

A critical review of evidence related to hand-arm vibration syndrome and the extent of exposure to vibration

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A critical review of evidence related to hand-arm vibration syndrome and the extent of exposure to vibration

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This report describes a systematic literature review on the nature of the exposure-response relationship between hand-transmitted vibration and the elements of hand-arm vibration syndrome (HAVS), ie the vascular, neurosensory and musculoskeletal components. Annex C of ISO 5349-1:2001 contains an exposure-response relationship for vascular HAVS, yet this review of the literature has not found any strong evidence of a precise quantitative relationship between exposure to vibration and health outcomes, either for vascular or neurosensory HAVS. There is some evidence that suggests possible limited reversibility of vascular HAVS after cessation of exposure. However, the limited evidence concerning neurosensory HAVS does not indicate any reversibility of the condition.

This review indicates that there are a number of unknowns with regard to the exposure-response relationships for HAVS. Despite on-going research in the area of HAVS, quantitative exposure-response relationships for HAVS remain elusive and ill-defined. It has still not been possible to establish if there is a no effect level for vibration exposure, other than the somewhat obvious zero exposure level.

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KEY MESSAGES

1. Annex C of ISO 5349-1:2001 contains an exposure-response relationship for vascular HAVS. However, this review of the literature has not found any strong evidence of a precise quantitative relationship between exposure to vibration and health outcomes, either for vascular or neurosensory HAVS.
2. Evidence suggests possible limited reversibility of vascular HAVS after cessation of exposure.
3. The limited evidence concerning reversibility of neurosensory HAVS does not indicate any reversibility of the condition.
4. There does not appear to be a significant body of appropriate research currently underway that would further our understanding of the quantitative relationship for either vascular or neurosensory HAVS.
5. No new evidence has been found to corroborate or refute the limited existing evidence for a no effect level for vibration exposure, other than the somewhat obvious zero exposure level.
6. There are still a number of unknowns with regard to the exposure-response relationship for HAVS. These include;
 - how best to quantify exposure,
 - the inter-relationship between cumulative exposure, current exposure and periods of non-exposure in the development of the symptoms of HAVS,
 - the relative importance of different vibration characteristics, such as frequency or impulsiveness, in relation to the different health outcomes.

EXECUTIVE SUMMARY

Background

In 2004, the Health and Safety Laboratory (HSL) undertook a systematic review of the literature entitled 'Clinical testing and management of individuals exposed to hand-transmitted vibration'. Part of this review covered literature related to the exposure-response relationships in hand-arm vibration syndrome (HAVS), noting that the relationship between vibration and injury was poorly defined for vascular HAVS and not defined for the neurosensory component of HAVS.

The increasing recognition that neurosensory HAVS is an important health outcome, together with the publication, post September 2004, of a number of papers related to the HAVS exposure-response relationship, suggested it was timely to re-review the literature. Additionally, it was considered appropriate to consult with international experts about current unpublished or future planned activity and identify any gaps in the evidence on relationships between exposure and health outcomes.

Main Aims

The aims of this work are:

- (a) to seek out and critically appraise information relating to the relationship between exposure to vibration and HAVS;
- (b) to establish areas of consensus of opinion and identify gaps in the evidence;
- (c) to consult with international experts in the area to establish if any further information is likely to become available;
- (d) to produce a report outlining the evidence available, any consensus of opinion and any gaps in knowledge.

The main research question was formalised as: '*To review the nature of the exposure-response relationships between hand-transmitted vibration and the elements of hand-arm vibration syndrome (HAVS), i.e. the vascular, neurosensory and musculoskeletal components*'. The main research question led to twelve inter-related questions being developed.

The evidence statements for each specific question were rated as follows:

- (+++)
(++)
 - (+)
 - (-)
- Strong evidence from more than one good quality study or a meta-analysis;
Moderate evidence, but from fewer, smaller or lower quality studies;
Limited evidence from a few studies or from studies of lower quality;
Lack of published evidence that specifically addresses the question.

Main findings

Quantitative relationships

This review has found no strong evidence that establishes precise quantitative relationships between exposure to vibration and associated health outcomes, including the key well-recognised endpoints of vascular or neurosensory HAVS.

There are a number of factors that may influence success in investigating exposure-response relationships for HAV from workplace studies. These include the following:

- The metric for hand transmitted vibration, A_h , is defined in ISO 5349 and is widely used. However there is a lack of consensus as to what is the most appropriate metric for assessing exposure.
- Recent guidance and legislation has led to significant reduction in exposure. Thus, retrospectively constructed estimates of past exposures, with their inherent greater uncertainty, are more dominant in the assessment of cumulative exposure.

- There is a lack of longitudinal studies, which are more appropriate than cross-sectional studies for defining exposure-response where the health outcome is related to chronic exposure.
- HAVS has become less prevalent in working cohorts, with longer latencies to occurrence of HAVS, since the time of the initial efforts to construct an exposure response relationship in the 1980s. This causes practical difficulties in establishing appropriate study cohorts of the necessary statistical power and with appropriate follow-up periods.
- Diagnosis and staging of HAVS is still based on reported (non-pathognomonic) symptoms, rather than on quantifiable measures of damage or physiological deficit. Consequently, diagnosis is open to misclassification through confounding conditions, which are relatively common in the general working population.

Vascular HAVS

A meta-analysis of studies by Brammer [1, 2] was used as the basis to develop the ISO 5349:1986 exposure-response relationship, which related to vascular HAVS only. The British Standard BS 6842:1987 [3] contained a more cautious interpretation of this relationship, which did not include so much data as the 1986 version of ISO 5349. By 2001, when the current version of ISO 5349-1 was published, the information contained on the exposure-response relationship had been greatly reduced and was accompanied by a large number of qualifying statements and notes. This reflected the known uncertainty in the exposure-response relationship at the time of publication. This uncertainty still persists today. This review has confirmed that the quantitative relationship suggested in ISO 5349-1 is not universally applicable. Some studies show agreement, whilst others show, in roughly equal proportions, that the ISO 5349-1 relationship both over-and under-predicts the risk of vascular HAVS. There are many possible reasons for this, which are explored in the report.

Neurosensory HAVS

Over recent years as understanding has developed, the importance of the neurosensory component, in comparison with vascular HAVS, has been recognised with regard to disability and quality-of-life. Most of the studies that have looked at the neurosensory effects of vibration exposure have found that there is a relationship between vibration exposure and the onset of neurological symptoms. However, any quantitative relationship is not well defined. There are in fact very few good quality, published epidemiological studies that investigate the quantitative relationship between exposure to vibration and severity of neurological symptoms. What few studies do exist eg. Bovenzi 2011, have collected appropriate data, but the data have apparently not been analysed to attempt to draw out any relationship. The result is that there is still very little information available on the quantitative relationship between exposure and health outcomes for neurological HAVS.

Evidence suggests that there is a relationship between cumulative exposure and quantitative tests of physiological damage, such as vibrotactile perception threshold (VPT) and thermal perception threshold (TPT). TPT may also be related to daily vibration exposure and appears more sensitive to cumulative vibration exposure than VPT.

No effect level

Early work by Brammer [4] suggested the possibility of a no effect level of exposure in the range $1\text{m/s}^2 < a_k < 2\text{m/s}^2$ where a_k is the single axis, frequency weighted acceleration magnitude. ISO 5349-1:2001 records that reports of ill-health are rare below $2\text{m/s}^2 A(8)$ and not known at exposures below $1\text{m/s}^2 A(8)$. This review has not found any recent evidence to either substantiate or refute this implied no effect level.

Reversibility

Evidence suggests some possible reversibility of vascular HAVS after cessation or reduction of exposure, which may happen over a period of years and depend on the initial severity of the symptoms. As there is evidence that the risk of vascular HAVS also relates to recent or current daily exposure, this suggests that the risk of vascular HAVS may not be simply driven by the extent of cumulative vibration exposure over a working lifetime.

The possibility remains that, if the diagnosis is solely based on reported extent and frequency of blanching, the apparent reversibility of vascular HAVS over time, may simply reflect life-style modifications made by sufferers to avoid blanching attacks, that are well established and documented in people with primary Raynaud's Phenomenon.

There is less evidence concerning reversibility of neurosensory HAVS than for vascular HAVS, but that which is available does not indicate any reversibility of the condition. The prevalence of the key, but non-specific, symptoms of tingling and numbness in the hands and fingers of workers has been reported as being around 15-20% in the general working population. This is higher than estimates of Raynaud's Phenomenon, especially for males. The prevalence of the key symptoms in the general population makes defining the complete reversibility of neurosensory HAVS problematic in both absolute terms and relative to vascular HAVS.

Frequency weighting

Most evidence from good quality epidemiological studies, measurements of finger systolic blood pressure, biodynamics, and limited experimental data, lends support to consideration of frequencies higher than those emphasised by the current frequency weighting defined in ISO 5349-1:2001, when estimating the risk of vascular HAVS. Evidence does not however point to a universally better alternative to the ISO 5349-1 frequency weighting in defining exposure.

Other Musculo-Skeletal Disorders

The extent and quality of the evidence for cumulative vibration exposure causing disorders such as Carpal Tunnel Syndrome (CTS), Dupuytren's contracture and other upper limb problems, is much lower than for vascular and neurosensory HAVS. However, there is evidence for a causal link specifically between CTS and Dupuytren's contracture and exposure to vibration.

Consultation with experts

In the consultation phase of the work, a total of 40 national and international experts were contacted by email. Responses were received from 10 of those contacted. This consultation did not bring to light any immediate opportunities for collaboration, or reveal any on-going research which might contribute greatly to the outcome of this review. Some very useful and interesting background to the origins and development of the ISO 5349 exposure response relationship was provided by Tony Brammer.

Recommendations

Despite on-going research, there are still a number of significant gaps in knowledge with regard to the exposure-response relationship for HAVS. These include;

- how best to quantify exposure
- the inter-relationship between cumulative exposure, current exposure and periods of non-exposure in the development of the symptoms of HAVS, and
- the relative importance of different vibration characteristics, such as frequency or impulsiveness, in relation to the different health outcomes.

HAVS and vibration-associated ill-health remains an international problem, where knowledge of current and future research work and pooling of appropriate data across national boundaries

remains important. There are example(s) of successful international collaboration (eg. The EU ‘VIBRISKS’ project: EC FP5 project no. QLK4-2002-02650). There appear to be one or two studies around neurosensory outcomes, where reworking on the original data, if made available, may help with an initial exposure-response relationship for neurosensory HAVS.

Despite the fact that there are difficulties in mounting workplace studies that focus on exposure-response relationships, there remains a need for such work. Given the realisation of its importance, the lack of any exposure-relationship for neurosensory HAVS suggests that additional effort is needed to address this question. The wide acceptance and availability of quantitative measures of vibration-induced neurosensory deficit, such as VPT and TPT, suggests that any such studies should employ quantitative measures in addition to physician-led diagnosis, as well as being longitudinal in nature. There appears currently only one, small scale Italian study focussing on the neurosensory outcomes that reflect these criteria, while a larger scale study from the same Italian research group is focussing on vascular HAVS outcomes.

Given the continuing prevalence of some degree of HAVS in workforces and the continuing reliance on health surveillance to prevent progression, better definition of the influence of current exposure on progression of HAVS would aid occupational physicians with management of affected individuals. Again, the involvement of quantitative measures of deficit, where available, rather than simple reporting of symptoms, is warranted.

An alternative approach to setting up new longitudinal studies, with their inherent problems and significant costs, might be analysis within the large amount of on-going physician-led health surveillance data. This could be combined with appropriate estimates of relevant workplace current exposure levels, to better define exposure-response relationships for risk of HAVS and its progression or regression.

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1. INTRODUCTION

1.1 BACKGROUND

In 2004 HSL published a systematic review of the literature related to exposure to hand-arm vibration and health outcomes [5]. This review found that the information related to the exposure-response relationship between vibration and vascular hand-arm vibration syndrome (HAVS) was poorly defined and had not been defined for the neurosensory (sensorineural) component of HAVS.

There is now increasing evidence that neurosensory HAVS is an important driver of the disability associated with HAVS [6, 7]. A number of publications related to the exposure-response relationship for HAVS have been published since the review in 2004 and since 2009 the International Standards committee on hand-arm vibration (HAV) has encouraged work into improving assessment methods for HAV. In addition, HSL has in recent years been involved in analysing data from referrals to the HAVS assessment centre, (not yet published). With all of this recent activity, it is now timely to bring all of the latest information together, to critically appraise the available information, consult with international experts to establish if there is any consensus of opinion, and, identify any gaps in the evidence.

1.2 AIMS

The aims of the work are:

- To seek out and critically appraise information relating to the relationship between exposure to vibration and HAVS.
- To establish areas of consensus of opinion and identify gaps in the evidence.

1.3 OBJECTIVES

- To review the published literature.
- To consult with international experts in the area to establish if any further information is available (e.g. other data available or unpublished information).
- To produce a report outlining the evidence available, any consensus of opinion and details of any gaps in knowledge.

2. REVIEW METHODOLOGY

2.1 RESEARCH QUESTIONS

The main research question can be formalised as;

‘To review the nature of the exposure-response relationships between hand-transmitted vibration and the elements of hand-arm vibration syndrome (HAVS), i.e. the vascular, neurosensory and musculoskeletal components’.

The main research question led to twelve inter-related questions being developed. These concerned the nature and strength of the relationships between vibration exposure and both the incidence and severity of the three elements of HAVS and their severity. Other health outcome measures were considered such as other upper limb musculoskeletal disorders (MSDs), and quantitative measures of functional, physiological and perceived disability or quality of life (QoL). The nature of the exposure metric was also reviewed in terms of the possible influence of frequency weighting of vibration and the relative importance between vibration acceleration and duration of tool use in representing risk of ill-health. The international standard ISO 5349 that remains central in defining how to measure hand transmitted vibration and express ‘daily exposure’ has a defined frequency weighting and ‘acceleration-duration’ function, the validity of which are recognised within the scientific community to need ongoing review against available evidence. The influence of intermittency and rest breaks in influencing the risk of ill-health were omitted as research questions, as a subsequent review will focus on this important area.

2.2 SEARCH TERMS

The following search term were used:

*(hand-arm vibration syndrome OR HAVS OR
vibration white finger OR VWF OR
Raynaud’s OR RP OR
hand-transmitted vibration OR HTV OR
hand-arm vibration OR HAV)*

AND

(dose response OR exposure response OR exposure outcome relationship)

Terms were searched across titles, abstracts and key words.

As well as including the publications identified using this search strategy in the review, the references were scrutinised for further publications missed through the above search terms.

2.3 SEARCH STRATEGY

The search strategy consisted of two elements:

For literature published after January 2004, after consultation with HSE’s search team, searches were made using two search engines, using the noted search terms and overarching research question. For literature published prior to 2004, the computerised ENDNOTE paper reference database established at HSL as part of authoring the Faculty of Occupational Medicine (FOM) review on ‘Clinical testing and management of individuals exposed to hand transmitted

vibration' [5] was the primary resource of appropriate material. The database contains over 8000 titles and abstracts in electronic form, with HSL holding about 1,500 as hard copies. Publications concerning exposure-response relationships were reviewed as part of addressing the FOM review evidence question '*How does the pattern and magnitude of exposure affect the likelihood of any hand-transmitted vibration-induced illness*'.

The search strategy also involved an iterative process, whereby those publications identified from the initial keyword search process, and passing the criteria for review, were scrutinised for any possible appropriate referenced publications not identified through the search terms. These publications were obtained and then subjected to the standard selection criteria.

An ENDNOTE electronic database specifically related to this review has been established.

2.4 CRITERIA FOR SELECTION ON PAPERS FOR REVIEW

Papers were selected for review by the research team according to criteria of containing data that explicitly addresses an exposure-response relationship described within the research questions.

Pre-2004 publications were identified from the FOM review as addressing exposure-response relationships and those identified in the existing ENDNOTE HAVS reference database as containing the search terms. Two reviewers then re-assessed these papers as meeting the current research questions.

For post 2004 publications, two reviewers assessed the abstracts from the literature searches in order to see if the paper met the selection criteria. Where there was doubt from the abstract that the paper could be rejected, the full text paper was obtained for consideration against the selection criteria. Papers were also sought, which contained data or described studies that might lead towards developing exposure-response relationships, e.g. by reworking of primary data not presented in the publication, as part of a meta-analysis or as an on-going prospective study.

A total of 184 titles and abstracts were identified through the search strategy. Of the total of 184 papers, 36 papers were discarded as being of little or no relevance to the review, 10 were retained as having relevance of a narrative nature for the commentary but were excluded from the review itself. A total of 138 papers were subjected to full independent review by the two reviewers.

2.5 DATA EXTRACTION AND PRESENTATION

The 138 papers were mapped to a matrix of areas of interest as an aid to gap identification. During the process of reviewing and mapping papers, the original matrix was modified to take account of additional factors that came to light during the course of the review. Amongst these was the need to distinguish between research items that related to incidence, prevalence, latency or severity of HAVS symptoms;

1. Latency – relates to the time period before symptoms start to appear in the exposed population
2. Prevalence – relates to the number of people with a disease in a given population at a specific time, either a point in time (point prevalence) or over a period of time (period prevalence).
3. Incidence – relates to the number of *new* cases of a disease that occur within a given time period

4. Severity – relates to the degree to which individuals are affected by the symptoms, for vascular and neurosensory HAVS usually measured by the Stockholm Workshop scale.

Also during the review, it was decided that the other area of interest relating to intermittency of exposure would actually form part of a separate review on intermittency and rest breaks and consequently these papers were omitted from this review. The mapping matrix is shown in Table 1.

Table 1 - Final mapping matrix

		VIBRATION EXPOSURE METRICS AND CHARACTERISTICS		
		Cumulative exposure metrics	Influence of frequency weighting	Power relationship between vibration magnitude and exposure time*
HEALTH OUTCOMES	Incidence and prevalence of vascular HAVS	Q1 para 4.1	Q8 para 4.8	Q12 para 4.12
	Severity of vascular HAVS identified by Stockholm workshop scale or other severity gradation	Q2 para 4.2		
	Incidence and prevalence of neurosensory HAVS	Q3 para 4.3	Q9 para 4.9	
	Severity of neurosensory HAVS identified by Stockholm workshop scale or other severity gradation	Q4 para 4.4		
	Incidence and prevalence of other associated symptoms.	Q5 para 4.5	Q10 para 4.10	
	Severity of other associated symptoms	Q6 para 4.6		
	Quantitative measures of functional or physiological damage (e.g. VPT)	Q7 para 4.7	Q11 para 4.11	
* Includes time dependency				

Due to the large numbers of papers that contain information relating to more than one of the cells in the matrix, the evidence table given in the Annex to this report includes a column showing to which research question each of the papers reviewed has contributed and also relates the main findings for each paper to the research question addressed. This is done using the paragraph numbers from Section 5 of this report.

Each paper was rated independently by the two reviewers as to the quality of data presented in each study. The generic criteria were:

- Clear study objectives
- Appropriate study design for objectives
- Adequate statistical power and analyses for objectives
- Consideration of possible biases and their influences on conclusions
- Outcome measures appropriate to address the research question
- Conclusions are compatible with the data presented.

Prior to undertaking the rating of individual publications the two reviewers met and agreed common approaches to application of the generic criteria.

Key findings from each paper are summarised in the evidence table in the Annex to this report.

2.6 EVIDENCE STATEMENTS AND RATING

In terms of synthesising and rating evidence statements, hierarchical considerations were included where the hierarchy of evidence is:

- systematic reviews and meta-analyses
- randomised control trials (invariably not found in occupational health studies)
- cohort studies
- case-referent studies
- cross-sectional studies
- case reports

The evidence statements were rated as follows:

(+++)
(++)
(+)
(-)

Strong evidence from more than one good quality study or meta-analysis

Moderate evidence but from fewer smaller or lower quality studies

Limited evidence from few studies or from studies of lower quality

Lack of published evidence

2.7 EXPERT CONSULTATION

The aim of consulting with international experts in the area of exposure to vibration and health outcomes is to establish if any further information is available. This might take the form of historical unpublished data either available for, or undergoing analysis, and recently commenced or on-going studies that have not yet produced any peer-reviewed publications. Forty international experts, identified from those publishing in the topic area, were sent emails requesting such information.

The process of expert consultation did not bring to light any major areas of work that were on-going at the time of the review. Nor did the process identify any opportunities for immediate collaboration with other researchers.

3. BACKGROUND TO RESEARCH QUESTIONS

The following background provides the reader with important information regarding the current standards and techniques for measurement and assessment of exposure to vibration. It also covers the health outcomes that have been linked with vibration exposure and their diagnosis. This will assist in understanding the outcomes of the review.

3.1 DEVELOPMENT OF THE ISO 5349 EXPOSURE-RESPONSE RELATIONSHIP FOR VASCULAR SYMPTOMS

The original exposure response relationship was developed for vascular symptoms only. Brammer presented two papers to the third International Symposium on HAV in Ottawa in 1981 which were published in the proceedings. The first of these papers [1] proposes functional relations between habitual exposure of the hands to vibration and the development of the early stages of vascular HAVS. The paper describes the choice of latent interval to onset of finger blanching as a useable health effect by which to identify affected individuals. The data presented for 15 separate studies of chainsaw operators report the latent interval in terms of mean and standard deviation years. These data show that the average latent interval from the studies which relate to exposures documented up to the year 1971, is in the range 4 ± 2 years.

Brammer's 1982 paper [1] describes the statistical techniques he uses and how he arrives at a set of selection rules for epidemiological data that can be used to develop the exposure-response relationship for vascular HAVS. The selection criteria devised include the number of people in the study population. This was set at a minimum of 30, which is low compared with typical selection criteria for epidemiological studies. Of these 30 exposed individuals, at least 20 must experience finger blanching and at least 6 must be at stage 3, according to the Taylor Pelmear scale. The minimum prevalence of finger blanching must be 50% of the population if the latent interval is less than 6 years, or 75% if the latent interval is more than 6 years. The average duration of the exposure of the group in years must exceed the latent interval reported by those affected. The pattern of vibration exposure of each population must include regular daily, or near daily exposure to one type of machine. A measure of the magnitude of the vibration was also required. From the studies that fitted all the selection criteria at the time of the first study, an equation was developed that could be used to predict the latent interval before finger blanching starts from the magnitude of the vibration stimulus.

In 1986, Brammer [2] went on to produce a further meta-analysis of studies. The selection criteria already defined in the earlier paper were applied to every epidemiological study of vibration published prior to 1980 and also any new studies available since. The results of each of the new studies were compared with the relationship defined in the original paper [1] and discussed.

The exposure-response relationship developed by Brammer was incorporated into the first version of ISO 5349, published in 1986. Its Appendix A contained a figure showing the estimation of risk with exposure-response curves to indicate the time in years of regular vibration exposure before episodes of finger blanching occur in 10, 20, 30, 40 and 50 % of exposed persons. There were three footnotes accompanying the data that qualified the use of the exposure-response relationship. The British Standards Institute (BSI) were more cautious than ISO in producing an exposure response relationship, because the rules applied to populations in the development of the original relationship can not be applied to all exposed populations. BSI published their own version of the exposure-response relationship in the Standard BS 6842:1987[3]. This standard did not include so much data as the 1986 version of ISO 5349.

Instead it contained only a relationship between the exposure time in years and the vibration magnitude which might be expected to cause finger blanching in 10% of an exposed population.

In the current version of ISO 5349-1, published in 2001, the information in the relevant Appendix (Appendix C) has been converted to take account of the requirement to measure vibration in three orthogonal axes and report the vibration total value, which is the root-sum-of-squares of the vibration magnitudes in each of the three axes. The information in Appendix C is greatly reduced from that in the 1986 version of the standard and is accompanied by a larger number of qualifying statements and notes. This reflects the known uncertainties that existed with regard to the exposure-response relationship at the time of publication. For example, the original relationship was based on populations of workers who were only exposed to one type of tool, whereas, typical vibration exposures often involve the use of more than one tool. The 2001 version of Appendix C only relates daily exposures to a 10% prevalence level “*in order to limit the potential for inappropriate use of the relationship*”.

3.2 NO EFFECT LEVEL

The second of Brammer’s 1982 papers [4] explains how the exposure-response relationship can be extrapolated to predict the vibration magnitude at which the latent interval corresponds to a working lifetime. This means that an operator could theoretically be exposed at this level for a lifetime without developing symptoms. The value obtained by Brammer is compared with two other studies [8] [9]. The conclusion is that the no effect level for an operator whose hands are exposed to vibration throughout the working day is in the range $1\text{m/s}^2 < a_K < 2\text{m/s}^2$ where a_K is the single axis, frequency weighted acceleration magnitude. Since this is based on the same exposure-response relationship discussed in 3.1, the same uncertainties apply to this conclusion.

In Appendix C of ISO 5349-1:2001 Figure C.1, the single prevalence level line on the graph is dotted below $3\text{ m/s}^2 A(8)$. This reflects uncertainty regarding the applicability of the relationship at low daily exposures and was intended to discourage any prediction of HAVS prevalence for exposures below $2\text{ m/s}^2 A(8)$. ISO 5349-1:2001 states ‘*Studies suggest that symptoms of the hand-arm vibration syndrome are rare in persons exposed to an A(8), at a surface in contact with the hand, of less than 2 m/s^2 and unreported for A(8) values of less than 1 m/s^2 .*

3.3 EXPOSURE LIMIT VALUE

Brammer produced a further paper published in a french journal [10] that suggested a maximum single axis value of 2.9m/s^2 , at which 50% of a working population would experience finger blanching symptoms after 25 years. This figure was used as the basis for the Exposure Limit Value (ELV) in the Control of Vibration at Work Regulations 2005.

