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Optimising case definitions of upper limb disorder for aetiological research and prevention – a review

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Abstract

Background—Experts disagree about the optimal classification of upper limb disorders (ULDs). To explore whether differences in associations with occupational risk factors offer a basis for choosing between case definitions in aetiological research and surveillance, we analysed previously published research.

Methods—Eligible reports (those with estimates of relative risk (RR) for >1 case definition relative to identical exposures were identified from systematic reviews of ULD and occupation and by hand-searching five peer-review journals published between January 1990 and June 2010. We abstracted details by anatomical site of the case and exposure definitions employed and paired estimates of RR, for alternative case definitions with identical occupational exposures. Pairs of case definitions were typically nested, a stricter definition being a subset of a simpler version. Differences in RR between paired definitions were expressed as the ratio of RRs, using that for the simpler definition as the denominator.

Results—We found 21 reports, yielding 320 pairs of RRs (82, 75 and 163 respectively at the shoulder, elbow, and distal arm). Ratios of RRs were frequently 1 (46%), the median ratio overall and by anatomical site being close to unity. In only 2% of comparisons did ratios reach 4.

Conclusion—Complex ULD case definitions (e.g. involving physical signs, more specific symptom patterns, and investigations) yield similar associations with occupational risk factors to those using simpler definitions. Thus, in population-based aetiological research and surveillance, simple case definitions should normally suffice. Data on risk factors can justifiably be pooled in meta-analyses, despite differences in case definition.

Introduction

Musculoskeletal disorders of the upper limb (ULDs) are important causes of morbidity and sickness absence, resulting, for example, in an estimated loss of 3.75 million working days per year in the UK in 2008/9 [1]. However, their optimal classification remains controversial [2–5]. Difficulty arises because of the multiplicity of disorders, disease labels, and diagnostic criteria adopted by therapists and researchers; ambiguity in the coverage and boundaries of case definitions; and the lack of a suitable reference standard [6].

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This want of an agreed diagnostic classification has hindered the pooling and interpretation of research data, and also attempts at standardised occupational surveillance. Additionally, it limits the scope for compensation.

Editorials and commentaries have highlighted the impasse and called on experts to agree consensual case definitions [7,8], and several classificatory schemes have been proposed based upon this approach [9-15]. However, in a systematic review by Van Eerd *et al*, no two of 27 schemes identified were identical [4], underscoring the scale of continuing disagreement.

There has been only limited debate about the rationale for preferring one scheme to another. However, a “diagnosis” can be thought of as a means to an end, possible goals being to identify modifiable risk factors as an aid to prevention, and to improve the clinical management of patients. According to this utilitarian logic, good case definitions will be those which ‘add value’ by distinguishing categories of disorder that differ importantly in their associations with potential causes and/or in their prognosis and responses to different treatments. It will be worth distinguishing subgroups (splitting rather than lumping) only where such differences are demonstrable and materially influence follow-on actions [16].

Optimal case definitions for prevention may not necessarily be identical to those for clinical care. To assess the relative merits of competing case definitions for ULDs in aetiological research, prevention, and surveillance, we compared their utility by analysis of results from previously published research.

Methods

We sought peer-reviewed reports in which more than one case definition had been analysed against occupational risk factors that were defined identically.

Several sources were screened to find papers with these characteristics:

1. In the Medline and Embase electronic bibliographic databases we combined terms for ULD with those for relevant occupational physical risk factors (e.g. repeated movements of the wrists/fingers, repeated bending and straightening of the elbow, repeated movements of the shoulder, work with the hands above shoulder height, lifting, use of a computer keyboard or mouse, vibration, cumulative trauma), and retrieved all systematic reviews and meta-analyses published since 1990 that met these search criteria (21 in all, listed in the online supplement). All primary research reports cited in these reviews were itemised, and cross-tabulated to eliminate duplicates.
2. Also, in case this strategy lacked sensitivity to detect reports containing more than one ULD case definition, we supplemented our electronic search with hand searches of five relevant and accessible occupational journals (*Occupational and Environmental Medicine*, *Scandinavian Journal of Work, Environment and Health*, *American Journal of Industrial Medicine*, *International Archives of Occupational and Environmental Health*, and *Occupational Medicine*) published between January 1990 and June 2010. This search provided three potentially relevant additional primary reports for consideration.

