0 (CI: 2.4, 33.4) for exertion (force > 1 kilogram), 8.8 (CI: 1.8, 44.4) for repetitiveness (elementary operation 10 seconds or less), 6.0 (CI: 1.8, 20.2) for changes in activity or breaks less than 15 % daily work time, 6.3 (CI: 2.1, 19.3) for lack of job rotation, and 5.0 (CI: 2.2, 21.2) for manual work station supply.

The authors reported point estimates and confidence intervals only for the occupational variables that were statistically significant in the final model. When exposure was re-defined as the total number of occupational risk factors accumulated by each participant in the study, ORs for CTS increased from 5.6 (CI: 1.6, 24.5) for those with three risk factors to 93.7 (CI: 13.4, 93.8) for four risk factors and 90 (CI: 8.0, 367) for those with five or more occupational risk factors compared to participants with one or two of the occupational risk factors for CTS.

Frost et al. [17] carried out a cross-sectional study within a group of 743 Danish slaughterhouse employees and 398 chemical plant employees. Individual ergonomic assessments were conducted for all of the slaughterhouse employees, and 90 % of job tasks were covered. However, exposure status was reduced in the analysis to three parameters for comparison with work in the chemical factory: any work in the slaughterhouse, de-boning work, and non-de-boning work. The latter two categories represent subgroups of the slaughterhouse employees. CTS cases were identified by the combination of symptom reports and NC test results or history of CT surgery.

The overall prevalence of likely CTS was 5 % among the slaughterhouse employees and 1 % among the chemical plant employees, in spite of the latter group's slightly older average age. After controlling for age, history of wrist trauma, body mass index (BMI), smoking habit, gender, and history of medically diagnosed rheumatoid arthritis, diabetes, myxedema, or connective tissue disease, the ORs for CTS in either hand was four times higher (OR = 4.01, CI: 1.72, 9.32) among slaughterhouse versus chemical plant employees. Slaughterhouse employees engaged in de-boning tasks had ORs for CTS 5.5 times higher than chemical workers (OR = 5.53, CI: 2.2, 13.9), and those in jobs other than de-boning had OR = 3.25 (CI: 1.27, 8.33) compared to chemical plant employees. The reported ORs were similar when CTS in the dominant or non-dominant hand was analyzed separately.

Three selection biases may have played minor, conflicting roles in the *Frost* et al. results: The chemical workers participated at a lower rate than the slaughterhouse workers, and they had both longer duration of service and older average ages. The lower participation rate suggests an inflation of the OR, since people who suspected health problems might be more likely to volunteer for health studies, while the older age and duration of service among the chemical workers suggests possible out-migration from the slaughterhouse employees experiencing symptoms; such a survivor effect that would tend to attenuate any effect of occupational exposures on CTS risk.

Latko et al. [18] conducted a cross-sectional study of 352 persons employed in three manufacturing facilities in North America. Participants completed a symptom questionnaire and hand diagram, and underwent NC testing. Individual exposure assessments were completed based on video tapes of participants at work. A total of 109 exposure variables were compiled, including ten anthropometric measures, 25 medical history factors, five demographic characteristics, four tobacco use measures, and 13 psychosocial factors. Fifty-two physical stressor variables were quantified for each job, including repetition, force, mechanical stress, posture, temperature, and vibration. However, repetitiveness was the primary exposure of interest. *Latko* et al. evaluated CTS according to several definitions. In this section, we discuss cases identified by the combination of symptoms and NC test results. Symptoms alone and NC test results alone are described in the relevant sections, below.

After excluding 16 diagnosed diabetics, the prevalence of CTS was 5.6 % (19 cases), and the authors noted a trend of increasing prevalence across categories of increasing job repetitiveness, ranging from 2.7 % of those in low repetition jobs to 7.9 % of those in high repetition jobs. After controlling for gender, age, and wrist shape (depth : width ratio at least 0.73 versus less than 0.73), the OR for repetition rating was 1.22 (CI: 0.98, 1.53).

The strengths of this study include its detailed exposure assessment and reliance on validated survey instruments. However, since only 19 CTS cases were identified by the combination of symptoms and NC test results, the multivariable model had limited statistical power to detect any effects. In addition, participation was limited to persons who had worked for at least six months. While intended to allow time for disease development, this restriction could have introduced a survivor bias if participants most susceptible to CTS developed symptoms and changed jobs before the six month minimum had elapsed.

A cross-sectional study in an electronics manufacturing facility in Egypt by *Abbas* et al. [19] included 198 employees. The 104 people engaged in assembly or quality control (QC) were considered exposed, while 94 in clerical, administrative or maintenance jobs were considered unexposed to workplace risk factors for CTS. Cases were identified by symptom reports, physical exam, and NC tests. The assembly and QC jobs were assessed individually for demands characterized by weight lifted, work pace, and predominant grip type. Each workstation was also assessed for its ergonomic properties.

The prevalence of CTS was 33.7 % in the exposed and 4.3 % in the unexposed group, yielding an unadjusted OR for CTS of 11.4 (95% CI: 3.6, 40.2). Among the assembly workers, precision grip was associated with a nearly seven-fold increase in ORs for CTS (adjusted OR = 6.5, CI: 1.08, 39.23), and the OR for intermediate grip was 1.98 (CI: 0.32, 11.9) compared with power grip. Each additional year of employment among the assembly workers was associated with an 11 % increase in ORs for CTS (OR = 1.11, CI: 1.03, 1.20). These estimates were based on only 35 cases and, since the model also adjusted for age, gender, marital status, job satisfaction, neck posture, body posture, production rate, and weight of parts used, the statistical power and stability of the model is questionable. Estimates for these other covariates were not presented by the authors, presumably due to their lack of statistical significance. In addition, women comprised over 90 % of the assembly group, so control for gender in this model is irrelevant and may further compromise the power of the analysis.

Nathan et al. [20] reported on a North American cohort, followed for eleven years, in which five work factors were evaluated for their association with CTS incidence: force, repetitiveness, vibration, keyboard use, and heavy lifting. Cases were identified by the combination of symptoms and positive NC tests. Occupational exposure to the CTS risk factors listed above was assessed at the 1984 baseline by direct observation and by questionnaires in 1988 and 1994 to 1995.

About 60 % of the original cohort of 471 people could be traced after 11 years. The majority of losses occurred in the interval between baseline and the first follow-up and were attributed to layoffs at one of the four worksites contributing study participants. Since no follow-up was initially planned, the authors reported inadequate contact information had been collected at baseline. Two hundred and fifty-six of the 471 original participants were followed at both contact points, and 35 of these (13 %) developed CTS.

After adjustment for gender, age, endocrine conditions, cigarette smoking status, and BMI, only exposure to vibration was associated with CTS: OR = 3.4 (CI: 1.09, 10.7). When stratified by gender, the strength of the association between CTS and vibration was doubled, to 7.3 for men and 8.2 for women. Confidence intervals for these estimates were not provided, but the authors indicated that the p-values were between 0.05 and 0.10. In contrast with the results of the other studies reported in this section, *Nathan* et al. found the highest magnitude ORs from their adjusted model were for the non-work factors of age 50 or older versus less than 30 years (OR = 10.6, CI: 2.7, 42.0) and BMI greater than or equal to 28.2 versus 21.6 or less (OR = 5.4, CI: 1.2, 23.0). Cigarette smoking was also associated with a two-fold increase in ORs for CTS in this cohort (OR = 2.03, CI: 0.68, 6.03).

The large proportion of the original cohort lost to follow-up raises the concern of selection bias in the remaining group, as does the younger average age and lower BMI at baseline (both negatively associated with CTS) among those not followed; however, these factors should not affect the internal validity of the reported associations between work factors and CTS incidence, unless age and BMI were also associated with exposure. In addition, the power of the multivariable model was compromised by the large number of covariates (11) and the relatively small number of cases (35).

Rosecrance et al. [21] completed a cross-sectional analysis of apprentice construction workers in several U.S. states. Exposure assessment comprised a descriptive list of 15 job factors, each of which respondents were asked to rate as a contributor to work-related musculoskeletal symptoms. The ratings ranged from zero (no problem) to ten (major problem). Ratings of five or above were considered positive contributors in the analysis; factors rated up to four were not considered to contribute to work-related musculoskeletal problems. Cases were identified by a combination of self-reported symptoms and median mononeuropathy assessed by NC testing.

A total of 1,325 apprentices were eligible to participate in the study. Participation rates were high, but varied by trade group, from 76.5 % of operating engineers to 100 % of sheet metal workers. After excluding 20 participants for incomplete data or the presence of comorbidity associated with CTS, the prevalence of CTS in this population was 8.2 % (91 of 1,115). After adjustment for age and BMI, the OR for each of the fifteen work factors analyzed ranged from 0.87 for bending/twisting the back (CI: 0.54, 1.41) to 1.7 for working overhead (CI: 1.06, 2.72). The latter was the only work factor statistically significantly associated with CTS. For each work factor, the analyses compared the ORs for CTS among participants rating that factor as a moderate-major problem versus those rating the factor as no problem or a minor problem. As has been described for several other studies, age and BMI seemed to have higher magnitude associations with CTS than did occupational factors. A model containing both age and BMI yielded OR = 4.9 (CI: 2.4, 10.0) for the highest versus the lowest quartile of BMI and OR = 4.12 (CI: 2.1, 8.1) for the highest versus the lowest quartile of age. Unfortunately, no estimates for age and BMI were presented for models that also contained work factors.

This study was conducted within a fairly young population, ranging from 18 to 53 years but with an average age of 27 years. CTS prevalence tends to increase with age. Therefore, independent of workplace exposures, this represents an otherwise low-risk group, which might increase the likelihood of identifying work-related factors associated with CTS. However, the exposure assessment method used in this study represents its major weakness. The self-ratings and the apparent wording of the questionnaire items suggests that participants might apply the highest ratings to those work activities that caused the most symptom aggravation, rather than to those activities bearing an etiological association with symptoms.

Thomsen et al. [22] completed a short-term (six to 18 months) prospective study of 731 employees at three worksites in Denmark. Cases were defined at the two follow-up contacts by a sequential process of

- reporting symptoms on a mailed questionnaire,
- positive findings at a clinical interview, and
- NC tests.

Only the "questionnaire cases" were invited to the clinical interview, and only the cases suspected after the interview underwent NC tests. In this section, we report results for the two combination case definitions. Findings for the questionnaire cases are reported below, in the "symptoms only" section. Occupational exposures were individually assessed at baseline. All jobs at the three participating worksites were categorized after walk-through assessments into

- repetitive,
- forceful,
- repetitive and forceful, and
- varied.

Participants reported hours per week spent in each task observed at their worksite. In addition, the investigators made individual measurements of handled weights, finger movements and cycle times, and all participants underwent goniometer measurement while performing work tasks.

At baseline, there were 35 CTS cases in the working hand and 22 cases in the non-working hand, based on symptoms plus clinical interview. Of these, eight working hand and two non-working hand cases were confirmed by NC testing, yielding an estimated prevalence of 1.4 % and 0.4 %, respectively. The annual incidence of cases identified by symptoms plus interview was 3.82 % per year in the working hand and 2.29 % in the non-working hand. When the more restrictive case definition was used, the annual incidence of CTS was 0.27 % for both hands.

Since there were no significant differences between exposure groups in incidence by symptoms plus clinical interview, and since the incidence of cases identified by additional NC testing was so low, the authors focused on analyzing prevalent cases for this report. After controlling for age, gender, BMI and seniority, hours of repetitive work per week and hours of forceful work per week were associated with CTS. For symptoms plus interview cases, the adjusted OR for repetitive work compared to varied work was 1.27 (CI: 1.01, 1.61) for the working hand and 1.25 (CI: 0.93, 1.68) for the non-working hand. Similar estimates were obtained for hours of forceful work per week, OR = 1.12 (CI: 0.86, 1.48) for the working hand, and OR = 1.34 (CI: 1.01, 1.87) for the non-working hand. For cases confirmed by NC, each hour of repetitive work per week was associated with an 84 % increase in the OR for CTS in the working hand (OR = 1.84, CI: 1.06, 3.19). The two NC cases in the non-working hand were not analyzed separately.