3.4 FREQUENCY WEIGHTING

The widespread application of ISO 5439 since its introduction has undoubtedly led to a greater degree of standardisation and hence comparability between vibration magnitude measurements than would be possible in the absence of a standard. However, with regard to certain aspects, such as the frequency weighting, there is still considerable scope for improvement. Annex C of ISO 5349-1:2001 states:

*"It is not known whether this frequency weighting [Wh] represents, separately, the hazard of developing vascular, neurological or musculoskeletal disorders. At present, it is used for the assessment of **all** biological effects of hand transmitted vibration."*

The application of the weighting for assessment of all biological effects is made for convenience rather than following strong scientific evidence. The frequency weighting fulfils the requirement to have a single figure measure of the magnitude of the vibration from a stimulus for the purposes of developing an exposure-response relationship. It is based on two small-scale experimental studies of threshold of sensitivity and equal sensation contours made by Miwa et al in the 1960s [11]. It has no epidemiological, pathological or physiological basis in its original state, other than subjective sensitivity measurements. Consequently, it may not be an optimal weighting for the best known component of HAVS, namely VWF or vascular HAVS, as described in the ISO 5349 exposure-response risk model or the other health outcomes, such as the neurosensory component of HAVS.

3.5 CUMULATIVE EXPOSURE METRICS

The techniques for assessing cumulative exposure to vibration are not standardised in the same way that assessment of daily vibration exposure has been. This means that there are a number of different techniques that have been applied in the published literature, reflecting that duration of exposure and vibration magnitude may be combined in various ways to define cumulative exposure.

Measures of exposure used include:

- Lifetime exposure time in years or cumulative hours of tool use
- Lifetime dose (e.g. [12-15] combining vibration magnitude and lifetime exposure time
- Daily vibration dose normalised to either a four or an eight hour day
- Daily vibration dose normalised to either a four- or an eight-hour day and multiplied by an estimate of the cumulative days of exposure. .

Techniques for assessing the number of working days in a year may also vary. The wide variability in techniques for assessment of lifetime exposures means that it is usually not possible to compare exposures across studies.

ISO 5349-1:2001 only defines a system for estimating the vibration exposure on one working day, referred to as the A(8) daily vibration exposure. It is clearly stated (in a note to Clause 5.5 of ISO 5349-2) that it cannot be assumed that the method provided by ISO 5349-1 can be extrapolated to allow the averaging of exposures over periods greater than 1 day. The exposure-response relationship in Annex C of ISO 5349-1 is based on the assumption that operators' exposures are the same "nearly-daily" throughout the working life. In practice it is unlikely that real lifetime exposure will meet this criterion. In many industries exposure patterns are highly variable from day to day and daily exposures are likely to be altered over the working lifetime. However, the ISO 5349 exposure-response curve in ISO 5349-1 is used often regardless of exposure patterns.

3.6 ISO 5349 FREQUENCY WEIGHTING, ITS INFLUENCE AND IMPLICATIONS

Versions of ISO 5349 (1986 and 2001) have been internationally pivotal in both exposure assessment within research studies and the regulatory development of workplace exposure standards. Both ISO 5349:1986 and ISO 5349-1:2001 have contained a number of inter-related elements:

- the practical means of how to measure vibration, the frequency-weighting that assumes the importance of different frequencies in causing injury,
- the calculation of daily vibration exposures based on 8 hour (previously 4 hour) energy-equivalent frequency-weighted vibration magnitudes (A(8)) and

- a risk model for VASCULAR HAVS based on years of exposure at various $A(8)$ values.

Without doubt, the promulgation of a standard for the measurement of vibration has been important for both routine workplace assessments and in allowing inter-research study comparisons. The importance of ISO 5349 guidance is reflected in that most of the studies reviewed in this report, where vibration measurement data were given, stated that their vibration measurements were according to the appropriate ISO 5349 standard. However, the scientific basis of elements within ISO 5349, such as the frequency weighting, the calculation of cumulative vibration exposure and its relation to risk of ill-health, have been questioned and investigated by many researchers over the years.

3.6.1 Conversion to triaxial $A(8)$ measurements

ISO 5349-1:2001 introduced a number of changes to the contents and requirements of the standard to reflect the increasing level of knowledge concerning measurement of exposure. The 2001 version of the standard changed to triaxial from single axis assessment of vibration magnitudes and the adoption of an 8-hour rather than the previous 4-hour normalisation period for daily exposure. These changes were assimilated into Appendix C of ISO 5349-1:2001 containing guidance on estimation of risk by using simple multiplication factors to convert single axis data to total values. However this conversion will introduce some variability and can only result in an approximation of the total value.

3.6.2 Applicability of data to different machine types

The data that contributed to the development of the exposure-prevalence relationships (Figure 2, Appendix A, ISO 5349:1986 and Figure C.1, Appendix C, ISO 5349-1:2001) were based on studies of operators whose exposure was solely from chain saws, grinders and rock drills. They did not include machines such as road breakers, impact wrenches and chipping hammers, which have a more impulsive action. There is considerable debate about whether or not the relationship is applicable to operators who use machines with impulsive vibration, or more than one type of machine.

3.6.3 Validity of the frequency weighting

In ISO 5349 the assessment of vibration magnitude is achieved by measuring the acceleration at the vibrating surface and applying the frequency weighting in which low frequencies (8 –16Hz) are given more weight than medium frequencies (31.5 to 100Hz) and even less weight is given to high frequencies (above 100Hz). The validity of the ISO 5349 frequency weighting has been repeatedly questioned and a number of papers have been identified in this review that look at alternative assessments of vibration exposure. An ISO committee is currently considering options for the revision of the frequency weighting in ISO 5349-1:2001.

A number of epidemiological studies have reported whether their findings related to VASCULAR HAVS are in line with the predictions given in ISO 5349 (both 1986 and 2001 versions) and have tended to interpret the outcomes as justifying or not the currently applied frequency weighting. However, it is important to recognise that predictions of risk of VASCULAR HAVS based on assessment of daily vibration exposure according to ISO 5349 involve not only the application of frequency-weighting in terms of defining the exposure term, but also a power function implicit in combining the measured frequency-weighted acceleration of the tool and the hours of its use to give the daily energy-equivalent vibration exposure $A(8)$.

3.6.4 Coupling forces

Currently exposure-response relationships are defined between the magnitude of the vibration on the tool and the health outcome. However, the measured vibration on the tool does not necessarily define the vibration that is transferred from the tool to the hand and arm to potentially cause harm. Therefore among criticisms of the current assessment technique for HAV is that no account is taken of the coupling forces between the exposed individual and the vibrating surface. Greater coupling forces cause greater damping of the vibrating surface that results in a lower vibration magnitude being measured. However the likelihood is that the greater coupling results in more of the energy being dissipated into the hand and arm, thereby increasing the likelihood of adverse effects.

Some investigators have proposed alternative assessment techniques for HAV that quantify the absorbed power. This can be done by simultaneously measuring both the velocity and the coupling force, from which the absorbed power can be calculated. However, measurements of coupling force are difficult to perform, and are currently impractical for in-use assessments on power tools. An alternative method of accounting for coupling forces has been proposed. This applies a correction factor to the measured vibration magnitude, based on simple coupling force measurements. This method currently has limited international support.

Improvements in instrumentation and measurement capabilities have made it possible to more thoroughly investigate the biodynamics of the hand arm system and to develop models that explain how the hand-arm system behaves under different conditions. Using these techniques, recent studies by Dong [16] have demonstrated that there are considerable differences between the vibration absorbed by the various anatomical structures of the upper extremity. The results of biodynamic investigations imply that if the exposure-response relationship is ever to be fully understood, it may be necessary not only to use different exposure assessment techniques for different health outcomes, but also for different parts of the hand arm system.

3.6.5 Use of band-limited and unweighted data

Some studies have investigated using “unweighted” vibration magnitudes as an alternative to ISO 5349 frequency weighted values; others have used “band-limited” magnitudes. The term “band-limited” is defined in ISO 5349-1 and ISO 8041 as the band-limiting component of the W_h frequency weighting. It has cut-off frequencies at the lower end of the 5Hz and the upper end of the 1250Hz 1/3 octave bands. Unfortunately the term “unweighted” is undefined, and in principle could include vibration at frequencies much higher than 1500Hz, which for impulsive machines can make a very significant difference to overall measured vibration magnitude. There is a need for clarity and definition when using “unweighted” measures of vibration magnitude. Most if not all of the papers that have investigated the difference between weighted and unweighted have in reality used band-limited data. .

3.6.6 The future of the ISO 5349 frequency weighting

It has long been suggested that the use of a single frequency weighted magnitude is not the most effective way to represent the various components of HAVS. The suitability of the current hand arm frequency weighting for the assessment of health outcomes associated with exposure of the hand and arm to vibration has been a subject for investigation and discussion since it was first introduced. ISO standards committees continue to investigate this area.

3.7 POWER RELATIONSHIP BETWEEN VIBRATION MAGNITUDE AND EXPOSURE TIME

The current standard technique for assessment of an individual's exposure to vibration is to combine an estimate of the magnitude of vibration being imparted by the vibrating surface with an estimate of the duration for which the vibration exposure persists. The exposure value is normalised to an eight hour period to give an energy equivalent $A(8)$ daily vibration exposure.

The combination of vibration and time is achieved using:

$$A(8) = a_{hv} \sqrt{\frac{T}{T_0}}$$

where a_t = the energy equivalent frequency weighted vibration magnitude
 T = the exposure duration
 T_0 = the reference period of 8 hours.

This relationship between vibration magnitude and exposure duration in the $A(8)$ calculation gives greater relative importance to the vibration magnitude compared with exposure time (e.g. to halve the $A(8)$ value you only need to halve the vibration magnitude but the exposure time needs to be reduced to one quarter of its original value to make the same change in $A(8)$).

There is no standard technique for estimating cumulative exposure. However, it should involve comprehensive knowledge of all the tools used by workers over their working life, the tools' exposure characteristics and both the work patterns and duration of use of each tool. For cross-sectional studies relying on retrospective assessment of cumulative exposure, such assessments may involve a great deal of uncertainty. A commonly adopted approach is to combine information on the current daily exposure or $A(8)$ with an estimate of the number of hours or years of exposure. This approach assumes that the daily exposure has been unchanged throughout the exposure period, which for lifetime exposure durations is unlikely, given the improvements in power tools that have been seen in recent years and the natural changes that occur in working processes.

The method of combining vibration magnitudes and exposure time information to estimate cumulative exposure inherently involves a power relationship if $A(8)$ daily exposure are used. Some investigators have combined measured vibration magnitudes for each tool with hours of total use of the working lifetime in order to investigate the nature of the using the generic equation:

$$\sum a_i^m . t_i$$

The varying approaches mean that it can be very difficult to compare outcomes across studies due to the use of different metrics.

3.8 HEALTH OUTCOMES

Hand Arm Vibration syndrome (HAVS) is commonly described as having three components;

- the vascular, also known as Vibration White Finger (VWF),
- the neurosensory or sensorineural, and
- the musculoskeletal.

The vascular and neurosensory components have been most widely investigated.

Vascular HAVS or vibration white finger (VWF) was first described in the early 1900s, holding for a considerable time a central position of interest, largely due to the conspicuous characteristic symptom of finger blanching. The neurosensory component became of increasing interest from the mid-1970s and recently has been suggested as more disabling than vascular HAVS for sufferers [6, 17, 18]. While the symptoms of episodes of numbness and tingling are less obvious symptoms than blanching attacks in workers using vibrating tools, the neurosensory loss leads ultimately to a significant deficit in the hands as sense organs and loss of manipulative dexterity skills affecting both work and social life. Loss of strength in hand muscles, pain in hands and joint of the distal upper extremity have all been linked with the musculoskeletal component of HAVS.

The exact mechanistic cause(s) of the blanching attacks of vascular HAVS remains unclear, although a number of theories have been put forward involving both local and central factors [19-22]. The mechanism causing the neurosensory element of HAVS is probably based on the ultimate loss of nerve-ending receptors and nerve fibres in the distal upper extremities through repeated insult, ultimately over-whelming any repair mechanisms for the on-going damage. Histopathology in biopsies from humans exposed to vibration [23-29] and animal models [30-36] has shown significant damage to the vascular, peripheral neurological and muscle systems.

A number of other upper limb conditions, e.g. entrapment disorders, including carpal tunnel syndrome (CTS), Dupuytren's contracture, and both anatomically specific and non-specific pain, have been linked with the use of vibrating tools. However, differentiating causality from vibration or from other factors, such as ergonomic issues, has not always been clear. The differentiation of HAVS and CTS by symptoms or signs is also not clear, and confounded by the gold-standard of nerve conduction velocity (NCV) measurements for CTS diagnosis potentially showing slowing of velocities in the distal upper extremities of those exposed to vibration [37-39].

3.8.1 Diagnosis of HAVS.

The staging of the severity of HAVS internationally uses the Stockholm Workshop scale (SWS), which addresses both the vascular and neurosensory components of HAVS. Developed and established in the late 1980s to early 1990s, it is very largely symptom driven [40, 41], reflecting the reality of diagnosis by occupational health professionals. Therefore the SWS is subject to issues concerning worker recall about the nature and severity of their symptoms. While it has not been without its critics about ill-defined terminology [42], there is no doubt that its universal adoption has greatly aided the identification and control of HAVS by occupational health professionals.

The diagnosis of HAVS is accepted to be largely an exclusory diagnosis, relying on medical interview and assessment techniques to elicit descriptions of symptoms and their severity from the worker, and exclude alternative causes. While finger blanching can be caused by non-vibrational reasons (e.g. iatrogenic, constitutive Raynaud's disease, vascular trauma, thoracic outlet syndrome), expert medical interview and clinical assessment can largely exclude these confounding causes of blanching. Neurosensory diagnosis is driven by symptoms of numbness and tingling beyond the normal physiological paraesthesia of the hands encountered while using vibrating tools; thus posing a diagnostic challenge given the non-specificity of such symptoms.

Given the current central role of presenting symptoms in the diagnosis and classification of HAVS, diagnostic tests have tended to play a secondary or adjunct role, rather than being embedded in the criteria for diagnosis. A number of tests have been suggested and utilised in research and routine clinical assessment of the symptom-led diagnosis. Such tests could be

described as ‘quantitative measures of functional deficit, physiological damage or underlying pathology’. They include;

- invasive techniques such as semi-quantitative biopsy analysis, or the less invasive, provocation technique of intradermal injection of vasoactive substances [26, 43] that unfortunately has not been followed-up
- tests of peripheral neurosensory deficit, including mechano- and thermo-receptor loss, which have wide acceptance in other disease areas where peripheral neuropathy investigation is warranted, and include both simple and more complex tests e.g. Semmes-Weinstein monofilaments, single and two point discrimination, vibrotactile perception thresholds (VPT) and thermal perception thresholds (TPT)
- nerve conduction velocity measurements in the distal upper extremity
- integrative tests of sensory and motor skill e.g. Purdue pegboard and other tests of manual dexterity
- grip and intrinsic hand muscle strength
- Tests of abnormality in vasoconstrictory, vasodilatory responses in the hands to cold challenge e.g. finger skin temperature recovery (FST) after cold challenge, or finger systolic blood pressure (FSBP) response to cold challenge.

No overall accepted consensus has currently been reached on the diagnostic value of any individual test. The diagnostic value of some tests, such as the FST, may be unclear to some extent because of the differing conditions used for the test. For the FSBP, there has been conflicting opinion between the few centres that have employed the test, on its diagnostic value in supporting a symptom-led diagnosis. One centre has found the FSBP both diagnostically and prospectively useful in confirming or predicting future vascular HAVS status [44, 45], while at least one other centre has struggled to confirm its diagnostic power [46, 47].

Such discrepancies and lack of consensus on the diagnostic power of any specific test may lie not only with differences in the equipment used, methodology, environmental conditions etc, but also with the inherent uncertainty and misclassification possibilities associated with symptom-led diagnosis and staging. Given the lack of embedding of quantitative tests within the diagnostic framework for the various components of HAVS, we have considered such tests separately from health outcomes within this review of exposure-response relationships.

4. EVIDENCE STATEMENTS

4.1 **WHAT IS THE STRENGTH OF EVIDENCE THAT THE INCIDENCE OF VASCULAR HAVS IS RELATED TO CUMULATIVE VIBRATION EXPOSURE AND DOES THE PUBLISHED DATA FIT THE ISO 5349 (1986) PREDICTION OF VIBRATION WHITE FINGER (VASCULAR HAVS) ONSET?**

Evidence drawn from largely cross-sectional epidemiological studies has indicated an increasing risk of vascular HAVS with either duration of exposure or various measures of cumulative vibration exposure, involving combinations of vibration magnitude and exposure time (+++). Where only duration of exposure is considered in relation to risk of vascular HAVS, the use of cumulative exposure based on total hours of tool use is a better predictor of vascular HAVS than years of exposure (++) .

Evidence that both complete recovery from vascular HAVS (or amelioration of severity), is possible after cessation or reduction in exposure, and that the risk of vascular HAVS also relates to recent/current daily exposure suggests that risk of vascular HAVS may not be simply driven by the extent of cumulative vibration exposure (++) .

The vascular HAVS risk model in ISO 5349 is not universally supported by the more recent body of largely cross-sectional, epidemiological studies; some studies tend to agree with it, while others suggest that ISO 5349 both over- and under-predicts the risk of vascular HAVS (++) .

4.2 **WHAT IS THE STRENGTH OF EVIDENCE THAT THE SEVERITY OF VASCULAR HAVS IS RELATED TO CUMULATIVE VIBRATION EXPOSURE?**

The weight of published evidence suggests that there is a relationship between increasing severity of vascular HAVS (defined by blanching frequency, Griffin score, Taylor Pelmear scale, Stockholm Workshop vascular scale) and cumulative exposure, expressed as years, cumulative hours, combinations of vibration magnitude and durations of exposure (++) .

There is very little published data that establishes the nature of the exposure-response relationship with the Stockholm Workshop scale; several investigators have concluded that the use of extent of blanching, as recorded for example by the Griffin scale, is a more robust measure of severity than the Stockholm workshop in this context (+) .

4.3 **WHAT IS THE STRENGTH OF EVIDENCE THAT THE INCIDENCE OF NEUROSENSORY HAVS IS RELATED TO CUMULATIVE VIBRATION EXPOSURE?**

A significant weight of evidence shows that the risk of neurosensory symptoms of HAVS is related to cumulative exposure to vibration, but the nature of the relationship is ill-defined (+++) .

There is less data available relating reduction in severity or complete reversibility of neurosensory HAVS than for vascular HAVS, but what there is suggests a relative lack of reversibility (+) .

4.4 WHAT IS THE STRENGTH OF EVIDENCE THAT THE SEVERITY OF NEUROSENSORY HAVS IS RELATED TO CUMULATIVE EXPOSURE TO VIBRATION?

There is evidence that severity of neurosensory HAVS, graded by the Stockholm Workshop scale, is related to cumulative vibration exposure (+).

A defined relationship between Stockholm Workshop for staging of neurosensory HAVS and measurement of the amount of cumulative exposure is lacking (-).

4.5 WHAT IS THE STRENGTH OF EVIDENCE THAT THE INCIDENCE OF OTHER (NON-HAVS) UPPER LIMB DISORDERS ARE RELATED TO CUMULATIVE EXPOSURE TO VIBRATION?

The extent and the quality of the evidence for cumulative vibration exposure causing other upper limb disorders (ULDs) such as CTS, muscle weakness, pain, etc., is much lower than for vascular HAVS and neurological symptoms (+).

There is evidence for a causal link specifically between CTS and Dupuytren's contracture and exposure to vibration, however, the exposure-response relationship is unclear, confounded by work factors such as repetition, force and posture (+++).

A number of other ULDs have been noted in vibration-exposed populations, but there is no convincing evidence that the vibration exposure on its own is causal (+).

4.6 WHAT IS THE STRENGTH OF EVIDENCE THAT THE SEVERITY OF OTHER (NON-HAVS) UPPER LIMB DISORDERS ARE RELATED TO CUMULATIVE EXPOSURE TO VIBRATION?

The evidence relating to the severity, rather than the incidence of non-HAVS ULDs and its relation to vibration exposure is very limited (-).

4.7 WHAT IS THE STRENGTH OF EVIDENCE THAT QUANTITATIVE MEASURES OF FUNCTIONAL DEFICIT, PHYSIOLOGICAL DAMAGE OR PATHOLOGY ARE RELATED TO CUMULATIVE EXPOSURE TO VIBRATION?

Evidence from one particular centre strongly suggests that finger systolic blood pressure (FSBP) may be related to both cumulative exposure involving vibration magnitude and duration of tool use and recent or current A(8). This latter finding is consistent with reported improvement in FSBP in vascular HAVS cases dependent on the degree of exposure reduction or cessation (++)

Evidence from a number of centres suggests that there is a relationship between quantitative tests of neurosensory function, such as vibrotactile perception threshold (VPT) and thermal-perception threshold (TPT), and cumulative exposure (++)

There is limited evidence that TPT may be related to A(8) daily exposure and is more sensitive to cumulative exposure than VPT (+).

4.8 HOW DO THE EMISSION CHARACTERISTICS OF VIBRATION (PARTICULARLY FREQUENCY) INFLUENCE THE RELATIONSHIP BETWEEN THE INCIDENCE AND SEVERITY OF VASCULAR HAVS AND EXPOSURE TO VIBRATION?

Good quality epidemiological studies (cohort and meta-analysis) support the idea that frequency weightings, which emphasise intermediate and higher frequencies more than the current frequency weighting in ISO 5349-1:2001, may be more appropriate in defining the risk of vascular HAVS. Biodynamic considerations and limited experimental data are consistent with this (+++).

There is one study (a meta-analysis, but one based on a collection of cross-sectional studies using retrospective assessment of exposures) that suggests that unweighted acceleration is superior to ISO 5349 in predicting the severity of HAVS, as defined by the extent of finger blanching (+).

4.9 HOW DO THE EMISSION CHARACTERISTICS OF VIBRATION (PARTICULARLY FREQUENCY AND THE APPLICATION OF ISO 5349) INFLUENCE THE RELATIONSHIP BETWEEN THE INCIDENCE AND SEVERITY OF NEUROSENSORY HAVS AND EXPOSURE TO VIBRATION?

The limited available evidence does not help confirm the applicability of the ISO 5349 frequency weighting or suggested alternative frequency weightings in relation to incidence and severity of neurosensory HAVS (+).

4.10 HOW DO THE EMISSION CHARACTERISTICS OF VIBRATION (PARTICULARLY FREQUENCY) INFLUENCE THE RELATIONSHIP BETWEEN THE INCIDENCE AND SEVERITY OF OTHER UPPER LIMB DISORDERS AND EXPOSURE TO VIBRATION?

There appears no epidemiological studies that address whether the incidence of upper limb disorders, not including HAVS components, is influenced by the frequency content of the vibration (-).

4.11 HOW DO THE EMISSION CHARACTERISTICS OF VIBRATION (PARTICULARLY FREQUENCY) INFLUENCE THE RELATIONSHIP IDENTIFIED BETWEEN QUANTITATIVE MEASURES OF FUNCTIONAL DEFICIT, PHYSIOLOGICAL DAMAGE OR PATHOLOGY?

There is very limited data from epidemiological and experimental studies that attempt to characterise the influence of vibration frequency on quantitative measures of physiological or pathological response (+).

Data from the same cohort study where unweighted vibration was a better predictor of vascular HAVS risk also found that vascular response to cold challenge (FSBP) over time was better predicted by unweighted frequency acceleration than weighted according to ISO 5349 (++)

4.12 WHAT IS THE NATURE OF THE RELATIONSHIP BETWEEN VIBRATION MAGNITUDE AND EXPOSURE DURATION WHERE EXPOSURE-RESPONSE RELATIONSHIPS FOR VIBRATION-INDUCED HEALTH OUTCOMES ARE APPARENT?

There is limited data that have been used to specifically explore the relative importance of vibration magnitude and exposure duration within cumulative exposure metrics predictive of the risk of vascular HAVS, and considerably less that can be used to address its severity (+).

The limited, but nevertheless high quality available data, about the relative importance of vibration acceleration and duration of tool use in predicting the risk of vascular HAVS fail to reach consensus (++).

There is a lack of evidence that can confirm the nature of the relationship between vibration magnitude and exposure duration within cumulative exposure metrics with regard to the risk of neurosensory HAVS and its severity, other upper limb disorders, or quantitative measures of functional or pathological damage (-).

5. DISCUSSION OF RESEARCH QUESTIONS AND EVIDENCE STATEMENTS

In the following sections, the main headings are the research questions being addressed, and for each question this is followed by two sub-sections; the first on the "Evidence Statements" which have been produced as a result of the review, the second a commentary on the literature.

There is a general acceptance that poor health outcomes in those exposed to hand-transmitted vibration derive from chronic exposure to vibration, although the exposure time to precipitation of health problems can vary considerably. Therefore the first seven questions focus on defining the strength of evidence for exposure being associated with a specific health outcome, while the subsequent questions attempt to distil the extent of current knowledge on the influence of temporal and vibration characteristics on any apparent exposure-response relationship.

Each evidence statement has an assessment of its strength (from (+++) for strong evidence to (-) for lack of evidence).

5.1 WHAT IS THE STRENGTH OF EVIDENCE THAT THE INCIDENCE OF VASCULAR HAVS IS RELATED TO CUMULATIVE VIBRATION EXPOSURE AND DOES THE PUBLISHED DATA FIT THE ISO 5349 (1986) PREDICTION OF VASCULAR HAVS ONSET?