We then excluded papers which were: (1) not in English; (2) published before 1980; (3) did not allow upper limb problems to be analysed separately from neck problems; (4) did not distinguish upper limb problems by anatomical site (e.g. elbow as opposed to arm); (5) did not include at least two explicit case definitions; (6) did not quantify risk estimates for one or more exposures in common against these alternative case definitions.

Figure 1 (online supplement) details the number of reports screened, retrieved, excluded and analysed in PRISMA [17] format. Altogether, 162 reports were screened for eligibility (86 of these in full). Finally, 21 reports (from 16 studies) were included in data synthesis. The main reasons for exclusion were: irrelevant hits ($n=76$), failure to analyse by anatomical site ($n=29$), absence of two case definitions ($n=15$), and insufficient quantification of risks ($n=11$).

From each eligible report we abstracted the main study characteristics (authors, date, setting, study design, study populations and numbers); and separately for each anatomical site (shoulder, elbow, forearm, wrist/hand), the occupational exposure definitions and case definitions employed; also, we abstracted or derived paired estimates of relative risk (RR – sometimes expressed as an odds ratio or prevalence ratio) with 95% confidence intervals (95% CI), for alternative case definitions with the same occupational exposures. Data abstraction was piloted and then undertaken by two of us (ECH and CL) and checked in full by KTP.

Various categories of comparison were identifiable, most of which had a natural hierarchy. Distinguishable were definitions based on: 1) symptoms vs. symptoms plus signs (e.g. elbow pain vs. elbow pain with tenderness on palpation); 2) symptoms defined generally vs. symptoms defined specifically (e.g. tingling/numbness in the hand vs. nocturnal tingling/numbness in the median nerve distribution); and 3) symptoms/signs vs. symptoms/signs plus a positive investigation (e.g. Tinel's sign positive vs. this and delayed median nerve conduction). Additionally, 4) one report allowed a comparison with no implicit hierarchy (one examination finding vs. another).

Differences in association between pairs of case definitions were expressed as a ratio of RRs – based, for the hierarchical groupings, on the stricter definition (C2) as numerator divided by the simpler one (C1) as denominator, and for the sole non-hierarchical pairing, on an arbitrary choice of denominator.

As hierarchical comparisons tended to be nested (i.e. subjects fulfilling the stricter case definition, C2, were subsets of those fulfilling the simpler definition, C1, rather than statistically independent samples), or the degree of overlap was uncertain from published reports, standard errors and CIs for their ratios could not be derived by standard statistical methods. Instead, the ratios were categorised into bands by magnitude and summarised by their median and interquartile (IQR) values. To gauge crudely the potential contribution of chance to any differences in RR, a comparison was also made between the lower 95% confidence limit of that for the stricter definition and the central estimate of that for the simpler definition. Separate summary statistics were compiled by anatomical site and for each category of comparison.

A limitation of this method is that the reference groups for the RRs under comparison were not always identical. For example, one RR might be for C1 vs. “not C1” and the other for C2 vs. “not C2”, rather than for C2 vs. “not C1”. Each report was assessed for this potential bias and the size of bias (% by which the ratio changed when analysis was restricted to “not C1” as compared with “not C2”) was estimated for all reports where it was known or calculable from the data supplied. The distribution (median and interquartile range) of estimated biases was then summarised.

Results

The 16 studies (21 reports) [10,18-37] yielded by our search provided a total of 320 paired comparisons of RR. The main characteristics of the reviewed studies are listed in Table 1. Reports came mostly from Northern Europe and the workplace setting; 13 of the 16 studies

were cross-sectional in design. Sample sizes ranged from 96 to 6,943, and in six of the studies (11 of the 21 reports), they exceeded 1,000.

Tables 2 to 4 provide, separately for the shoulder, elbow, and distal upper limb, details of the paired case definitions employed in reports; the occupational exposures analysed; the number of comparisons of RRs provided by each report; and the frequency distribution of the ratios of RRs.