As with several other studies discussed in this section, the major strength of *Thomsen* et al. [22] is the detailed, individual-level exposure assessment. However, the short follow-up interval and relatively small study size limits the utility of these data and allows for only a cross-sectional analysis. Among epidemiological designs, cross-sectional studies generally offer the least possibility for causal inference, as they are plagued by uncertain temporal associations as well as the possible action of selection biases, particularly by factors that might favour the inclusion of less severe cases in occupational groups. However, to acquire sufficient information to analyze CTS incidence, the authors calculated that 4,000 person years in the exposed and unexposed groups would be necessary to detect a relative risk of 2.0 with 80 % power and a type I error rate (alpha level) of 5 %.

Andersen et al. [23] investigated CTS among 6,943 computer users in Denmark participating in the baseline and one-year follow-up assessment of the Neck and Upper Extremity Disorders Among Technical Assistants (NU-DATA) study. This group represents about 60 % of the target population of 9,480 members of a trade union. At baseline, cases were identified by symptom reports and clinical interviews; after one year, new cases were identified from among the participants with no or mild symptoms at baseline. Information on personal characteristics and work exposures, including hours per week using a keyboard and mouse and in non-computer work tasks, posture-related variables and work-related psychosocial factors, was collected via questionnaire.

The baseline prevalence of interview-confirmed CTS was 4.8 % (n = 255). Logistic regression models describing the association between work factors and prevalent CTS were adjusted for psychosocial work characteristics (high demands, low control, low social support, and time pressure) and personal factors (negative affect, type A behaviour, age, gender, high or low BMI, poor social network, high physical activity, medical disorder, and smoking). Among the work factors analyzed, mouse use in categories above ten hours per week was associated with a statistically significant two- to three-fold increase in ORs for CTS, and participants reporting dissatisfaction with their work place design had 70 % increased ORs for CTS (CI: 1.1, 2.6). Point estimates for all other work factors (arm/wrist support during mouse use, hours per week of keyboard use, arm/wrist support during keyboard use, abnormal mouse or keyboard positions, poor adjustment of work chair or desk) were between 0.7 and 1.1.

At follow-up, 198 participants reported new or worsened CTS symptoms, and 41 of these were confirmed by clinical interview. Logistic models for incident CTS were adjusted for the same personal and psychosocial work factors listed above. As was seen for prevalent CTS, mouse use in categories of hours per week above ten was associated with a two- to three-fold increase in odds of incident CTS. Although the 95% CI for all categories were fairly narrow, only those for 20 to 25, 25 to 30 and more than 30 hours per week (the three highest categories) excluded one. Participants who reported using arm/wrist supports up to half the time while doing mouse work had OR = 1.5 (CI: 0.7, 3.3). Point estimates for all other work factors were approximately 1.0, and no CI excluded 1.0.

Although the types of exposures considered by *Andersen* et al. [23] were quite different from those evaluated by *Thomsen* et al. [22], it is interesting to note that these two prospective studies reported risk estimates for work factors of similar magnitude, and that were much lower than the estimates reported from the case-control and cross-sectional studies. It should also be noted, however, that the exposure assessments used in the two prospective studies were probably less precise than the individual-level exposure assessments used in the other studies summarized in this section. Misclassification of exposure, if non-differential, tends to result in risk estimates biased towards the null.

The large number of people included and the prospective design of the NU-DATA study represent its two main strengths. However, one year of follow-up seems not to be long enough to detect a sufficient number of new CTS cases to accurately assess risk factors for incident disease: Only 41 people reported new or worsening CTS after one year. Since the logistic regression model employed by the authors included 15 covariates and up to eight indicator variables describing work exposure categories, the analyses certainly suffered from low statistical power. The validity of the results is also threatened by differential participation in the one-year follow-up for participants with and without symptoms at baseline: 39 % of participants who were symptom-free at baseline were lost to follow-up, compared to 26 % lost among those with the most frequent symptoms at baseline. The differential participation rate suggests selection bias that might serve to overestimate the true effects at follow-up, due to preferential inclusion of those with symptoms.

3.2 CTS identified by combination definitions: nine limited studies

There were nine limited studies which used combination definitions to identify CTS. *Werner* and colleagues published two studies describing a cohort of about 700 employees at six worksites in the U.S. [14; 24]. Five were manufacturing facilities in different industries, and the sixth worksite contributed clerical staff. Jobs from three of the industrial sites were rated by industrial engineers and hygienists as consisting of high, medium or low levels of repetitive movements. The ratings were applied to all jobs in all sites, presumably on the basis of job title. For about half of the jobs represented in the cohort, force and posture measurements were also obtained. In addition, psychosocial work factors were assessed via self-administered questionnaire at two of the industrial sites and at the clerical worksite.

Werner et al. [24] describe the baseline cross-sectional analyses conducted to assess the factors associated with abnormal NC test results and prevalent median nerve symptoms. All participants underwent NC testing, and 25 % of the population (n = 184) had results indicating slowing of median NC. Symptoms were assessed by self-administered questionnaires. The prevalence of symptoms among subgroups of participants identified by presence or absence of median nerve slowing was nearly equal: 49.5 % with symptoms, 50.5 % without symptoms.

Job repetition rating was available for all members of the cohort and was statistically significantly higher among those with symptoms compared to those without symptoms (average rating of 5.8 versus 4.5 on a 10 point visual analogue scale, $p = 0.002$). Several other ergonomic and psychosocial work factors were also statistically significantly associated with the presence of symptoms, but these measurements were only available for half the cohort and the authors presented insufficient information for a reader to assess the presence of bias (e. g., no information about the distribution of cases among the subset with data). A logistic regression analysis on the factors that were available for all participants yielded an OR for repetition rating of 1.2 (CI: 1.05, 1.37). Gender was also a statistically significant predictor of symptoms among those with abnormal NC tests; OR = 2.9 (CI: 1.5, 5.8) for women versus men.

After 17 months of follow-up, the incidence of hand/wrist symptoms was assessed among the subset of participants who, at the baseline examination, had positive NC tests but were free of nerve symptoms [14]. Participants were matched on age, gender, and worksite. Five of the original six worksites, including the clerical site, were represented in the follow-up analysis. Cases were identified by self-reported symptoms using a mailed questionnaire.

Of those participating in the follow-up, 49 had positive NC test results at baseline (exposed), and 59 had normal NC test results (unexposed). Although the exposed and unexposed were matched on several characteristics, only the results of unconditional analyses were reported, and these indicated little or no difference in the rate of development of symptoms for the two groups:

12 % of the exposed (n = 6) and 10 % of the unexposed (n = 10). An under-powered logistic regression model indicated positive associations between the development of median nerve symptoms and both job repetition rating (OR = 1.35, CI: 1.03, 1.77) and months of follow-up (OR = 1.19, CI: 1.04, 1.36), and an inverse association between symptom development and the peak latency of the median sensory nerve in the right hand (OR = 0.27, CI: 0.05, 1.32). The model also contained terms for BMI (OR = 1.07, CI: 0.92, 1.24) and median sensory nerve amplitude in the right hand (OR = 0.94, CI: 0.87, 1.02). The authors did not comment on the expected association between the various nerve conduction measures, or on the effect of including both measures in the same model.

Given the lack of a "gold standard" diagnostic tool for CTS, the basic study design employed by *Werner* et al. represents an important innovation and acknowledges the lack of information available as to the correspondence between abnormal NC test results and the presence or development of problematic hand/wrist symptoms.

Unfortunately, this study was hampered by the small number of cases and use of inappropriate statistical methods. These factors render the results difficult to interpret. In addition, the loss to follow-up was higher among participants with abnormal NC tests at baseline (35 % versus 22 %). The authors did not state the method of follow-up contact; if through the workplace, then a higher proportion of the group with abnormal NC tests at baseline might have left their jobs due to the development of symptoms compared to those who had normal NC tests at baseline. If so, this would lead to an underestimate of the association between NC tests and development of median nerve symptoms. The use of unconditional statistical techniques with matched data would also result in an underestimate of any effect evaluated.

Atroshi et al. [9] completed a community-based cross-sectional study in southern Sweden. Two-thousand, four-hundred and sixty-six persons responded to a questionnaire eliciting symptom reports and details on occupational activities. Three hundred and fifty-four respondents (14 %) reported median nerve symptoms; 262 of these (74 %) participated in a clinical examination and NC testing, as did 125 asymptomatic respondents.

Among the population as a whole (not just those participating in the clinical exam), CTS identified by the presence of symptoms and NC test results was statistically significantly more common among blue-collar (3.5 %) than white-collar (1.7 %) workers. The authors reported that the difference in CTS prevalence remained statistically significant after adjusting for BMI, age, and gender, but did not present any specific estimates. Other work factors (use of force with the hand more than one hour per day, working with flexed or extended wrist, repetitive hand or wrist motion, and use of hand-held vibrating tools) were similarly associated with higher prevalence of CTS. However, the authors did not report the results of any adjusted analyses of these exposures.

Gorsche et al. [25] conducted a prospective analysis of CTS among 665 employees of a Canadian meat packing plant. Cases were identified by the combination of self-reported symptoms and clinical signs (Phalen's or Tinel's tests). Jobs were categorized according to whether hand-held tools were required; the jobs that did require tools were described as highly repetitive (cycle time less than 30 seconds or continuous hand movement for over half of a task cycle).

The prevalence of CTS at baseline was estimated at 37 % of the population (n = 244). Employees without CTS at baseline were re-examined at two intervals of just under one year, each; the combined incidence was 11 %. The only occupational characteristic analyzed by these authors was hand-held tool use. The association between tool use and prevalent CTS was statistically significantly positive in a model that included age, BMI, gender, and ethnicity; but the point estimate was not reported. The model describing risk of incident CTS did not include any occupational factors.

Gorsche et al. offer useful prevalence and incidence estimates for one industry, but the failure to report work exposure data limits the utility of this study for the current purpose of identifying occupational risk factors for CTS. In addition, there were some problems with study execution. The initial response rate among employees of the plant was relatively low, at 73 %. Only 55 of the original 665 participants had supervisory or clerical jobs; if this represents the total group of non-tool users, then the authors' ability to analyze work factors was substantially limited. Unfortunately, the study groups were not described clearly enough to determine if this was or was not the case. The prospective study design allowed for an assessment of CTS incidence rates, but high rates of loss to follow-up at each contact point and low initial participation rates by clerical personnel both suggest selection bias might have played a role in the results.

Roquelaure et al. [26] conducted a one-year follow-up study among shoe factory employees in France. Individual level exposures were assessed via questionnaire and work station analyses in which eleven separate factors were assessed. Additional information was collected by questionnaire regarding psychosocial factors, health history, and leisure time physical activities. Cases were identified by symptoms and clinical exam findings.

The prevalence of CTS at the baseline examination was 16.6 % (33 of 199). Nineteen new cases of CTS were identified at the follow-up examination, and performance of rapid trigger movements with hand tools was found to be statistically significantly associated with CTS incidence (OR = 3.8, CI: 1.0, 17.2). This was the only objectively assessed factor associated with the outcome. The model also contained indicators for BMI above 30 kg/m^2 (OR = 4.4, CI: 1.1, 17.1); psychological distress indicated by scoring above the 90th percentile on the 12-item General Health Questionnaire[2] (GHQ-12) (OR = 4.3, CI: 1.0, 18.6); and lack of individual job control (OR = 0.5, CI: 0.2, 1.3). Categories of age and indicators for female gender and the inability to take breaks were also included in the model, but the authors reported their associations were not statistically significant and omitted the point estimates.

While generally quite well-planned and executed, there were two important limitations to this study: First, there was insufficient variability in ergonomic exposures in the study population to be able to detect gradients in risk, since all participants were exposed to at least one of the items included in the work station assessment; and 93 % had highly repetitive jobs (work cycles less than 30 seconds and/or at least half the cycle repeating the same motions). Second, too few incident cases accrued after one year to allow for thorough statistical analysis. In addition, the average duration of employment was about 20 years, suggesting that the study population might be weighted towards individuals less susceptible to CTS.