5.1.1 Evidence statements

Evidence drawn from largely cross-sectional epidemiological studies has indicated an increasing risk of vascular HAVS with either duration of exposure or various measures of cumulative vibration exposure, involving combinations of vibration magnitude and exposure time (+++).

Where only duration of exposure is considered in relation to risk of vascular HAVS, the use of cumulative exposure based on total hours of tool use, is a better predictor of vascular HAVS than years of exposure (++).

Evidence that both complete recovery from vascular HAVS (or amelioration of severity), is possible after cessation or reduction in exposure, and that the risk of vascular HAVS also relates to recent/current daily exposure suggests that risk of vascular HAVS may not be simply driven by the extent of cumulative vibration exposure (++).

The vascular HAVS risk model in ISO 5349 is not universally supported by the more recent body of largely cross-sectional, epidemiological studies; some studies tend to agree with it, while others suggest that ISO 5349 both over- and under-predicts the risk of vascular HAVS (++).

5.1.2 Commentary

There is a considerable body of evidence drawn from epidemiological studies, albeit largely cross-sectional, that have indicated a trend towards increasing risk of vascular HAVS with increasing magnitude of hand-transmitted vibration [12, 48, 49], duration of exposure [12, 49-61] or various cumulative vibration dose measures involving combinations of vibration magnitude and exposure time (years or total hours of tool use) [2, 12, 14, 49, 51, 52, 62-64].

Where only duration of exposure is considered in relation to risk of vascular HAVS, published studies in five different populations, albeit relying on retrospective exposure estimations, have

shown that the use of cumulative exposure based on total hours of tool use, rather than years of exposure, is a better predictor of vascular HAVS [12, 13, 15].

A one year time-lagged regression analysis of 3 year follow-up data from a cohort study has highlighted that daily exposure (A(8)) is a significant predictor of the risk of vascular HAVS [49]. The FOM evidence review in 2004 [5] had highlighted a number of longitudinal studies that have reported a decrease in the point prevalence of vascular HAVS over time, or that vascular HAVS symptoms are no longer reported in some individuals [65-71]. However, Brubaker [72] identified the possible influence of inconsistency in symptom reporting over time. Later longitudinal studies [73] reported that in a follow-up period of 10 years, 2 out of 15 (one retired; one active) foresters with vascular HAVS recovered from symptoms. In another follow-up study, largely of foresters but including some stone workers [74], the recovery from vascular HAVS at one and three year follow-up was 13% and 21% of the affected workers at the initial assessment. These surprisingly high recovery percentages in a relatively short follow-up period may reflect that under the study's definition for vascular HAVS, prior vascular HAVS cases who had not blanched for up to two years were still recorded as vascular HAVS cases at the initial time point. However, evidence from longitudinal studies that the risk of HAVS relates to 'current or recent' daily vibration exposure and the possibility of reversibility of HAVS suggests that the risk of vascular HAVS is not solely related to the extent of cumulative vibration exposure, but possibly influenced by periods without vibration exposure and by current level of vibration exposure.

Some studies have directly compared the prevalence in their populations to the risk prediction relationship between vascular HAVS prevalence and exposure found in ISO 5349:1986. Where this is the case, some agree [49, 51, 59, 75, 76] and some disagree [50, 53, 54, 58, 60, 77, 78]. The studies that disagree produced data to show that ISO 5349 may both under-estimate [53, 54, 58, 60] and over-estimate [50, 77, 78] the risk of developing HAVS. A study by Bovenzi [51] produced data that agreed with the model in a population of stone masons using rotary tools, but found that the model over-estimated for workers using percussive tools. Of the studies that found the ISO 5349 relationship to over-estimate risk, three of them were studies of workers using tools that are impulsive or percussive in nature. However, in the wider study, most of the papers that have looked at the contribution of different frequencies to the risk of vascular HAVS have concluded that the frequency weighting should take more account of medium and high frequency vibration. If it were the case that higher frequencies are under-represented, then studies involving impulsive tools might be expected to under-estimate the risk, rather than over-estimate it as found in three studies [50, 77, 78]. This indicates that the suitability or otherwise of the frequency weighting for prediction of the risk from impulsive tools may not be the only factor having an influence on the applicability of the current ISO 5349 vascular HAVS risk model.

A review by Bovenzi [79] looked at many epidemiological studies of the vascular exposure-response relationship. Of the 21 studies examined, 17 were cross-sectional and four were longitudinal. Eleven studies reported over-estimation of risk, seven studies reported underestimation of risk and three found good agreement. Reasons suggested by the various authors for the lack of agreement include the use of the ISO 5349 frequency weighting and the uncertainties over the energy-equivalence relationship in ISO 5349.

Table 2 of this report has been drawn up to consider the outcomes of some of the best quality, most suitable and relevant studies when compared with the ISO 5349 model. This has been done in an attempt to identify if there is any pattern to the rate at which studies agree or disagree with the exposure-response model in ISO 5349. The table shows that even when only nine optimum studies are considered, there is no identifiable pattern or trend to the agreement, or otherwise. Three studies show ISO 5349 over-estimates, three show ISO 5349 under-estimates,

one shows ISO 5349 agrees, and two studies show mixed outcomes depending on the type of workforce. Even different studies by the same principal authors have different outcomes in terms of their findings for different cohorts.

The development of the original exposure-response relationship by Brammer [75] contained some very stringent stipulations on the details of studies that could be included in the meta-analysis for the development of the exposure-response model. For example, only populations with a minimum of 50% prevalence of symptoms or more could be included. Looking at the studies that have been reported since the original development work, there are seldom any reports of symptom prevalence at this level. In itself, this is an indication that control measures to reduce damaging exposures may have been effective or that current occupational health practise applies much more stringent fitness-to-work decisions regarding vibration than were applied historically. The modification of the exposure-response model in ISO 5349:2001 to give only the 10% prevalence curve also reflects the lowering of incidence and prevalence of symptoms in the vibration exposed population.

A further issue when attempting to compare recent studies with the exposure-response model is the large uncertainty that exists on the assessment of the mean latent interval, as well as the daily vibration exposure associated with a particular workforce or subset. This may simply reflect the heterogeneity of exposure within a group of workers, who may be apparently undertaking the same task or using the same tool. It may reflect the reliance on recall for defining latency in individual workers and individual vascular susceptibility to vibration. It may also be a reflection of the individual susceptibility to vibration exposure. The latent intervals quoted in studies typically have an associated standard deviation on the mean latency, which in many cases is almost as large as the mean itself. This makes consideration of the margin of over- or under-estimation almost impossible.

Differences in outcome from studies concerning agreement with the ISO 5349 vascular HAVS risk model may also be a reflection of the extent of uncertainty in retrospective exposure assessment in the individual studies. However, there are also many other aspects of HAV research that may affect the success or otherwise of studies in investigating the appropriateness of the vascular HAVS risk model in ISO 5349; for example factors of study design, use of retrospective exposure assessment, (particularly in cross-sectional studies), changes in vibration magnitude due to changes in tooling over working lifetime etc.

Table 2. Summary of study outcomes for suitable, relevant work.

Reference	Study	Impulsive/ non impulsive	Outcomes	ISO 5349 underestimates Overestimates, or agrees
Bovenzi, (2009) #7498 and Bovenzi (2010) #7493	Epidemiological PS-Longitudinal over 3 years; forestry and stone workers.	Both	Forestry - observed incidence 4.3 % , ISO 5349 expected 3.5% Stoneworkers – observed incidence 14.3%, ISO 5349 expected 6%	ISO 5349 underestimates for stone workers. Agrees (within limits) for Forestry workers
Bovenzi et al (1994) #320	Epidemiological, cross sectional study of 828 quarry workers	Both	Prevalence of VWF and neurosensory HAVS 30% & 40% respectively	Agrees for rotary tools Overestimates for percussive tools
Burstrom #6167	Cross sectional study of 87 manual workers in a pulp-mill machinery manufacturer.	Both	Average time to onset of symptoms (vascular and neurological) was 12 years (5500 to 7200 hours of exposure). A(8) values were in the range 2.1 to 2.5 m/s ² . Accumulated exposures were between 38200 and 45300 mh/s ² .	Underestimates
Keith & Brammer (1994) #5356	Canadian jack leg rock drill operators	Impulsive	Mean observed latency = 9.5yrs, Observed prevalence = 43% Measured single axis ahw =18m/s ² ±2 Mean daily exposure time = 1.9hrs, A(4) =12.4m/s ² ISO 5349 predicts latency of 5.3 years	Overestimates up to factor of 2
Barregard et al 2003 #5958	Cross sectional study of 806 Swedish car mechanics	Both	Prevalence of ~15% VWF among car mechanics in Sweden, rising to 25% after 25 years. Estimated mean (sd) magnitude 3.5(0.6)m.s ⁻² in nut-runners. Average of 14 minutes vibration exposure per day.	Underestimates
Bovenzi & Franzinelli (1995) #1080	Epidemiological, cross sectional study of forestry workers in Italy	Non-impulsive	Overall prevalence of VWF is 23.4%. (13.4% in users or AV saws and 51.7% in users of both AV and nonAV saws). Risk estimates for VWF are lower than predicted by ISO 5349.	Overestimates
Burdorf and Monster (1991) #828	Cross sectional study of 194 riveters in aircraft industry	Impulsive	Data predicts p=0.18 at 10yrs, P= 0.29 at 20 yrs	Agrees
Nilsson et al (1989) #173	Cross-sectional epidemiological study of 89 platers and 61 controls	Both	VWF point prevalence among currently exposed platers was 42%. Latency for the study population was shorter than that predicted by ISO 5349. (Mean latency was 9.8 years)	Underestimates
Bovenzi et al 1988 #312	Cross sectional study in 76 stone drillers and cutters	Both	35.5% had symptoms of VWF with a median latent period of ten years . ISO 5349 over estimates risk in these stone workers	Overestimates

5.2 WHAT IS THE STRENGTH OF EVIDENCE THAT THE SEVERITY OF VASCULAR HAVS IS RELATED TO CUMULATIVE VIBRATION EXPOSURE?

5.2.1 Evidence statements

The weight of published evidence suggests that there is a relationship between increasing severity of vascular HAVS defined by blanching frequency, Griffin score, Taylor Pelmear scale, Stockholm Workshop vascular scale and cumulative exposure expressed as years, cumulative hours, combinations of vibration magnitude and durations of exposure (++).

There is very little published information, including that published since the previous review [1], that establishes the nature of the exposure-response relationship with the Stockholm Workshop scale; several investigators have concluded that the use of extent of blanching as recorded for example by the Griffin scale, is a more robust measure of severity than the Stockholm workshop in this context (+).

5.2.2 Commentary

Some studies use only exposure time, either in hours or years, as the metric of cumulative exposure [48, 56, 57, 80]. In a meta-analysis of three cross-sectional studies that used both weighted and unweighted (band-limited) single axis vibration exposure magnitudes, Griffin [12] investigated relationships with extent of finger blanching and various lifetime exposures, including simple duration of tool use. Mason [15] largely replicating the various lifetime exposures derived by Griffin [12] in another cross-sectional study, but employing physician-led Stockholm workshop staging, found significant relations with all the various indices of cumulative exposure, but was unable to clearly distinguish the best metric. Burdorf and Monster [76] used $A(4)$ daily vibration exposure, but considered also the number of years of exposure. The majority of the studies have found that there is an increase in severity of vascular HAVS with some measure of increasing exposure [12, 15, 51, 56, 57, 62, 63, 81]. Only two studies reported finding no relationship between severity of vascular symptoms and cumulative exposure [76, 80]. In both these cases, the assessment of symptoms and exposure duration was fairly coarse and one of the authors actually states that they would not expect their study to be able to find any such relationship. Those cross-sectional workplace studies that have addressed this question are susceptible to bias from loss of the most serious cases from investigation, therefore weakening any real relationship between exposure and severity.

In a longitudinal study of vascular HAVS cases over varying follow-up periods of 1-11 years and with continuing vibration exposure, a significant deterioration in the vascular HAVS stages (Stockholm Workshop) and number of phalanges affected by blanching was reported [48]. No attempt was made to investigate the effect of available exposure data (daily hours and follow-up time) on these outcomes.

The severity of vascular HAVS is defined by the extent and frequency of blanching attacks, and therefore subject to both environmental factors and subject recall. It has been suggested that vascular HAVS sufferers learn to modify their lifestyle to limit the frequency of blanching attacks, which may be perceived as reversibility of the severity of HAVS. At least two investigators [48, 82] highlighted that the use of the Griffin score (numerical assessment of extent of blanching) may be the most robust technique for the purposes of studying progression or regression of vascular HAVS severity. However, this still relies on accurate subject recall.

A review [5] had noted that reversibility in severity of vascular HAVS, or subjective amelioration of symptoms had been reported where vibration exposure had ceased or been reduced [70, 82-86]. Any recovery is likely to be over periods of years, as one short term follow-up study of just one year found no recovery in symptoms or staging in cases that were no longer exposed to vibration and a recent publication [87] suggests little improvement in the majority of HAVS cases over a five year period.

5.3 WHAT IS THE STRENGTH OF EVIDENCE THAT THE INCIDENCE OF NEUROSENSORY HAVS IS RELATED TO CUMULATIVE VIBRATION EXPOSURE?

5.3.1 Evidence statements

A significant weight of evidence shows that the risk of neurosensory symptoms of HAVS is related to cumulative exposure to vibration, but the nature of the relationship is ill-defined (+++).

There is less data available relating reduction in severity or complete reversibility of neurosensory HAVS than for vascular HAVS, but what there is suggests a relative lack of reversibility (+).

5.3.2 Commentary

Most of the studies that have looked at the neurosensory effects of vibration exposure have found that the onset of neurological symptoms is related to increasing vibration exposure [14, 15, 51-53, 56, 57, 62-64, 81, 88-90], although the nature of the relationship is not well defined.

Four studies [55, 76, 80, 91] failed to find a relationship. The Burdorf and Monster [76] study had also failed to find a relationship between severity of vascular HAVS and exposure. A study by Cherniak [55] found that the neurological symptoms in his 2001 study were more prevalent in the least exposed (by duration only) group. All four studies seem to have based their cumulative exposure assessments on measures of exposure time only. This raises the question of whether the magnitude of the vibration is of more relevance in the development of the neurosensory component of HAVS than in the vascular element.

Bovenzi [92] in a small cohort study of naval engine workers that staged workers by the Stockholm workshop scale, reported at 1-3 year follow-up that 4 out of 12 of those initially at SN0 were subsequently equally split between SN1 and SN2. Although good exposure measurements were made, no analysis of the incidence of neurosensory HAVS and extent of vibration exposure was made; the mean $A(8)$ in the cohort was $2.5 \text{ m/s}^2 \pm 0.6 \text{ m/s}^2$. The prevalence of neurosensory HAVS at follow-up albeit in a small study size, suggests a very different risk model than that for vascular HAVS described in ISO5349.

5.4 WHAT IS THE STRENGTH OF EVIDENCE THAT THE SEVERITY OF NEUROSENSORY HAVS IS RELATED TO CUMULATIVE EXPOSURE TO VIBRATION?

5.4.1 Evidence statement

There is limited evidence that severity of neurosensory HAVS, graded by the Stockholm Workshop scale, is related to cumulative vibration exposure (+).

A defined relationship between Stockholm Workshop for staging of neurosensory HAVS and measurement of the amount of cumulative exposure is lacking (-).

5.4.2 Commentary

There is a relatively small amount of published epidemiological studies that have directly addressed whether there is an exposure-response relationship between cumulative or daily exposure and severity of neurosensory HAVS, whether described by non-specific associated symptoms, or classifications such as the Stockholm Workshop scale. Many studies may have collected appropriate data but without this question being an outcome in any publication. For example, Bovenzi [51] staged neurosensory severity according to a Stockholm workshop-like scale in a large cross-sectional study of stone workers, calculating both $A(8)$ and lifetime dose. However, his analyses were restricted to exposure-response relationships in terms of incidence/prevalence rather than severity. Likewise the small longitudinal study in naval engine workers [92] staged subjects according the Stockholm workshop scale and calculated $A(8)$ at initial study, but reported neither data on lifetime exposures nor attempted to analyse any changes in SN staging during a relatively short follow-up period according to exposure metrics. These two studies by Bovenzi [45, 86] contain data which could potentially be used in re-analysis to attempt to elucidate an exposure-response relationship for neurosensory HAVS.

The diagnosis of HAVS, whether vascular or neurosensory, is very largely a symptom driven definition. Unlike quantitative tests associated with vascular HAVS, which remain contentious with the HAVS research community, neurosensory tests such as VPT and TPT are more widely established as possibly relating to the severity of neurosensory dysfunction. Therefore changes in such neurosensory tests may be taken as additional evidence of exposure-severity relationships for neurosensory HAVS.

Both Letz [56] and Jang [63] reported analyses on neurosensory staging by Stockholm Workshop scale and cumulative vibration exposure in shipyard workers. Letz [56] found a statistically significant relationship with cumulative years of exposure, while Jang [63] found a significant relationship between severity of neurosensory HAVS grade and categorised lifetime vibration exposure calculated according to (Griffin). Pitts [14] and Mason [15] investigated cross-sectionally largely the same populations where neurosensory staging was available, Mason [15] investigated a number of measures of cumulative exposure (years, total hours, combinations of acceleration and duration with different power functions.) Modelling suggested that the various cumulative exposure models were significantly related to neurosensory Stockholm Workshop staging, but without indicating any preferential exposure model, except that total years was the weakest exposure measure. Lundstrom [88] investigating platers, assemblers and a group of office workers (total population of 109) appeared less convinced of a relationship between cumulative vibration dose and staging by Stockholm workshop scale, noting a 'tendency' to an increase in staging with exposure. It is noteworthy that 13% of his office workers appeared to have stages SN2 or SN3, suggesting possible difficulties in case definition or staging.

A review by Mason and Poole [5] concluded that any reversibility of neurosensory HAVS was less apparent than for vascular HAVS. However, the prevalence of the key, but non-specific, symptoms of tingling and numbness in the hands and fingers has been reported as around 15-20% in the general working population and is higher than estimates of RP in the general UK population, especially male. This may tend to make defining the complete reversibility of neurosensory HAVS in both absolute terms and relative to vascular HAVS problematic. More recently, no reversibility of sensory symptoms was apparent over 1-3 year follow-up in the seventeen workers with neurosensory symptoms at baseline and with continuing exposure at a mean $A(8)$ of 2.5 m.s^{-2} [92].

5.5 WHAT IS THE STRENGTH OF EVIDENCE THAT THE INCIDENCE OF OTHER (NON-HAVS) UPPER LIMB DISORDERS ARE RELATED TO CUMULATIVE EXPOSURE TO VIBRATION?

5.5.1 Evidence statement

The extent and the quality of the evidence for cumulative vibration exposure causing other upper limb disorders (ULDs) such as CTS, muscle weakness, pain etc. is much lower than for vascular HAVS and neurological symptoms (+).

Evidence for a causal link specifically between CTS and Dupuytren's contracture and exposure to vibration has been found, but the exposure-response relationship is unclear, confounded by work factors such as repetition, force and posture (+++).

A number of other ULDs have been noted in vibration-exposed populations, but there is no convincing evidence that the vibration exposure on its own is causal (+).

5.5.2 Commentary

For ULDs other than HAVS, there is more difficulty establishing whether vibration is implicated as being causal. Vibratory operations invariably also involve manual handling and other ergonomic considerations that have been linked with ULDs. It is, therefore, not always possible to separate the contribution of the various potential causative hazards in leading to the health outcome of interest.

An authoritative review by Gemne [93] concluded that the available data showed a lack of causal relationship between vibration and the formation of bone cysts and vacuoles. A longitudinal study by Kivekas [61] found that there was no relationship between osteoarthritis and exposure time after allowing for age. Une [94] found a tendency for radiographic changes to occur in the elbow joints of chain saw operators to become more pronounced with longer chainsaw use, but differences were not significant at the 5% level. Therefore studies related to skeletal/joint health outcomes failed to find a significant relationship with cumulative exposure to vibration.

There appear to be more positive results when upper limb health outcomes are considered. Some studies have found a relationship [57, 62, 64, 76, 80, 89, 95] that relates vibration exposure to soft tissue injuries and CTS as opposed to other bone and joint disorders. These studies tend to assess cumulative vibration exposure only in terms of exposure time, taking no account of vibration magnitude [57, 64, 80, 95]. Also, some of the studies suggest that there is a relationship, although they do not contain sufficient statistical evidence to confirm this [80, 94].

Bernard [96] in a critical review of epidemiological studies up to 1997 found evidence of a causal relationship between CTS and vibration exposure, but not for neck and shoulder MSDs. A recent meta-analysis [97] on appropriate studies from 1980 to 2009 confirmed vibration as a risk factor for CTS. A recent systematic review [98] concluded that Dupuytren's contracture, which has a strong familial component, was on balance linked with high levels of work exposure, involving both manual work and vibration exposure, but without any evidence of an exposure-response relationship.

So it appears that there is a tendency for a number of ULDs to be associated with vibration exposure but, except particularly for CTS and also Dupuytren's contracture, it is not possible to be able to define vibration alone as causal. One study of female workers using orbital sanders [99] showed that the occurrence of soft-tissue disorders of the upper limb increased significantly with increase of both daily vibration exposure and strain index score. It was estimated that the

risk for CTS increased by a factor of 1.30 for each unit of increase in *A*(8) and by 1.09 for each unit of increase in the strain index score.

5.6 WHAT IS THE STRENGTH OF EVIDENCE THAT THE SEVERITY OF OTHER (NON-HAVS) UPPER LIMB DISORDERS ARE RELATED TO CUMULATIVE EXPOSURE TO VIBRATION?

5.6.1 Evidence statement

The evidence relating to the severity rather than the incidence of non-HAVS ULDs and its relation to vibration exposure is very limited (-).

5.6.2 Commentary

When it comes to the effects of vibration related to upper limb disorders other than HAVS, there are complications with the associations with manual handling activities as already described. For many health outcomes, the severity of the injury is not easily assessed. A study by Une et al [94] showed a tendency for radiographical changes in the arms of chainsaw operators to become more pronounced with longer chainsaw use, but the differences were not significant at the 5% level. While this study included a significant number of vibration exposed subjects (n=375), only a relatively small number of controls were employed for comparison (n=26).

Most of the other studies that looked for a relationship, found that there was evidence that increasing exposure to vibration was related in some way to increasing *incidence* of ULDs [51, 57, 62, 76, 89, 95] as already described, but there is little or no information on severity. This may reflect the lack of standardisation of recording of such symptoms. Whereas for vascular and neurological symptoms of HAVS, use of the Stockholm Workshop or Griffin scale are common place, the literature did not appear to contain any commonly recognised or utilised method for scoring and recording different levels of vibration related ULDs.

5.7 WHAT IS THE STRENGTH OF EVIDENCE THAT QUANTITATIVE MEASURES OF FUNCTIONAL DEFICIT, PHYSIOLOGICAL DAMAGE OR PATHOLOGY ARE RELATED TO CUMULATIVE EXPOSURE TO VIBRATION?

5.7.1 Evidence statements

Evidence from one particular centre strongly suggests that finger systolic blood pressure (FSBP) may be related to both cumulative exposure involving vibration magnitude and duration of tool use and recent or current *A*(8). The finding regarding the latter relationship is consistent with reported improvement in FSBP in vascular HAVS cases, dependent on the degree of exposure reduction or cessation (++).

Evidence from a number of centres suggests that there is a relationship between quantitative tests of neurosensory function, such as vibrotactile perception threshold (VPT) and thermal-perception threshold (TPT), and cumulative exposure (++).

There is limited evidence that TPT may be related to *A*(8) daily exposure and is more sensitive to cumulative exposure than VPT (+).

5.7.2 Commentary

While the diagnosis of HAVS and the staging of its severity are very largely differential, based on signs and reported symptoms, there are a number of quantitative tests that have been employed as an adjunct in diagnosis and staging. Many of these tests reflect functional or damage-related physiological changes caused by hand-transmitted vibration. Thus the tests employed in investigating workers exposed to hand-transmitted vibration have tended to address detecting abnormalities in vasoconstrictor or vasodilatory response, loss of receptors and associated small nerve fibres in fingers and hands, muscle loss in the hands and manual dexterity. However, with many of these quantitative measures, the test protocol and equipment used to perform the test may well influence the outcomes. There have been moves to standardise such quantitative measures, e.g. through the ISO committee activity, but often their level of diagnostic power in diagnosing and staging HAVS is less well defined compared with accepted standards for clinical diagnostic tests.

Vascular changes reflected by monitoring finger skin temperature and FSBP changes after cold challenge have been applied in a number of published research studies. While forms of these tests have been reported as diagnostically powerful [44, 49, 100], other researchers have not confirmed this [101, 102]. This lack of agreement has not been resolved, although the tests have relied on different test apparatus or different forms of the test. It has been noted that environmental conditions and the nature of cold challenge as part of FSBP testing may influence diagnostic power [103, 104].

VPT and TPT tests have been employed as quantitative tests of neurosensory loss in fingers. They reflect loss of mechano- and thermo-receptors at nerve endings in the dermis, or even loss of the small nerve fibres in the hands. Other, simpler tests include Semmes-Weinstein monofilaments, single and two-point discrimination tests that largely detect the same physiological or pathological change.

Recently researchers have become interested in quantitative measures of perceived quality-of-life, upper limb disability and psychological effects in workers exposed to hand-arm vibration [18, 105, 106].

