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Effects of Varying Case Definition on Carpal Tunnel Syndrome Prevalence Estimates in a Pooled Cohort

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Abstract

Objective: To analyze differences in carpal tunnel syndrome (CTS) prevalence using a combination of electrodiagnostic studies (EDSs) and symptoms using EDS criteria varied across a range of cutpoints and compared with symptoms in both ≥1 and ≥2 median nerve–served digits.

Design: Pooled data from 5 prospective cohorts.

Setting: Hand-intensive industrial settings, including manufacturing, assembly, production, service, construction, and health care.

Participants: Employed, working-age participants who are able to provide consent and undergo EDS testing (N = 3130).

Interventions: None.

Main Outcome Measures: CTS prevalence was estimated while varying the thresholds for median sensory latency, median motor latency, and transcarpal delta latency difference. EDS criteria examined included the following: median sensory latency of 3.3 to 4.1 milliseconds, median motor latency of 4.1 to 4.9 milliseconds, and median-ulnar sensory difference of 0.4 to 1.2 milliseconds. EDS criteria were combined with symptoms in ≥1 or ≥2 median nerve–served digits. EDS criteria from other published studies were applied to allow for comparison.

Results: CTS prevalence ranged from 6.3% to 11.7%. CTS prevalence estimates changed most per millisecond of sensory latency compared with motor latency or transcarpal delta. CTS prevalence decreased by 0.9% to 2.0% if the criteria required symptoms in 2 digits instead of 1.

Conclusions: There are meaningful differences in CTS prevalence when different EDS criteria are applied. The digital sensory latency criteria result in the largest variance in prevalence.

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Carpal tunnel syndrome (CTS) is a common and costly musculoskeletal disorder with annual U.S. costs estimated at $2 billion.1 Prevalence has been estimated at 1.5% to 5.8% in the general population, with higher prevalence rates in specific subpopulations.2-7

The case definition of CTS used in epidemiologic research often includes documentation of dysesthesias in the median nerve distribution of the hand and electrodiagnostic study (EDS) results...
consistent with median nerve mononeuropathy at the wrist. Clinical studies often rely on similar criteria, but they may also use a more detailed medical history, presence of nocturnal symptoms, and additional diagnostic maneuvers. However, diagnostic maneuvers (eg, Phalen or Hoffman-Tinel test) contribute relatively little to the predictive value.

Prior studies have used a variety of criteria for evaluating the slowing of median nerve conduction results consistent with CTS. Nerve conduction outcomes are a continuous measure reported as either latency (ms) or velocity (m/s). Therefore, when using nerve conduction outcomes to distinguish results that are consistent with CTS from those that are not, investigators must select a cutpoint or threshold at which to dichotomize the distributions. Such values have ranged from 3.4 to 4.0 milliseconds for median sensory nerve latencies, 4.0 to 4.6 milliseconds for median motor nerve latencies, and 0.3 to 1.0 millisecond for the median-ulnar nerve sensory latency difference (transcarpal delta).

There appears to be no consensus on optimal EDS criteria for CTS in either epidemiologic or clinical settings. Research is also relatively sparse regarding the impacts of varying EDS criteria on observed disease prevalence.

The purpose of this study was to evaluate the effect of a range of EDS criteria in combination with 2 symptom criteria on observed CTS prevalence in a large population of workers from a wide range of industries and across multiple regions of the United States.

Methods

Study design

Data from 5 prospective cohort studies that used comparable methods and have been previously described were pooled for the current analyses. In short, all studies were prospective cohort studies enrolling workers in a variety of industrial settings. The common objective of these studies was to quantify relations between EDS factors and two case definitions of CTS. These analyses are of cross-sectional baseline symptoms data and relationships between EDS factors and the ipsilateral ulnar sensory nerve across the wrist were collected in the dominant hand on all participants regardless of symptoms at the time of enrollment.

Participants

Study participants were 18 years old, able to provide consent, and currently employed in a broad variety of industrial settings in which the enrolled workers performed a wide range of hand-intensive activities. Industrial settings included manufacturing, production, service, construction, and health care. Data collection for these studies’ baseline enrollments were conducted from 2001 to 2006. A total of 4321 subjects were enrolled.