Hamann et al. [10] surveyed 1,079 dentists attending a national meeting in the U.S. Just under 3 % of the participants were diagnosed with CTS based on median nerve symptoms and NC tests demonstrating median nerve latencies of 0.5 milliseconds or longer. Although the authors collected data on a substantial number of potential covariates, only bivariate descriptions were presented. For example, participants meeting the case definition for CTS were, on average, about six years older than those without CTS (55.2 versus 49.4 years) and had been in practice for about six years longer

[2] A measure of current mental health used extensively in different settings and countries.

(27.5 versus 21.4 years). The lack of controlled analyses limits the utility of the results of this study.

Stevens et al. [11] surveyed 257 computer users employed in a U.S. medical center. Cases were identified by self-reported symptoms and NC test results. CTS prevalence rates were compared for computer versus typewriter users. No differences in CTS prevalence were observed between these two occupational groups, but only the results of descriptive analyses were reported.

Anton et al. [27] recruited dental hygienists attending an ergonomics conference in the U.S. to complete a survey and undergo NC testing. The survey elicited demographic information, ergonomic work factors, work load, symptoms of job-related pain, and hand symptoms. A hand diagram was also included to evaluate specific median nerve symptoms. The authors evaluated CTS identified by symptoms alone (discussed below) and the combination of symptoms and positive NC tests.

The response rate to the questionnaire was 100 % of 109 conference attendees. Due to time constraints, only 89 of 95 (93 %) female hygienists underwent NC testing. The prevalence of CTS by the combination of symptoms and NC tests was 8.4 % (n = 8 cases). No bivariate or multivariate analyses could be carried out with such a small number of cases.

This study was limited due to the recruitment of subjects during a professional conference about ergonomics. While this assured a good response rate, conference participants might have been more likely to be affected by or aware of musculoskeletal disorders than their non-conference attending peers (selection bias). With 93 % reporting at least one work-related musculoskeletal symptom, there was little or no possibility of detecting an association between symptoms and work factors. The study also suffered from inadequate statistical power. Not only were too few cases detected by these authors (n = 8) for any multivariable analyses to be carried out, a post-hoc power analysis indicated only 51 % probability of rejecting the null hypothesis with the number of participants included.

Werner et al. [13] described the results of a cross-sectional study of female dental hygienists attending an annual meeting in the U.S. The prevalence of CTS among study participants, assessed by symptoms and NC tests, was compared to the prevalence among the general population of Sweden as well as the subset of the population working in white-collar occupations. Nine of 305 participants (2.95 %) were identified as cases, defined as having median sensory nerve latency of 0.8 milliseconds or longer in the dominant hand. This was similar to the rate reported for both comparison groups (2.7 % and 1.7 %, respectively). The small number of cases among the participants precluded any detailed analysis.

3.3 CTS identified by symptoms: three adequate studies

Three adequate studies identified CTS by symptoms only. The well-done study by *Latko* et al. [18] is described in detail, above. After controlling for age, gender, and wrist shape (ratio of depth to width), the authors reported that repetitiveness of work was statistically significantly associated with prevalence of CTS (OR = 1.16, CI: 1.00, 1.34 per unit of repetition; OR = 2.32, CI: 1.07, 4.99 for high versus low repetition). In the same multivariable model, the participants with a ratio of wrist depth to width 0.73 or more had OR = 2.59 (CI: 1.35, 4.96) compared to those with ratio less than 0.73.

As summarized above, *Thomsen* et al. [22] identified CTS cases using symptoms reported on a mailed questionnaire. There were 70 cases in the working hand and 44 cases in the non-working hand reported at baseline in a cohort of 731 Danes employed at a bank and two postal centres. After controlling for age, gender, BMI, and seniority, the odds of CTS were statistically significantly increased by 20 to 30 % with each ten hour per week increase in repetitive (OR = 1.21, CI:1.01, 1.46) and forceful work (OR = 1.28, CI: 1.08, 1.52). Due to the small number of incident cases, the authors were only able to analyze prevalent CTS.

Andersen et al. [23] studied a wide distribution of both mouse and computer use in a cohort study of computer users (above). A self-administered questionnaire was sent to 9,480 members of a Danish trade union, with responses received from 6,943 (73 %)

at baseline and 5,658 (82 %) at the one-year follow-up. Respondents answered questions about symptoms, work-related physical and psychosocial factors, and personal characteristics.

The overall self-reported prevalence of tingling or numbness in the right hand at baseline was 10.9 %. The proportion with prevalent CTS was reduced to 4.8 % when clinical confirmation was required. About 1/3 of respondents (1.4 %) experienced symptoms at night. Tingling or numbness in the right hand was associated with time spent using a computer mouse, but not time spent using a keyboard. No posture or psychosocial variables were associated with CTS symptoms, but participants who were dissatisfied with their physical workplace design had slightly elevated odds of CTS symptoms compared to those without complaints (OR = 1.6, CI: 1.2, 2.1). Female gender, smoking, older age, and some medical conditions were also associated with slightly increased ORs for prevalent CTS symptoms.

After one year of follow-up, mouse use for more than 20 hours per week was associated with incidence of possible CTS. The OR for 20 to 25 hours per week of mouse use was 2.6 (CI: 1.2, 5.5), and OR = 3.2 (CI: 1.3, 7.9) for 25 to 30 hours of mouse use per week. Mouse use for more than 30 hours per week had OR = 2.7 (CI: 1.0, 7.6). In addition, being female, having a medical disorder, and smoking were also related to the development of possible CTS.

Overall, the study was comprehensive and well-described. There were some problems with differential rates of loss to follow-up, however: The proportion of those lost was highest among participants with no symptoms and lowest among those who reported more frequent symptoms at baseline. The study was also somewhat limited by the modest number of cases, only 166 at baseline and 173 at one year. This accounts for the relatively large CIs in models including up to eight exposure categories.

3.4 CTS identified by symptoms: three limited studies

There were three limited studies which identified CTS by symptoms only. *Lalumandier* et al. distributed 6,320 surveys to U.S. Army military and civilian dental personnel to assess the number of hand symptoms, job information, and healthcare utilization for hand problems. Ethnicity, age, gender, years in the current job, military or civilian status, and number of patients treated per week was also collected [28; 29]. Over 5,000 questionnaires (response rate = 80.9 %) were returned with complete information, and the number of symptoms reported was used to group respondents into three categories describing the likelihood of CTS.

The overall prevalence of CTS was 25.4 %. Among all dental professionals responding to the questionnaire, dental therapy assistants had the highest rate of hand problems (86 %) and probable CTS (73 %) identified by three or more symptoms of median nerve entrapment. Of the dental hygienists responding, 75 % reported some hand problem and 57 % had probable CTS. Increased age was positively associated with the development of hand problems. For respondents younger than 25 years, 13.7 % reported probable CTS; the proportions increased to 22.8 % (25 to 34 years); 28.4 % (35 to 47 years); and 34.3 % (45 years and older). Women were more likely to report CTS symptoms compared to their male counterparts (33.4 % versus 19.1 %).

These studies were clearly designed and had an excellent response rate, thorough discussion and results tied to the existing literature. Unfortunately, the authors provided descriptive analyses only, and there was no consideration of confounding in spite of the availability of data.

The prevalence of CTS among dental hygienists was also assessed by *Anton* et al. [27]. These authors used a cross-sectional design and recruited 95 dental hygienists at a continuing education conference in the U.S. Subjects completed a self-administered questionnaire and were considered CTS cases if they reported at least "moderate" symptoms of numbness, tingling, burning or aching, and shaded two of the four fingers in the median nerve distribution of either hand in a diagram. In addition, symptoms must have occurred sometime in the past 12 months, been present for at least one month, and have occurred while practicing as a dental hygienist.

Approximately 93 % of the dental hygienists stated that they had at least one job-related ache, pain, or discomfort in the 12 months prior to the survey. The majority of these were in the wrist/hand region (69.5 %). The overall prevalence of CTS based solely on symptoms was 44.2 % and decreased to 23.2 % if a more conservative definition including nocturnal symptoms was included. No additional analyses were performed using the symptoms only definition. Details about the strengths and limitations of this study can be found above.

3.5 CTS identified by nerve conduction test results: one adequate study

Only one study rated as adequate defined cases on the basis of NC test results in the absence of symptoms or clinical exams. The adequately rated study by *Latko* et al. [18] included this outcome definition in addition to symptoms, only, and the combination of symptoms and NC test results; study details can be found in the combination definition section. The prevalence of CTS based on NC test results was 24 % in this industrial cohort. After excluding 16 of 352 participants with diabetes, the authors found no trend in the association between CTS based on NC test results and repetition level. The prevalence was 26.8 % for those in low repetition jobs, 16.4 % for medium repetition jobs, and 25 % for those in high repetition jobs. None of 52 ergonomic factors considered by these authors were associated with abnormal NC test results in a multiple logistic regression model controlling for age, gender, wrist shape, and BMI.

3.6 CTS identified by nerve conduction test results: two limited studies

There were two studies rated as limited which defined cases based on NC test results alone. In the study by *Kutluhan* et al. [30], rated as limited, 70 Turkish carpet weavers were compared to 30 housewives using a cross-sectional design. Data on age at beginning work, length of employment, and amount of work produced per year were collected for each weaver. The authors queried for CTS symptoms and examined for Tinel's, Phalen's, and reverse Phalen's signs, sensory loss and atrophy of the thenar eminence, but limited their case finding to NC tests. A distal latency difference of greater than 0.5 milliseconds between the median and ulnar sensory nerves was considered indicative of CTS. Participants with slowing of the median sensory conduction velocity and delayed distal motor latency were regarded as severe cases; those with slowing of the median sensory conduction velocity, only, were considered as moderate cases; and those with normal median sensory conduction velocities but greater than 0.5 milliseconds distal latency difference between median and ulnar sensory nerves were regarded as mild CTS cases.

In their analyses, the authors treated each hand independently, and found 31 (22.1 %) with CTS among the weavers. There was severe involvement in 11, moderate involvement in six, and mild involvement in 14 hands. Among the controls, CTS was present in four hands, bilaterally in one, and unilaterally in two persons. All cases were mild. Carpet weaving was associated with an OR of 3.3 (CI: 1.23, 8.9) compared to controls. There was no correlation between CTS and employment duration or amount of work produced per year. However, in the CTS positive group (31 hands), there was a positive correlation between the amount of work produced per year and the severity of CTS ($r = 0.639$, $p = 0.014$).

This study has two main limitations. First is the selection of the study population. It is not clear how weavers were identified and invited to participate, nor was the response rate stated. Likewise, selection criteria for the ten "healthy housewives" were not specified. Second, evaluation of potential confounders was not adequately described. The authors collected a large amount of data about symptom prevalence, physical examination results, employment duration, age, etc., but these factors were not sufficiently used or described in the analyses. These factors limit the interpretability of the study results.

In the second study, *Liu* and colleagues [31] studied 45 frequent computer users (6 to 8 hours per day). CTS was defined as: median digit II and ulnar digit V sensory latency difference of greater than 0.4 ms; median distal motor latency greater than 4.0 ms; and median sensory velocity less than 40 m/sec. In addition to NC, subjects completed a questionnaire to gather information about age, dominant hand, employment duration, severity of symptoms and any painful sensation in the involved hands. Pain severity was measured using a visual analogue scale. Wrist angle measurements (the exposure of interest) were determined by goniometry during work activities.

In their analysis, the authors treated each hand (n = 90) independently. NC findings were consistent with CTS in 15 of 90 hands. This included seven dominant hands, two non-dominant hands, and six hands bilaterally. There was no significant correlation between CTS development and duration of employment, but a significant positive correlation was found between wrist angle while typing and motor latency. In addition, there was a significant negative correlation between wrist angle and median sensory velocity. The authors concluded that "the larger the wrist angle when typing on a keyboard, the higher the risk of developing CTS." Wrist angle extension of greater than 20 degrees was defined as "large." The clinical severity of wrist pain was also significantly correlated with both motor latency and sensory conduction velocity in this study.

The main limitations of this paper stem from its cross-sectional design and inadequate data analysis. Although information on a variety of potential confounders was collected, no multivariate analyses were described. No firm conclusions can be drawn from this work.