Bovenzi [107] reported a five year follow-up (1990-1995) in forestry workers who underwent FSBP tests with cold challenge at 10°C (FSBP(10°C)) to the fingers with subgrouping in those without initial vascular HAVS with continuing exposure or subsequent retirement, and those with vascular HAVS at the initial time point. In those workers who retired during follow-up, improvements in FSBP(10°C) were correlated with years since cessation of chainsaw use. This study also suggests that effects on FSBP are reversible to some extent and that recent exposure may also play a role in defining FSBP(10°C). Bovenzi more recently had established a longitudinal study largely of forestry workers and some stone workers. Bovenzi has reported findings at the one and three year follow-up stages [13, 44, 49]. The one year follow-up suggested that FSBP(10°C) was related to daily exposure (A(8) weighted and unweighted) but had a stronger relationship with various measures of cumulative exposure involving combinations of acceleration magnitude and duration of tool use. The 3 year follow-up analysis using a one year time lagged regressive model also confirmed that responses in FSBP(10°C) over follow-up were most significantly related to measures of daily exposure expressed as A(8) weighted or unweighted rather than daily exposure duration [49]. Interestingly the same author [73] reported in a 10 year follow-up study of foresters that a reduction in FSBP(10°C) over the follow-up period was associated, but not significantly, with an increase in daily exposure A(8), but inversely related to Griffin score in both active and retired workers. Petersen [86] has also employed a cold challenge FSBP test, including whole body cooling of the subject, in a study

involving 1-13 year follow-up periods. The FSBP at follow-up was unchanged in 45%, increased (improved) in 43% and decreased (worsened) in 12%. There was no real analysis of such changes against exposure in the follow-up period, although confirming the possibility of reversibility of abnormality in FSBP.

Ho [108] in a paper published in 1986 concerning grinders, reported that total exposure measured in hours was significantly correlated with a number of median and ulnar nerve conduction velocity (NCV) parameters, VPT and skin rewarming after cold challenge, but not pain threshold, skin temperature or the 'nail press' test. The latter had been widely used in Japan as a simple test of circulatory function. The reported correlation coefficients for the significant tests were relatively weak to moderate, possibly reflecting the limitations of cumulative exposure assessments based on cumulative total hours employing subject recall. Ekenvall [81] in a case study of 55 patients noted that higher VPTs had higher mean exposure scores, using a relatively simplistic combination of years of tool use and tool acceleration banded into three categories. Nilsson [109] reported a significant relationship between cumulative exposure and increasing abnormal neutral zone in the TPT test after controlling for various potential confounders. Sauni [62] showed an increase in VPT in metal workers across a range of testing frequencies against cumulative exposure divided into quartiles. Lundstrom [110, 111] also investigated VPT against cumulative exposure divided into tertiles of increasing exposure in a similar working population to Sauni [62]. Lundstrom reported that there was not a clear relationship between exposure and reduced VPT on an individual basis, but that on a group basis, VPTs tended to be higher across the increasing exposure tertiles. He concluded that reduced tactile sensitivity based on VPT is related to the degree of vibration exposure, but the exposure-response relationship is not clear. Virokannas [112] concluded that higher VPT testing frequencies (>63Hz) are more sensitive in detecting the effects of cumulative vibration than the lower testing frequencies (16 & 32 Hz), and also reported a significant relationship (correlation coefficients around 0.6) between VPT (250 Hz testing) and total hours of exposure in both workers using tamping machines and those using chain saws [113]. Brammer [114] reported VPT measurements in a 13 year follow-up (1990-2003) study of foresters using chainsaws and latterly increased use of brush-cutters from 1999 leading to a reduction in exposure. The authors interpret the results as suggesting an arrest in the deterioration of VPT from 1995 to 2003; at the last time point the z-axis A(8) daily vibration exposures for the two tool types were 1.5 and 3.1 m.s⁻² respectively.

Su [89] investigated a number of quantitative tests reflecting manual dexterity, temperature sensation and light touch detection in construction workers in Malaysia. Cumulative exposure was based on Griffin's [12] lifetime dose measure, but simply dichotomised into two groups: low to moderate exposure and high exposure. Significant increased abnormality was only detected in light-touch detection using Semmes-Weinstein monofilaments in the higher exposure group; increased abnormalities for the Purdue pegboard (manual dexterity) and temperature sensation were not statistically significant. However, these outcomes may well be influenced by the cut-offs of abnormality used for each test. Cherniak [115, 116] has investigated nerve conduction velocity (NCV) in shipyard workers and dental hygienists using high frequency hand pieces. While the author showed significant slowing of various segmental NCVs in exposed shipyard workers compared to controls, no attempt at correlation with quantitative measures of exposure was presented. Bovenzi [92] has recently carried out a longitudinal study with a follow-up period of 1-3 years in a small (n=29) group of naval engineers. This study showed deteriorations in TPT (warmth and cold perception and thermal neutral zone) that were significantly related to daily exposure expressed as A(8), while changes in VPT at 31.5 & 125Hz were not similarly related.

Sauni [117] reported that the well-established and validated EQ-5D quality-of life questionnaire suggested poorer outcomes related to cumulative vibration exposure (p<0.001). Although the

author highlights the possible influence of ULDs and CTS on quality-of-life measures that may not be directly related to vibration exposure, but associated with ergonomic aspects of using vibrating tools. This appears to be the only published paper that examines quality-of-life in terms of cumulative vibration exposure.

5.8 HOW DO THE EMISSION CHARACTERISTICS OF VIBRATION (PARTICULARLY FREQUENCY) INFLUENCE THE RELATIONSHIP BETWEEN THE INCIDENCE AND SEVERITY OF VASCULAR HAVS AND EXPOSURE TO VIBRATION?

5.8.1 Evidence statements.

Good quality epidemiological studies (cohort and meta-analysis) support the idea that frequency weightings, which emphasise intermediate and higher frequencies more than the current frequency weighting in ISO 5349-1:2001, may be more appropriate in defining the risk of vascular HAVS. Biodynamic considerations and limited experimental data are consistent with this (+++).

There is one study (a meta-analysis, but based on a collection of cross-sectional studies using retrospective assessment of exposures) that suggests that unweighted acceleration is superior to ISO 5349 in predicting the severity of HAVS defined by the extent of finger blanching (+).

5.8.2 Commentary

Dong (2005) [118] described the categories of studies that could underpin investigation of frequency weightings in relation to health outcomes. These include:

- Psycho-physical studies of subjective sensation, such as the Miwa [11] study that underpins the current frequency weighting within ISO 5349. However, it seems unclear how subjective sensation relates to pathological outcomes associated with excessive vibration exposure.
- Epidemiological studies. Those studies that are available are largely workplace studies and often cross-sectional in design that often rely on worker recall about their past exposure history, type of tools used and presentation of initial symptoms. However, such studies truly reflect the effects of cumulative exposure in humans. Data derived from prospective cohort studies would be more powerful and possibly less open to recall and survival population bias.
- Animal and human volunteer studies of the frequency dependencies of pathological and physiological effects of vibration exposure. Animal studies need to be considered as to whether they reflect likely human pathology and that the exposure regimes are appropriate, rather than reflecting severe acute vibration exposures. Human volunteer studies need to be considered as to whether the short-term physiological changes monitored are likely to reflect a long-term pathological process.
- Biodynamic studies of the fingers-hand-arm system. While the exact processes of vibration-induced injuries are not sufficiently defined, Dong [118] suggests that vibration-induced stresses and deformations that act directly on various tissues and cells cause the development of the disorders and that these processes relate to the internal dynamic forces associated with transmission of vibration to anatomical locations in the hand-arm system. Methods to determine these biodynamic forces and their relation to frequency weighting have had some limited investigation [119]. The total power absorption of the entire hand-arm system has also been used as a measure of exposure and its relation to frequency. Thus, a frequency weighting based on measured

biodynamic characteristics, reflects a means of exposure assessment that is based on a plausible damage mechanism.

A relatively small number of studies have directly addressed issues about the appropriate frequency weighting for vascular HAVS. For example, Bovenzi has reported on a cohort study of mostly forestry workers together with a smaller number of stone-workers at 1, 3 and 4 years follow-up [13, 44, 49, 120]. At the three year follow-up analysis using a time-lag model, he suggested that cumulative exposures derived from combinations of acceleration to various powers and duration of exposure were better fits to the incidence of vascular HAVS when the acceleration was unweighted as opposed to using frequency weighted acceleration according to ISO 5349 [13]. The author concluded that for the prediction of vascular HAVS, dose measures constructed from unweighted r.m.s. acceleration are appropriate. In a further publication [49] using the same study and follow-up period, Bovenzi additionally explored the relationship between the incidence of vascular HAVS and daily vibration exposure, finding that $A(8)$ unweighted over the frequency range 6.3-120Hz was a better predictor than $A(8)$ weighted according to ISO 5349. In the analysis at the four year follow-up Bovenzi [120] applied four different frequency weightings in determining $A(8)$ values, including the ISO 5349 weighting as well as additional weightings that gave more weight to intermediate and higher frequencies. These latter, additional weightings also gave a better model fit for the incidence of vascular HAVS than the ISO 5349 weighting.

Griffin [12] reported a meta-analysis of three cross-sectional studies covering over 1500 users of power tools including stone grinders and carvers, dockyard workers and forestry workers. Various measures of cumulative dose were used in logistic regression analysis to model the occurrence of vascular HAVS. Measures of cumulative exposure involving acceleration and duration were stronger predictors of vascular HAVS when calculated using unweighted (band-limited) acceleration. Some analysis of the severity of vascular HAVS using the Griffin or blanching score and exposure measures was also made. Again, dose measures using band-limited acceleration provided better fits for vascular HAVS severity.

Mason [15] and Pitts [14] investigated the influence of frequency weighting in largely the same population. Mason studied the influence of frequency weighted and unweighted acceleration in both the incidence and severity of vascular HAVS according to the Stockholm Workshop scale. Pitts focussed on a range of frequency weightings including the current ISO 5349 weighting and others, both under consideration by the appropriate ISO committee and used in German guidance [121]. Essentially these reports could not find, for vascular HAVS, one weighting system that gave a better model for the incidence of HAVS or differentiated between unweighted versus ISO 5349 weighting for the severity of HAVS. Mason [15] highlighted that the uncertainty in retrospective exposure history constructions, largely based on worker recall, may obscure the best exposure-response relationship.

Tominaga [122] has attempted to define better frequency weightings for the risk of developing vascular HAVS. This involved the selection and re-analysis of subjects from pre-1990 studies with significant levels of vascular HAVS and aggregating workers into groups of around 20 individuals according to their unique use of a particular type of tool, carrying out similar work and within a certain exposure duration range. The author constructed a family of five weighting curves that gave significantly better fits for vascular HAVS exposure-response than ISO 5349, but highlighted possible limitations of the analysis in terms of not all tool types being represented (chipping hammers, jack hammers, rock drills, sand rammers and chain saws included), the relatively small size of groups and the possibility that not all vibration exposure was accounted for. Essentially Tominaga suggests that his analysis shows that high frequencies should be weighted at the expense of lower frequencies in terms of predicting the risk of vascular HAVS.

At least one epidemiological study [58, 60] has suggested that the observed increased prevalence of vascular HAVS in a particular population (riveters) from that predicted by ISO 5349 was due to impulsive acceleration, or higher frequencies not being represented by the ISO 5349 weighting. Brammer in two modelling meta-analyses of exposure-response relationships [2, 75] noted in the latter study that there was a lack of fit in cohorts using impulsive tools. Explanations for this are suggested, however it may be that the lack of fit for impulsive tools is due to early loss of cases from workplace based cross sectional studies, possibly due to damaging exposures. The consequences of this are that observed vascular HAVS prevalences for impulsive tool users are lower than predicted.

Dong [123] in an authoritative review of biodynamics of hand-arm vibration derived from theoretical considerations and experimental studies suggests that ISO 5349 over-estimates the potential of low frequencies to cause problems while underestimating the outcomes from higher frequency exposure. A few experimental studies have also addressed the issue. Bovenzi [124] found 15-minute exposure to 5.5 m.s^{-2} weighted acceleration at various frequencies in healthy subjects caused post-exposure vasoconstriction in both vibrated and non-vibrated hands, but in the vibrated hand vasoconstriction was higher at higher frequencies. A later human experimental study [125] employing FSBP suggested that increasing vibration magnitude caused greater reduction in finger blood flow (FBF) in all fingers and that 125Hz caused a greater reduction in FBF than 31.5Hz applying equal levels of frequency weighted (ISO 5349) vibration. These results were interpreted by the author as suggesting that the ISO 5349 frequency weighting may not be appropriate for the vascular effects of vibration. However, these are acute effects from short-term exposures and their relevance to chronic effects from long-term exposure is unknown. In a rat model study Curry [34] investigated arterial damage using 4-hour duration of a high constant acceleration of 49 m.s^{-2} at 30, 60, 120 & 800Hz. A complex relationship between frequency of vibration and histological damage was observed, with the same damage markers increased after 30, 60 and 120Hz. The author suggested that smooth muscle contraction is a major contributor to arterial damage, and that the damage found at 800Hz and above may indicate resonance effects on elastic membranes.

5.9 HOW DO THE EMISSION CHARACTERISTICS OF VIBRATION (PARTICULARLY FREQUENCY AND THE APPLICATION OF ISO 5349) INFLUENCE THE RELATIONSHIP BETWEEN THE INCIDENCE AND SEVERITY OF NEUROSENSORY HAVS AND EXPOSURE TO VIBRATION?

5.9.1 Evidence statements

The limited available evidence does not help confirm the applicability of the ISO 5349 frequency weighting or suggested alternative frequency weightings in relation to incidence and severity of neurosensory HAVS (+).

5.9.2 Commentary

Based on a combination of theoretical and experimental data, a biodynamic approach to frequency weighting suggested separate frequency weightings for the fingers, hands and wrists, which are anatomical structures associated with the neurosensory component of HAVS [118]. The biodynamic analysis would suggest that the frequency weighting in ISO 5349 underestimates the risk from higher frequencies in causing neurosensory problems associated with the hands and fingers, but correlates approximately for the wrist and more proximal upper limb structures [118]. Dong [123] suggested that using transmitted acceleration based (TAB) weightings for fingers, unweighted acceleration may be more appropriate, but pointed out that

other TAB weightings may be appropriate for non-vascular HAVS disorders. This author [126] also highlighted that finger grip forces significantly altered the absorption of vibration power, and that force and coupling between tool and hand may influence frequency weighting. In another experimental study, but based on an acute exposure rat model, Govindaraju [127] found evidence of nerve damage occurring at 800Hz, again questioning the relevance of the frequency weighting within ISO 5349, although the severity of damage (disrupted myelin/axons and oedema) did not correlate directly with frequency of stimulus. Govindaraju [32] applied acute high acceleration shock-wave vibration simulating a bucking bar in a rat tail model and concluded that shock wave vibration can cause severe nerve damage. However, the relevance of these animal findings from acute exposures in an animal model to human chronic exposure appears conjectural.

The evidence provided by Dong [118] and Govindaraju [32] tends to suggest that the ISO 5349 frequency weighting possibly underestimates the importance of higher frequencies in causing neurosensory problems. The cross-sectional studies by Mason [15] and Pitts [14] employed largely the same study population and statistical analysis, based on that used by Griffin [12]. Pitts [14] employed various weightings including ISO 5349, a band-limited unweighted approach, a frequency weighting system suggested by Tominaga [122], and two weightings contained in German guidance [121](VDI 2057). There was some suggestion that ISO 5349 and one of the German VDI 2057 frequency weightings indicated better models of the risk of neurosensory HAVS. Mason [15] found no clear evidence that acceleration weighted according to ISO 5349 or unweighted was superior within various combinations of acceleration to the first and second power and duration of tool use in predicting the incidence or severity of neurosensory HAVS, and highlighted the problems inherent in retrospective exposure constructions. Sauni [62] in a cross-sectional study of metal workers reported that impulsive HAV was significantly associated with neurosensory symptoms but not vascular or other symptoms. Tominaga [122] re-analysed data from a number of pre-1980 studies where workers had used a particular type of tool, in order to construct an alternative frequency weighting by comparing vibration exposure and effects. Numbness was the neurosensory outcome measure of relevance. Tominaga stated that, like vascular HAVS, there was a tendency for high frequency to have a strong influence, but without being able to make a statistically significant frequency weighting descriptor from the data. He highlighted some limitations of this study which included the data being drawn from small groups, the sampling of tool type was biased as it did not include grinders or impact wrenches, and that the vibration magnitudes used might not fully reflect the workers' exposure where there was potential for variation between tasks.

There is no body of data from epidemiological studies that unequivocally support the limited experimental and theoretically based studies that suggest that higher frequencies should be given more weight for predicting neurosensory outcomes in vibration exposed hands and fingers.

5.10 **HOW DO THE EMISSION CHARACTERISTICS OF VIBRATION (PARTICULARLY FREQUENCY) INFLUENCE THE RELATIONSHIP BETWEEN THE INCIDENCE AND SEVERITY OF OTHER UPPER LIMB DISORDERS AND EXPOSURE TO VIBRATION?**

5.10.1 **Evidence statement**

There appears no epidemiological studies that address whether the incidence of upper limb disorders, not including HAVS components, is influenced by the frequency content of the vibration (-).

5.10.2 Commentary

Dong's biodynamic analysis [118, 123, 126]) may also apply to other upper limb disorders in those exposed to vibration. However, it is based on uncomplicated assumptions of how vibration may cause damage at various anatomical structures in the upper limbs. This is possibly more appropriate for acute effects from exposure rather than chronic biological effects as it takes no account of damage-repair mechanisms and temporal effects. It is also without any supportive experimental human data for either acute or chronic effects. However it suggests that biodynamic frequency weightings may be applicable for conditions in the fingers/hands and wrist/elbows/shoulder, although biodynamic weighting for the latter anatomical structures correlate with ISO 5349.

An epidemiological study in female dentists with frequency weighted exposures below $2.5 \text{ m.s}^{-2} \text{ A(8)}$ [128] concluded that dentists with a long work history of dental filling and root treatment involving use of very high frequency (above 1250Hz) hand pieces seemed to be associated with finger symptoms which were perceived as vibration-related particularly where tests of "pinch-grip" were used. However this study did not appear to have excluded other possible influences such as exposure to mercury or other chemicals which cause peripheral circulatory disturbances.

Tominaga [122] re-analysed data from a number of pre-1980 studies where workers had used a particular type of tool in order to construct an improved frequency weighting by comparing vibration exposure and effects. Joint pain was the outcome measure of relevance. Tominaga found that the complaint rate did not vary between groups and was not related to vibration.

5.11 HOW DO THE EMISSION CHARACTERISTICS OF VIBRATION (PARTICULARLY FREQUENCY) INFLUENCE THE RELATIONSHIP IDENTIFIED BETWEEN QUANTITATIVE MEASURES OF FUNCTIONAL DEFICIT, PHYSIOLOGICAL DAMAGE OR PATHOLOGY ?

5.11.1 Evidence statements

There is very limited data from epidemiological and experimental studies that attempt to characterise the influence of vibration frequency on quantitative measures of physiological or pathological response (+).

Data from the same cohort study where unweighted vibration was a better predictor of vascular HAVS risk also found that vascular response to cold challenge (FSBP) over time was better predicted by unweighted frequency acceleration than weighted according to ISO 5349 (++).

5.11.2 Commentary

Bovenzi has relatively recently established a cohort for longitudinal study, consisting predominantly of forestry workers together with a smaller number of stone workers. A cold provocation finger systolic blood pressure (FSBP) test using 30°C & 10°C appears to be part of the longitudinal monitoring of this cohort. Analysis at the one year follow-up period used linear regression models relating FSBP(10°C) at follow-up to various measures of cumulative exposure of the form:

$$\sum a_i^m t_i \text{ where } m = 0,1,2,4$$

Use of both ISO 5349 weighted and unweighted acceleration, suggested only minor differences between unweighted and weighted values (perhaps slightly favouring the weighted dose

measures). Further analysis was published at the 3-year follow-up period, allowing regression analysis of changes in FSBP(10°C) over time against alternative measures of A(8) daily vibration exposure, after adjusting for covariates [49]. This analysis was carried out in three groups: all subjects, those without vascular HAVS at initial study and those with normal FSBP(10°C) at initial study. In all three groups the A(8) daily vibration exposure unweighted over the range 6.3-1250Hz gave better model fits than using the A(8) weighted as per ISO 5349. Bovenzi has also reported recently a longitudinal study of neurosensory function using thermal perception thresholds (TPT, hot and cold) and vibrotactile perception thresholds (VPT) at 31.5 and 125 Hz (Bovenzi, 2011). This is a relatively small study of 29 naval engineers and a similar number of controls, with follow-up periods of between 1-3 years. However, while changes in time for TPTs, but not VPTs, were significantly related to measures of daily exposure, such metrics were only calculated as frequency-weighted according to ISO 5349 rather than including unweighted calculations as in the studies involving FSBP.

A study by Virokannas [113] produced data that suggested that the relationship between the frequency-weighted acceleration and duration of tool use is not of equal weight in causing abnormality in VPT. The presented data suggest that $a_{hw}^2 \cdot t$ is a better fit.

Alternative frequency weightings, based on biodynamic responses derived from theoretical and experimental assessments, have been described for various anatomical structures in the upper limbs, and may suggest that differing frequency weightings apply to physiological and pathological responses reflecting sites of damage [118, 123]. However, data to support these frequency-weightings is lacking.

There are only a limited number of human and animal experimental studies that are relevant to the research question. Burstrom [129, 130] reported human volunteer studies where vibration magnitude, frequency weighted according to ISO 5349, was unable to predict temporary threshold shifts in VPT. Bovenzi [125] reported a human volunteer study where 125Hz caused a greater reduction in finger blood flow than 31.5Hz when equal levels of frequency-weighted vibration were applied. This could be seen as consistent with epidemiological findings for both incidence of finger blanching and FSBP response, where higher frequencies have greater effect than lower frequencies, thus again calling into question the validity of the current ISO 5349 frequency weighting. Ye [131] showed that different repetition rates and peak magnitudes, but the same frequency weighted rms acceleration, caused similar decreases in blood flow, implying that the ISO 5349 model is applicable for shock vibration. Govindraju [127], Curry [34] and Okada [132] report studies in rats that include a range of physiological parameters and tissue damage markers and vibration frequencies covering 30Hz to 800Hz, or 3Hz to 1000Hz. Complex patterns of changes were noted, but without any evidence of how this relates to the frequency weighting of ISO 5349. As with all experimental studies, the question of how short-term effects from acute exposures relate to the risk from chronic exposure, is unclear.

5.12 WHAT IS THE NATURE OF THE RELATIONSHIP BETWEEN VIBRATION MAGNITUDE AND EXPOSURE DURATION WHERE EXPOSURE-RESPONSE RELATIONSHIPS FOR VIBRATION-INDUCED HEALTH OUTCOMES ARE APPARENT?

5.12.1 Evidence statements

There is limited data that have been used to specifically explore the relative importance of vibration magnitude and exposure duration within cumulative exposure metrics predictive of the risk of vascular HAVS, and considerably less that can be used to address its severity (+).

The limited, but high quality available data about the relative importance of vibration magnitude and duration of tool use in predicting the risk of vascular HAVS fails to reach consensus (++).

There is a lack of evidence that can confirm the nature of the relationship between vibration magnitude and exposure duration within cumulative exposure metrics with regard to the risk of neurosensory HAVS and its severity, other upper limb disorders or quantitative measures of functional or pathological damage (-).

5.12.2 Commentary

Data from a single cohort study suggests that within a cumulative exposure metric, acceleration is more important than exposure duration (i.e. $a^2.t$ as implicit in the ISO 5349 or higher powers) as a better risk predictor than employing equal weighting to both acceleration and duration (i.e. $a.t$), or using simple total hours of exposure. However, this result appears at odds with a meta-analysis [12] of the data from three cross-sectional studies where equal weighting or simple total cumulative hours appeared a better risk predictor than employing higher powers of acceleration (i.e. $a^2.t$ or $a^4.t$). The evidence from these limited studies for the use of unweighted acceleration rather than the weighted as in ISO 5349 appeared somewhat stronger than the relative importance of acceleration and duration in defining risk of vascular HAVS.

The A(8) daily vibration exposure calculation, and thus implicitly also the vascular HAVS risk model, are explicitly based on the premise that frequency-weighted vibration (a_{hv}) is more important than the time that a worker uses vibrating tools. Recently a relatively small number of studies or retrospective analyses of prior collected data have attempted to investigate various functions involving both vibration magnitude (frequency weighted or band limited) and exposure duration ($a_{\text{weighted or unweighted}}^m.t$ where m is an integer) as risk predictors. These recent studies have used various statistical techniques to compare the effect of the different combinations in order to identify which models provide the best fit of data.

One of the first publications that specifically addressed the question of the nature of the relationship between acceleration magnitude and exposure time [12] was a meta-analysis of three cross-sectional studies involving a range of tools. This study concluded that a combination of hours of tool use and unweighted acceleration ($a_{\text{unweighted}}.t$) was the best risk model for both incidence and severity of vascular HAVS, based on the extent of blanching. For severity of HAVS, giving higher weight to vibration magnitude was a poorer fit than using simple total exposure hours. Thus the authors' analysis for the incidence of vascular HAVS suggests that the relationship in ISO 5349 may be flawed. However, while a meta-analysis, this study involved only cross-sectional data and the vibration measurements used the values for the highest axis, possibly under-representing magnitudes for rotary tools. Interestingly for stone grinders, whose exposure was limited to only rotary tools, higher powers of frequency weighted acceleration gave a better fit.

In contrast to Griffin's meta-analysis [12] Bovenzi [44] reported that higher orders of acceleration in relation to duration gave better statistical fits with little influence of using either weighted or unweighted acceleration for vascular HAVS. As this was data from a one-year follow-up on a cohort consisting predominantly of forest workers, this analysis obviously also relies heavily on retrospective exposure data from employee and employer recall. The same author reported further analysis after a three-year follow-up on the same cohort, which involved statistical techniques such as time-lag regression analyses, that are more appropriate for discerning exposure relationships within time points of a longitudinal study.