All studies were approved by the appropriate institutional review board and were performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and all subsequent amendments. All participants provided informed consent prior to participation.

Baseline questionnaires collected information on demographics, medical history, psychosocial factors, work history, and musculoskeletal symptoms. EDSs of the median motor nerve and median sensory nerve and the ipsilateral ulnar sensory nerve across the wrist were collected in the dominant hand on all participants regardless of symptoms at the time of enrollment.

Participants were excluded from these analyses if they were missing baseline symptoms or had invalid EDS latency results (n=856, 19.4%).

Symptoms data collection

Most participants had symptoms recorded by digit in the first (thumb), second (index finger), third (middle finger), and fourth (ring finger) digits. Symptoms in the fifth digit were not used in analyses. In 2 studies, a hand symptom diagram was used to collect symptom location and characteristics in all but the fourth digit (eg, tingling, numbness, pain). In the remaining 4 studies, symptoms were recorded during standard interviews conducted by a medical professional. For the purpose of the current analyses, 2 symptom criteria were applied separately: tingling, numbness, burning, or pain in ≥1 median innervated digit (thumb, index, middle, ring), and these symptoms in ≥2 median innervated digits.

EDS measures

All study sites collected 3 measures often used to characterize median nerve function at the wrist: median sensory latency, median motor nerve latency, and the difference between the median and ulnar nerve sensory latencies across the wrist (transcarpal delta). All sensory latencies were peak measures, and all motor latencies were onset measures. All EDSs were performed unilaterally on the dominant hands. Three study groups used conventional clinical electrophysiology/electromyography equipment (XLTEK NeuroMax 1002, Cadwell 6200A, Teca Synergy N2), and 2 studies used a portable nerve testing device (NC-stat5). The NC-stat has preconfigured sensors on the electrodes to accommodate different hand dimensions. The specific model numbers used were NC-S51, NC-S52, and NC-S53 for small, medium, and large median motor and sensory latencies and NC-S61 and NC-S62 for right and left ulnar motor and sensory latencies, respectively. Each sensor has anatomic locations to facilitate ease of use, and strict cleaning procedure was followed per the manufacturer’s recommendations. The NC-stat has demonstrated agreement with conventional EDS devices for measures of median motor and sensory nerve latencies. EDSs were performed according to standard electrodiagnostic testing protocols. Stratified analyses comparing distributions of symptoms and EDS criteria by study showed no statistically significant differences between electrodiagnostic testing devices across the 5 studies; therefore, all data were pooled into a single dataset for analyses.

Most sensory latency values were measured at the standard distance of 14 cm; however, some hands were too small. If not measured at 14 cm, they were standardized to a 14-cm distance. No motor latencies were corrected. All median sensory measures were antidromic. Skin temperature was measured prior to testing, and hands were warmed to a minimum skin temperature of 30°C to 32°C by 4 of the 5 study groups included in the analyses. Regression analyses were used to adjust latency values to a standard temperature of 32°C as described in a prior publication.

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List of abbreviations:

- CTS: Carpal tunnel syndrome
- EDS: Electrodiagnostic study

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Nominal changes were observed when temperature correction was applied.

**CTS case definitions**

An analysis was conducted by calculating the prevalence of CTS over a range of EDS threshold (ie, cutoff) values in combination with each of the 2 symptom-based criteria: symptoms in ≥1 digits and symptoms in ≥2 digits. Only 1 of the 3 EDS measures was varied at the time, while the others were held constant at an a priori selected reference value. For example, median sensory and median motor latencies were held at 3.7 and 4.5 milliseconds, respectively, whereas the transcarpal delta varied from 0.4 to 1.2 milliseconds, in 0.1-millisecond increments. Consequently, a set of 6 analyses were conducted (ie, 3 EDS criteria by 2 symptom criteria). The reference values used for these calculations were 3.7 milliseconds for median sensory latency, 4.5 milliseconds for median motor latency, and 0.8 millisecond for transcarpal delta latency. These reference values were selected based on criteria commonly used in prior publications.