3.7 CTS identified by clinical exam findings: two adequate studies

There were two studies of adequate quality that used clinical examination findings as the only criterion for diagnosis of CTS.

Leclerc et al. [32] used a cross-sectional design to evaluate 1,547 workers from 53 different companies. The work was considered "repetitive" by the authors and included assembly line, clothing and shoe industry, and the food industry. A total of 39 occupational physicians participated by establishing a list of about 50 workers each, 40 of whom were exposed to repetitive work and ten controls not exposed to repetitive work. Each participant completed a self-administered questionnaire inquiring about demographics, co-morbid conditions, job characteristics, and psychosocial measures. In addition, each participant underwent a standardized clinical exam. CTS was considered to be present if either Tinel's sign or Phalen's test was positive, or if a definite diagnosis based on nerve conduction velocity had been established before the medical examination.

One thousand, two hundred and ten subjects were classified by the occupational physician as engaging in repetitive work. The remaining 337 were workers with a similar distribution of age and gender, who worked in the same company but did not have repetitive work. A total of 151 hands were diagnosed with CTS; these were found in 11.8 % of respondents with repetitive work and 2.4 % of controls. In a logistic regression model, neither age nor gender was associated with CTS. Job sector was associated with CTS, with the highest ORs observed for those employed in packaging (OR = 6.55, CI: 3.02, 14.2). Psychosocial health was related to CTS such that increasing numbers of psychological problems were related to increased ORs for CTS. The highest category (out of 3) had OR = 2.32 (CI: 1.48, 3.63). Finally, compared to those with BMI less than 27, respondents with BMI between 27 and 31 had OR for CTS = 2.16 (CI: 1.35, 3.45), and those with BMI greater than 31 had OR = 1.91 (CI: 1.09, 3.37).

In a second logistic model, the authors added several work-related variables, including work satisfaction, need to press with the hand, job control, and cycle time. This model yielded almost no statistically significant findings, except for BMI greater than 26 (OR = 2.16, CI: 1.41, 3.29), psychological problems (OR = 2.32, CI: 1.40, 3.82), and cycle time of less than ten seconds (OR = 1.90, CI: 1.04, 3.48).

In a third logistic model, the authors included sex, age, BMI, psychological problems, job sector, need to press with the hand, job control, and "just in time" inventory practices. Those with BMI greater than 26 and psychological problems again showed increased ORs for CTS. In addition, low job control had OR = 1.59 (CI: 1.04, 2.43), and "just in time" inventory had OR = 2.24 (CI: 1.40, 3.57).

While the definitions of CTS and "repetition" were somewhat poorly described, they were consistently applied across many companies and industries. The analyses were thorough and thoughtful, although there were too many parameters in some of the models for only 127 cases. The findings were consistent with the literature and also added to existing knowledge by modelling job factors across companies and industries.

The same cohort was followed after three years with a questionnaire and physical examination by *Leclerc* et al. [33]. During that interval, 57 new cases of CTS were identified among the 467 participants free of CTS at baseline (incidence = 12.2 %). Industrial sector, age group, and number of other upper-limb disorders were not related to the development of CTS. For men, work factors related to the development of CTS were "tighten with force" (OR = 4.09, CI: 1.43, 11.7) and "hold in position" (OR = 3.59, CI: 1.06, 12.1). For women, the only factor associated with the development of CTS was an increase in BMI since baseline of more than 2 kg/m^2 (OR = 2.38, CI: 1.04, 5.47).

The poorly described definitions of CTS and "repetition" were problematic at follow-up as they were in the initial report for this study. The diversity of participants allowed for analysis of job factors, physical characteristics, and psychosocial problems. Though these studies would be substantially strengthened by a more complete description of case ascertainment and exposure measures, they are still able to add to our understanding of CTS.

3.8 CTS identified by Worker's Compensation claims: two limited studies

Two studies of limited quality described CTS using Worker's Compensation (WC) claims as a case-finding technique. The first, by *Silverstein* et al. [34], examined the claims incidence rate, cost and industry distribution of work-related upper extremity disorders in Washington State. The authors abstracted WC claims filed between 1987 and 1995 from a state-wide database and categorized them into general and specific disorders of gradual and sudden onset.

On average, 3,132 WC claims for CTS were submitted annually during the study period. There were 2,918 individuals involved, yielding a yearly claim rate per 10,000 full time equivalents of 27.3. The largest claims incidence rates per 10,000 workers were as follows: shake mills (216 per 10,000), seafood canneries (188), meat/poultry dealers-wholesale (169), creameries (165), meat products manufacturing (139), meat dealers-wholesale (133), wallboard insulation (131), aluminium smelting (127), roofing (117), and logging (116).

This study provides an unbiased estimate of the number of work-related CTS claims in Washington State over time. Unfortunately, information on only the most severe cases is provided by this data source, as workers were required to have sought medical care and filed a WC claim to be included in the sample. Controlled analyses were not possible due to the use of administrative data, so confounding is quite likely to have affected the results.

The second study using WC claims was conducted by *Davis* et al. [35]. The authors used physician case-reports and WC disability claims to document patterns of work-related CTS in Massachusetts from March 1992 through June 1997. Work-related CTS was identified in 4,836 cases. Nineteen percent were identified through physician reports, only; 75 % through WC claims, only; and 6 % of cases were identified from both sources.

Overall, there were 4.0 cases per 10,000 employees, and 70 % of cases were women. The incidence of claims for CTS increased with age from 1.4 among those under age 25 years to 6.0 among those aged 45 to 54 years. Industry sector was related to the rate of CTS cases per 10,000, including: agriculture (2.4), mining (5.5), construction (2.5), manufacturing (8.6), transportation (4.0), wholesale trade (3.4), retail trade (3.4), finance/insurance/real estate (3.3), services (2.4), and public administration (2.6). The rate of CTS cases was lower for those in white-collar (e. g. managerial and professional specialty: 1.0 per 10,000) versus blue-collar (e. g. operators and labourers: 7.7 per 10,000) jobs. The industries with the highest case rates included aircraft and parts manufacturing: 26 per 10,000; fabricated textile products manufacturing: 24.5 per 10,000; and scientific and controlling instrument manufacturing: 24.2 per 10,000.

The use of WC claims and physician surveillance provides an excellent estimate of burden of occupational CTS by industry and job category for the Commonwealth of Massachusetts. Again, however, these estimates are likely to include only the most severe cases, as reports are supplied by specialty physicians and are limited to persons with at least five days lost from work. In addition, confounding is likely as the authors provided descriptive analyses, only.

3.9 CTS identified by prior CT release surgery or physician diagnosis: one adequate study

One study rated as adequate identified CTS on the basis of prior CT release surgery or physician diagnosis. *Rossignol* et al. [36] used a cross-sectional design to study the rates of CTS release for adults 20 to 64 years of age on the island of Montreal, Canada, for 12 months in 1993 to 1994. The number of surgical cases within demographic categories was compared to the 1991 population census for Montreal, so annual surgical incidence rates could be calculated. In addition, surgical patients were identified by 20 plastic surgeons participating in the study. These subjects were interviewed about their CTS symptoms, any diagnostic testing, co-morbidities, job tasks, and functional limitations prior to surgery.

There were 969 surgeries during the study period, yielding a rate of 0.9 per 1,000 adults in the population. The majority of cases (74 %) were women. The highest rates were found for women aged 45 to 54 years (2.4 per 1,000 compared to 0.7 per 1,000 for males in the same age group). Two hundred and thirty-eight surgical patients met the inclusion criteria for interview, and 94 % of them reported having had at least one diagnostic test prior to surgery. Half the patients reported experiencing symptoms for at least two years prior to surgery. Functional limitations prior to surgery included difficulties with: carrying grocery bags (51 %), unscrewing the cap of a jar (43 %), carrying a full cup (30 %), writing (28 %), and holding a telephone receiver (27 %). Of all the patients interviewed, 53 % reported that when their symptoms first began, they had a job with physically demanding tasks for the hands and wrists. Work demands included the use of force, vibrating hand-held power tools, or exposure to cold. Forty percent reported the presence of a medical condition known to be associated with the development of CTS.

For manual workers, the standardized incidence rate (SIR) for surgical CT release was 1.8 (CI: 1.4, 2.2) for women and 1.9 (CI: 1.4, 2.5) for men. The highest risk was identified for those in housekeeping occupations, including commercial and domestic categories (SIR = 7.2, CI: 2.8, 13.4 and SIR = 67.2, CI: 17.3, 148.0; for women and men, respectively). The second highest risk group was data processors (SIR = 3.1, CI: 1.0, 6.3 for women and SIR =11.2, CI: 1.1, 31.8 for men). "Data processor" was the only job category among all clerical occupations that showed an increased incidence of CT release. Among participants in material handling occupations, the SIR for women was 6.0 (CI: 2.2, 11.8) and the SIR for men was 5.5 (CI: 1.4, 12.3).

This study capitalized on the broad accessibility of medical care in Canada and was enhanced by the inclusion of a majority of surgeons performing CT release in Montreal. The major strength of this study was its use of census data to calculate incidence rates and SIRs. However, the ability to evaluate and control for confounding, except for age and gender, was limited by the reliance on administratively collected data. In addition, the occupational categories used were broad, and exposure categories were based only on job titles. These factors suggest residual confounding and misclassification of exposure, respectively, might have influenced some of the reported results.

3.10 CTS identified by prior CT release surgery or physician diagnosis: one limited study

There was one limited study which identified CTS on the basis of prior CT release surgery or physician diagnosis. *Dryson* et al. [37] identified 964 patients referred to an occupational physician for CTS in New Zealand. The patients were categorized according to occupation, and their distribution was compared with the general population distribution of occupational categories. For women, CTS cases were more likely than women in the general population to be identified as working in clerical occupations (RR = 1.78, CI: 1.03, 3.07), or to be manual labourers in industry (plant/ machine operators, RR = 2.83, CI: 01.21, 6.62; labourers, RR = 2.70, CI: 1.22, 5.98). For men, the CTS cases were more likely than their general population counterparts to be identified as working in trades (RR = 3.55, CI: 1.88, 6.68). As with the other studies summarized in this section, the usefulness of these results is limited by the lack of information on potential confounders or effect modifiers. However, all of these studies may be considered hypothesis-generating tools that draw attention to particular industries or jobs that might be targeted for closer examination in the future.

4 Discussion

A large amount of research on the association between occupation and CTS has been completed since 1997. Much of this work has been of high quality and represents substantial methodological improvement over the six cross-sectional studies identified as the best available by NIOSH in their 1997 review [5]. For example, the literature now includes a number of prospective studies, and many authors have attempted to employ individual level exposure measures. Careful definitions and descriptions of both exposure and outcome measures have also added to the quality of the available literature.

The NIOSH panel identified three occupational exposures as potentially related to CTS: force, repetition, and vibration. Posture was also considered by the panel, but the evidence for a connection with CTS was deemed "insufficient". In Table 7 (see page 86) we summarize the evidence provided by the eleven best quality studies included in the current synthesis with respect to occupational exposures identified by NIOSH.

Three studies addressed the association between forceful movements and CTS [16; 20; 22]. All three employed a combination technique for identifying cases of CTS that included at least self-reported symptoms and NC test results, but none of the exposure measures were comparable. The largest magnitude estimate, OR = 9.0 (CI: 2.4, 33.4), resulted from the smallest of the three studies and the only one employing the case-control design. The estimate was adjusted for gender, parity (among women), and other occupational exposures. This was also the only one of the three studies that employed individual level exposure assessments using job-task analyses: exposed employees were defined as those who lifted tools and materials in excess of one kilogram. Cases reported symptoms and had either a positive clinical examination or positive NC test results [16].

Nathan et al. [20] observed participants at work at a baseline contact point, and rated each job along a five-point scale describing the consistency of use of force (0 = not at all, 5 = consistent). These ratings were used to categorize participants eleven years later. The authors reported a negative association between the rating and risk of CTS identified by symptoms plus NC test results (OR = 0.75, CI: 0.21, 2.72) after controlling for cigarette smoking, age, gender, non-white race, BMI, leisure activity, presence/absence of hormone use or endocrine conditions, duration of employment, and several other work exposures.