This further analysis [13] reiterated that higher powers of acceleration, and especially unweighted acceleration, gave a better statistical fit for risk of vascular HAVS. Certainly from

the modified Akaike's Information Criterion (QIC) used to compare the statistical fits between various exposure-response models, inclusion of vibration magnitudes combined with simple total exposure hours strongly improved the models for the risk of vascular HAVS. Changes in QIC values from parity between acceleration and duration to higher powers of 2 & 4 for acceleration relative to duration were less obvious, although they tended to support higher powers for acceleration. Overall the data from this cohort, consisting largely of foresters, suggested that employing acceleration in combination with exposure duration was a better predictor of vascular HAVS risk than simple cumulative hours of tools use. Higher powers of acceleration were better predictors than using equal weighting of acceleration and cumulative hours and using unweighted acceleration (over the frequency range of 6.3-1250 Hz) was better than using weighting according to ISO 5349. However, all the cumulative exposure metrics applied in this study were significant predictors of vascular HAVS risk.

Mason [15] attempted to replicate the analysis of Griffin [12], but looking at both incidence and severity of both vascular and neurosensory HAVS that had been Stockholm Workshop staged by medical assessment. This cross-sectional study was based on retrospective exposure assessment on a combination of subjects from a HAVS referral unit with varying tool use and a workplace study. The data suggested that for both vascular and neurosensory HAVS the incidence and severity were significantly related to a number of cumulative exposure metrics, but no power of acceleration or use of weighted versus band-limited was statistically superior. This appears to be the only study that has addressed the nature of the acceleration-exposure relationship for the incidence and severity of neurosensory HAVS. However, the authors stressed the inadequacies and difficulties in retrospective exposure assessment and cross-sectional studies in deriving exposure-response relationships.

Bovenzi in his cohort study of mainly foresters, also included finger systolic blood pressure measurements with cold challenge to the fingers as a quantitative means of defining vasoconstrictor response [44, 49]. At the one-year follow-up [44], the vasoconstrictor response was only significant when exposure time and vibration acceleration were combined to give cumulative exposures, and higher powers of acceleration (2 and 4) appeared to give a better fit than using a simple combination of acceleration and duration. Interestingly using frequency weighted acceleration according to ISO 5349 or unweighted acceleration had little influence, with the use of the unweighted giving marginally better fits. The papers [13, 44, 49] reporting the analysed data from this cohort after the 3-year follow-up period confirmed that higher powers of acceleration gave better fits to the vasoconstrictor response, but that unweighted acceleration performed better than frequency weighted acceleration.

A small longitudinal study [92] in naval engineering using thermal perception thresholds (TPT) as indicators of neurosensory deterioration, suggested that changes in TPT were significantly related to magnitude of vibration exposure and daily duration of exposure in hours (both components of $A(8)$), but failed to assess their relative importance.

6. DISCUSSION AND CONCLUSIONS

6.1 SOURCES OF BIAS AND UNCERTAINTY IN OUTCOMES OF RESEARCH

For the purposes of studying an exposure-response relationship, the most powerful studies are prospective cohort studies of sufficient duration to ensure the sufficient development of health outcomes in the exposed population. These studies may however suffer from significant attrition rates that may introduce bias and are relatively uncommon because of cost and their time consuming nature.

The majority of epidemiological studies reported in the literature relating to HAVS are cross-sectional in nature. Of necessity, these studies contain exposure estimates which are based on reconstruction of vibration exposure patterns, depending often on worker recall and also the estimation of the likely vibration emissions from tools used. The nature and degree of uncertainty between the two elements of retrospective cumulative exposure may obscure their respective relevance in defining exposure-response relationships. It is also possible that the nature of the exposure-response relationship may be different depending on the nature of the vibration and the tools used. Thus a relationship derived from investigation of workers using almost solely a single tool (e.g. chainsaws) may not be appropriate for other exposures, and studies involving multiple tool use may not show a clear relationship.

Another possible source of bias in cross-sectional workplace investigations is that a survivor population is studied, with the most severe cases no longer in the workplace, thus introducing a bias in the results towards detecting a weaker relationship than exists in reality. A more general source of potential bias is the favouring of studies with positive findings compared to studies with negative outcomes.

While the diagnosis and staging of the severity of the components of HAVS relies on largely symptom-driven criteria within the Stockholm workshop scale, it is likely that any exposure-response relationship will be less well defined than if the diagnosis was based on quantitative measures of vibration-induced pathology. Some of the uncertainty in exposure-response relationships in symptom-led HAVS diagnosis and staging may simply reflect the additional uncertainties from the influence of environmental factors, subject recall and the non-specific nature of the symptoms, which can be relatively common in any working population. For example, a study in Japanese forestry workers showed the same degree of vascular damage by finger punch biopsy, but the reporting of blanching symptoms was driven by the nature of the climate they were working in.

6.2 EVIDENCE RELATING TO VASCULAR HAVS

As found in the previous review [1], there appears strong evidence of an increasing risk of vascular HAVS with cumulative exposure to vibration, either based on duration of exposure or various metrics involving both vibration magnitude and duration of exposure. The risk of vascular HAVS also appears related to recent or current daily exposure. This, in combination with the potential reversibility of vascular HAVS after cessation or reduction in exposure, suggests that risk of vascular HAVS is not simply linked to accumulated vibration exposure. Evidence from one particular centre strongly suggests that finger systolic blood pressure (FSBP) under cold challenge shows similar relationships to both cumulative exposure and current daily exposure as for the risk of vascular HAVS. (Significant potential diagnostic and prognostic outcomes for FSBP from this research group have not been substantiated, and need

confirmation.) While there is also moderate evidence for a relationship between the severity of vascular HAVS and cumulative exposure, any relationship based on recent or current exposure is unclear.

Most evidence from good quality epidemiological studies (a cohort and meta-analysis), could challenge FSBP in the same cohort study, biodynamic considerations and limited experimental data, supports the idea that frequency weightings emphasising more intermediate and higher frequencies compared with current ISO 5349-1:2001 frequency weighting, may be more appropriate in defining the risk of vascular HAVS. The meta-analysis also suggested that unweighted frequency is superior to the frequency weighting in ISO 5349 in predicting the severity of vascular HAVS, as defined by the extent of finger blanching.

There is limited data that has specifically explored the relative importance of vibration magnitude and exposure duration within cumulative exposure metrics for predicting the risk of vascular HAVS, and considerably less that addresses its severity. The limited, but high quality, available data about the relative importance of vibration acceleration and duration of tool use in predicting the risk of vascular HAVS fails to reach consensus.

6.3 EVIDENCE RELATING TO NEUROSENSORY HAVS

Over recent years the importance of the neurosensory component in comparison with vascular HAVS has been recognised with regard to upper limb disability or quality-of-life. However, the symptom drivers of diagnosis and staging of neurosensory HAVS (i.e. numbness and tingling) are relatively non-specific and commonly reported outside vibrationally exposed cohorts.

As with vascular HAVS, there is significant weight of evidence that shows that the risk of neurosensory symptoms of HAVS and their severity is related to cumulative exposure to vibration, although the weight and quality of evidence may not be as strong as for VASCULAR HAVS. There is, however, very little evidence that attempts to actually quantify the relationship. There is a lack of evidence concerning current or recent vibration exposure and risk of neurosensory HAVS, while neurosensory HAVS appears less reversible than vascular HAVS.

Evidence from a number of centres suggests that there is a relationship between cumulative exposure and well-founded quantitative tests such as vibrotactile perception threshold (VPT) and thermal-perception threshold (TPT) that indicate loss of small nerve fibres and their associated receptor nerve endings. TPT may also be related to A(8) daily exposure and appears more sensitive to cumulative vibration exposure than VPT.

Less is known about the nature of the relationship between cumulative exposure and neurosensory HAVS compared with vascular HAVS. The limited available evidence does not help confirm the applicability of the ISO 5349 frequency weighting, or suggested alternative frequency weightings, in relation to incidence and severity of neurosensory HAVS. Also, there is no evidence to indicate how frequency weighting may influence the relationship between exposure and VPT and TPT measurements. There is also a lack of evidence that can confirm the relative importance of vibration magnitude, or exposure duration, within cumulative exposure metrics, in defining the risk and severity of neurosensory HAVS, and changes in VPT or TPT.

6.4 REVERSIBILITY OF VASCULAR AND NEUROSENSORY HAVS AND THE 'NO EFFECT' LEVEL

There is not a great deal of evidence on the reversibility of vascular HAVS, or any relationship to the levels of continuing exposure, apart from complete cessation of vibration exposure. The

evidence would seem to suggest that vascular HAVS may show some reversibility, but over a time frame of years and to a greater degree in the less severe cases. The evidence for reversibility of neurosensory HAVS is sparse. However, based on an understanding of the neurological pathology and the very limited evidence available, it seems unlikely that neurosensory HAVS shows reversibility.

The symptom-driven diagnosis and staging of both vascular and neurosensory HAVS may raise complications in terms of defining reversibility however. It seems well established with occupational health professionals who are experienced in assessing HAVS, that many sufferers of significant vascular HAVS modify their lifestyle to reduce the number of blanching attacks that are suffered. This phenomenon is well known in those with primary Raynaud's. Such lifestyle modifications that can influence frequency, although not the extent of blanching, become the norm for a sufferer and consequently they may be perceived as reduction in the severity of vascular HAVS over time and reported as such to a project investigator. Lifestyle modification to ameliorate symptoms of numbness and tingling is not possible, although those with significant neurosensory HAVS may avoid undertaking any work requiring manual dexterity. Quantitative measures that may reflect the underlying pathology of HAVS could be a better way of defining reversibility of HAVS. However, for vascular HAVS, there is only one Italian group (Bovenzi et al) that has reported the value of a vascular test (FSBP) in staging severity and identifying reversibility [49, 133]. This has not been confirmed by other groups. For neurosensory HAVS, both VPT and TPT have proven status in defining peripheral neurosensory loss in a number of clinical conditions, but there is dearth of evidence that has specifically studied changes in these tests in HAVS sufferers after reduction or cessation of exposure.

6.5 NO EFFECT LEVEL

Brammer [4] explains how the exposure-response relationship can be extrapolated to predict the vibration magnitude at which the latent interval corresponds to a working lifetime. This could then be regarded as a no effect level of exposure, since an operator could theoretically be exposed at this level for a lifetime without developing symptoms. The value obtained by Brammer is in the range $1\text{m/s}^2 < a_K < 2\text{m/s}^2$ where a_K is the single axis, frequency weighted acceleration magnitude.

ISO 5349-1:2001 states; "*Studies suggest that symptoms of the hand-arm vibration syndrome are rare in persons exposed to an $A(8)$, at a surface in contact with the hand, of less than 2m/s^2 and unreported for $A(8)$ values of less than 1m/s^2 .*" The graphical representation of the proposed exposure-response relationship for vascular HAVS (Figure C.1 in Appendix C) indicates this with a dotted line, rather than a solid line, below $3\text{m/s}^2 A(8)$.

6.6 EVIDENCE RELATING TO OTHER UPPER LIMB DISORDERS

The extent and the quality of the evidence for cumulative vibration exposure causing other ULDs such as CTS, muscle weakness, pain etc. is much lower than for vascular HAVS and neurological symptoms, although evidence for a causal link, specifically between CTS and Dupuytren's contracture and exposure to vibration has been found. A number of other ULDs have been noted in vibration-exposed populations, but there is no convincing evidence that the vibration exposure on its own is causal. The evidence relating to the severity rather than the incidence of non-HAVS ULDs and its relation to vibration exposure is very limited.

For those few non-HAVS upper limb disorders where a causal link with vibration has been found, there is no epidemiological evidence that addresses whether their incidence is influenced

by the frequency content of the vibration or the nature of the relationship between vibration magnitude and exposure duration within exposure metrics.

6.7 EXPERT CONSULTATION

Responses were received from 10 of the 40 experts contacted, or from representatives where a team of researchers work together. Three of these contacts gave details of current research programmes and recent publications that allowed crosschecking of the validity of literature searches undertaken. Details of work currently in progress in the field of research included; continuing study of the mechanisms of vibration injury in rat-tail models that simulate sinusoidal vibration and impact shock wave vibration from powered hand tools and on-going work within the area of exposure-response relationships for HAVS.

Two researchers also gave details of papers that are currently in the process of being published but which are not yet available for inclusion in the review. One paper deals with frequency dependent effects in animal models; the other does directly concern exposure-response relationships. A significant contribution was made by Tony Brammer, who provided a considerable amount of helpful supplementary information on the background to the formulation of the original exposure-response relationship and suggested no effect level.

6.8 GAPS IN KNOWLEDGE

This review indicates that there are still a number of unknowns with regard to the exposure-response relationships for HAVS. Despite on-going research in the area of HAVS, quantitative exposure-response relationships for HAVS remain elusive and ill-defined.

It has still not been possible to establish if there is a “no effect” level for vibration exposure, other than the somewhat obvious “zero exposure” level.

Other unknowns include:

- The technique for quantification of the exposure, in terms of how to combine information on vibration magnitude and exposure duration, that best reflects the risk and severity of the different health outcomes;
- The inter-relationship between cumulative exposure, current exposure and periods of non-exposure in the development of the symptoms of HAVS;
- The relative importance of different vibration characteristics, such as frequency or impulsiveness, in relation to the different health outcomes.

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ANNEX

Ref	Matrix ID/para number	Study	Outcomes
Aiba et al (2012)[134]	4.1	<p>Type Longitudinal study of impact wrench users 1981 to 2008</p> <p>Population 704 workers</p> <p>Outcome definition. VWF by medical examination by questionnaire and doctor</p> <p>Exposure assessment TOT from questionnaire, based on hrs/day x days /year x years. Total vibration magnitude in terms of n according to ISO 5349.</p> <p>Analysis: Association between risk of RP and operating years from Kaplan-Meier survival curve</p>	<p>4.1 Mean TOT 11,689 hours. 39 cases of VWF over the period of study</p> <p>4.2 Incidence rate of 6.27 persons per 1000 person years. Survival curve showed risk of developing RP was 0.002 to 0.004 for 7-12 years after which there was an exponential increase. Gender age and smoking were not significantly associated with risk. Prevalence peaked at 6.2% in 1987. Prevalence was 4.9% in 2008. Many exposures above the limit value.</p>
Anttonen & Virokannas (1994)[59]	4.1 4.3	<p>Type Cross sectional study of 3720 reindeer herders, using snow mobile, chain saws</p> <p>Population 2705 respondents to questionnaire</p> <p>Outcome definition Exposure time, hand numbness and white finger attacks reported by self-administered questionnaire</p> <p>Exposure assessment A(4) exposure to vibration, annual usage time and number of years used.</p>	<p>4.1 VWF prevalence 19% compared with ISO 5349 prediction of 17% based on A(4) daily exposure values</p> <p>4.1 Increasing VWF prevalence with increasing exposure in hours. Shows clear monotonic linear relationship of cumulative hours exposure with prevalence of age adjusted VWF (age adjusts to account for primary Raynauds onset).</p> <p>4.3 Increasing hand numbness with increasing exposure, but starting from 29% in controls.</p>
Astrom et al (2006)[80]	4.1 4.3 4.5	<p>Type Epidemiological Cross sectional study of 769 drivers of terrain vehicles in Sweden</p> <p>Population Driver of forest machines (273) snowmobiles (176) snowgroomers (101) Reindeer herders (218) and referents (296) 61 –79% response rate.</p> <p>Outcome definition: Self administered questionnaire to rate symptoms of HAVS and Nordic questionnaire on MSDs</p>	<p>4.1, 4.3 No obvious increase in risk of VWF or numbness by categorised increasing exposure hours</p> <p>4.5 Monotonic increase in risk of wrist, elbow and shoulder by categorised increasing exposure hours, but only in left arm not right arm. Some evidence of increased neck problems with increasing exposure, but relationship between duration of exposure and</p>

Ref	Matrix ID/para number	Study	Outcomes
		<p>Exposure assessment Cumulative exposure time in hours estimated from questionnaire</p> <p>Analysis Prevalence odds ratios using multiple logistic regression analysis, adjusted for age and nicotine use. 95% confidence interval used</p>	severity of symptoms is poor. Study indicates that HAV exposure <i>could</i> have contributed to symptoms. Cannot distinguish between HAVS and CTS.
Barregard et al (2003) [53]	4.1 4.3	<p>Type A cross sectional study of 806 Swedish car mechanics</p> <p>Population 806 Swedish car mechanics, exposed mainly via nut runners</p> <p>Outcome definition: Self administered questionnaire followed up by clinical examination of 187 individuals reporting symptoms. Classified according to Stockholm Workshop scale.</p> <p>Exposure assessment Vibration measurements on wrenches to ISO 5349 1986 (single axis) in a brake device. Estimated magnitude 3.5m/s/s. No calculations of lifetime dose.</p> <p>Analysis. Survival analysis. 95% confidence interval using binomial distribution, analysis of variance and linear and logistic regression all used to examine the association between exposure time, age, nicotine and prevalence of HAVS.</p>	<p>4.1 Prevalence of ~15% VWF among car mechanics in Sweden, rising to 25% after 25 years. Estimated mean (sd) magnitude 3.5(0.6)m.s⁻² in nut-runners. Average of 14 minutes vibration exposure per day.</p> <p>4.1 Increase in prevalence of VWF with duration of exposure. The prevalence of VWF is far higher than would be predicted by ISO 5349 model. (3%). The validity of the frequency weighting is called into question.</p> <p>4.3 Clear linear relationship between years of exposure and prevalence of neurosensory HAVS. About 25% of the cohort had neurological symptoms at stage 1-2 rising to 40% after 20 years</p>
Bovenzi et al (1998) [107]	4.1 4.2 4.7	<p>Type Cohort, prospective study in forestry workers</p> <p>Population 68 forestry workers in three groups, first examined in 1990, re-examined 1995. Categorised into group A- active workers without VWF; Group B-workers without VWF who retired during study period, and group C active or retired workers with VWF at initial time point.</p> <p>Outcome definition Medical interview, physical examination and cold provocation test to measure FSBP₁₀</p> <p>Exposure assessment ISO 5349 vibration total values and lifetime dose based on vibration magnitude and total hours of use.</p>	<p>4.1 4.2 Reduction in or cessation of exposure has beneficial effect on VWF. VWF may be reversible on cessation of, or reduction in exposure (using AV saws) Evidence that relationship between vibration and incidence and severity of VWF may not reflect a simple relationship of irreversible outcome based on cumulative exposure.</p> <p>4.7 FSBP has a significant (p<0.001) inverse relationship with VWF symptoms. A significant improvement in FSBP was seen in groups B and C, again suggesting underlying reversibility in vasoconstriction when vibration exposure is stopped or reduced</p>

Ref	Matrix ID/para number	Study	Outcomes
		<p>Analysis Mann-Whitney rank-sum test, Kruskal-Wallis one way ANOVA</p> <p>to compare independent groups. Wilcoxon's ranked signs to compare paired observations. Chi square statistic. GEE to assess relationship between exposure variables and repeated measures of FSBP</p>	<p>over a time frame.</p> <p>4.1 Use of AV chainsaws can still contribute to health outcomes? .</p>
Bovenzi et al (1988) [135]	4.1 4.7	<p>Type cross sectional study in 76 stonedrillers and stonecutters</p> <p>Population 32 stonedrillers and 44 stonecutters</p> <p>Outcome definition Questionnaire and physician lead interview. FST following cold provocation test. Taylor scale used</p> <p>Exposure assessment A(4) daily vibration exposure and Vibration Exposure Level (VEL) which is log sum of A(4) daily exposure converted to dB and lifetime exposure T/T₀ where T₀ = a reference year = 180 days</p> <p>Analysis Student's t-test, chi-square test, Cochran's test, Kendall's tau-b significance p < 0.05</p>	<p>4.1 35.5% had symptoms of VWF with a median latent period of ten years</p> <p>4.1 VWF prevalence within ISO5349 not suitable, over estimates risk in these stone workers</p> <p>4.2 A significant association between vibration exposure level (VEL) and severity of VWF stages was observed</p> <p>4.7 Rewarming of the fingertips was more prolonged in operators with VWF.</p>
Bovenzi et al (2000)[124]	4.1 4.7	<p>Type Experimental study</p> <p>Population 10 healthy male subjects</p> <p>Outcome definition Measures of FBF and FST to determine the effect of different frequencies of vibration on blood flow.</p> <p>Exposure assessment Vibration exposures of 15 mins at 16, 31.5, 63, 125 and 250Hz and 5.5m/s² weighted acceleration.</p> <p>Analysis Student's t-test for paired and unpaired comparisons. Repeated measures ANOVA. GEE approach to assess relation between continuous variables with repeated measures.</p>	<p>4.1 Finger blood flow but not skin temperature reduced by vibration exposure. Large FBF reduction in both vibrated and non-vibrated fingers during vibration, post vibration immediate return to normal with subsequent decreasing FBF above 16Hz for 45 minutes.</p> <p>4.7 Greater reduction in circulation at 31.5Hz to 250 Hz when compared with 16Hz.. Vasoconstriction in the post exposure period increases with increasing frequency.</p> <p>4.7 ISO 5349 frequency weighting overestimates vasoconstriction at 16Hz.</p>
Bovenzi (2005) [136]	4.1 4.3	<p>Type Review</p>	<p>4.3 1.7 to 5.7 % workers are estimated to be exposed to potentially harmful HTV. With prevalence of neurosensory symptoms from a</p>

Ref	Matrix ID/para number	Study	Outcomes
	4.5		<p>few to 80%.</p> <p>4.3 Increase in neurosensory symptoms with increasing daily exposure, duration of exposure or lifetime dose of exposure.</p> <p>4.5 Increase in CTS in vibration exposed populations but hard to draw a conclusion about the causes. Same with bone and joint disorders.</p> <p>4.1 Prevalence of VWF among vibration exposed workers is up to 100% for some situations.</p>
Bovenzi et al (1994)[51]	4.1 4.3 4.5	<p>Type Epidemiological, Cross sectional study</p> <p>Population 828 quarry workers and stone carvers;-145 quarry drillers, 425 stone carvers, 258 controls</p> <p>Outcome definition: Occupational physician administered questionnaire. Stockholm classification of vascular symptoms and sensorineural and MSDs</p> <p>Exposure assessment Total hours of exposure to tools estimated. Vibration measured to BS 6842. Lifetime dose calculated according to Griffin</p> <p>$\left[\sum a_{hw}^2 t_h \right]^{0.5} td.ty$ categorised into 4 groups of almost equal size by lifetime exposure on log scale</p> <p>Analysis Standard tests including ANOVA, linear regression, chi-squared test, multivariate logistic regression</p>	<p>4.1 4.3 Prevalence ORs for all health effects were higher in exposed versus controls taking account of confounders. Prevalence of VWF and neurosensory HAVS 30% & 40% respectively</p> <p>4.1 Risk of VWF increased with increase vibration exposure. Linear relationship between log VWF prevalence and log lifetime vibration dose.</p> <p>4.1 Effects of A(8) and duration of exposure combined to increase VWF risk. The OR for VWF increased by 1.1 for each unit of daily vibration exposure ($m.s^{-2}$) [A(8)] and by 1.07 for each year of exposure.</p> <p>4.1 Good agreement with ISO 5349 predictions for VWF in stone-masons using rotary tools, and overestimation for those using percussive tools.</p> <p>4.3 Risk of neurosensory disturbance did not show a clear monotonic increase of risk with increasing vibration exposure</p>

Ref	Matrix ID/para number	Study	Outcomes
			<p>4.5 Risk of signs/symptoms of CTS, Dupuytren's contracture, muscle weakness and pain in upper limbs did not show increasing risk with increasing exposure.</p>
Bovenzi et al (1995) [77]	4.1 4.6	<p>Type Epidemiological, cross sectional study of forestry workers in Italy</p> <p>Population 222 forestry workers (164 AV saws only, 58 AV and non AV) and 195 controls (shipyard labourers)</p> <p>Outcome definition Health and workplace assessment questionnaires. VWF diagnosis by positive history of blanching and positive cold provocation FSBP test. Classified by Stockholm Workshop scale</p> <p>Exposure assessment Vibration total values measured for AV and non AV saws. Exposure time estimates from questionnaires backed up by work records, interviews with employers and employees and amounts of fuel used.</p> <p>Lifetime dose as Griffin i.e. $(\sum(a_{h,w}^2 \cdot (\text{hrs per day}))^{1/2} \cdot \text{days} \cdot \text{years})^2$. Also A(8) according to BS6842.</p> <p>Analysis All the usual statistical techniques were employed. Goodness of fit of logistic models assessed by Hosmer-Lemeshow statistic.</p>	<p>4.1 Overall prevalence of VWF is 23.4%. (13.4% in users of AV saws and 51.7% in users of both AV and non-AV tools).</p> <p>4.1 When cohort split into 4 equally sized groups, significant associations between VWF prevalence and lifetime dose. VWF increased monotonically with vibration dose.</p> <p>4.1 If vibration exposure (A(8)) is doubled, total duration of exposure should be halved to produce an equivalent effect.</p> <p>4.1 Risk estimates for VWF are lower than predicted by ISO 5349.</p> <p>4.6 Cold provocation FSBP showed linear decrease across categorised lifetime dose</p>
Bovenzi et al (2005)[48]	4.1 4.6	<p>Type Epidemiological cohort, longitudinal study of VWF claimants from different industries. Average follow-up period of 4.1 years (range 1-11)</p> <p>Population 177 claimants, 104 successful. Study concentrates on 73 claimants who were unsuccessful in the first examination, continuing to be vibration exposed.</p> <p>Outcome definition Anamnestic diagnosis based on positive history of blanching, first attacks after start of exposure and</p>	<p>4.1 14 new cases of VWF were reported during the study period. 3 VWF cases recovered by follow-up. 16 deteriorated in VWF staging; 20 stationary and 4 cases showed improvement (by one stage) over follow-up period.</p> <p>4.1 Incidence of VWF symptoms significantly influenced by daily vibration exposure in hours, but not follow-up time, age or smoking status.</p>