Taking, as an example, the findings at the shoulder by Brandt [22]: a comparison was drawn between a simple symptom definition (at least moderate shoulder pain over the past 7 days) and a stricter definition involving these symptoms together with substantial tenderness on palpation in various pre-specified anatomical locations. RRs for each case definition were obtainable for use of the computer mouse and use of the computer keyboard – two pairs of comparisons, the ratio of RRs (stricter vs. simpler definition) being in each case 1; in neither did the lower 95% confidence limit for the stricter definition exceed the central estimate of the simpler definition.

On the same basis, some 82 paired comparisons were found at the shoulder, 75 at the elbow, and 163 in the distal arm, with some reports contributing in excess of 40 comparisons. However, ratios of RRs were seldom as high as 4 (2% of all comparisons), and often 1 (46%), the median ratio overall and by anatomical site being close to unity (Table 5). In only 5% of comparisons were RRs sufficiently divergent for the lower 95% confidence limit of the stricter case definition to exceed the central estimate of that for the simpler one. Different patterns of hierarchical comparison (whether involving a contrast of symptoms, or symptoms with symptoms and signs, or additional investigation) yielded similar estimates of the ratio, as did comparisons at each anatomical site, although ratios above two were somewhat more common at the shoulder.

In a sensitivity analysis, we excluded data from the influential NUDATA and Finland Health 2000 studies [20-23,36], the linked reports from which contributed all but 116 of the 320 comparisons. Among the remainder, ratios of 2 and 4 were relatively less frequent, but the median and IQR values were scarcely different.

Finally, Table 6 (which appears online) presents estimates of potential bias arising from use of different reference groups in comparisons of RRs. In nine studies (11 reports) it was either absent or calculable from the published data; in three it was present but not calculable; and in five studies (seven reports) the potential for bias was neither clear nor calculable. Eventually, estimates of potential bias were made for 45 comparisons. Effects were small, the median bias being 0% (IQR 0% to 1.7%, range -4.9% to 14.6%), and in 87% of comparisons it was <5%.

Discussion

This analysis indicates that hierarchical case definitions of increasing sophistication, involving confirmatory physical signs, more specific symptom patterns, or additional investigations, yield remarkably similar associations with putative occupational risk factors to those obtained using simpler case definitions.

Our analysis has certain limitations. In particular, the search strategy is unlikely to have discovered every occupational report over the two decades of inquiry that involved multiple case definitions. Specifying sensitive electronic search terms for this topic is challenging. To make the task manageable, we focussed on systematic reviews of occupational risk factors at each anatomical site as our main source of references to primary research reports, but to improve the detection rate we also hand-searched five leading peer-reviewed occupational

journals. In the event, hand-searching identified only three potentially eligible papers missed by the database screen, lending some validity to our search. More importantly, papers were selected blind to information on the ratios of interest, and we have no reason to suppose that the reports retrieved were unrepresentative of the universe of relevant studies in the peer-reviewed literature.

A second area of difficulty lies in evaluating the role of chance in the ratio measures obtained. Scope to estimate CIs for the ratios was limited by the nested nature of many observations and the indeterminate extent of overlap in others. However, the infrequency of ratios of >2 across all 320 comparisons, and of lower confidence limits of RRs for stricter definitions exceeding the central estimates for simpler definitions, argue against important differences being overlooked by chance. Additionally, findings were insensitive to the exclusion of two large influential studies that contributed more than half the observations, suggesting that this possible non-independence of data points from the same study was not a cause of material bias. A further sensitivity analysis suggested that the potential for bias arising from differences in the reference group for paired risk estimates was inconsequential.

A lack of detectable difference between case definitions (ratio close to unity) could arise if the occupational exposures studied were not risk factors for symptoms or disorders at the sites in question, or were defined with substantial measurement error, such as to appear so. However, many of the exposures evaluated were well established or plausible risk factors, and RRs exceeded 1.0 for 81% of the 640 estimates of RR identified during the review. True differences might also be masked by confounding. However, estimates were adjusted in the same statistical models and any superiority in favour of the stricter definition could only be masked by systematic negative confounding relative to the simpler definition. Differences in approach to exposure assessment between studies are unlikely to have biased findings, given the focus on ratios of RRs derived within-study comparisons in which exposures were defined identically.