Thomsen et al. [22] reported a 40 % increase in odds for CTS with each ten hour increment of forceful work per week (OR = 1.41, CI: 0.86, 2.30) after adjustment for hours of repetitive work, age, gender, seniority, and BMI. Exposure categories were based on questionnaire data, and cases were identified from symptom reports, clinical exam, and NC test results. When the authors re-defined cases based only on symptoms, the effect was reduced to OR = 1.28 (CI: 1.08, 1.52), although the number of cases in the working hand increased from eight to 70.

Although the evidence provided by the NIOSH 1997 review [5] and these three studies generally supports a positive association between forceful movements and CTS, the lack of comparability of the exposure metrics and the wide range of effect estimates reported leave this conclusion open to question.

Repetitive actions were measured by cycle times in several studies [16; 18; 20 to 22; 32]. The reported effect estimates were of similar magnitude, ranging from OR = 1.14 (CI: 1.00, 1.34) per unit of exposure based on a five-point rating scale for cases based on symptoms only [18] up to OR = 1.90 (CI: 1.01, 3.48) for clinically diagnosed CTS among those with jobs involving cycle times of ten seconds or less compared to those whose operations lasted one minute or more [32]. An unusually high effect estimate, OR = 8.8 (CI: 1.8, 44.4), was provided by *Roquelaure* et al. from their case-control study with individual level exposure assessment and cases based on a combination of symptoms and either clinical exam findings or NC test results [16]. Each of these estimates was controlled for a variety of occupational and non-occupational factors.

Taken together with the material reported in the 1997 NIOSH review [5], the epidemiological evidence is limited in quantity, but appears to consistently indicate a small positive association between repetitive actions and the risk of CTS.

The 1997 NIOSH panel reported weak evidence in favour of a positive association between occupational exposure to vibrations and CTS [5]. Only one of the 11 studies rated adequate in the current review addressed this exposure. The 11 year follow-up study reported by *Nathan* et al. identified cases of CTS based on self-reported symptoms and NC tests. Based on individual observation, jobs that were classified as entailing exposure to vibration were found to be positively associated with risk of CTS (OR = 3.73, CI: 1.04, 13.33) [20]. This represents an addition to the body of epidemiological evidence in favour of an association between vibration and CTS, but the evidence as a whole is insufficient for a firm conclusion to be reached.

The evidence available in 1997 was deemed by NIOSH to be insufficient for determining whether or not an association exists between wrist postures (flexion) and risk of CTS [5]. We identified one adequate study that addressed this exposure. *Frost* et al. [17] compared slaughterhouse with chemical plant employees. CTS cases were defined on the basis of either symptoms alone, or symptoms combined with NC test results, and job tasks were analyzed to assess the frequency of wrist movements out of the neutral position. Slaughterhouse employees were found to work in non-neutral positions "a substantial part of the time", and to be at increased risk of CTS relative to chemical factory employees. However, wrist posture, per se, was not assessed as an independent determinant of CTS. We conclude that no additional evidence for or against a connection between CTS and wrist posture has become available since 1997.

None of the other occupational activities that were evaluated in the best quality studies were assessed in a sufficient number of investigations for any conclusion about the evidence for or against an association with CTS to be reached. Pressing with the hand, computer keyboard use, and changes in activity during the work day/job rotation were each evaluated in two studies. Grip type, manual work station supply, holding items in position, computer mouse use, and de-boning work were each evaluated in one study. Even if of excellent quality, single studies or pairs of epidemiological studies cannot provide sufficient evidence to either establish or reject an association between work activities and CTS. An additional question that remains open is that of the association between CTS and combinations of any of the four major occupational exposures discussed here, e. g., work that is both repetitive and forceful.

5 Summary

Our conclusions are based on a review of the epidemiological literature that was published in either the English or the German language since 1997. Three-hundred and thirty-four studies were screened for content, and the 34 that addressed the association between CTS and occupational exposures were assessed for quality. The final quality ratings were based primarily on study design and analysis methods.

Papers rated “Adequate” were free of major bias; residual confounding was unlikely to have substantially influenced the results; there was reasonably complete ascertainment of cases and adequate exposure assessment. “Limited” studies were free of major bias, but residual confounding might have influenced the results; there was reasonably complete ascertainment of cases and reasonable exposure assessment methods were used. “Inadequate” studies were judged likely to be substantially influenced by major bias, or residual confounding was likely to have influenced the results; or the study outcome was not specifically carpal tunnel syndrome.

Among the 27 studies rated either “adequate” or “limited”, we found substantial methodological improvements over the work as summarized in [5]. These improvements include the use of stronger analytical study designs in addition to the cross-sectional design, and the use of individual-level or group-level job task analyses to assess exposure. For example, several of the best studies included in this review used prospective research methods [20; 22; 23; 33], which offer the best support for causal associations among epidemiological methods. Unfortunately, all but one of the prospective studies employed follow-up intervals of less than two years, which limited the number of incident cases available for analysis.

Studies published prior to 1997 generally used exposure categories based on job title, occupation, or industry. This technique offers a general impression of high-risk jobs or industries, but is likely to result in substantial misclassification of exposure because job, occupation and industry serve as surrogates for more specific tasks.

The best of the more recent investigations employed individual level task analyses or used detailed task assessments for representative jobs that were generalized to employees in the same or similar job categories. We recognize that group level job task analyses may result in misclassification of exposure due to inter-individual variability in task performance. However, the degree of misclassification is likely to be less than that arising from the use of broader categories, such as occupation.

Even with these methodological improvements, the key issue yet to be fully addressed is the definition of CTS, itself. The lack of a "gold standard" diagnostic technique represents a major hurdle to be overcome. Nerve conduction (NC) tests are considered the most objective measure of median nerve entrapment. However, the lack of overlap between cases identified by NC tests compared to other methods, and the low predictive value of abnormal NC tests among asymptomatic individuals followed over time, suggest the need for improvements in medical diagnostic techniques. Any future original research or literature review of risk factors for CTS must address the fact that the prevalence, incidence, and risk factors for CTS, as well as the practical impact of the disease on patient populations, will depend strongly on the case definition used.

As of 1997, repetition, force, vibration, and wrist posture (flexion) were judged to be potentially related to the risk of occupational CTS [5]. Based on our review of the English and German language epidemiology literature published between 1997 and 2003, we conclude that there is consistent evidence for a small, positive association between repetitive work and CTS. The evidence for an association between CTS and forceful work is weak and of questionable validity, and there is insufficient evidence for a conclusion to be drawn about the existence or direction of an association between CTS and occupational exposure to vibration, work in non-neutral wrist postures, or combinations of work exposures.

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7 Annex: Tables

List of Tables

Table 1:
Summary of criteria for evaluating study quality[1)]

Study attribute	**Criteria**
Study objectives	Clearly stated, relevant to research questions
Study methods	Adequately described, appropriate for objectives minimize selection and information bias
Outcome measurement	Well-defined, reasonably specific, accurate measurement or diagnosis, proper time frame for risk of outcome
Exposure measurement	Individual level data (vs. ecologic), direct quantitative measurements (vs. indicators), account for changes over time
Control of confounding	Known risk factors considered and measured, reasonable method(s) used (stratification, multi-variate)
Interpretation	Consider alternative explanations, assess potential for and magnitude of bias, reasonable statistical power

1) *Sulsky* et al. 2002 [38]

Table 2:
Characteristics of 34 studies of carpal tunnel syndrome (CTS) and occupation

First author (Year)	Study population	Country	Comparison	Design	Size[1]	Gender
Abbas (2001) [19]	Electronics manufacturing facility employees	Egypt	Internal	Cross-sectional	198	Both
Andersen (2003) [23]	Danish Association of Professional Technicians	Denmark	Internal	Cohort	6,943	Both
Anton (2002) [27]	Dental hygienists attending a professional conference	United States	Internal	Cross-sectional	95	Women
Atroshi (1999) [9]	Age- and gender-stratified population random sample	Sweden	Internal	Cross-sectional	2,466	Both
*Bekkelund** (2001) [39]	Cleaners	Norway	Secretaries	Cross-sectional	83	Women
*Budak** (2001) [40]	Carpet weavers in a single company	Turkey	Undefined internal control group	Cross-sectional	47	Women
*Cosgrove** (2002) [41]	Railroad employees suing for compensation for CTS	United States	None	Cross-sectional	900	Men
Davis (2001) [35]	All cases of work-related CTS reported to the SENSOR program and all WC claims[2]	United States	None	Cohort	4,836	Both
*Diaz** (2001) [42]	Nurse anaesthetists	United States	Operating room nurses	Cross-sectional	244	Women
Dryson (2001) [37]	Patients referred to an occupational physician for CTS	New Zealand	General population	Cross-sectional	2,647	Both
Frost (1998) [17]	Slaughterhouse employees	Denmark	Chemical plant employees	Cohort	1,141	Both
Gorsche (1999) [25]	Meat packing employees who worked >1 month	Canada	Internal	Cohort	665	Both
Hamann (2001) [10]	Dentists attending one ADA meeting in 1997 or 1998[3]	United States	Internal	Cross-sectional	1079	Both
*Hess** (1997) [43]	State agency employees who routinely use computers	United States	Internal	Cross-sectional	274	Both
Kutluhan (2001) [30]	Carpet weavers	Turkey	Healthy housewives	Cross-sectional	100	Women

Table 2 (continued):

First author (Year)	**Study population**	**Country**	**Comparison**	**Design**	**Size[1]**	**Gender**
Lalumandier (2000) [28]	U.S. Army military and civilian dental personnel	United States, Panama, Europe, Asia	Internal	Cross-sectional	5,115	Both
Lalumandier (2001) [29]	U.S. Army military and civilian dental hygienists	United States, Panama, Europe, Asia	Internal	Cross-sectional	177	Both
Latko (1999) [18]	Employees of 3 manufacturing facilities	United States	Internal	Cross-sectional	352	Both
Leclerc (1998) [33]	Employees in 4 sectors exposed to repetitive work	France	Internal	Cross-sectional	1,547	Both
Leclerc (2001)	Employees who participated in a baseline study 1993-94	France	Internal	Cohort	598	Both
Liu (2003) [31]	Frequent computer users randomly selected from hospital departments	Taiwan	Internal	Cross-sectional	45	Unknown
Nathan (2002) [20]	Employees in 4 industrial sites in March to October 1984	United States	Internal	Cohort	471	Both
Roquelaure (1997) [16]	Television, shoe and auto-mobile brake production employees	France	Internal	Case-control	130	Both
Roquelaure (2001) [26]	Footwear assembly employees	France	Internal	Cohort	199	Both
Rosecrance (2002) [21]	Construction apprentices	United States	Internal	Cross-sectional	1,142	Both
Rossignol (1997) [36]	Patients with CTS release	Canada	General popula-tion of Montreal	Cross-sectional	238	Both
Silverstein (1998) [34]	Washington state employed population	United States	None	Cohort	26,262	Both
Stevens (2001) [11]	Computer users	United States	Internal	Cross-sectional	257	Both
Thomsen (2002) [22]	Employees of a bank and two postal centers	Denmark	Internal	Cohort	731	Both
Werner (1997) [14]	Employees at 5 manufacturing sites and 1 clerical site	United States	Internal	Cohort	154	Both

Table 2 (continued):

First author (Year)	**Study population**	**Country**	**Comparison**	**Design**	**Size**[1]	**Gender**
Werner (1998) [24]	Employees at 5 manufacturing sites and 1 clerical site	United States	Internal	Cross-sectional	724	Both
Werner (2002) [13]	Dental hygienists attending ADHA meeting in Washington, DC[4]	United States	Clerical and industrial workers	Cross-sectional	305	Women
*Yagev** (2001) [44]	Patients referred for electro-physiological tests	Israel	Other examinees in the clinic	Case-control	396	Both
*Zetterberg** (1999) [45]	Car assemblers	Sweden	Internal	Cross-sectional	564	Both

[1] Total sample size: (exposed plus unexposed) or (cases plus controls)

[2] SENSOR: Massachusetts (US) Sentinel Event Notification System for Occupational Risks.
WC: Workers' Compensation

[3] ADA: American Dental Association

[4] ADHA: American Dental Hygiene Association

* Study was rated inadequate for inclusion in critical review.