Ref	Matrix ID/para number	Study	Outcomes
		<p>recent (within 2 years) attacks. Stockholm classification modified to remove ambiguity; staged on extent of blanching in fingers. FSBP cold provocation test used.</p> <p>Exposure assessment Questionnaire based estimates of exposure time.</p> <p>Analysis Kruskal-Wallis one way ANOVA to compare independent groups. McNemar test , χ^2 tests. GEE (generalised estimating equations) method for longitudinal data. Logistic regression accounting for repeated measures within subject of both dependent and independent variables during follow-up.</p>	<p>4.6 Abnormality in FSBP significantly related to follow-up time in years; zero FSBP not related to exposure time but to VWF status. Deterioration in FSBP over follow-up time was significant in those without VWF symptoms and incident VWF cases.</p>
Bovenzi (2007) [73]	4.1 4.7	<p>Type Epidemiological, cohort study, Longitudinal prospective study of 128 forestry workers followed up over a 9 year period</p> <p>Population 128 forestry workers from 5 different companies in Italy, most of which had only used AV saws</p> <p>Outcome definition Finger blanching measured by medical assessment using Griffin scale. FSBP measured after cold provocation</p> <p>Exposure assessment Vibration measurements to ISO 5349. Exposure time using questionnaire for employees and employers and company records to produce daily duration of exposure and total years of tool use.</p> <p>Analysis Wilcoxon's signed-ranks test used to compare paired observations. Kruskal-Wallis one way ANOVA to compare more than two independent groups. Least squares regression used to study association between FSBP and independent variables.</p>	<p>4.1 Mean $A(8)=3.7 \text{ m/s}^2$. Initial prevalence of VWF in exposed workers was 26.6%. 11 new cases over the 9 year period giving cumulative incidence of 11.7%. total exposure duration during follow-up in active workers was 6579 hours (sd 5342). Prevalence at end of follow up was 33.6%.</p> <p>4.1 Those non-retired with persistent VWF during follow-up showed an increase in median Griffin score (18 to 24) but not significant (those retired showed similar pattern)</p> <p>4.7 The study showed an increase in the FSBP of retired workers at follow-up. No significant change in FSBP over follow-up period in active workers. By regression analysis changes in FSBP in active workers were not significantly related to either $A(8)$ or follow-up time, but with VWF score.</p> <p>4.7 Hyper-responsiveness of the digital arteries (FSBP) at initial examination was a significant predictor of the VWF</p>

Ref	Matrix ID/para number	Study	Outcomes
Bovenzi et al (2008) [44]	4.1 4.7 4.10 4.11	<p>Type Epidemiological, longitudinal prospective cohort study of power tool users. 1 year follow-up.</p> <p>Population 216 HTV workers (183 forestry workers 33 stone workers) and 139 control men from the same companies.</p> <p>Outcome definition Trained occupational health physicians carried out interviews using the VIBRISKS questionnaire. VWF staged according to Stockholm Workshop scale. Griffin scoring method used to assess extent of finger blanching. Cold provocation test of FSBP; finger cooling 30C to 10C.</p> <p>Exposure assessment Vibration measured according to ISO 5349, weighted and unweighted magnitudes recorded. Exposure time using questionnaire, company records and direct observation . Various lifetime doses were calculated $\sqrt{a_i^m \cdot t_i}$ where m=0,1, 2 or 4.</p> <p>Analysis Students t-test for independent groups, one way ANOVA for more than 2 independent groups. Wilcoxon's for paired observations. Regression models employed LR statistic, and BIC used for overall fit and model comparisons</p>	<p>4.1 Initial VWF prevalence & 1 year incidence 1.7%.</p> <p>4.7 HTV workers had greater cold response of digital arteries (FSBP) at follow up compared with controls (stone workers p<0.001; forestry workers p<0.05). No significant changes in cold challenge FSBP results between examinations for asymptomatic HTV workers or VWF cases.</p> <p>4.7 Data showed a dose –response relationship between cold induced vasoconstriction (FSBP) at follow-up and some measures of daily and cumulative exposure values but not total years or hours of tool use.</p> <p>4.10, 4.11 BIC values suggested higher powers of acceleration performed statistically better in regression models for cumulative exposure Only minor differences noted between using unweighted or frequency-weighted acceleration.</p> <p>4.1 During the follow-up period; SWS vascular staging did not change for 26 cases; improved in 4 and deteriorated in 7, plus 3 new VWF cases. Improvements solely in forestry workers.</p>
Bovenzi (2010) [49]	4.1 4.6 4.8 4.11	<p>Type Epidemiological, longitudinal study of power tool users. 3 year follow-up</p> <p>Population 249 HTV workers (forestry workers and stone workers), 138 controls</p> <p>Outcome definition Trained occupational health physicians carried out interviews using the VIBRISKS questionnaire. Cold provocation FSBP test. VWF with or without abnormal FSBP results.</p> <p>Exposure assessment VIBRISKS used to assess exposures.</p>	<p>4.1 Mean A(8) 3.5 m/s² in foresters and 6.7 m/s² in stoneworkers.</p> <p>4.1 Incidence of VWF related to measures of daily vibration exposure duration alone or in combination with frequency weighted (ISO5349) acceleration or unweighted over 6.3-1250Hz.</p> <p>4.1 Incidence of VWF significantly related to daily exposure in hours, A(8) both weighted and unweighted.</p>

Ref	Matrix ID/para number	Study	Outcomes
		<p>Vibration measured according to ISO 5349, weighted and unweighted. Exposure time using questionnaire for employees and employers and company records and direct observation techniques. Daily vibration exposure assessed as A(8) weighted or unweighted.</p> <p>Analysis Non parametric tests for independent groups. GEE analysis using time lag models to investigate the temporal relationship. QIC used to compare the fit of GEE models</p>	<p>4.8, 4.11 Time-lag regression model suggested unweighted frequency gave better predictions of VWF incidence than employing weighted accelerations or duration alone (m=2 better than m=0)</p> <p>4.6 Unweighted acceleration better prediction of the cold response of digital arteries (FSBP) in those exposed workers without VWF</p>
Bovenzi et al (2011) [120]	4.1 4.7	<p>Type A longitudinal prospective cohort study; 3 year follow-up</p> <p>Population 206 forestry and stone workers with no VWF at initial survey; 43 VWF cases also participated in follow-up.</p> <p>Outcome definition Presence of VWF from medical interview assisted by colour charts, plus VIBRISK questionnaire</p> <p>Exposure assessment Four frequency weightings applied to the vibration data: W_h (as per ISO5349), W_{h-bl}, W_{hf} and W_{hT}. Exposure time by direct observation. A(8) daily exposures calculated using all four weightings.</p> <p>Analysis GEE method to assess relationships for four weightings. Odds ratios and 95% confidence intervals were estimated from GEE logistic regression coefficients. The model with smallest QIC value was chosen as best fit for relation between VWF and exposure.</p>	<p>4.1 Overall incidence of VWF was 5.3% over 3 years; 4.3% in foresters, 14.3% in stone workers (11 new cases). Median A(8) [IOS5349] 3.4 and 6.4 m/s² in forestry and stone workers respectively.</p> <p>4.1 Cumulative incidence of VWF related to all measures of daily exposure. Duration of follow-up in years also significant.</p> <p>4.7 Measures that give more weight to intermediate and high frequencies fit the VWF outcome better than W_h</p>
Bovenzi (2010)[74]	4.1 4.7 4.11	<p>Type Epidemiological prospective cohort study; 3 year follow-up.</p> <p>Population exposed n=310 baseline; 249 1st follow-up; 213 2nd follow-up & n=177 3rd follow-up. 92% forestry workers; 8% stone workers. Controls n=143,138,118 & 99 at respective follow-ups;</p> <p>Outcome definition for vascular HAVS:- (a) reliable history of VWF symptoms assisted by colour charts. (b) as (a) but</p>	<p>4.1 All cumulative exposure measures were significant predictors of VWF incidence. Duration of exposure in years poorest predictor Cumulative hours of tool use better predictor than exposure years but poorer than involving acceleration (weighted or unweighted)</p> <p>4.7, 4.11 Based on QIC incorporation of acceleration and duration (i.e. m>0) seems to give better model fits and higher powers (m>1)of unweighted acceleration in dose estimates more predictive</p>

Ref	Matrix ID/para number	Study	Outcomes
		<p>supported by cold challenge FSBP measurements.</p> <p>Exposure assessment Field vibration measurements for tools- expressed as per ISO5349-1 & unweighted over 6.3-1250Hz frequencies. Observation of exposure patterns over 1 week, and estimates of historical exposure for each tool.</p> <p>Dose= $\sum a_i^m t_i$ where m=0,1,2,4</p> <p>Analysis vascular outcomes over time to alternative measures of cumulative exposure, controlling for confounders, using GEE methods</p>	<p>than equal weighting to acceleration and duration (m=1)</p> <p>4.7 Evidence that unweighted acceleration better predictor to weighting according to ISO5349-1</p>
Bovenzi et al (2006)[125]	4.1 4.8	<p>Type Human volunteer study, on finger blood flow and vibration and contact force</p> <p>Population 10 healthy male volunteers</p> <p>Outcome definition FBF in middle finger.</p> <p>Exposure assessment 11 occasions, 5 periods of 5 minutes with combinations of force and vibration exposure. 31.5 Hz 4 and 16m/s² o R 125Hz 16 and 64m/s² equivalent to 2 and 8m/s² weighted at both frequencies</p> <p>Analysis Mean SD and standard error, students t-test for paired means. Repeated measures ANOVA. 95% confidence intervals. GEE method for relationship between variables with repeated measures.</p>	<p>4.1 Increasing vibration magnitude caused greater reduction in FBF in all fingers.</p> <p>4.8 125Hz caused greater reduction in FBF than 31.5Hz when equal levels of frequency-weighted (ISO5349-1) vibration were applied. Increasing force caused greater reduction in FBF in affected finger.</p>
Bovenzi et al (2005) [99]	4.1 4.5	<p>Type: Epidemiological cross-sectional study (exposed & control groups)</p> <p>Population: Females; furniture manufacture-exposed using orbital sanders; NHS workers as controls</p> <p>Outcome definition : prevalence of RP and CTS (using consensus diagnostic criteria for epidemiological studies)</p>	<p>4.1 No increase in prevalence of RP in exposed population compared with controls, but higher prevalence for CTS, peripheral sensorineural disturbances and upper limb musculoskeletal complaints.</p> <p>4.5 Upper limb and sensorineural disorders related to increase in</p>

Ref	Matrix ID/para number	Study	Outcomes
		<p>Exposure assessment: HTV measured according to ISO 5349; daily exposure to standard A(8)</p> <p>Analysis: log binomial regression analysis; PR adjusted for covariates.</p>	daily vibration exposure. PR for CTS, other ULMSDs (shoulder, elbow wrist) and neurosensory symptoms increased by 1.3, around 1.15-1.36 and 1.26 for each unit increase in A(8).
Bovenzi et al (2011) [92]	4.3 4.4 4.7 4.12	<p>Type Cohort, prospective Longitudinal study; follow-up period of 1-3 years.</p> <p>Population 29 naval engine workers and 27 controls</p> <p>Outcome definition Thermal and vibrotactile perception thresholds. Subjects Stockholm workshop staged for neurosensory HAVS</p> <p>Exposure assessment VIBRISKS questionnaire used to help assess exposures; A(8), duration of exposure in hours & equivalent frequency weighted acceleration. Direct timed observation by supervisor.</p> <p>Analysis Students t-test, analysis of covariance, chi-squared or Fisher's exact test, Spearman's rho. GEE analysis (autoregressive)</p>	<p>Study showed impaired thermal acuity in vibration exposed in index and little fingers. 58% symptoms of numbness/tingling at initial time point. Mean A(8)=2.5(0.6)m/s²</p> <p>4.3 4/29 new cases of tingling & numbness during follow-up [but none of VWF]</p> <p>4.4 No case of reversibility observed in those with symptoms at initial time point.</p> <p>4.7 Significant exposure-response relationship between thermal sensory impairment and all 3 measures of vibration exposure. But no relationship or changes over time for vibrotactile perception. No evidence that duration of exposure or A(8) was significantly more important than the other</p>
Bovenzi & Griffin (1997) [137]	4.7 4.11	<p>Type: Experimental study</p> <p>Population: 8 healthy male subjects, 5 white 3 oriental.</p> <p>Outcome definition: Measurement of changes in FST and FBF</p> <p>Exposure assessment: N/A</p> <p>Analysis: Regression analysis</p>	<p>4.7 Digital circulatory response depends on magnitude and frequency of vibration.</p> <p>4.7 Vasomotor systems mediated both centrally and locally are involved in the reaction of digital vessels to acute vibration.</p> <p>4.11 The pattern of haemodynamic changes does not support the ISO 5349 frequency weighting.</p>
Bovenzi (2011) [79]	4.1 4.2	<p>Type: Review and prospective cohort study (VIBRISKS work already reviewed in Bovenzi et al 2011).</p>	<p>4.1 Table of literature on exposure-response relationship and comments on levels of agreement/disagreement with the VWF prevalence predictions included in ISO5349.</p>

Ref	Matrix ID/para number	Study	Outcomes
			<p>4.1 Out of 21 studies, 11 overestimate - mostly in percussive machines 7 underestimate and 3 agree Forestry worker studies; agree, underestimate and overestimate.</p> <p>4.2 In the study: Observed incidence = 14% Predictions without uncertainties: A(8) Wh = 8% A(8) Wh bl 12% A(8) Whf/ WhT 11%</p> <p>In previous longitudinal studies of the VIBRISKS research project, significant associations were found between VWF and some predictors such as age at entry, body mass index and smoking. These have not been considered to simplify the relationship and make it comparable with the ISO model.</p> <p>4.2 Data show that exposure to medium and high frequencies is important in the development of VWF.</p>
Brammer (1986) [2]	4.1 4.8	<p>Type Meta analysis; subsequent review using additional data. Population Equations 1& 2 (see below), and the VWF risk relationship contained in ISO5349 are based on an original meta-analysis using criteria of (a) >30 people with at least 50% or 75% blanching prevalence if latency <6 years or >6 years respectively, (b) On average the duration of exposure must exceed latency interval (c) used a recognised experimental technique for vibration measurement. 14 studies were used for equation 2; data from 7 studies contributed to equation 1. All</p>	<p>4.1 A simple model of exposure-response relationships is proposed.</p> <p>4.1 Eq 1 is supported by subsequent data, although slight modification is suggested. Eq 2 is not supported by the one study which fulfils the criteria, but this is suggested to be due to the effect of operating time/day which is not taken in to account in the model.</p> <p>4.8 Concludes that lack of fit of a miners' study is not due to inadequacies of frequency weighting and not due to the impulsive</p>

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		<p>were retrospective , cross-sectional studies. This papers reviews 3 additional studies fulfilling almost all the above criteria and 1 study fulfilling all criteria for comparison with equation 1 & 2.</p> <p>Outcome definition</p> <p>Eq 1 $\bar{t}_{LI} = 78.7/a_k^{1.07}$ linking mean latency in a group to acceleration (frequency weighted)</p> <p>Eq 2 $s = 0.01 + 0.46\bar{t}_{LI}$ linking the standard deviation of the group response</p>	<p>nature of the vibration signal.</p>
Brammer (1990) [138]	4.1	<p>Type Meta analysis Population Criteria for inclusion are the same as set in Brammer 1986. <i>Review attempts to establish a relationship between:</i> t_{avLI} = the average latent interval, s = the standard deviation and the “hazard intensity” for which frequency weighted acceleration is used. From this an attempt to establish the threshold of vibration magnitude to which an operator can be exposed without developing HAVS is made.</p>	<p>4.1 A simple model of exposure-response relationships previously proposed for VWF is supported by new data. The exposure-response pattern follows a cumulative normal distribution curve.</p> <p>4.1 The relationship between s and t_{avLI} is given by: $s = 0.5t_{avLI}$ The relationship between t_{avLI} and the hazard intensity a_k is given by $t_{avLI} = 78.7/(a_k)^{1.07}$ and forms the basis of the ISO 5349 model.</p> <p>4.1 Estimation of a vibration threshold value by four different methods produces values in the range from 1 – 4 m/s²</p> <p>4.8, 4.12 Explanations are offered as to why the studies which disagree with the proposed model do so. No explanation could be found for the discrepancies between studies using impulsive tools implying that the model may not be appropriate for these types of exposure.</p>

Ref	Matrix ID/para number	Study	Outcomes
Brubaker et al (1986) [50]	4.1 4.3	<p>Type Cross sectional study</p> <p>Population 95 rock drillers in British Columbia</p> <p>Outcome definition Professionally administered questionnaire used to classify symptoms according to Taylor Pelmear scale</p> <p>Exposure assessment: Years of exposure only.</p> <p>Analysis: simple categorical analysis.</p>	<p>4.1 Statistically significant association between years of exposure and presence of symptoms amongst drillers</p> <p>4.1 46% showed VWF symptoms compared with 4% in controls.</p> <p>4.1 Latency is greater 7.5 years than the 3-5 years indicated by ISO 5349 at these magnitudes</p> <p>4.3 29% of drillers also reported Neurological symptoms compared with 12% of controls</p>
Brubaker et al (1987) [72]	4.1	<p>Type Longitudinal cohort study of 202 fallers in British Columbia</p> <p>Population 71 fallers surveyed in 1979-80 and 55 repeated in 1984-85</p> <p>Outcome definition Questionnaire administered by trained interviewer. Taylor Pelmear staging. FSBP test</p> <p>Exposure assessment A(4)daily exposures</p>	<p>4.1 Prevalence of VWF was 51% in 1979-80 and 53% in 1984-85</p> <p>4.1 7 out of 28 VWF cases on initial investigations reported no symptoms on follow up and 4 reported improvement but 30% reported onset of symptoms in 1984-85. Study suggests that regression of VWF may occur</p>
Burdorf & Monster (1991)[76]	4.1 4.3 4.5	<p>Type Cross sectional study of riveters</p> <p>Population 194 riveters and 194 controls from single firm in aircraft industry. 101 riveters and 76 controls included in analysis, (responders & meeting inclusion criteria of 1 year employment, no exposure in previous employment). Tool types and working techniques reported not to have changed in 20 years</p> <p>Outcome definition Self administered questionnaire. Stockholm Workshop scale used for classification. Nordic questionnaire used for MSDs</p> <p>Exposure assessment Vibration measurements to ISO 5349 1986. Calculated A(4) were 2.8m.s⁻² and 1.0m.s⁻² for riveters and controls respectively</p>	<p>4.1 Comparison of data with ISO 5349 shows (prevalence rates of VWF compatible with predictions in ISO 5349) results within the range suggested for VWF.</p> <p>4.1, 4.5 After 10 years of exposure, statistically significant age adjusted odds ratios were found for VWF (1.9) and pain or stiffness of the wrist (3.2).</p> <p>4.3, 4.5 Although not statistically significant, odds ratios much greater than 1 were found for numbness of fingers and pain or stiffness in elbow or shoulder. Numbness in fingers only showed p values between 0.5 and 0.1 for regression coefficients of duration of exposure in logistic regression.</p>

Ref	Matrix ID/para number	Study	Outcomes
		Analysis chi-squared tests and students t-tests, logistic regression analysis, Odds ratios P<0.05. Odds ratios for symptom outcomes in riveters versus controls predicted from logistic regression models using duration of exposure after adjusting for age	4.5 The results of logistic regression show a clear exposure-response relationship for pain and stiffness in the wrist elbow and shoulder when compared with controls. Risk of wrist pain in riveters showed stronger regression with duration of exposure than pain in elbows or shoulder
Burstrom et al 2006 [52]	4.1 4.3	Type Cross sectional study of workers in heavy engineering Population 87 manual workers in a pulp-mill machinery manufacturer. Outcome definition Occurrence of vascular/neurological symptoms by registering symptoms on a sketch of the hand and stating year of onset. Exposure assessment Vibration measured to ISO5349. Exposure time estimated by objective and subjective means. Subjective included diary, questionnaire and interview. Accumulated vibration exposure calculated for each individual, as well as energy-equivalent acceleration Analysis Analysis of differences in correlations using 95 % confidence interval.	4.1, 4.3 Average time to onset of symptoms (vascular and neurological) was 12 years (5500 to 7200 hours of exposure). 4.1, 4.3 A(8) values were in the range 2.1 to 2.5 m/s ² . Accumulated exposures were between 38200 and 45300 mh/s ² 4.1, 4.3 Best correlation between latency and vibration exposure was with lifetime exposure suggesting that the magnitude and duration of the vibration are both important 4.1, 4.3 New cases of vascular and neurological symptoms were found at exposures below A(8) 2.5 m/s ² implying that the EAV is not a safe exposure level. 4.1, 4.3 Study supports the view that ISO 5349 underestimated the risk for both types of vibrational energy
Burstrom et al (2009) [129]	4.7 4.11 4.12	Type Volunteer study Population 10 healthy subjects, 5 male, 5 female. Outcome definition Vibrotactile and thermal perception thresholds measured before and after exposure to vibration Exposure assessment 5m/s ² at 125Hz for an overall A(8) exposure that did not change although the temporal pattern was varied, between 2 and 16 minutes, and frequencies of 31.5 & 125Hz used. Analysis SAS stats package. Repeated measures ANOVA.	4.7 Study confirms the TTS in both thermal and vibrotactile perception thresholds although thermal effects were only significant for the cold threshold. 4.7 Pre-exposure to vibration had a significant acute effect on vibrotactile thresholds 30 secs after exposure (p<0.001) which was still significant 25 minutes after the exposure. 4.7 Different patterns of exposure had different effects on VPT with

Ref	Matrix ID/para number	Study	Outcomes
			<p>VPT less affected when the exposure includes rest breaks.</p> <p>4.11 Frequency weighting according to ISO 5349-1 was unable to predict the produced acute changes in VPT i.e. vibrotactile TTS much lower at 31.5Hz than 125Hz.</p> <p>4.12 Calculation of energy-equivalent frequency-weighted acceleration does not reflect the acute changes of VPT</p> <p>4.12 Different patterns of exposure had no significant effect on thermal perception thresholds.</p>
Cherniak et al (2004) [115]	4.7	<p>Type Epidemiological, cross sectional study of shipyard workers</p> <p>Population 214 shipyard workers, 199 men, 15 women.</p> <p>Outcome definition Measured SNCVs, assessed CTS</p> <p>Exposure assessment 3 exposure groups low, medium and high.</p> <p>Analysis T-tests for differences between groups, ANOVA used for differences in nerve conduction velocity. Multiple linear regression analysis for relationship between SNCVs and other variables. Multiple regressions looked at age, gender, finger circumference, BMI and hand temperature as possible explanatory variables</p>	<p>4.7 SNCV varied between quartiles but not in a way that differentiated long from short segments.</p> <p>4.7 Wrist-palm and digital segments were slower than palm-proximal digit segments.</p> <p>4.7 Temperature had an effect on nerve conduction velocity, but not equally across segments.</p> <p>Reduced SNCVs may be a consequence of industrial exposure to vibration.</p>
Cherniak et al (2004) [55]	4.1 4.3	<p>Type 2 cross sectional studies of shipyard workers.</p> <p>Population 288 shipyard workers in 1988. 214 shipyard workers in 2001</p> <p>Outcome definition Stockholm Workshop scale for both vascular and sensorineural symptoms Unclear as to whether SWS staging was based simply on questionnaire responses.</p> <p>Exposure assessment Vibration measurements were made but not used directly. Exposure time estimates in terms of current</p>	<p>4.1 Techniques for managing exposure such as job rotation led to increased exposure for some groups and elimination of the highest exposure group.</p> <p>4.1 VWF did not increase with cumulative exposure except for exposures >18000hrs.</p> <p>4.1, 4.3 In 2001 for each log unit of cumulative exposure the</p>

Ref	Matrix ID/para number	Study	Outcomes
		<p>weekly exposures, cumulative years and hours.</p> <p>Analysis Polychotomous logistic regression to assess relationship between independent variables.</p>	<p>estimated OR was 1.44 (CI 1.04-1.98) for sensorineural and 1.70 (CI 1.06-2.71) for vascular. In 1988 study respective ORs were 2.35 (CI 1.48-3.73) and 3.99 (CI 2.27-7.01)</p> <p>4.1, 4.3 Reduction of exposure duration alone is not sufficient to reduce health effects.</p> <p>4.1, 4.3 The hierarchy of fit for symptom stage was log-cumulative hours > vibration years > current weekly vibration exposure.</p>
Cherniak et al (2006)[116]	4.5 4.7	<p>Type Epidemiological, Cross sectional study of dental hygienists</p> <p>Population 94 experienced dental hygienists and 66 dental students described as inception cohort.</p> <p>Outcome definition Self administered questionnaire, Physical examination including 20 different clinical provocation tests. Measurement of VPTs for 3 different mechanoreceptors, SNC tests, pinch force</p> <p>Exposure assessment No. of years in practice and no. of hours using vibratory and manual tools from self administered questionnaire.</p> <p>Analysis SPSS and SAS stats packages, one and two way ANOVA, linear regression, confidence intervals.</p>	<p>4.5, 4.7 Experienced dental hygienists were more likely to be diagnosed with CTS than non-symptomatic hygienists and were more likely to have slower SNVCs along the median nerve.</p> <p>4.5 CTS was not associated with increased VPTs, but trend towards use of vibratory tools accompanying CTS.</p> <p>4.5, 4.7 A subgroup of dental hygienists have a combination of subjective hand weakness, low pinch force, parasthesias and raised VPTs particularly at 125Hz.</p> <p>4.7 Age, differing exposures and RP do not account for much difference in VPTs.</p>
Cherniak et al (2009)[139]	4.5 4.7	<p>Type Epidemiological, Cross sectional study of 5 groups of workers [although drawn from the longitudinal HAVIC study]</p> <p>Population 217 shipyard workers, 94 dental hygienists, 66 dental hygiene students, 61 forestry workers and 54 truck cab workers.</p> <p>Exposure assessment No details in this paper as to how exposure information was combined. Data logging of force and vibration made using palm measurements.</p>	<p>4.5 CTS was less common in cohorts with lower vibration exposures (forestry and truck cab workers) although numbness and tingling symptoms were present.</p> <p>4.7 SNCV-PDDD was elevated in cohorts with higher vibration exposure implying an effect of vibration on nerve conduction velocity.</p>