Alternatively, and more plausibly, little “added value” is created by case definitions of increasing sophistication relative to simple ones in population-level studies, and if so a good case exists for simplification. In planning field studies of ULDs and occupational risk factors, or employers’ surveys of hazard and risk, resource expended on additional physical examinations or investigations will generally yield marginal or no benefits; whereas costs will be predictably higher, with added problems of inconvenience and non-compliance. Similarly, in health surveillance, a complex case definition will be more difficult to implement uniformly across settings and over time, with no clear offsetting benefits.

Our findings do not identify a preferred set of case definitions for ULDs in the context of prevention and surveillance at the population level. Rather, they suggest that variations make little difference. Thus, the preferred starting point for aetiological investigation will normally be a broad case definition that is simpler to apply and may give more cases and therefore greater statistical power. This does not preclude additional exploratory analyses on subsets of cases defined according to more stringent diagnostic criteria, if researchers wish to seek evidence of differential associations with risk factors. It may also be more efficient to use stricter criteria when cases have already been defined in this way (for example, if cases of CTS are readily identifiable from the records of a neurophysiology department, all of whom meet certain criteria following nerve conduction testing). In most situations, however, simple case definitions will suffice. Similarly, in surveillance, simple choices which are easier to implement will usually be preferable.

Finally, in appraising the research literature, our findings imply that heterogeneity of case mix and variations in approach to case classification have less impact than might be

supposed. This gives a justification in systematic reviews and meta-analyses for pooling data on associations with risk factors at a given anatomical site between studies, even though such studies may have differences of case definition.

More generally, the utilitarian framework offers an empirical basis for moving towards a simpler, more rational basis on which to classify ULDs for preventive purposes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What is already known on this subject: There is widespread disagreement between experts on the optimal classification of upper limb disorders and the best case definitions.

What this study adds: Complex case definitions yield similar associations with occupational risk factors to simpler definitions. This provides encouragement to adopt simpler case definitions in population-based aetiological research and surveillance, and to pool data in meta-analyses despite differences in case definition.

Table 1

Characteristics of the reviewed studies

First author	Date	Country	Setting	Design	Study population(s)
Frost [18]	199 9	Denmark	Workplac _e	X	576 current and 167 former slaughterhouse workers; 398 referent chemical workers
Thomsen [19]	200 2	Denmark	Workplac _e	X/C	790 workers from various workplaces (e.g. postal centres, bank) - sub-population of the PRIM study
Andersen [20]	200 3	Denmark	Workplac _e	X/C	6,943 technical assistants (draftsmen) & machine technicians from the NUDATA study
Kryger [21]	200 3	Denmark	Workplac _e	X/C	As for Andersen 2003
Brandt [22]	200 4	Denmark	Workplac _e	X/C	As for Andersen 2003
Lassen [23]	200 4	Denmark	Workplac _e	X/C	As for Andersen 2003
Svendsen [24]	200 4	Denmark	Workplac _e	X	1886 male machinists, car mechanics & housepainters from 258 local garages and workshops
Vitkari Juntura [10]	199 1	Finland	Workplac _e	X	102 meat-cutters, 125 sausage makers, 150 packers; 332 meat processors in non-strenuous jobs
Shiri [25]	200 6	Finland	Communit y	X	4,784 30-64 yr olds sampled from Finnish residents during 2001-2 (the Health Survey 2000)
Shiri [26]	200 9	Finland	Communit y	X	6,254 30-64 yr olds sampled in the Finnish Health Survey 2000
Ritz [27]	199 5	Germany	Workplac _e	X	290 male gas and water work employees, classified by intensity of elbow straining work
Bovenzi [28]	199 1	Italy	Workplac _e	X	65 chainsaw-using forestry operatives; 31 hospital maintenance workers with no vibration exposure
Bonfiglioni [29]	200 7	Italy	Workplac _e	X	71 full time and 155 part time cashiers; 98 other office workers
Ono [30]	199 8	Japan	Workplac _e	X	209 nursery school cooks aged 40-59 yrs; 366 other social welfare workers
Chiang [31]	199 3	Taiwan	Workplac _e	X	207 fish processing workers from 8 plants, classified by repetition and force in their job
Reading [32]	200 3	UK	Communit y	X	2,142 adults aged 25-64 yrs from primary care registers, classified by pattern of hand symptoms
Walker-Bone [33]	200 6	UK	Communit y	X	496 adults aged 25-64 yrs with upper limb pain and 2,248 without, from primary care registers
Bamhart [34]	199 1	USA	Workplac _e	X	106 ski assembly workers in repetitive jobs; 67 other employees from the same workforce