Table 3:
Design details for 34 studies of carpal tunnel syndrome (CTS) and occupation

First author (Year)	Case definition(s) [1)]	Details	Investigator blinded?	Participation rate
Abbas (2001) [19]	Sx + NC + Exam	Sx: self-reported pain and/or paresthesia NC: < 42 msec [2)] + normal f-test and/or delay of > 4.2 sec	Not clear	> 90 %
Andersen (2003) [23]	1. Sx + Exam 2. Sx only	Baseline Sx: tingling/numbness > 1 per week in last 3 months; Sx at night Follow-up Sx: Tingling/numbness in right hand >1/week in last 3 months	Yes	70 to 79 %
Anton (2002) [27]	1. Sx + NC 2. Sx only	Sx: numbness, burning, tingling or aching, and 2/4 fingers of median nerve distribution of either hand NC: median-ulnar difference ≥ 0.5 msec or median motor latency ≥ 4.4 msec.	No	> 90 %
Atroshi (1999) [9]	Sx + NC	Sx: Nocturnal and/or activity-related pain, numbness, tingling in 2/4 fingers NC: Median ulnar sensory latency difference ≥ 0.8 msec	Yes	80 to 89 %
*Bekkelund** 2001) [39]	NC only	Vibratory, warm-cold and heat-pain detection thresholds	Yes	Not stated
*Budak** (2001) [40]	NC only	Median sensory latency > 3.7 msec, median motor latency > 4.4 msec	No	Not stated
*Cosgrove** (2002) [41]	NC only	Motor median-ulnar difference > 1.2 msec Sensory median-ulnar difference > 0.6 msec Mid-palmar median-ulnar difference > 0.4 msec	No	> 90 %
Davis (2001) [35]	Worker's Compensation Claim or physician diagnosis	Not applicable	Yes	Database study
*Diaz** (2001) [42]	Sx + Exam or history of CT release	Sx: Nocturnal hand pain, hand pain diagram Exam: Positive Tinel's sign and Phalen's test	Yes	< 70 %
Dryson (2001) [37]	Physician diagnosis	Not specified	Not applicable	> 90 %

Table 3 (continued):

First author (Year)	Case definition(s) [1)]	Details	Investigator blinded?	Participation rate
Frost (1998) [17]	Sx + NC or prior CT release	Sx: ≥ 1 night per week, ≥ 3 fingers NC: Distal-motor latency ≥ 4.3 msec or conduction velocity < 50 msec for at least 1 of sensory median finger nerves and sensory conduction velocity ≥ 50 msec in ulnar nerve	Yes	70 to 79 %
Gorsche (1999) [25]	Sx + Exam	Sx: Pain/numbness lasting > 1 week and positive Tinel's or Phalen's sign	No	70 to 79 %
Hamann (2001) [10]	Sx + NC	NC: Median latency ≥ 0.5 msec or 0.8 msec Sx: Numbness, tingling or pain	No	Not stated
*Hess** (1997) [43]	Sx only	Numbness/tingling/pain in fingers, hands, wrists or arms and decreased hand strength and upper back pain and neck and/or shoulder pain	Yes	< 70 %
Kutluhan (2001) [30]	NC only	Mild: Normal sensory conduction, but > 0.5 msec distal latency difference, median-ulnar sensory nerve Moderate: Slowing of median sensory conduction Severe: Slowing of median sensory conduction *and* delayed motor distal latency.	No	Not stated
Lalumandier (2000) [28]	Sx only	≥ 3 of: Pain at night, tingling, clumsiness, activity-induced symptoms, and swelling	No	80 to 89 %
Lalumandier (2001) [29]	Sx only	≥ 3 of: Pain at night, tingling, clumsiness, activity-induced symptoms, and swelling	No	> 90 %
Latko (1999) [18]	1. Sx only 2. NC only 3. Combination	Sx: Hand diagram NC: Ulnar-median nerve latency difference ≥ 0.5 msec	Yes	Not stated
Leclerc (1998) [32]	Exam or previous NC	Exam: Positive Tinel's sign or Phalen's test	No	Not stated
Leclerc (2001) [33]	Exam	Sx: Not specified Exam: Positive Tinel's sign or Phalen's test	No	80 to 89 %
Liu (2003) [31]	NC only	Median digit II and ulnar digit V sensory latency must differ by greater than 0.4 ms; median distal motor latency must be greater than 4.0 ms; median sensory velocity must be less than 40 m/sec	No	Not stated

Table 3 (continued):

First author (Year)	Case definition(s) 1)	Details	Investigator blinded?	Participation rate
Nathan (2002) [20]	Sx + NC OR prior CT release	Sx: Presence of hand/wrist symptoms, undefined NC: Not specified	No	< 70 %
Roquelaure (1997) [16]	≥3 of: Sx, NC, Exam, prior CT release	Sx: ≥3 of tingling, pain/numbness, worse at night ≥ 20 times or lasting ≥ 3 weeks Exam: Positive Tinel's and Phalen's or hypoesthesia NC: Sensory or motor conduction velocity < 40 msec	Yes	Not stated
Roquelaure (2001) [26]	Sx and/or Exam	Sx: Paresthesia, pain, or numbness ≥ 1 week or ≥ 10 times during the last year Exam: Tinel's or Phalen's or diminished sensation	Not stated	80 to 89 %
Rosecrance (2002) [21]	Sx + NC	Sx: Numbness, tingling, pain and/or burning NC: Median mononeuropathy latency difference ≥ 0.5 msec	Yes	80 to 90 %
Rossignol (1997) [36]	Surgery for CTS release	Not applicable	No	< 70 %
Silverstein (1998) [34]	Worker's Compensation claim	Not applicable	Not applicable	Database study
Stevens (2001) [11]	1. NC only 2. Sx + NC	Sx: Awakened by paresthesia; hand goes to sleep; relieved by shaking NC: Median mid-palmar latency > 2.2 msec or median-ulnar palmar latency difference > 0.4 msec	Yes	80 to 89 %
Thomsen (2002) [22]	Sx + NC Sx only	Sx: Tingling, "CTS symptoms reported" NC: Sensory conduction velocity < 50 msec or abnormal median-distal motor latency vs. controls	Yes	70 to 79 %
Werner (1997) [14]	Sx + NC	Sx: Pain, numbness, tingling, or burning in the hand or fingers > 1 week or 3+ times since initial screening NC: Median sensory latency ≥ 0.5 msec or ≥ 0.8 msec	Unclear	70 to 79 %
Werner (1998) [24]	Sx + NC	Sx: Not specified NC: Median sensory evoked response ≥ 0.5 msec or ≥ 0.8 msec	Unclear	Not stated

Table 3 (continued):

First author (Year)	Case definition(s) [1)]	Details	Investigator blinded?	Participation rate
Werner (2002) [13]	Sx + NC	Sx: Numbness, tingling, or pain; hand diagram NC: Median sensory latency ≥ 0.5 msec or ≥ 0.8 msec	No	Not stated
*Yagev** (2001) [44]	NC Only	Median sensory latency ≥ 3.9 msec or motor latency ≥ 4.5 msec	Yes	Not stated
*Zetterberg** (1999) [45]	Sx + Exam	Sx: Numbness Exam: Tinel's or Phalen's test	No	< 70 %

1: Sx = Median nerve symptoms; NC = Nerve conduction; Exam = clinical examination, possibly including Tinel's sign or Phalen's test. Case definitions described, not necessarily reported in analyses.

2: msec = milliseconds

* Study was rated inadequate for inclusion in critical review.

Table 4:
Exposure assessments used in 34 studies of occupation and carpal tunnel syndrome (CTS)

First author (Year)	**Exposure**			**Comment**
	Classi-fication	**Assessment method**	**Metrics**	
Abbas (2001) [19]	Qualitative	1. Observation, job task analysis 2. Industrial Hygiene – ergonomic measurement at the individual level	1. Likelihood of exposure based on group level measurement 2. Ranking based on individual measurements	Jobs were characterized according to weight lifted, pace, and grip type needed. Work stations were measured for each person. Years of work also used as an exposure measure.
Andersen (2003) [23]	Quantitative	Self-report via questionnaire/interview	Time in task	Tasks included overall computer use and mouse and keyboard use separately.
Anton (2002) [27]	Semi-quantitative	Self-report via questionnaire/interview	Time in task	Clinical practice variables included years of work as dental hygienist, days worked per week, patients per day. Time spent doing specific dental procedures (probing, scaling, flossing, etc.) was also quantified.
Atroshi (1999) [9]	Semi-quantitative	Self-report via questionnaire/interview	Job category (white- or blue-collar) and job task descriptors	Job task descriptors were use of excessive hand force, excessive wrist flexion/ extension, repetitive hand or wrist motion, and vibratory tool use.
*Bekkelund** (2001) [39]	Qualitative	Cleaners compared to secretaries	Years at work	Both cleaners and secretaries worked at least 19 hours/week for 3 or more consecutive years.
*Budak** (2001) [40]	Qualitative	Weavers compared to non-weavers		Mean years worked by weavers was 8.4 years.
*Cosgrove** (2002) [41]	Semi-quantitative	Self-report via questionnaire/interview	Likelihood of exposure based on group level measurement	Used the *Silverstein* method to classify jobs into force/repetition categories.
Davis (2001) [35]	Qualitative	Industry sector and occupational category		Classification of industry and occupation based on information in physician case reports and workers' compensation records.

Table 4 (continued):

First author (Year)	Exposure			Comment
	Classi-fication	**Assessment method**	**Metrics**	
*Diaz** (2001) [42]	Qualitative	Self-report via questionnaire/interview	Likelihood of exposure based on group level measurement	Nurse anaesthetists vs. operating room nurses
Dryson (2001) [37]	Qualitative	Occupational group		Occupational groups were managers, professionals, technicians, clerical, sales/service, agriculture, trades, plant/machine operators, and labourers.
Frost (1998) [17]	Qualitative	1. Self-report via questionnaire/interview 2. Observation, job task analysis	1. Likelihood of exposure based on group level measurement 2. Frequency of wrist movements out of neutral position	Slaughterhouse vs. chemical factory employees
Gorsche (1999) [25]	Qualitative	Self-report via questionnaire/interview	Likelihood of exposure based on group level measurement	Unclear: exposure assess-ment might have been based on job title. These included production workers, supervisors, and administrative staff.
Hamann (2001)	Semi-quantitative	Self-report via questionnaire/interview	Time in task	Hours worked per week and weeks worked per year
*Hess** (1997) [43]	Semi-quantitative	Self-report via questionnaire/interview	Mean perceived stress score (PSS) and percep-tion of having ergonomi-cally correct work station (Likert scale).	Other variables were perceived knowledge of prevention of repetitive strain injuries and whether was action taken to improve workstation.
Kutluhan (2001) [30]	Semi-quantitative	1. Occupational group 2. Self-report via questionnaire/interview	Employment duration, amount produced per year, and began work	Carpet weavers vs. housewives
Laluman-dier (2000) [28]	Qualitative	1. Occupational group 2. Self-report via questionnaire/interview	1. Dental subspecialties 2. Job characteristics	Job characteristics included number of patients with heavy calculus, job satisfac-tion, and time in practice.
Laluman-dier (2001) [29]	Qualitative	Self-report via questionnaire/interview	Likelihood of exposure based on group level measurement	

Table 4 (continued):

First author (Year)	Exposure			Comment
	Classi-fication	Assessment method	Metrics	
Latko (1999) [18]	Semi-quantitative	Observation, job task analysis	Likelihood of exposure based on group level measurement	Visual analog scale to rate job stress (0 = no stress, 10 = most stress). Repetition measured by how busy the hands were during the work cycle, accounting for recovery time within cycle and hand speed. Ratings applied to videotaped workers.
Leclerc (1998) [32]	Qualitative	Observation, job task analysis	Likelihood of exposure based on group level measurement	Occupational physician enrolled subjects based on judgment about repetitive nature of work.
Leclerc (2001) [33]	Qualitative	Job title	Likelihood of exposure based on group level measurement	"Workers whose occupations required repetitive work".
Liu (2003) [31]	Quantitative	Observation	Goniometric measure of wrist flexion	The maximum extension of wrists during work was measured, and the data were recorded as an average of 3 measures.
Nathan (2002) [20]	Qualitative	1. Observation, job task analysis at baseline 2. Self-report via questionnaire/interview at subsequent follow-ups	Likelihood of exposure based on group level measurement	Occupational hand use assessed by direct observation in 1984 and stratified into 5 categories based on relative intensity of force, repetition, and presence of keyboard tasks. At subsequent follow-ups, the presence of vibration and additional information regarding intensity of occupational hand use was gathered with 5-point Likert scales.
Roquelare (1997) [16]	Semi-quantitative	1. Industrial hygiene – ergonomic measures at the individual level 2. Work station used 6 months prior to diagnosis (for cases) or at the end of 1992 (for controls)	Time in task	Work classified as repetitive if cycle time < 30 seconds and high force if prehensive efforts >1 kg. Work defined as continuous if breaks and secondary tasks < 15 % of job duration.