For the analyses, median sensory latency, median motor latency, and transcarpal delta latency thresholds were each varied separately in 0.1-millisecond intervals up to 0.4 millisecond above and below the reference values, for a total of 9 threshold values each. For example, given the reference value of 3.7 milliseconds for the median sensory latency, the prevalence of CTS was estimated for median sensory latency values ranging from 3.3 to 4.1 milliseconds, in 0.1-millisecond intervals, for each of the 2 symptom-based criteria while holding the reference values for motor latency at 4.5 milliseconds and the transcarpal delta latency at 0.8 millisecond. Similarly, median motor nerve latency values were varied from 4.1 to 4.9 milliseconds, and transcarpal delta latency values were varied from 0.4 to 1.2 milliseconds.

The CTS case definitions used symptoms (eg, numbness, tingling, burning, pain) in either ≥1 or ≥2 digits innervated by the median nerve and the specific EDS criteria previously described. CTS prevalence was also calculated based on EDS criteria used in prior studies to allow for comparison.

**Results**

Data from a total of 3130 participants were included in these pooled analyses. Demographic characteristics of the pooled sample are provided in Table 1. Both sexes were well represented (women: n = 1523, 48.7%), and the mean body mass index (28.5 kg/m²) indicates that a large proportion of participants were overweight or obese. Approximately half (50.3%) were lifelong nonsmokers. Relatively few, 115 (3.7%) and 156 (5.0%), had physician-diagnosed diabetes mellitus or thyroid disorder, respectively.

The estimated prevalence of CTS for each of the 6 analyses is reported in Figure 1 and ranged from 6.3% to 11.7%. As expected, the lowest cutpoint values for sensory latency, motor latency, and transcarpal delta each yielded the highest number of observed cases. Substantial differences in prevalence were observed as each cutpoint value was increased. The largest change in relative prevalence occurred when varying the sensory latency, whereas the smallest change in relative prevalence occurred when varying the motor latency. As expected, the observed CTS prevalence for symptoms in ≥1 digit was between 0.9% and 2.0% higher than the prevalence requiring symptoms in ≥2 digits.

In addition, prior published criteria for EDS thresholds consistent with CTS were applied to the pooled data sample of the current study to calculate CTS prevalence (Table 2). The prevalence rates ranged nearly 2-fold, from 5.9% to 11.6%, depending on the EDS criteria and symptom definition used (eg, ≥1 digit or ≥2 digits).

For reference purposes, the prevalence rates were also calculated using only 1 EDS measure instead of all 3 (eg, sensory, motor, transcarpal delta) (Table 3). The prevalence rates are therefore lower than in Figure 1.

**Discussion**

These results suggest that varying the threshold of the median motor nerve latency or the transcarpal delta latency has less effect, per millisecond of change, on observed CTS prevalence than varying the threshold of the median sensory nerve latency. In this population of industrial workers, changes to the median sensory nerve latency criterion has more than 3-fold greater impact on the observed CTS prevalence than changes to either the median motor nerve latency or transcarpal delta latency. The effects of changing the cutpoints in this study were also not linear. The largest effects were observed over changes to the lower cutpoint values.

Although it is known qualitatively that changes in EDS cutpoints will result in changes in the observed prevalence of CTS, our study findings quantify these effects across a range of values for 3 common EDS metrics in a large and representative sample. To our knowledge, these effects have not been quantified before. These results help to illuminate the extent to which the variability of CTS prevalence reported in the published literature may be solely attributed to differences in CTS case definition criteria.

The estimated prevalence of CTS decreased by between 0.9% and 2.0% when comparing the symptom criterion from paresthesias or pain in ≥1 digits with paresthesias or pain in ≥2 digits, regardless of the EDS criteria used. Few studies evaluating CTS provide sufficient description of case definitions to allow for differentiation between symptoms in ≥1 and ≥2 median nerve–served digits. Most published case definitions of CTS in peer-reviewed research rely on combinations of symptoms in ≥1 of multiple areas, including the fifth digit (not normally innervated by the median sensory nerve) and the hand and wrist.