Ref	Matrix ID/para number	Study	Outcomes
			<p>4.5 Highest combined pathologies were found in shipyard workers.</p> <p>4.5 Reducing vibration exposures appears to effectively eliminate HAV as an independent risk factor for CTS</p>
Cherniak et al (2007) [140]		<p>Review paper by HAVIC HAVIC aims to characterise the exposure-response relationship for HAV through a study design incorporating multiple cohorts, some having existing historical data.</p>	
Cherniak et al (2008) [141]	4.5 4.7	<p>Type 2 Cohort studies Population 214 Shipyard workers and 94 dental hygienists studied in 2001/02 and 2004 Outcome definition Nerve conduction velocities, Vibrotactile threshold, questionnaire and physical examination classification according to Stockholm Workshop scale. CTS according to 2 definitions Exposure assessment Questionnaire assessment Analysis SPSS and SAS packages. F tests and t-tests to establish differences between groups. McNemar and Mantel-Haenzel, chi square test used to test association between variables. Significant = $p < 0.05$ two tailed.</p>	<p>4.5 Diagnosis of CTS differs widely.</p> <p>4.7 Combining clinical criteria to create a more narrow or specific case definition of CTS does not appear to predict SNCV.</p>
Curry et al (2005) [34]	4.11	<p>Population Experimental animal study Male Sprague-Dawley rats. Outcome definition 6 groups: control, sham vibrated, 30, 60, 120 and 800Hz 4hrs duration, 49m/s² Arterial damage investigated. Exposure assessment Analysis Light microscopy and electron microscopy, immunostaining with NFATc3 as an early marker of cell damage.</p>	<p>4.11 Immunostaining and vacuolisation, both indicators of damage, increased after 30, 60 and 120 Hz, but not 800Hz. Complex relationship between frequency of vibration and site of damage.</p> <p>4.11 The relationship between vibration frequency and tissue damage severity is complex with the pattern influenced by relative contributions of multiple factors; neurally and stretch-mediated smooth muscle contraction, vasoconstriction, vibration amplitude, and resonance energy absorption.</p>

Ref	Matrix ID/para number	Study	Outcomes
			4.11 Vibration stress and smooth muscle contraction are the major contributors to arterial damage.
Dandanell and Engstrom (1986) [60]	4.1 4.8	Type Cross sectional study of Riveters Population 288 workers who had worked for up to 25 years Outcome definition Finger blanching Exposure assessment Vibration measurements to ISO/DIS 5349.2 but also including ultrasonic measurements. Calculations of vibration intensity in Watts/m ² -	4.1 59 out of 288 workers who had worked up to 25 years showed finger blanching. 4.1 50 % of those who had worked for more than 10 years had finger blanching. 4.8 The number of workers suffering finger blanching was four times greater than predicted by ISO/DIS 5349. The author suggests that the risks from higher frequencies, possibly even ultrasonic frequencies could explain the differences in predicted and actual rates of finger blanching.
<u>Dong J et al (2007) [16]</u>	4.1 4.8	Type Experimental study of absorbed power in the hand and arm.	4.8 Total power absorbed by the entire hand arm system correlates very well with the ISO frequency weighting 4.8 Power absorbed by the palm-wrist forearm correlates with ISO 5349 weighting, but power absorbed by the fingertips correlates with unweighted vibration. 4.8 ISO 5349 weighting could overestimate low frequency and greatly underestimate high frequency effects on the fingers 4.1 Data show a relationship (although non-linear) with 4h energy equivalent absorbed power and prevalence of VWF.
Dong R (2012) [123]	4.8 4.9 4.10	Type Review of biodynamics of human hand-arm vibration Population not applicable Outcome definition not applicable Exposure assessment not applicable	4.8 The frequency weighting in ISO5249-1 overestimates the low frequency effect but underestimates the high frequency effect on the fingers and hand. Transmitted acceleration-based (TAB) weighting for fingers is near unity to 200Hz therefore unweighted acceleration

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			<p>may be better assessment</p> <p>4.9, 4.10 Consideration of TAB weightings to other structures in the hand-arm may be needed when considering exposure risk for non-VWF disorders</p>
Dong (2005) [126]	4.8 4.9 4.10	<p>Type Experimental, human volunteer</p> <p>Population 10 male subjects</p> <p>Outcome definition biodynamic response of human fingers in a power grip subjected to a random vibration.</p>	<p>4.8, 4.9, 4.10 Under constant velocity vibration, the finger vibration power absorption at frequencies above 200Hz is approximately twice that at frequencies below 100Hz.. This suggests that the frequency weighting specified in ISO5349-1 may underestimate the high frequency effect on vibration induced disorders.</p> <p>4.8, 4.9, 4.10 Increasing finger grip force significantly increases vibration power absorption. Below 100Hz the influence is more significant under the pull-only and grip-only, rather than combined grip and push action</p> <p>4.8 Frequency, force and coupling type all affect BR, especially at frequencies below 50Hz.</p> <p>4.8 ISO 5349 weighting may under-estimate the effect of higher frequencies and ISO weighting should take account of coupling forces.</p>
Dong (2005) [118]	4.8 4.9 4.10 4.11	<p>Type Review on biodynamic modelling</p>	<p>4.8, 4.9, 4.10, 4.11 By biodynamic analysis, frequency weightings can be divided into 3 groups: weightings for fingers/hands; wrist/elbow/shoulder & head. The ISO5349-1 weighting is highly correlated with wrist/elbow/shoulder, but not the other 2 groups (fingers/hands & head).</p> <p>4.8, 4.9, 4.10, 4.11 Two weightings derived from biodynamic analysis (TAB & BFB) have higher influence of frequencies >20Hz</p>

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			<p>than in ISO5349-1</p> <p>4.8 Results indicate that more weight should be given to the mid range frequencies. Three weightings are proposed: 1.) fingers and hand 2.) wrist, elbow and shoulder 3.) head The wrist, elbow, shoulder weighting correlates best with the ISO weighting</p>
Dong (2012) [142]	4.11	Theory paper - development of a biodynamic frequency weighting for the finger tip.	<p>4.11 Proposes a theory on frequency weighting that suggests that a weighting should include two components: W1 = biodynamic frequency weighting W2 = biological frequency weighting</p> <p>Describes work to develop W1. Measurements of the vibration power absorption at different locations on the hand arm system.</p> <p>Tries to split the ISO weighting in to W1 and W2 to assess ISO weighting suitability.</p> <p>Identifies differences for fingers compared with entire hand-arm system and concludes that because of the way Miwa did his experiments, W1 ISO represents the entire HA system, not individual components such as fingers.</p> <p>Uses measures of VPAD (vibration power absorption density) which is a combined measure of the vibration stress and strain rate.</p>

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Ekenvall and Carlsson (1987) [84]	4.1 4.7	<p>Type Cohort, Follow up study</p> <p>Population Initial 68 patients with VWF; 55 followed-up</p> <p>Outcome definition Physician lead interview with questionnaire. Taylor Pelmear scale and FSBP measurements. Subjective assessment of condition</p> <p>Exposure assessment No information on vibration dose</p> <p>Analysis Wilcoxon's test, Fisher's exact test.</p>	<p>4.1 10 patients reported subjective improvement in symptoms after ceasing exposure to vibration</p> <p>4.1 Symptoms only improved in workers who had ceased or reduced exposure for more than 3 years</p> <p>4.7 On a group basis, there was no change in the results of FSBP measurements in the 43 patients who attended both examinations</p>
Ekenvall et al (1989) [81]	4.1 4.3 4.7	<p>Type Case-series study</p> <p>Population 55 patients after exclusions</p> <p>Outcome definition Symptom scaling according to Taylor Pelmear and neurological symptoms according to Brammer. Thermal and vibration perception measurements</p> <p>Exposure assessment 3 indices of vibration magnitude and a multiplication factor based on number of years of exposure to give estimated exposure dose value</p> <p>Analysis t-test with p<0.05 significant. Chi-squared test to analyse relation between neurological and vascular symptoms.</p>	<p>4.1, 4.3 Patients with advanced vascular and neurological symptoms had a higher mean exposure index (p<0.0005)</p> <p>4.7 Patients with above median vibration thresholds had higher mean exposure dose scores (p<0.05).</p>
Engstrom and Dandanell (1986) [58]	4.1 4.8	<p>Type Cross sectional study of Riveters</p> <p>Population 340 workers who had worked for up to 40 years.</p> <p>Outcome definition Raynaud's phenomenon according to Taylor Pelmear scale. No cold provocation test.</p> <p>Exposure assessment Questionnaire to give tool time per day, chronometer to measure tool usage, time studies. Measurement of shock acceleration</p>	<p>4.1, 4.8 More than 50% of riveters had VWF after more than 10 years of exposure. This is a greater risk of RP that predicted from ISO-5349 (59/288 versus 14/288).</p> <p>4.8 Impulsive acceleration not appropriately represented in ISO5349</p>
Futatsuka et al (1989) [66]	4.1	<p>Type Longitudinal study over 30 years</p> <p>Population 1551 Japanese Forestry workers who used a saw for >100 hours per year</p> <p>Outcome definition Questionnaire based diagnosis of VWF, cross-references with compulsory annual medical examination</p>	<p>4.2 Peak prevalence of VWF overall was 30.9% in 1973 and peak incidence was 4.9% in 1972</p> <p>4.1 Overall latent interval was 6.2 ±3.9 years.</p>

Ref	Matrix ID/para number	Study	Outcomes
		conducted since 1965. 1042 subjects were examined by objective measurements including FSBP and FST Exposure assessment Vibration magnitudes taken from reports by Japanese Ministry of Agriculture and Forestry	4.1 When split in to groups for assessment, both incidence and prevalence rates decreased significantly in groups that began use in 1969/70 onward 4.1 Suggestion that VWF may be reversible.
Futatsuka et al (2005) [90]	4.1 4.3 4.5 4.7	Type Epidemiological , cross-sectional study of 102 quarry workers Population 73 rock drill operators and 29 controls Outcome definition: Subjective measures of ill health as well as functionality tests. Vascular by FST, nail compression test, recovery of finger skin temperature after cold provocation for 10C for 10 minutes. Sensorineural by threshold of vibration and pain. Tapping ability and grip strength Exposure assessment Acceleration measured to ISO 5349 Analysis Students t-test used for comparison with p<0.05 = significant. Factor analysis with factor loadings computed by Maximum-Likelihood extraction and promax rotation.	4.1 No workers had a history of white finger. 4.3 Subjective results: Prevalence of finger hypoesthesia 67.6% in operators vs 3.8% in controls. 4.5 Weakness and coldness significantly higher than in controls. 4.7 In the function tests there were no significant differences for any tests. This is as reported for other cohorts in tropical climates eg. Chainsaw operators in Papua New Guinea and Indonesia. Reasons are concluded to be due to climate, young workforce, breaks from exposure for 2-3 months in rainy season and healthy worker effect. 4.3 Sensorineural symptoms exist in 5-10% of exposed workers.
Gemne and Saraste (1987) [93]	4.5	Review of literature on bone and joint pathology in relation to vibration exposure defining exclusion/inclusion criteria, as well as search strategy	4.5 Evidence of an association of elbow and wrist osteoarthritis and use of low frequency percussive tools, but not related to the vibration exposure. 4.5 Constitutional susceptibility may be required to produce osteoarthritic lesions. 4.5 Available data show a lack of causal relationship between vibration and formation of bone cysts and vacuoles.
Gerhardsson	4.1	Type Cohort study of workers exposed to vibration	4.1 Subjective assessments of exposure times lead to over-estimates

Ref	Matrix ID/para number	Study	Outcomes
et al (2005) [143]	4.7	<p>Population 19 male machine shop workers exposed to vibration</p> <p>Outcome definition Measurement of vibrotactile thresholds, motor nerve conduction velocities, sensory nerve conduction velocities, fractionated conduction velocities, vibration thresholds, temperature thresholds,</p> <p>Exposure assessment Physical examination followed by structured interview using administered questionnaire. Timings of exposures</p> <p>Analysis SPSS used to perform Wilcoxon's signed ranks test Spearman's correlation coefficients, $p < 0.05$ = significant. Linear regression analysis</p>	<p>of cumulative lifetime exposure but objective measurements indicated VWF prevalence rates which agree with ISO 5349. [Duration of exposure four-fold higher by subjective estimation].</p> <p>4.7 Vibration perception thresholds and nerve conduction velocities were the most sensitive outcome measures.</p>
Govinda Raju et al (2011)[32]	4.7 4.8	<p>Population Experimental study of male Sprague-Dawley rats.</p> <p>Outcome definition Pain sensitivity and light/electron microscopy of tissue histology.</p> <p>Exposure assessment Groups of 8 rats. 12 minutes exposure to shock from a riveting hammer.</p> <p>Analysis Two way repeated measures ANOVA to compare tail flick response. One way ANOVA to compare means for effects on nerves $P < 0.05$ significance</p>	<p>4.7 Immediately after exposure tails were hyperalgesic with disrupted myelinated axons, fragmented nerve endings and mast cell degranulation.</p> <p>4.7 After 4 days, tails were hypoalgesic, nerve endings were lost in the skin indicating that shock vibration causes severe nerve damage.</p> <p>4.8 Frequency weighting underestimates the risk of nerve injury</p>
Govinda Raju et al (2008) [127]	4.9 4.11	<p>Population Experimental animal study in Male Sprague-Dawley rats</p> <p>Outcome definition behavioural changes, histopathology for nerve damage</p> <p>Exposure assessment</p> <p>Analysis One way ANOVA to compare means and pairwise comparisons using Newman-Keuls tests. $P < 0.05$ significance</p>	<p>4.9 All three vibration conditions produced significant oedema and significant increase $p < 0.01$ in the number of disrupted axons.</p> <p>4.11 Severity of nerve damage did not correlate directly with frequency.</p> <p>4.11 800Hz generated less myelin disruption but most oedema.</p>
Griffin M (2012) [144]	4.7 4.11	<p>Review of experimental studies of frequency-dependence of perception thresholds, comfort contours, TTS and finger blood flow.</p>	<p>4.7 Frequencies at 250 -315Hz have the most influence on vasoconstriction.</p>

Ref	Matrix ID/para number	Study	Outcomes
			<p>4.11 Showed that duration doesn't influence vasoconstriction</p> <p>4.11 Suggests that the mechanoreceptors responsible for perception are involved in the vascular response.</p> <p>4.11 Shows that Wh frequency weighting underestimates vasoconstriction between 63Hz and 315Hz.</p>
Griffin et al (2003)[12]	4.1 4.8 4.12	<p>Type Epidemiological Meta-analysis – combination of 3 cross-sectional studies</p> <p>Population 1557 users of power tools in 7 groups. Stone grinders, stone carvers, quarry drillers, dockyard caulkers, dockyard boilermakers, dockyard painters and forest workers.</p> <p>Outcome definitions positive history of finger blanching using Griffin's scoring system. Exclusion of subjects with possible non-vibration related causes.</p> <p>Exposure assessment Exposure time obtained both as total hours of use and years of use. Vibration magnitudes were from representative samples of tools for each population. 7 alternative dose measures, varying combinations of exposure duration with weighted and unweighted magnitudes.</p> <p>Dose= $\sum a_i^m t_i$ where m=0,1,2,4</p> <p>Analysis Unconditional logistic regression analysis. Measures of dose were either quintile based design variables or continuous covariates.</p>	<p>4.1 Taking account of age and smoking, exposure measures using lifetime duration only were better than those where m >1 (ie giving more influence to acceleration) at predicting VWF.</p> <p>4.1 Some evidence from logistic regression analysis, adjusted for age and smoking, that vibration magnitude is significant in predicting VWF, even though to a lesser extent than duration of exposure</p> <p>4.1 All measures of dose were also associated with severity of symptoms .</p> <p>4.12 data suggest that m=1 rather than M>2 gave best fit for severity of VWF based on Griffin score; involving acceleration m>1 gave no better (by LR test) than exposure hours alone.</p> <p>4.1 Total hours duration was a better predictor of VWF than years of exposure. Duration of exposure</p> <p>4.8 Unweighted acceleration measures were better than frequency weighted acceleration measures of exposure.</p>

Ref	Matrix ID/para number	Study	Outcomes
			<p>4.12 Combination of unweighted acceleration and hours exposure gave the best fit for the risk of VWF, counter to the weighting and time dependency in ISO5349-1</p> <p>4.8 Authors state additional analysis (not presented) showed that Σa_{uwi-t_i} for dockyard painters & caulkers and forestry workers gave fit as good or better (stone carvers and boilermakers than other dose measures. Stone grinders were only occupation in which higher powers of m ($m>1$) were better, and had lowest prevalence of VWF and only group where vibration was limited to rotary tools</p>
Hagberg et al (2008) [145]	4.1	<p>Type Cohort study of engineering workers both retrospective and prospective.</p> <p>Population 147 manual workers and 94 office controls</p> <p>Outcome definition Raynauds at baseline, 5, 10 and 15 years by questionnaire and physician examination</p> <p>Exposure assessment Vibration magnitudes to ISO 5349. Subjective assessments of daily exposure time by diary, questionnaire and interview. Lifetime exposure = multiply hours/day x days/year x years x vibration magnitude. 5 exposure classes developed: Class 0 = not exposed, class 4 was >18086 h.m/s²</p> <p>Analysis Cumulative incidence, survival analysis using proportional hazards model.</p>	<p>4.1 Retrospective incidence of VWF was 15.9 for exposed and 2.43 for not exposed compared with the prospective incidence of 13.6 for the exposed and 4.97 for the not exposed</p> <p>4.1 Based on the retrospective survivor analysis, there was no significant monotonic relationship between increasing cumulative exposure categorisation and survival curves; hazard ratio confidence intervals overlapped for Q2-Q4.</p> <p>4.1 Authors show that retrospective and prospective incidence rates in exposed and controls are similar.</p>
Ho & Yu 1986 [108]	4.7	<p>Type: cross-sectional with exposed & control groups</p> <p>Population: 70 grinders & 72 age matched controls in warm climate, Taiwan.</p> <p>Outcome definition: NCV in median and ulnar nerves, including motor conduction (MCV), sensory conduction elbow-fingers (pSCV) & wrist-fingers (dSCV); VPT (125 Hz),</p>	<p>4.7 Significant correlation ($p<0.05$) between TOT (after adjusting for age) and;</p> <p>(a) NCV median (MCV, pSCV, dSCV)</p> <p>(b) NCV ulnar (MCV pSCV, dSCV)</p> <p>(c) VPT</p> <p>(d) pain threshold</p>

Ref	Matrix ID/para number	Study	Outcomes
		<p>skin temperature, nail press, pain threshold, grasping power (grip).</p> <p>Exposure assessment: total tool operating time (TOT)</p> <p>Analysis: t-tests & multiple regression analyses, including age & TOT</p>	<p>but not skin temperature & nail press test (reflecting circulatory function). Correlation coefficients (r) tended to be between 0.28-0.4 for significant relationships</p>
Ho and Yu (1989) [146]	4.7	<p>Type Experimental animal study, 20 male albino rabbits exposed to 60Hz 0.35mm (51m/s²) 150, 250, 450 and 600 hours, (2hours/day for 6 days/week. Leg and whole body vibration</p> <p>Outcome definition: Electron microscopy of nerves post mortem</p>	<p>4.7 Vibration caused:</p> <ul style="list-style-type: none"> disruption of the myelin sheath accumulation of vacuoles disorganisation of paranodal end loops dilatation of SLI and disappearance of neurotubules <p>4.7 Extent of the disruption in myelin sheath was related to the amount of vibration dose</p>
Jang et al (2002) [63]	4.1 4.3	<p>Type PS Epidemiological, cross-sectional study of 344 shipyard workers in Korea</p> <p>Population 344 vibration exposed workers from one shipyard and 53 unexposed white-collar controls</p> <p>Outcome definition: Stockholm Workshop classification of vascular and neurological symptoms by questionnaire only</p> <p>Exposure assessment Vibration measurements made on most tools according to ISO5349. Lifetime dose measured according to Griffin.</p>	<p>4.1 Positive relationship between presence of VWF symptoms and lifetime exposure (p<0.00001) in logistic regression analysis after adjusting for age, alcohol and smoking. Prevalence of VWF 22.7%</p> <p>4.1 Prevalence and severity of VWF by SWS staging increased (significantly) by increasing lifetime exposure category.</p> <p>4.3 Prevalence of sensorineural symptoms 78.2% (Controls 0% and 34%)</p>

Ref	Matrix ID/para number	Study	Outcomes
		$\left[\sum a_{hw}^2 t_h \right]^{0.5} td.ty \Big]^2$ <p>Exposure time assessed by questionnaire and work study timings to obtain actual exposure. Exposure categorised into 4 groups</p> <p>Analysis chi-squared tests and logistic regression analysis. Adjustments made for compounding factors eg. Age, smoking, alcohol.</p>	<p>4.3 Prevalence of SN symptoms also increased with lifetime exposure (p=0.0003) in logistic regression analysis after adjusting for age, alcohol and smoking. Severity of SN staging also increased by lifetime exposure category.</p> <p>4.3 90% of workers with lifetime exposure >21m²sec⁻⁴hd had SN symptoms.</p>
Jorulf (1986) [91]	4.1 4.3	<p>Type Epidemiological, Cross sectional study of impact wrench users.</p> <p>Population 904 workers at Volvo Truck Corporation.</p> <p>Outcome definition VWF and numbness by self administered questionnaire.</p> <p>Exposure assessment vibration measurements from National Board of Occupational Safety and Health in Sweden. (No standards in 1985.). Acceleration range of tools between 3.9-18.1 m.s⁻²</p> <p>Analysis Non parametric statistical tests used with p<0.05 as significant.</p>	<p>4.1, 4.3 23% prevalence of VWF and 33% prevalence of numbness in 7 –9 year exposure category, (but only 9% prevalence of VWF and 23 % prevalence of numbness in the >10 years exposure category).</p> <p>4.1, 4.3 The prevalence of numbness appears to increase more rapidly than VWF</p>
Keith & Brammer (1994) [147]	4.1 4.8	<p>Type Meta-analysis of Miners and Chainsaw operators</p> <p>Population. Rock drill operators and chainsaw operators</p> <p>Outcome definition. Observed latency in populations, technique for assessment not specified.</p> <p>Exposure assessment Highest axis frequency weighted and unweighted acceleration and estimated exposure times</p> <p>Analysis: Comparison of ISO 5349 predicted and observed latency</p>	<p>4.8 The drilling process investigated has a high frequency component (3kHz) which is weighted out by ISO 5349.</p> <p>4.1 Chainsaw vibration in the Bovenzi study and rock drill vibration in the current study are assumed to be equally hazardous. ISO 5349 predicts the latency for chainsaws but over estimates the hazard for rock drills.</p> <p>4.8 Their frequency contents being very different, the overprediction of hazard due to ISO 5349 for rock drills is</p>

Ref	Matrix ID/para number	Study	Outcomes
			attributed to the high frequency content of the signal.
Kent et al 1994 [148]	4.7	<p>Type Cross sectional study</p> <p>Population 43 people in 3 groups: 12 controls, 16 VWF patients, 15 Raynauds patients</p> <p>Stimulus 120Hz sine wave at 0.15mm amplitude on simulated handle. 15 to 17 N grip force. 1 minute of exposure to vibration.</p> <p>Measured response Beta-thromboglobulin levels, circulating platelet aggregate ratio and platelet sensitivity to aggregation were measured</p>	<p>4.7 Base line Beta-thromboglobulin levels were raised in Raynauds and VWF patients before exposure and in all three after exposure.</p> <p>4.7 Circulating platelet aggregate ratio showed no differences in any groups before or after vibration.</p> <p>4.7 Platelet sensitivity to aggregation with ADP and collagen showed varying levels of response. Controls tended to be more sensitive to aggregation with low dose ADP than those with VWF or RP.</p> <p>4.7 Results show that intravascular platelet aggregation occurs as a result of exposure to vibration. Release of vasoactive agents and platelet-derived growth factor may result in vasoconstriction and be responsible for observed decrease in blood flow ultimately resulting in hypertrophy of the smooth muscle.</p>
Kim et al (2007) [149]	4.8	Mathematical study of the effect of different approaches to signal analysis	<p>4.8 Proposes the use of AWT to characterise the vibration signal.</p> <p>4.8 Includes use of the finger weighting proposed by Dong et al which gives a much higher total acceleration in the frequency weighted time histories than the ISO 5349 weighting.</p>
Kivekas et al (1994) [61]	4.1 4.5	<p>Type Longitudinal study of Finnish lumberjacks with seven year follow-up</p> <p>Population 279 lumberjacks and 178 controls. In the follow up there were 213 lumberjacks and 140 controls</p> <p>Outcome definition Questionnaire based assessment, clinical examination and radiographs of wrist and hands</p> <p>Exposure assessment No exposure assessment made.</p> <p>Analysis Separate analysis of prevalence and cumulative</p>	<p>4.1 There was a significant increase in VWF prevalence at follow-up in exposed, but not in controls.</p> <p>4.1 The cumulative incidence in lumberjacks was 14.7% over the follow-up period; 2.3% in controls. Therefore crude RR was 6.5 (CI2.4-17.5)</p> <p>4.1 Taking account of age, there was a significant trend for both</p>