First author	Date	Country	Setting	Design	Study population(s)
Marcus [35]	200 2	USA	Workplac e	C	632 newly hired computer users following prospectively for neck-shoulder problems
Miranda [36]	200 5	Finland	Communit y	X	4,071 adults aged 30-64 yrs from a population health survey who held a job in the past 12 months
Ohlsson [37]	198 9	Sweden	Workplac e	X	148 women in assembly work and 60 sex- and age-matched controls from the general population

X = cross-sectional; C=cohort; X/C= including both baseline and follow-up analyses. PRIM = Project on Research and Intervention in Monotonous Work; NUDATA = Neck and Upper Extremity Disorder Among Technical Assistants

Table 2
Case definitions at the shoulder: comparison of relative risks for various occupational exposures in common

Author (comparisons)	Case definitions		Risk factors	Number of comparisons with Ratio (2)/(1):				LCLE2>E1
	(1) Simpler definition	(2) Stricter definition		1	>1 - <2	2 - <4	4	
	<i>Symptoms vs. Symptoms + signs ["diagnosis"]</i>							
Brant (2)	At least moderate pain, past 7 days	 + substantial palpation tenderness in: trapezius, levator, supraspinous or infraspinous muscles	Use of mouse (30/wk) Use of keyboard (20 h/wk)	2	0	0	0	0
Frost (2)	Pain/discomfort for 3/12, in past 12/12	... + signs of impingement on examination [supraspinatus tendonitis]	Slaughterhouse worker (current/ past/never)	0	0	2	0	1
Bovenzi (2)	Pain on most days for 1 month, in past 12 months	 + pain in shoulder during resisted supination with elbow flexed 90°, tenderness in bicipital tendon in palpation [bicipital tendonitis]	Hand-transmitted vibration (two daily vibration dose levels)	1	1	0	0	missing
Chiang (1)	Pain, past 30 days	... + unclear, but including tender points and/or palpable hardenings in neck-shoulder region [various unspecified diagnoses]	Highly repetitive and sustained forceful work vs. not	0	1	0	0	0
Svendsen (10)	Troublesome pain/discomfort, past 12 months	1 sign of indirect tenderness (painful arc test, pain on isometric abduction, Jobe's test) + 1 sign of direct tenderness (Hawkin's test, abduction internal rotation test) [supraspinatus tendonitis]	Upper arm elevation >90°, current % of working hours, lifetime estimate for dominant & non-dominant sides; high job demands; low job control; low support	6	2	2	0	2
Svendsen (10)	As above + limited daily activity	As above	As above	7	3	0	0	0
Walker-Bone (6)	Pain lasting 1 day in past 7 days	Any of: rotator cuff tendonitis, adhesive capsulitis, bicipital tendonitis, subacromial bursitis, or acromioclavicular joint dysfunction as defined in ref X and Table 8 [various diagnoses]	Blue-collar worker; arm elevated >1 h/day; carrying weights on one side; high job demands; low support; low job control	4	0	0	2	1
Miranda (48)	Shoulder pain in past 7 and 30 days	Pain in the rotator cuff region for past 1 & 3 months + pain on resisted active movements (abduction, external rotation, internal rotation, painful arc) [chronic rotator cuff disorder]	Driving a motor vehicle, frequent and/or heavy lifting, work with hands above shoulder height, high hand force, repeated hand or wrist movements, hand-transmitted vibration	14	12	20	2	8
	<i>Symptoms 1</i>	<i>Symptoms 2</i>						
Ohlsson (1)	Pain, past 12 months	Pain, past 12 months preventing everyday activities [Nordic questionnaire]	Assembly work (currently or in the past 4 years)	0	1	0	0	0

Author (comparisons)	Case definitions		Risk factors	Number of comparisons with Ratio (2)/(1):				LCLE≥ E1
				1	>1 - <2	2 - <4	4	
All (n= 82)				35	19	24	4	12

Table 3
Case definitions at the elbow: comparison of relative risks for various occupational exposures in common