Analysis of a subset of data where sites reported pain or burning independently of numbness or tingling was performed to evaluate differences in estimated prevalence when including pain

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>37.5±11.9</td>
</tr>
<tr>
<td>Female</td>
<td>1523 (48.7)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>28.5±6.3</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>115 (3.7)</td>
</tr>
<tr>
<td>Thyroid disorder</td>
<td>156 (5.0)</td>
</tr>
<tr>
<td>Smoking Current</td>
<td>956 (30.7)</td>
</tr>
<tr>
<td>Past</td>
<td>601 (19.3)</td>
</tr>
<tr>
<td>Never</td>
<td>1573 (50.3)</td>
</tr>
<tr>
<td>Median sensory latency (ms)</td>
<td>3.48±0.64</td>
</tr>
<tr>
<td>Median motor latency (ms)</td>
<td>3.86±0.75</td>
</tr>
<tr>
<td>Transcarpal delta (ms)</td>
<td>0.42±0.49</td>
</tr>
</tbody>
</table>

NOTE. Values are mean ± SD or n (%).
or burning as a symptom criteria. When using numbness or tingling in the median nerve–served digits alone, there was a reduction of prevalence by 11.5% to 8.7%. Of the prevalent cases in the subset analysis, 2.8% were symptomatic for pain or burning and did not report numbness or tingling in the median nerve–served digits. Therefore, these data suggest that when restricting the case definition to numbness or tingling symptoms, prevalence will decrease by approximately 25%.

**Table 2** CTS prevalence estimates using the study’s pooled data based on previously published EDS criteria

<table>
<thead>
<tr>
<th>Study</th>
<th>Previously Published EDS Criteria</th>
<th>Prevalence in Pooled Study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median Sensory Latency (ms)</td>
<td>Median Motor Latency (ms)</td>
</tr>
<tr>
<td>Uncini et al&lt;sup&gt;13&lt;/sup&gt;</td>
<td>4.2</td>
<td>0.5</td>
</tr>
<tr>
<td>Charles et al&lt;sup&gt;16&lt;/sup&gt;</td>
<td>4.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Seror&lt;sup&gt;17&lt;/sup&gt;</td>
<td>3.4&lt;sup&gt;1&lt;/sup&gt;</td>
<td>4.0&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Stevens&lt;sup&gt;18&lt;/sup&gt;</td>
<td>3.5</td>
<td>4.6&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Jablecki et al&lt;sup&gt;14&lt;/sup&gt;</td>
<td>3.4&lt;sup&gt;1&lt;/sup&gt;</td>
<td>4.1</td>
</tr>
<tr>
<td>Wong et al&lt;sup&gt;19&lt;/sup&gt;</td>
<td>4.0&lt;sup&gt;1&lt;/sup&gt;</td>
<td>4.1</td>
</tr>
<tr>
<td>Wong et al&lt;sup&gt;20&lt;/sup&gt;</td>
<td>3.4&lt;sup&gt;1&lt;/sup&gt;</td>
<td>4.0&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Kimura et al&lt;sup&gt;24&lt;/sup&gt;</td>
<td>3.5</td>
<td>4.5</td>
</tr>
<tr>
<td>Salerno et al&lt;sup&gt;21&lt;/sup&gt;</td>
<td>4.0&lt;sup&gt;1&lt;/sup&gt;</td>
<td>*</td>
</tr>
<tr>
<td>Makanji et al&lt;sup&gt;22&lt;/sup&gt;</td>
<td>3.6</td>
<td>4.4</td>
</tr>
<tr>
<td>Werner et al&lt;sup&gt;12&lt;/sup&gt;</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Armstrong et al&lt;sup&gt;23&lt;/sup&gt;</td>
<td>3.4&lt;sup&gt;1&lt;/sup&gt;</td>
<td>4.4</td>
</tr>
</tbody>
</table>

* No cutpoint listed for this criterion.
<sup>1</sup> Lowest criterion.
<sup>2</sup> Highest criterion.
A study of 1646 hands of 824 workers reported a prevalence of abnormal EDSs of 12.2% when applying a transcarpal delta value of 0.5 millisecond and 5.1% for a transcarpal delta value of 0.8 millisecond. When combined with any symptoms of the wrist, hands, or digits on 3 occasions over the last year, the prevalence of 1.9% (symptoms in 1 digit) and 1.8% (symptoms in 2 digits) observed in our study.