Table 4 (continued):

First author (Year)	**Exposure**			**Comment**
	Classi-fication	**Assessment method**	**Metrics**	
Roquelare (2001) [26]	Semi-Quantitative	1. Self-report via questionnaire/interview 2. Industrial hygiene – ergonomic measures at the individual level	Ranking based on indi-vidual measurements	Ergonomic factors included job rotation, work cycle time, repetitive movement patterns, rapid trigger movements, hand vibra-tion, and wrist flexion/ extension.
Rosecrance (2002) [21]	Qualitative	1. Job title 2. Self-report via questionnaire/interview	1.Likelihood of exposure based on group level measurement 2. Perceived contribution of 15 job factors to musculoskeletal injury (0-10 scale)	Main comparison across the following apprentice trades: electricians, sheet metal workers, operating engineers, and plumbers.
Rossingnol (1997) [36]	Qualitative	Self-report via questionnaire/interview	Likelihood of exposure based on group level measurement	Classified case occupation via interview. Denominators for each occupation from Canadian Census.
Silverstein (1998) [34]	Qualitative	Occupation and industry as reported by physician	Likelihood of exposure based on group level measurement	Denominators for each occupation from Washing-ton State Department of Labor and Industries.
Stevens (2001) [11]	Semi-quantitative	Self-report via questionnaire/interview	Time in task	Occupational variables included hours/day, years using keyboard and type-writer, and frequency of mouse use.
Thomsen (2002) [22]	Semi-quantitative	1. Self-report via questionnaire/interview 2. Observation, job task analysis	Likelihood of exposure based on group level measurement	Jobs at one bank and two postal centers classified as repetitive, forceful, repeti-tive and forceful, or varied.
Werner (1997) [14]	Semi-quantitative	Industrial hygiene – ergo-nomic measurement at the group level	Likelihood of exposure based on group level measurement	Employees in jobs meant to represent the range of tasks within each industry were recruited into the study. The jobs were videotaped and the tapes assessed by an Industrial hygiene team for levels of repetition.

Table 4 (continued):

First author (Year)	**Exposure**			**Comment**
	Classi-fication	**Assessment method**	**Metrics**	
Werner (1998) [24]	Qualitative	1. Industrial hygiene – ergonomic measurement at the group level 2. Self-report via questionnaire/interview	Likelihood of exposure based on group level measurement	Industrial engineers and hygienists rated repetition, hand force, wrist/forearm posture, and contact stress after viewing videotape of each job category. Ratings were made on a visual analog scale.
Werner (2002) [13]	Qualitative	Self-report via questionnaire/interview	Time in task	Years as hygienist, hours/week and weeks/year worked.
*Yagev** (2001) [44]	Qualitative	Self-report via questionnaire/interview	Likelihood of exposure based on group level measurement	Jobs were categorized as high/low force and high/low repetition. The criteria for categorization was not detailed.
*Zetterberg** (1999) [45]	Qualitative	1. Self-report via questionnaire/interview 2. Observation, job task analysis	Likelihood of exposure based on group level measurement	Details of the job/ergo-nomic factors assessed were not provided.

* Study was rated inadequate for inclusion in critical review.

Table 5:
Covariate data collected by the authors of 34 studies of occupation and carpal tunnel syndrome (CTS)

First author (Year)	Covariates collected[1]							
	Age	**Gender**	**BMI[2]**	**Medical factors[3]**	**Exposure level**	**Task**	**Duration of employment**	**Other[4]**
Abbas (2001) [19]	√	√			√	√	√	Marital status, job satisfaction, posture, amount of production
Andersen (2003) [23]	√	√	√	√	√	√		Psychosocial factors, leisure activities, smoking
Anton (2002) [27]	√	√	√	√	√	√	√	Psychosocial factors at work, handedness, hobbies, leisure activities, ergonomic factors; restricted to women
Atroshi (1999) [9]	√	√	√	√				Handedness, social status, education, exercise, smoking, employment activities
*Bekkelund** (2001) [39]	√						√	Skin temperature at testing, alcohol consumption, hand grip strength; restricted to women
*Budak** (2001) [40]						√		Restricted to women with no pre-existing medical conditions
*Cosgrove** (2001) [41]	√		√	√	√		√	Grip strength, leisure activities
Davis (2001) [35]	√	√						Industry sector, occupation
*Diaz** (2001) [42]	√		√			√	√	Restricted to non-obese women, no endocrine disorders
Dryson (2001) [37]		√						Occupation
Frost (1998) [17]	√	√	√	√	√	√	√	Smoking, handedness
Gorsche (1999) [25]	√	√	√	√		√	√	Alcohol, pregnancy, handedness, ethnicity, leisure activities
Hamann (2001) [10]	√	√	√	√	√		√	Hours worked per week and year
*Hess** (1997) [43]	√	√						Ethnicity, education, and dependents

Table 5 (continued):

First author (Year)	Covariates collected[1]							
	Age	Gender	BMI[2]	Medical factors[3]	Exposure level	Task	Duration of employment	Other[4]
Kutluhan (2001) [30]	√			√			√	Restricted to women, amount of work produced per year
Lalumandier (2000) [28]	√	√			√	√	√	Ethnicity, civilian vs. military status
Lalumandier (2001) [29]	√				√		√	Civilian vs. military status
Latko (1999) [18]	√	√	√	√	√		√	Race, education, tobacco use, ratio of wrist depth to width, history of acute injury
Leclerc (1998) [32]	√	√	√	√		√	√	Education, psychosocial work factors
Leclerc (2001) [33]	√	√	√	√	√	√	√	Smoking, psychological symptoms, psychosocial work factors, posture
Liu (2003) [31]	√			√	√		√	Dominant hand
Nathan (2002) [20]	√	√	√	√	√	√		Leisure activity, exercise habit, smoking, race
Roquelaure (1997) [16]	√	√	√	√	√	√	√	Smoking, education, number children in household, alcohol, handedness, non-occupational activities
Roquelaure (2001) [26]	√	√	√	√	√	√	√	Psychosocial, ergonomic factors, leisure activity
Rosecrance (2002) [21]	√	√	√	√	√	√	√	Trade, apprentice level, education, work history
Rossignol (1997) [36]	√	√						Occupational category
Silverstein (1998) [34]	√	√						Industrial classification
Stevens (2001) [11]	√	√			√	√		Occupation, handedness
Thomsen (2002) [22]	√	√	√		√	√	√	Hours worked per week
Werner (1997) [14]	√	√	√	√	√			Handedness, duration of follow-up

Table 5 (continued):

First author (Year)	Covariates collected[1]							
	Age	Gender	BMI[2]	Medical factors[3]	Exposure level	Task	Duration of employment	Other[4]
Werner (1998) [24]	√	√	√	√	√			Education, psychosocial, work organization factors
Werner (2002) [13]	√		√	√	√		√	Type of glove; restricted to women
*Yagev** (2001) [44]	√	√	√	√	√	√		Education, smoking, country of origin
*Zetterberg** (1999) [44]	√	√	√	√			√	Hand grip, wrist diameter, tobacco use, work satisfaction

[1] Covariate information collected, but not necessarily included in the analyses or presented in the report.

[2] BMI: Body Mass Index (ratio of weight to height^2) in kg/m^2

[3] Includes: hormonal status for women; metabolic and endocrine disorders, prior injury, etc.

[4] No study design considered disease latency

* Study was rated inadequate for inclusion in critical review.

Table 6:
Overall quality assessment of 34 studies of occupation and carpal tunnel syndrome (CTS)

First author (Year)	Ascertainment of [1)]		Likelihood of bias			Overall quality
	Cases	Exposure	Selection	Information	Residual confounding	
Abbas (2001) [19]	A	A	Possible: High participation by all invited, but no information about selection for invitation	Unlikely	Possible: Gender included in the model, but too few men in the analysis group	**Adequate**
Andersen (2003) [23]	L	A	Possible: Subjects without symptoms at baseline most likely to be lost to follow-up	Possible: Recall bias, if those with symptoms report computer and mouse use more than those without.	Unlikely	**Adequate**
Anton (2002) [27]	L	A	Possible: Participants recruited at a conference on ergonomics	Possible: Conference was about ergonomics	Likely: No multivariate analyses presented.	**Limited**: Small number of cases, no control or assessment of confounding.
Atroshi (1999) [9]	A	L	Unlikely	Unlikely	Possible: Mainly presented unadjusted results	**Limited**: Exposure assessment limited to blue-/white-collar job. No adjusted results presented.
*Bekkelund** (2001) [39]	L	L	Possible: No data on participation rates	Unlikely	Likely: Differences in tests not adjusted for age, BMI, temperature, or wrist biometrics	**Inadequate**: Outcome was nerve function, not CTS.
*Budak** (2001) [40]	A	L	Possible: Authors did not describe how participants were identified or selected.	Unlikely	Inadequate: no consideration of confounding in the analysis	**Inadequate**: Outcome was not CTS. Control group was not described.

Table 6 (continued):

First author (Year)	Ascertainment of [1)]		Likelihood of bias			Overall quality
	Cases	Exposure	Selection	Information	Residual confounding	
*Cosgrove** (2002) [41]	I	A	Unlikely	Possible: Significant measurement problems including: large hands, temperature variations, rough/calloused hands	Possible: Information on possible confounders not available	**Inadequate**: Significant measurement problems and all subjects were claimants for Worker's Compensation.
Davis (2001) [35]	L	L	Possible: Cases likely to be severe, requiring special care or > 5 days lost from work.	Unlikely	Unlikely	**Limited**: Descriptive analysis only
*Diaz** (2001) [42]	L	I	Possible: Non-responder bias possible. There is no information on participation rate.	Possible: Study initiated in response to CTS cluster	Likely: no confounders considered in analysis	**Inadequate**: Cross-sectional study, unclear why or nurses selected as comparison group. No consideration of confounding and incorrect calculations.
Dryson (2001) [37]	L	A	Unlikely	Possible: Subjects identified in an occupational clinic.	Likely: No adjustment attempted, no information on potential confounders or effect modifiers.	**Limited**: Exploratory research that examined the distribution of broad industry groups among patients in an occupational clinic.
Frost (1998) [17]	A	A	Possible: Fairly low response rate, differential by group	Possible: No formal assessment of work exposures among comparison group	Possible: Comparison group was older and had longer employment history.	**Adequate**

Table 6 (continued):