Author (comparisons)	Case definitions		Risk factors	Number of comparisons with Ratio (2)/(1):				LCLE2>E1
	(1) Simpler definition	(2) Stricter definition		1	>1 to <2	2 to <4	4	
	<i>Symptoms vs. Symptoms + signs ("diagnosis")</i>							
Bovenzi (2)	Epicondylar Pain on most days for 1 month, in past 12 months	... + tenderness at lateral/medial epicondyle, pain in resisted flexion/extension of fingers & wrist with elbow flexed, epicondylar palpation tenderness [epicondylitis]	Hand-transmitted vibration (two daily vibration dose levels)	0	2	0	0	missing
Chiang (1)	Pain, past 30 days	Local tenderness, pain in resisted extension/ flexion of wrist and fingers, and decreased hand grip vs. opposite hand [epicondylitis]	Highly repetitive and sustained forceful work vs. not	1	0	0	0	0
Vikari-Juntura (6)	Pain in past 7 days	Epicondylar tenderness	Packers, sausage makers, meat cutters, strenuous jobs vs. non-strenuous jobs (by sex)	2	4	0	0	0
Walker-Bone (5)	Pain lasting 1 day in past 7 days	... in lateral (medial) elbow + tenderness over lateral (medial elbow) + pain over lateral (medial) elbow region in resisted active extension (flexion) of the wrist [epicondylitis]	Blue-collar worker; elbow bending >1 h/day; high job demands; low support; low job control	3	2	0	0	0
	<i>Examination 1</i>	<i>Examination 2</i>						
Ono (2)	Lateral (medial) epicondylar palpation tenderness	Lateral (or medial) epicondylar pain on resisted active extension (flexion) of the wrist	Nursery school cooks (either arm) vs. controls	0	1	0	1	0
Ritz (4)	Palpation tenderness at epicondyle + pain on extension/flexion of wrist/fingers with extended elbow	+ pain on lifting a chair	10+ yrs of moderate or high elbow-straining work, separately for current & former job	2	2	0	0	0
Shiri (2)	Epicondylar palpation tenderness and/or pain on resisted active wrist extension (flexion)	Epicondylar pain on resisted active wrist extension (flexion) ['definite' vs. 'possible' epicondylitis]	Forceful activities: repetitive movements of hands or wrists	0	2	0	0	0
	<i>Symptoms 1 vs. Symptoms 2</i>							
Lassen (26)	Any elbow discomfort/pain in past 12 months	Any pain/discomfort for >30 days + at least 'quite a lot of trouble' in past 12 months ('severe' pain)	Mouse use (h/wk); keyboard use (h/wk); arm/wrist support for mouse	8	18	0	0	0

Author (comparisons)	Case definitions		Risk factors	Number of comparisons with Ratio (2)/(1):				LCLE2>E1
	(1) Simpler definition	(2) Stricter definition		1	>1 to <2	2 to <4	4	
			or keyboard use; abnormal mouse/keyboard position; work chair/desk not adjusted; high strain index; high job demands; low control; low support; high time pressure; dissatisfied with work design					
Lassen (26)	New pain/discomfort , past 12 months, absent at baseline	New pain/discomfort for >30 days + at least 'quite a lot of trouble' over past 12 months, absent at baseline (incident 'severe' pain)	As above	13	12	1	0	0
Ohlsson (1)	Pain, past 12 months	Pain, past 12 months preventing everyday activities [Nordic questionnaire]	Assembly work (currently or in the past 4 years)	0	1	0	0	0
All (n = 75)				29	44	1	1	0

Table 4
Case definitions at the distal upper limb: comparison of relative risks for various occupational exposures in common