There were large differences in observed prevalence across the EDS criteria used in this study. The difference in prevalence, when varying the sensory latency from 3.3 to 4.1 milliseconds, may have a substantial impact on researchers' abilities to accurately differentiate relations within studies evaluating potential risk factors or treatments for CTS. Selection of EDS criteria with maximum specificity to accurately diagnose true cases while not sacrificing sensitivity is needed. Strict EDS criteria would lead to lower prevalence estimates but may yield more accurate measures of disease than if less stringent EDS criteria were used. Conversely, less stringent EDS criteria will increase case numbers and study power but may lead to more false-positive cases and case misclassification and therefore may result in erroneous conclusions. This difference may partially explain different findings in studies evaluating risk factors for CTS. There also exists the possibility of directional misclassification in either direction, dependent on the criteria and symptoms, therefore allowing for bias. Careful, a priori consideration of the appropriate cutoffs to use, which balance sensitivity and specificity, may have a meaningful impact on study findings.

Additionally, there are meaningful implications regarding prevalence measures of CTS. Differences in EDS criteria and the resulting prevalence may have a meaningful impact on the proportion of those with a positive test result who are truly positive (positive predictive value), the proportion of those with a negative test result who are truly negative (negative predictive value), and the number needed to treat. Other authors have hypothesized that there may be a meaningful difference in case counts depending on the EDS criteria used. Werner and Andary discuss the potential impact of varying EDS criteria. These data quantify these differences in a large population of workers and allow for more direct comparisons between prior published studies.

Much of the literature has focused on the discussion relating to transcarpal delta measurements for the removal of potential intrapersonal variation by using an internal comparison between the median and ulnar nerve. The abnormal classification threshold for this value has increased over time from 0.3 millisecond in the 1980s, to 0.4 and 0.5 millisecond in the 1990s, to as high as 1.0 millisecond for patients who are mildly diabetic. Although the transcarpal delta is an important measure in the diagnosis of CTS, additional EDS measures have not received the same level of consideration in the literature. These data support further scrutiny of the sensory latency criterion, in addition to the transcarpal delta criterion, relating to clinical manifestation of symptoms in both ≥1 and ≥2 median nerve–served digits.

### Study limitations

Differences in symptomology between studies blur the potential relation between EDS criteria and the CTS case definition. Some studies include symptoms only in digits 1 through 3, whereas others rely on digits 1 through 4. When restricting these data to digits 1 through 3, there were no meaningful differences in trends (data not shown); however, prevalence measures were uniformly slightly lower. Differentiation between symptom criteria of digits 1 through 3 compared with digits 1 through 4 in future studies may further illustrate relations between EDS criteria and the CTS case definition.

Future research in this field will help to clarify the impacts of the CTS case definition on prevalence estimates in other populations and the impacts of these differences on CTS incidence. Although these data suggest that changing the cutpoint for motor latency or the transcarpal delta has relatively little effect on prevalence estimates, this may not be true in all populations and remains to be replicated. In these data there are multiple factors.
that have a relatively large impact on CTS prevalence estimates. These factors include the number of symptomatic digits and sensory latency cutpoint values used for CTS case definition. These differences are yet to be evaluated in incidence cases from prospective data.

Conclusions
There were meaningful differences in observed CTS prevalence in a pooled cohort of working individuals over a range of commonly used values to classify EDS as consistent with CTS. The effects on estimated CTS prevalence were greatest for the median sensory latency when compared with the median motor latency or trans-carpal delta. These results allow readers to quantify at least some of the variance observed in published studies of CTS prevalence.

Suppliers
a. XLTEK NeuroMax 1002; Natus Medical Incorporated, 5900 First Ave S, Seattle, WA 98108.
b. Cadwell 6200A; Cadwell Laboratories, Inc, 909 N Kellogg, Kennewick, WA 99336.
c. Teca Synergy N2; Oxford Instruments, 12 Skyline Dr, Ste 230, Hawthorne, NY 10532-2133.
d. NC-stat; NeuroMetrix, Inc, 62 4th Ave, Waltham, MA 02451.

Keywords
Carpal tunnel syndrome; Diagnostic techniques and procedures; Electrodagnosis; Prevalence; Rehabilitation; Standards

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References
26. Johnson EW, Kukla RD, Wongsam PE, Piedmont A. Sensory latency when compared with the median motor latency or trans-carpal delta. These results allow readers to quantify at least some of the variance observed in published studies of CTS prevalence.