First author (Year)	Ascertain-ment of 1)		Likelihood of bias			Overall quality
	Cases	Exposure	Selection	Information	Residual confounding	
Gorsche (1999) [25]	L	L	Possible: Differential participation by exposure status. Significant loss to follow-up may be more likely to include injured workers.	Unlikely	Unlikely	**Limited**: Potential for bias and confounding limit confidence in findings; errors in quantifying the study population and methods
Hamann (2001) [10]	A	A	Unlikely	Unlikely	Likely: only bivariate analyses conducted	**Limited**: External validity questionable; no multivariate analysis conducted
*Hess** (1997) [43]	L	I	Likely: poor response rate (44 %)	Unlikely	Unlikely	**Inadequate**: Flawed study with poor case definition
Kutluhan (2001) [30]	A	L	Possible: response rate for carpet workers and source and response rate of controls unknown	Possible: Subjective CTS measurement	Likely: Not clear when covariates adjusted and to what effect	**Limited**: Did not use physical exam findings and control of confounders not adequately described
Lalumandier (2000) [28]	L	L	Unlikely	Unlikely	Likely: descriptive analysis only	**Limited**: No consideration of confounding in analysis, though covariate data were collected
Lalumandier (2001) [29]	L	L	Unlikely	Unlikely	Likely: descriptive analysis only	**Limited**: Exposure assessed by job title: case ascertainment by symptom count
Latko (1999) [18]	A	A	Possible: Participation limited to those with 6+ months work which could impose survivor bias	Unlikely	Unlikely	**Adequate**

Table 6 (continued):

First author (Year)	Ascertainment of [1)]		Likelihood of bias			Overall quality
	Cases	Exposure	Selection	Information	Residual confounding	
Leclerc (1998) [32]	A	A	Possible: Occupational physician chose cases and controls based on estimated work repetitiveness.	Possible: The same physician who recruited subjects performed the exam and interview.	Possible: Only bivariate analysis presented	**Adequate**
Leclerc (2001) [33]	L	A	Unlikely	Unlikely	Possible: Only bivariate analysis presented	**Adequate**
Liu (2003) [31]	A	A	Unlikely	Possible: The same physician who recruited subjects performed the measures.	Possible: Only bivariate analysis presented	**Limited**: No consideration of confounding in analysis, though covariate data were collected
Nathan (2002) [20]	L	A	Possible: Differential loss to follow-up	Unlikely	Possible: Small number of cases suggests the analyses were underpowered.	**Adequate**
Roquelaure (1997) [16]	A	A	Unlikely	Unlikely	Unlikely	**Adequate**
Roquelaure (2001) [26]	A	L	Possible: Average time on the job was > 20 years, possible survivor bias	Unlikely	Possible: Only bivariate analyses presented	**Limited**: Excellent exposure measures but little variability in population
Rosecrance (2002) [21]	A	L	Unlikely	Unlikely	Unlikely	**Adequate**
Rossignol (1997) [36]	L	A	Unlikely	Unlikely	Possible: Exposure category based on broad job categories, not tasks.	**Adequate**

Table 6 (continued):

First author (Year)	Ascertain-ment of [1)]		Likelihood of bias			Overall quality
	Cases	Exposure	Selection	Information	Residual confounding	
Silverstein (1998) [34]	L	A	Unlikely	Unlikely	Likely: No controlled analyses presented	**Limited**: Provides unbiased estimate of the number of Worker's Compensation claims
Stevens (2001) [11]	L	L	Possible: Exclusion criteria not well-explained	Possible: Unlikely explanation for results	Likely: No control of potential confounders	**Limited**: No controlled analyses, prevalence estimates only; poor choice of comparison group
Thomsen (2002) [22]	A	A	Unlikely	Unlikely	Possible: Adequate for prevalent cases but not for incident cases	**Adequate**
Werner (1997) [14]	A	L	Possible: Follow-up rates differential by site and higher if abnormal NC observed at baseline; follow-up symptoms were self-reported.	Unlikely	Likely: Analyses were mainly univariate and the model was unconditional in spite of matched design.	**Limited**: Analyses and sample size were inadequate and follow-up may have been too short for some subjects (range 10 to 24 months).
Werner (1998) [24]	A	A	Possible: Volunteer rate was 45 to 89 % by site. Unclear how recruitment was handled.	Unlikely	Likely: Description of modeling unclear and unable to determine how covariates were coded	**Limited**: Description of modeling unclear and unable to determine how covariates were coded
Werner (2002) [13]	A	L	Possible: Unknown participation rate or criteria	Possible: Tests conducted in dominant hand only – could underestimate CTS.	Likely: Unadjusted prevalence estimates only.	**Limited**: Underpowered, no adjusted or stratified analyses; attempted logistic regression on only 9 cases

Table 6 (continued):

First author (Year)	**Ascertain-ment of [1)]**		**Likelihood of bias**			**Overall quality**
	Cases	**Exposure**	**Selection**	**Information**	**Residual confounding**	
*Yagev** (2001) [44]	A	A			Possible: Sample size likely inade-quate for number of variables in model	**Inadequate**: The nature and reasons for referral are not clear, pool of subjects not well-described nor is the process for catego-rizing exposure
*Zetterberg** (1999) [45]	L	L	Possible: Subjects included only those employees present at the time of evaluation.	Unlikely		**Inadequate**: Analy-ses compared men vs. women, no exposure groups

* Study was rated inadequate for inclusion in critical review.

[1)] Ascertainment of cases/exposure was: A = adequate, L = limited, I = Inadequate

Table 7:
Summary of adjusted estimates of effect of work exposures from 11 studies rated as "adequate"

Exposure	**First author (Year)**	**Design**	**Size**[1]	**Case definition**[2]	**Comparison**	**Effect estimate**
Force						
> 1 kg	*Roquelaure* (1997) [16]	Case-control	130 (65 cases)	Sx+(NC *or* exam)	< 1 kg	OR = 9.0 (CI: 2.4, 33.4)
Consistency rating 1 to 5	*Nathan* (2002) [20]	Prospective (11 years)	471	Sx+NC	Increment per rating unit	OR = 0.75 (CI: 0.21, 2.72)
Hours/week	*Thomsen* (2002) [22]	Prospective (6 to 10 months)	731	Sx+NC+Exam Symptoms	Increment per 10 hours/week	OR = 1.41 (CI: 0.86, 2.30) OR = 1.28 (CI: 1.08, 1.52)
Repetition						
Operation ≤ 10 seconds	*Roquelaure* (1997) [16]	Case-control	130 (65 cases)	Sx+(NC *or* exam)	Operation > 10 seconds	OR = 8.8 (CI: 1.8, 44.4)
Cycle 30 to 59 sec Cycle 10 to 29 sec Cycle < 10 sec	*LeClerc* (1998) [32]	Cross-sectional	1,210	Exam	Cycle ≥ 1 min	OR = 1.03 (CI: 0.56, 1.89) OR = 1.33 (CI: 1.75, 2.37) OR = 1.90 (CI: 1.04, 3.48)
10-point rating scale	*Latko* (1999) [18]	Cross-sectional	352	Sx+NC Symptoms NC	Increment per rating unit	OR = 1.22 (CI: 0.98, 1.53) OR = 1.16 (CI: 1.00, 1.34) Not associated
Consistency rating 1 to 5	*Nathan* (2002) [20]	Prospective (11 years)	471	Sx+NC	Increment per rating unit	OR = 1.14 (CI: 0.59, 2.20)
No variability Hours/week	*Thomsen* (2002) [22]	Prospective (6 to 10 months)	731	Sx+NC+Exam	Varied work Increment per 10 hours/week	OR = 1.84 (CI: 1.06, 3.19) OR = 1.21 (CI: 1.01, 1.46)
Moderate-major problem	*Rosecrance* (2002) [21]	Cross-sectional	1,115	Sx+NC	No or minor problem	OR = 1.54 (0.92, 2.56)
Vibration						
None	*Nathan* (2002) [20]	Prospective (11 years)	471	Sx+NC	Any	OR = 3.73 (CI: 1.04, 13.33)

Table 7 (continued):

Exposure	First author (Year)	Design	Size[1]	Case definition[2]	Comparison	Effect estimate
Tighten with force						
Any	*LeClerc* (2001) [33]	Prospective (3 years)	598	Exam	None	OR = 4.09 (CI: 1.43, 11.7) Men only
Grip type						
Precision Intermediate	*Abbas* (2001) [19]	Cross-sectional	104	Sx+NC+Exam	Power grip	OR = 6.52 (CI: 1.08, 39) OR = 1.98 (CI: 0.32, 11.91)
Changes in activity						
< 15 % of work-time	*Roquelaure* (1997) [16]	Case-control	130 (65 cases)	Sx+(NC *or* exam)	≥15 % of work-time	OR = 6.0 (CI: 1.8, 20.2)
Job rotation						
None	*Roquelaure* (1997) [16]	Case-control	130 (65 cases)	Sx+(NC *or* exam)	Any	OR = 6.3 (CI: 2.1, 21.2)
Manual workstation supply						
Yes	*Roquelaure* (1997) [16]	Case-control	130 (65 cases)	Sx+(NC *or* exam)	No	OR = 5.0 (CI:2.2, 21.2)
Job control						
Low	*LeClerc* (1998) [32]	Cross-sectional	1,210	Exam	High	OR = 1.43 (CI: 0.92, 2.23)
Press with hand						
Yes	*LeClerc* (1998) [32]	Cross-sectional	1,210	Exam	No	OR = 1.41 (CI: 0.92, 2.15)
Yes	*LeClerc* (2001) [33]	Prospective (3 years)	598	Exam	No	OR = 0.28 (CI: 0.09, 0.82), Men only
Hold in position						
Yes	*LeClerc* (2001) [33]	Prospective (3 years)	598	Exam	No	OR = 3.59 (1.06, 12.1) Men only

Table 7 (continued):

Exposure	First author (Year)	Design	Size[1]	Case definition[2]	Comparison	Effect estimate
Mouse use						
2.5 to 4 hours/week	*Andersen* (2003) [23]	Prospective (1 year)	173	Sx+Exam	0 to 2.4 hours/week	OR = 0.7 (CI: 0.3, 1.9)
5 to 9 hours/week						OR = 1.9 (CI: 0.9, 1.9)
10 to 19 hours/week						OR = 1.6 (CI: 0.8, 3.3)
20 to 24 hours/week						OR = 2.0 (CI: 0.9, 4.2)
25 to 29 hours/week						OR = 2.6 (CI: 1.2, 5.5)
30 to 34 hours/week						OR = 3.2 (CI: 1.3, 7.9)
> 30 hours/ week						OR = 2.7 (CI: 1.2, 7.6)
Keyboard use						
Consistency rating 1 to 5	*Nathan* (2002) [20]	Prospective (11 years)	471	Sx+NC	Increment per rating unit	OR = 0.88 (CI: 0.52, 1.47)
2.5 to 4 hours/week	*Andersen* (2003) [23]	Prospective (1 year)	173	Sx+Exam	0 to 2.4 hours/week	OR = 0.9 (CI: 0.4, 1.8)
5 to 9 hours/week						OR = 0.8 (CI: 0.4, 1.5)
10 to 14 hours/week						OR = 1.2 (CI: 1.6, 2.5)
15 to 19 hours/week						OR = 0.8 (CI: 0.4, 1.5)
> 20 hours/week						OR = 1.4 (CI: 0.5, 4.3)
Slaughterhouse work						
Any	*Frost* (1998) [17]	Cross-sectional	1,141	Sx+(NC or Dx)	Chemical workers	OR = 4.24 (CI: 1.77, 10.13)
De-boning						OR = 5.53 (CI: 2.20, 13.90)

[1] Total sample size

[2] Case definitions: Sx+(NC *or* exam) = median nerve symptoms and either positive nerve conduction test or clinical exam. Sx+NC = median nerve symptoms plus positive nerve conduction test. Sx+NC+Exam = median nerve symptoms plus positive nerve conduction test plus positive clinical exam. Symptoms = median nerve symptoms, only. Exam = positive clinical exam, only. NC = positive nerve conduction tests, only.

Table 8:
Conclusions regarding potential risk factors for CTS
(identified by the 1977 NIOSH panel [5])

Potential risk factor	**Number of studies included in review**[1]	**Case identification technique(s)**	**Conclusion**
Repetition	6	Symptoms, clinical diagnosis, combination techniques	Consistent, small, positive association
Force	3	Combination techniques	Weak positive association, questionable validity
Vibration	1	Combination techniques	Insufficient evidence
Posture	1	Symptoms, combination techniques	Insufficient evidence

[1] Number of studies rated "adequate" that considered each of the potential occupational risk factors for CTS identified by the 1997 NIOSH review panel.