Author (comparison s)	Case definitions		Risk factors	Number of comparisons with Ratio (2)/(1):				LCLE2> E1
	(1) Simpler definition	(2) Stricter definition		1	>1 to <2	2 to <4	4	
WRIST/HAN D	Symptoms vs. Symptoms + signs ["diagnosis"]							
Bovenzi (2)	Pain on most days for 1 month, in past 12 months - hand	pain/numbness/ tingling, distribution of median nerve + Tinel's/Phalen's sign, reduced sensitivity to touch/pain in 3 & a half fingers on radial hand, weakness in pinch/grip [CTS]	Hand-transmitted vibration (two daily vibration dose levels)	0	2	0	0	missing
Bovenzi (2)	As above - wrist	As above	As above	0	0	2	0	1 missing 1
Chiang (1)	Pain, past 30 days, wrist	All of: 1) pain, numbness, or tingling in median nerve innervated fingers; 2) +ve Tinel's or Phalen's sign; 3) onset in current job; 4) not due to systemic disease or injury [CTS]	Highly repetitive and sustained forceful work vs. not	1	0	0	0	0
Chiang (1)	Pain, past 30 days, hand	As above	As above	0	1	0	0	0
Marcus (13)	Discomfort on any day in past 7 days with severity 6 on visual analogue scale; or discomfort of any severity plus reported use of medication	... + any of: medial or lateral epicondylitis, flexor carpi radialis tendonitis, flexor carpi ulnaris tendonitis, digital flexor tendonitis, extensor tendonitis, intersection syndrome, trigger finger, CTS, or ulnar neuritis [various diagnoses]	Prescribed degrees of keyboard wrist ulnar deviation; mouse wrist ulnar deviation; mouse wrist extension angle; distance to J key from table surface or table edge; keyboard activation force. Also, wrist rest; sharp leading edge on table surface	8	5	0	0	0
Walker-Bone (6)	Pain lasting 1 day in past 7 days	... + dorsal wrist pain on resisted extension of fingers <i>or</i> palmar wrist pain on resisted flexion of fingers <i>or</i> medial wrist pain on resisted medial wrist movement <i>or</i> radial wrist pain on resisted radial wrist movement [tenosynovitis]; <i>or</i> ...radial pain + tenderness over radial wrist + +ve Finklestein test [de Quervain's]	Blue-collar worker; typing 1 h/day; repetitive movements > 4h/day; high job demands; low support; low job control	5	0	1	0	0
Walker-Bone (6)	As above	.. in fingers, with Heberden's nodes <i>or</i> .. in thumb base with focal tenderness (osteoarthritis, DIP joints or thumb base)	As above	2	4	0	0	0
Barnhart (1)	Hand pain (right)	...+ either Tinel's or Phalen's test positive [CTS]	Repeated /sustained flexion, extension or ulnar	0	0	1	0	1

Author (comparison)	Case definitions		Risk factors	Number of comparisons with Ratio (2)/(1):				LCLE2>E1
	(1) Simpler definition	(2) Stricter definition		1	>1 to <2	2 to <4	4	
			deviation of wrist by 45°, radial deviation > 30°, or pinch type grip					
Barnhart (1)	Nocturnal hand pain (right)	As above	As above	0	0	1	0	1
	<i>Clinical vs. Clinical + investigation</i>							
Barnhart (1)	Positive Tinetti's or Phalen's test	 + nerve conduction - distal sensory latency of median minus ulnar nerve ms [CTS]	As above	0	0	1	0	0
Thomsen (2)	Tingling 1x/wk + 1 of 3 radial fingers 1/wk, alone or with numbness or pain consistent with CTS - working hand	 + distal sensory latency at digit II <50 m/s or abnormal median distal motor latency, wrist to APB vs. control group [CTS]	Hrs/wk of repetitive work (e.g. data entry, loading/opening envelopes, sorting forms); h/wk of forceful work (e.g. emptying/sorting letter boxes)	0	2	0	0	0
Bonfiglioli (3)	Nocturnal +/- diurnal numbness, tingling, burning, or pain in 1 of first 3 fingers, in past 1 month (Katz diagram)	 + reduction in sensory conduction velocity, wrist to palm (according to Rempel) [CTS]	Full-time or part-time work as a cashier (classified as having repetitive movements and force) vs. not; previous 'at-risk' job vs. not	3	0	0	0	0
	<i>Symptoms 1 vs. Symptoms 2</i>							
Andersen (25)	Tingling/numbness at least once/week within last 3 months in the right hand	Tingling/numbness at least once/week within last 3 months in the right hand – in the median nerve distribution and at night [CTS]	Mouse use (h/wk); keyboard use (h/wk); arm/wrist support for mouse or keyboard use; abnormal mouse/keyboard position; work chair/desk not adjusted; high strain index; high job demands; low control; low support; high time pressure; dissatisfied with work design	15	9	0	0	0
Lassen (26)	Any hand/wrist pain/discomfort, past 12 months	Any pain/discomfort for >30 days + at least 'quite a lot of trouble' in past 12 months ('severe' pain)	As above for Andersen	12	14	0	0	0
Lassen (26)	Any new discomfort/pain, past 12 months, absent at baseline	Any new pain/discomfort for >30 days + at least 'quite a lot of trouble', past 12 months, absent at baseline (incident 'severe' pain)	As above for Andersen	13	11	2	0	2
Reading (4)	Numbness/tingling in 'limited' median distribution	Numbness/tingling in 'extensive' median distribution – for definitions see ref X [CTS]	Bending & straightening elbow, >1 h/d; keyboard use >4 h/d; carrying	1	0	3	0	0

Author (compariso ns)	Case definitions		Risk factors	Number of comparisons with Ratio (2)/(1):				LCLE2> E1
	(1) Simpler definition	(2) Stricter definition		1	>1 to <2	2 to <4	4	
			weights of . 5 kg in one hand; repeated wrist or finger movements, >4 h/d					
Ohlsson (1)	Pain, past 12 months	Pain, past 12 months preventing everyday activities [Nordic questionnaire]	Assembly work (currently or in the past 4 years)	0	1	0	0	0
	<i>Examination 1 vs. Examination 2</i>							
Shiri (18)	'Possible' CTS - i.e. symptoms in 1 of 3 radial digits + findings in 1 of 4 tests <i>and/or</i> 'Probable' CTS (see next column)	Probable' CTS – symptoms (pain/tingling/ reduced sensation) in 2 of 3 radial digits + findings in 2 of 4 tests (Tinel's test, carpal compression test, reduced sensation in median nerve distribution, weakness of thumb abduction/wasted thenar eminence)	In former or latest job or both; hands above shoulder, 1 h/d; handling loads; repeated hand/wrist movements, 2h/d; high hand grip forces, 1 h/d; work with vibrating tools, 2 h/d	4	14	0	0	0
FOREARM	<i>Symptoms 1 vs. Symptoms 2</i>							
Kryger (25)	At least moderate forearm pain, past 7 days	Quite a lot of pain/discomfort for > 30 days in past 12 months	As above for Andersen	20	5	0	0	0
All (n= 163)				84	68	11	0	4

LCLE2>E1 = lower 95% confidence limit for case definition 2 > central estimate for case definition 1

Table 5
Comparison of relative risks for alternative case definitions and occupational exposures in common, overall and by anatomical site

	Comparison s	Ratio, median (IQR)	% of comparisons with Ratio: LCLE2>E1*			
			1	2	4	
Anatomical site:						
Shoulder	82	1.2 (0.8 to 2.4)	41	34	4	14
Elbow	75	1.1 (0.9 to 1.4)	39	3	1	0
Wrist/hand/forearm	163	1.0 (0.8 to 1.3)	52	7	0	3
Hierarchical comparisons:						
Symptoms + signs vs. symptoms	128	1.1 (0.8 to 2.0)	44	26	3	10
Specific vs. general symptoms	160	1.0 (0.8 to 1.3)	47	4	0	1
Specific symptoms + signs vs. less specific symptoms + fewer signs	24	1.2 (1.0 to 1.5)	25	0	0	0
Clinical + investigation vs. clinical [§]	6	1.0 (0.9 to 1.4)	-	-	-	-
Non hierarchical comparisons:						
Examination 2 vs. examination 1 [§]	2	3.0 (-)	-	-	-	-
Sensitivity analysis:						
Excluding the NUDATA & Finland Health 2000 results	116	1.1 (0.8 to 1.7)	44	15	3	6
All	320	1.05 (0.83 to 1.50)	46%	13%	2%	5%

* L_{CLE2}>E1 = lower 95% confidence limit for case definition 2 > central estimate for case definition 1; this information was missing for 4 comparisons.

[§]s were not derived, as the number of compared ratios was small. (For the 6 clinical + investigation vs. clinical comparisons, 3 of the ratios were 1 and 3 were 2 -<4; for the 2 comparisons of differing examination methods, one ratio was >2 -<4 and one was 4. In none of these 8 comparisons was L_{CLE2}>1.)