Ref	Matrix ID/para number	Study	Outcomes
		incidence data. Risk ratios and 95% CI estimated.	<p>incidence and prevalence of WF with duration of exposure P<0.001.</p> <p>4.1 6 out of 78 lumberjacks who had reported symptoms in 1978 reported improvement in 1985, allowing for the notion of reversibility.</p> <p>4.5 After allowing for age, the prevalence of osteoarthritis was not related to exposure time. No significant differences in occurrence rates of wrist bone translucencies between lumber jacks and controls.</p> <p>4.1 White finger symptoms develop much more slowly in third generation (Vibration reduced) chain saw operators.</p>
Koskimies et al (1992) [68]	4.1 4.3	<p>Type Longitudinal study of Finnish forestry workers with follow-ups 1972 -1990.</p> <p>Population 118 – 205 forest workers</p> <p>Outcome definition Questionnaire, physical examination</p> <p>Exposure assessment No exposure assessment was made</p> <p>Analysis Data expressed as % of population at time of examination</p>	<p>4.1 The prevalence of VWF has reduced from 40% in 1972 to 5% in 1990. The main reason for the reduction is the reduction in vibration magnitude of the saws. Thus supporting the concept of reversibility of VWF depending on current exposure.</p> <p>4.3 The prevalence of numbness decreased from 78% in 1972 to 28% in 1990, thus supporting the concept of reversibility of neurosensory symptoms depending on current exposure</p>
Krajnak et al (2012) [150]	4.2 4.4	Review of literature on animal and computational modelling studies of the frequency-dependent effects of vibration	<p>4.2 4.4 Rat studies showed that frequencies that cause the most strain and stress on tissues have the greatest effects on morphology and vascular function. This occurs at the resonant frequencies of the fingers.</p> <p>4.2 4.4 Differences in frequency dependence between vascular and</p>

Ref	Matrix ID/para number	Study	Outcomes
			<p>neurological.</p> <p>Describes ‘blebs’ - a 2 stage mechanism of damage.</p> <p>Recognises limitations of rat studies for cumulative exposure investigation.</p>
Krajnak et al (2012) [151]	4.7 4.11	<p>Type Experimental study on rat tails.</p> <p>Outcome definition. Current perception thresholds, fold changes in transcript levels, immunostained area of the nerves, myelinated nerve number and myelin thickness</p> <p>Exposure assessment 4 hour bouts at 62.5, 125 and 250 Hz for ten days</p> <p>Analysis: One way ANOVA</p>	<p>4.7 Vibration at 250Hz more detrimental than other lower, frequencies.</p> <p>4.11 Current ISO 5349 frequency weighting under-estimates risk of injury above 100Hz.</p>
Letz et al (1992) [56]	4.1 4.3	<p>Type Epidemiological, cross sectional study of 375 shipyard workers</p> <p>Population 375 workers questioned. Of the 297 respondents (79%) 26 were excluded leaving 271 shipyard employees in three exposure groups, non-exposed, partially exposed and full time.</p> <p>Outcome definition: Self-administered questionnaire, leading to Classification according to Stockholm Workshop scale.</p> <p>Exposure assessment. Cumulative exposures in hours divided in to quintiles to give roughly equal groups</p> <p>Analysis Logistic regression to control for age, ethnicity and smoking. Highly significant association ($p < 0.001$) between cumulative duration and symptoms. Smoking related to vascular and neurological symptoms.</p>	<p>4.1, 4.3 Median latency 8400 hrs for VWF 8200 for numbness.</p> <p>4.1 Reporting of symptoms not significantly related to age but highly related to several indices of tool use.</p> <p>4.3 The effect of cumulative exposure to vibration is demonstrated. SN=0 drops from 82% in the not exposed to 19% for those with >17000 hrs cumulative exposure.</p> <p>4.1, 4.3 Incidence of vascular and sensorineural symptoms is among the highest reported in literature at the time. This is attributed to the specialised nature of the job tasks.</p> <p>4.1, 4.3 Polychotomous logistic regression analysis of SWS stage employing age, smoking status, ethnicity and either (cumulative hours, years of exposure. Logged cumulative exposure produced the best fit.</p>

Ref	Matrix ID/para number	Study	Outcomes
			<p>4.1 For the vascular stages OR was 2.9(CI 1.7-5.0) for each log unit increase in total hours of vibratory tool use</p> <p>4.3 For the neurosensory stages OR was 1.8(CI 1.2-2.9) for each log unit increase in total hours of vibratory tool use</p>
Lundstrom et al (1992) [88]	4.1 4.3	<p>Type Epidemiological, Cross sectional study of platers and assemblers</p> <p>Population 109 platers and assemblers and 45 office workers as controls.</p> <p>Outcome definition Self administered questionnaire. Stockholm Workshop classification of SN symptoms by medical examinations, subjective reporting of symptoms and clinical tests.</p> <p>Exposure assessment Self administered questionnaire on exposure time including life time exposure. Vibration measurements to ISO 5349. Platers used grinders and chipping hammers. Assemblers used nut runners. Lifetime exposure calculated from</p> $VD_{tot} = (a_{h,w}) \cdot t_d \cdot k \cdot t_y$ <p>where k=200 = no. working days/year.</p> <p>Analysis Regression analysis to produce correlation coefficients.</p>	<p>4.3 Increasing vibration doses (long-term exposure to moderate levels of vibration, or short-term exposure to high levels of vibration) lead to an increased prevalence of sensorineural disturbances.</p> <p>4.3 There was an unusually high prevalence (30%) in the controls. 15% reported symptoms at SN 2 and 3 when compared with 27% in assemblers. Assemblers had the lower vibration exposures than platers.</p> <p>4.3 The paper criticises the rating scale as some of the observed symptoms could not be fitted sensibly in to the classification eg. Abnormal vibrotactile perception but no numbness, or loss of manual dexterity on its own.</p> <p>4.1, 4.3 Findings support the idea that vascular and neurological components develop independently.</p>
Lundstrom et al (1999) [110]	4.7	<p>Type Cross sectional study of workers in heavy engineering</p> <p>Population 170 male workers from engineering plant, 125 vibration exposed, 45 non-exposed.</p> <p>Outcome definition VPT at 7 frequencies 8 –500 Hz to measure VPT_P, VPT_{NP}. P= Pacinian, NP = non-pacinian. VPT responses were scored & categorised into 4 groups based on comparison of mean and multiples of sd in non-exposed group (ie. VPT < (mean+1sd)= ‘normal’; VPT between mean +1sd &</p>	<p>4.7 When comparing non exposed and EC2 there was a 4 fold increase in relative risk of elevated VPT above 40Hz suggesting that there is an exposure-response relationship for sensorineural disorders.</p> <p>4.7 Correlation between CVE and VPT weak (r=~-0.2)</p> <p>4.7 A weakly significant relationship between decreasing tactile</p>

Ref	Matrix ID/para number	Study	Outcomes
		<p>mean +2sd = 'slightly reduced' etc. Thus case definition of VPT abnormality was above the mean +1 sd in unexposed. All VPT measurements had been age-adjusted according to published data.</p> <p>Exposure assessment Vibration assessed according to ISO5349.</p> <p>CVE = $(a_{hw})_{td.k.ty}$ where k = 200 days per year and categorised into 3 groups; non exposed, EC1 = CVE $0 \leq 24000$, EC2 = CVE $>24000 \text{mh/s}^2$</p> <p>Analysis Odds ratios 95 % confidence interval. Linear regression to give correlation coefficients</p>	sensitivity measured by VPT _P and VPT _{NP} and increasing CVE (r approximately 0.2).
Mason et al (2011) [15]	4.1 4.3	<p>Type Cross-sectional study of referrals to HAVS assessment unit</p> <p>Population HAVS referrals cases</p> <p>Outcome definitions Physicians assessment of Stockholm stage</p> <p>Exposure assessment Comparison of various techniques for assessment of exposures including time to onset of symptoms (latency).</p> <p>Dose = $\sum a_i^m t_i$ where m=0,1,2 and a_i is either mean weighted or unweighted acceleration.</p> <p>Analysis: based on repeating Griffin (2003) analysis</p>	<p>4.1, 4.3 Years of exposure gave the poorest model</p> <p>4.1, 4.3 Recommends use of cumulative hours of tool use across all tools for estimation of health outcomes</p> <p>4.1, 4.3 Unable to prove that frequency weighting (ISO5349) gives a better fit dose-response model than unweighted.</p>
McGeoch & Gilmour (2000) [152]	4.1 4.3	<p>Type: Cross sectional study of 165 heavy engineering workers</p> <p>Population: Welders, fitters, platers and dressers at a heavy engineering plant.</p> <p>Outcome definition: Questionnaire and objective tests including Adson, Allen, Tinel and Phalen. Stockholm Workshop staging.</p>	<p>4.1 33% had vascular symptoms</p> <p>4.3 62% had neurological symptoms</p> <p>4.1 Mean LI for vascular symptoms was 19.1 years</p>

Ref	Matrix ID/para number	Study	Outcomes
		<p>Exposure assessment: Years/total hours tool use</p> <p>Analysis: Chi² tests and one way ANOVA. Ordinal logistic regression</p>	<p>4.3 Mean LI for neurological symptoms was 19.7 years</p> <p>4.3 Shows probability functions/curves for SN and SV stages by years of tool use subdivided in some cases by type of job.</p>
Mirbod et al (1992) [153]	4.1 4.3	<p>Type Meta-analysis</p> <p>Population 164 dental technicians, 256 aircraft industry workers, 79 digging labourers, 46 sewing machine operators, 272 chain saw operators. 259 male and 657 female RP controls</p> <p>Outcome definition: Prevalence of VWF & numbness of hands.</p> <p>Exposure assessment Vibration measurements using transducer strapped to back of hand</p>	<p>4.1 Highest prevalences of VWF were for chain saw operators (9.6%), then dental technicians (4.8%). Others (aircraft industry workers, digging labourers and sewing machine operators) had similar rates of incidence to those found in the general population. (2.7 to 2.9%)</p> <p>4.3 No significant differences were found between machine operators and the general population in terms of neurological symptoms</p>
Mirbod (1997)[154]	4.1 4.3 4.5 4.7	<p>Type Epidemiological, cross sectional study of 447 male chainsaw operators</p> <p>Population 447 male chainsaw operators 43 VWF sufferers and matched controls</p> <p>Outcome definitions VWF from nurse administered questionnaire and objective tests skin temp, nail press test. Vibration threshold at 125Hz, Pain threshold using weighted needles. Grip strength test.</p> <p>Exposure assessment Frequency weighted vibration measured on operators' hands using a single axis device. Years of exposure used as metric, banded into 5 categories</p> <p>Analysis Simple comparison of matched controls using t-tests and chi-squared tests.</p>	<p>4.1 Linear monotonic Positive relationship between years of exposure and prevalence of VWF (20.9% prevalence after 30yrs) numbness (25.4% prevalence after 30yrs).</p> <p>4.1 Significant relationship between exposure duration and stage of VWF but using Taylor Pelmear scale</p> <p>4.3 Significant relationship between hand numbness and categorised exposure years (table 4)*</p> <p>4.5 Comparison of VWF sufferers and matched controls show significant differences (p<0.01) in skin temperature and nail press test and reduced grip strength.</p> <p>4.5 Significant relationships between elbow pain and back pain, but</p>

Ref	Matrix ID/para number	Study	Outcomes
			not shoulder stiffness or knee pain and categorised exposure years 4.5 229 chainsaw workers in subgroups 40s 50s and 60s were studied. Workers in their 60s with the same amount of exposure had lower functional capacities as indicated by nail press test, vibration threshold and grip strength tests.
Miwa T (1967)[11]	4.7	Type: Experimental study of threshold of sensation and equal sensation contours. Population: 10 healthy male subjects Outcome definition: The basis of the hand arm frequency weighting Exposure assessment: N/A	4.7 Develops threshold of sensitivity and equal sensation contours for hand transmitted vibration 4.7 Concludes that the hand arm system is equally sensitive to vibration in the vertical and horizontal directions
Miyashita et al 1994 [95]	4.1 4.3 4.7	Type: Epidemiological Cross-sectional study Population: 266 workers using chain-saws & 46 controls never exposed to vibration Outcome definition: Include skin temperature changes after cold challenge, pain and vibration perception before/after cold challenge and grip/pinch strength strength. Analysed outcomes derived as scores (0-25), where quantitative tests, clinical assessment and subjective symptoms are combined, and used separately for the vascular, sensory, musculoskeletal components. Exposure assessment: retrospective total chainsaw use (hours) [TOT] calculated from occupational history and banded into 8 groups. Analysis: Simple comparison of outcomes by exposure groups, t-tests and correlation coefficients	4.7 Significant increases in mean scores were found with increasing TOT between some of the exposure time groups and this confirmed the dose response relationship according to the author. 4.1, 4.3 Prevalence rates (scores) were higher for numbness than for Raynaud's phenomenon.
Nagata et al(1993)[155]	4.1 4.2 4.5	Type; Cross sectional study of forestry workers in Japan. Population: 179 chainsaw workers and 205 controls. Outcome definition: Interview and functional tests; FST, nail	4.1 RP 9.5 % prevalence, edema 1.7% in forestry workers. 4.5 Sclerodactylia in 31.8% of foresters but only 6.4 % of controls.

Ref	Matrix ID/para number	Study	Outcomes
	4.6	compression test, VPT at 125Hz and hand examination Exposure assessment: simple estimates based on previous study results. Analysis: Unconditional logistic regression analysis.	4.2 Increased OR of RP in long term vibration exposure groups 4.2 4.6 Significant dose-response relationships between RP and duration of exposure and Sclerodactylia and duration of exposure
Necking et al (2004)[27]	4.6 4.7	Type Study of Referees to Malmo University Dept of hand surgery. Population 20 right handed men with grip weakness and HAVS, 4 age matched controls Outcome definition Clinical examination, muscle biopsy from abductor brevis on right hand, light microscopy, enzyme and immunohistochemical analyses, morphometry. Exposure assessment Lifetime exposure $CVE = (a_{h,w})t_h.t_d.t_y$ where $t_h = 0.5$ 2 or 4 hrs per day $t_d =$ no. working days/year = 200 $t_y =$ no years. <i>Also categorised into 3 groups depending on increasing CVE dose</i> Analysis Linear regression and one way ANOVA	4.7 Centrally located myonuclei and fibre type grouping, angulated muscle fibres, ring fibres and regenerating fibres and fibrosis are believed to reflect damage to muscle fibres and the motor nerve. 4.7 Significant correlations were found with central nuclei and cumulated vibration exposure ($r=0.52$, $P<0.05$). But when split in to groups, the lowest CVE group had the strongest correlations ($r=0.77$) 4.7 Angulated fibres correlated significantly with total vibration exposure time ($r=0.46$, $P<0.05$) for group II (longer exposure time) this was even stronger ($r=0.75$, $P<0.05$). No other correlations with exposure were found. 4.6 Muscle abnormalities found could explain the subjective experience of hand weakness. 4.7 Significant correlation between 2 point discrimination and CVE in little finger but not index finger
Nelson & Griffin (1989)[156]	4.1 4.8	Type Cross sectional study of dockyard employees Population 1200 dockyard employees, 921 after exclusions Outcome definition Administered questionnaire to identify symptoms using Griffin scoring technique Exposure assessment Vibration measurements to ISO 5349 Analysis Multiple regression analysis, Kendall's tau, logistic regression analysis	4.1 Finger blanching score was only significantly related to measures of exposure time, not measures of vibration dose. 4.1 Latency period for the 20 th percentile was inversely proportional to daily vibration exposure time in hours per day. 4.8 No evidence that frequency weighted magnitude provided a

Ref	Matrix ID/para number	Study	Outcomes
			better prediction of VWF than unweighted magnitudes.
Nilsson et al (1989) [54]	4.1 4.2	<p>Type Cross-sectional epidemiological study of platers</p> <p>Population 89 platers and 61 controls</p> <p>Outcome definition VWF according to Taylor Pelmear scale and Stockholm scale. Chart used to document symptoms followed up by physician-lead examination and interview</p> <p>Exposure assessment Vibration measurements to ISO 5349. Subjective (by questionnaire) and objective measurements of exposure time. Total daily exposures computed</p> <p>Analysis Prevalence rates odds ratios and confidence limits were computed. Tow-tailed tests with $P < 0.05$ as significant. Multiple logistic regression used for interaction analysis.</p>	<p>4.1 VWF point prevalence among currently exposed platers was 42%.</p> <p>4.1 Latency for the study population was shorter than that predicted by ISO 5349. (Mean latency was 9.8 years).</p> <p>4.1 The ISO5349 prediction for 10% VWF prevalence and study population are generally in line but further progress in cumulative prevalence of VWF in study population suggests less risk compared with ISO5349.</p> <p>4.1 Relatively linear montonic relationship between years of exposure and prevalence of VWF. Logistic regression suggested years of vibration exposure significant after adjusting for age.</p> <p>4.2 While successive increase in SWS staging 1-3 was found with length of vibration exposure. No correlation between SWS and vibration years found.</p>
Nilsson and Lundstrom (2001)[109]	4.7	<p>Type Cross sectional study</p> <p>Population 123 vibration exposed and 62 non-exposed workers from 500 employees. HTV mostly from using grinders (65%), hammers (25%)</p> <p>Outcome definition Thermal perception thresholds (TPT) on the distal phalanx and thenar eminence. Case definition of 'abnormal' TPT was determined from overall mean threshold value +/- 1 SD.</p>	<p>4.7 The study shows an increased risk of disturbed thermal perception among vibration exposed workers and a relationship between cumulative exposure to vibration and thermal sensory function. The effect occurred at vibration levels below the (then) guidance. 4000 m.h.s^{-2} change in CVE increased risk of an 'abnormal' neutral zone by 18% after controlling for age and skin temperature</p>

Ref	Matrix ID/para number	Study	Outcomes
		<p>Exposure assessment Vibration measurements to ISO 5349 and estimation of CVE. Individual's exposure time calculated from observation, questionnaire and diaries.</p> <p>Analysis Specifically the association between CVE and neutral zone was tested using multiple logistic regression with age, height, smoking (Y/N) and skin temperature as confounders. (age, exposure interactions were explored).</p>	
NIOSH (1997) [96]	4.5 4.6	<p>Review 20 selected epidemiological studies</p>	<p>4.5, 4.6 This critical review of the epidemiologic literature identified a number of specific physical exposures which are strongly associated with specific upper extremity and low back musculoskeletal system disorders (MSDs) when exposures are intense, prolonged, and particularly when workers are exposed to several risk factors simultaneously.</p>
Nyantumbu et al (2007) [157]	4.1 4.3	<p>Type Cross sectional study of South African Gold miners</p> <p>Population 156 occupational exposed and 140 other mine workers. 95% power to detect 10% difference</p> <p>Outcome definition Clinical HAVS assessment following HSL protocol carried out by an occupational physician. Thermal aesthesiometry, vibrotactile threshold and cold provocation test. Staged according to Stockholm workshop scale</p> <p>Exposure assessment Interview to establish previous exposure and medical history. Ambient temperatures from mines were also recorded.</p> <p>Analysis Students t-tests, Mann Whitney test, χ^2 test. P set to 0.05</p>	<p>4.1, 4.3 The prevalence of HAVS was 15% with a mean latency of 5.6 years. 13 vascular and neurological. 8 neurological only, 3 vascular only (16/156 with vascular symptoms)</p> <p>4.1, 4.3 5% (7/140) controls had symptoms indistinguishable from HAVS</p> <p>4.1, 4.3 Low prevalence may be due to existence of a survivor population (NIHL sufferers had been removed from exposure as had those with reduced grip strength) and warm ambient temperatures</p>
Okada A (1986) [132]	4.11	<p>Type Experimental study in rats</p> <p>Population 153 male wistar rats</p> <p>Outcome definition Measurements of skin temp, blood flow and peripheral nerve conduction velocities</p> <p>Exposure assessment Exposed tail and hind legs separately to</p>	<p>4.7, 4.11 Varying effects (skin temperature blood flow and NCV) at varying frequencies were observed except at 960Hz. Effects on the muscles, evidenced by a circulating muscle damage marker were amplitude dependent.</p>

Ref	Matrix ID/para number	Study	Outcomes
		50m/s/s vibration at 30, 60,120, 240, 480 and 960 Hz Analysis Students t-test for paired comparisons	
Petersen et al (1995) [86]	4.1 4.7	Type Follow-up cohort study of VWF patients, with history of chipping hammers and angle grinders. Variable follow-up period of 1-13 years Population 132 out of 318 patients examined for VWF between 1978 and 1990 were invited. 102 attended. Outcome definition Questionnaire and interview techniques used to collect information. FSBP under cold provocation measured. Exposure assessment Acceleration classes used were <3 m/s/s, 3-10 m/s/s and >10 m/s/s. Analysis Logistic regression	4.1 Results show that symptoms improve after a reduction in exposure and aggravate in unchanged or increased exposure. 4.7 No relation found between subjective evaluation of change in frequency of attacks and FSBP. FSBP can improve in VWF. Interestingly improvement in FSBP was not reflected in subjective symptoms
Pitts et al (2012) [158]	4.8 4.9 4.12	Reconstruction of lifetime histories for referred HAVS cases using a range of different frequency weightings.	4.8 4.9 4.12 Nine frequency weightings (including ISO) were compared and four power relationships between a and t (0, 1, 2 and 4) using statistical techniques applied to data in the two HSL databases looking for: Any form of HAVS Vascular HAVS Sensorineural HAVS Wh and Wh50lp and first power relationship provide the strongest indicators of HAVS in general. No clear evidence for any of the evaluated dose measures for vascular HAVS
Pitts (2011) [14]	4.8 4.9	Type Modelling study based on epidemiological cross-sectional data Population Referral subjects to a specialised HAVS assessment unit	4.8 No particular weighting system proved superior to the others. 4.9 First power of ISO5349 and one of the German VDI2057 weightings suggested better in modelling the risk of sensorineural HAVS

Ref	Matrix ID/para number	Study	Outcomes
		<p>Outcome measures vascular and neurosensory HAVS by physician-led assessment</p> <p>Exposure assessment Lifetime exposure in the form $\sum a_{xi}^m \cdot t_i$ where m= 0,1,2,4 and x reflects various frequency weighting. Vibration magnitudes from HSL HAV database; exposure duration from history. Exposures categorised into quintiles. Various weightings applied including ISO5349, band-limited (unweighted), Tominaga weighting, two based on German guidance VDI2057.</p> <p>Analysis logistic regression with Bayseain Information Criteria to assess strengths of various models</p>	
Rytönen (2006) [128]	4.10	<p>Type Cross sectional study</p> <p>Population 295 female Finish dentists.</p> <p>Outcome definition self reported finger symptoms perceived to be vibration associated (exact nature of the symptoms not well clarified) and measurements of pinch grip</p> <p>Exposure assessment Questionnaire and self reporting of exposure. Single axis vibration measurements to ISO 5349 using contact and non-contact techniques. Weighted magnitudes and unweighted high frequency magnitudes. Estimated total values and daily exposures .</p>	<p>4.10 Dentists daily exposures were below 2.5 m/s² A(8).</p> <p>4.10 Finger symptoms were reported as experienced sometimes by 12.2% and continuously by 1.7%.</p> <p>4.10 Finger symptoms were correlated with high BMI and age as well as total exposure time during work history.</p> <p>4.10 Total exposure time was associated with a two-fold risk of symptoms (OR 1.92, 95% CI: 1.03 –3.6)</p>
Saito K (1987) [159]	4.7	<p>Type Longitudinal study of Japanese forest workers</p> <p>Population 155 Foresters aged 24 to 53</p> <p>Outcome definition Health examinations over 6 years. Subjective symptoms recorded. Skin temp and VPT, nail compression test, sensitivity to pain.</p> <p>Exposure assessment Exposure times assessed</p>	<p>4.7 No significant difference by year but, skin temp recovery faster for men in their 20s.</p>
Sauni et al (2009) [62]	4.1 4.4 4.6	<p>Type Epidemiological cross sectional study of 530 Finnish metal workers</p> <p>Population 530 workers surveyed, 285 responded.</p>	<p>4.1. Cumulative exposure associated with symptoms of VWF (OR=2.4-4.5).</p>

Ref	Matrix ID/para number	Study	Outcomes
	4.7	<p>Questionnaire based with clinical assessment follow-up of those reporting symptoms</p> <p>Outcome definition: HAVS, CTS, upper limb MSD + VPT measurements</p> <p>Exposure assessment cumulative exposure index, I, based on vibration magnitudes from database and exposure times from questionnaire.</p> $I = \sum A_i(8)^2 \text{ years d}$ <p>Where A(8)= average daily exposure, years = exposure time in years and d = annual exposure time in days.</p> <p>Analysis: Logistic regression for VWF & CTS adjusted for age and smoking with cumulative and current daily exposure and impulse as separate explanatory variables.</p>	<p>4.6. Cumulative exposure associated with symptoms of CTS (OR=4.6-6.1). Cumulative exposure associated with symptoms of MSD (OR=4.7-5.4).</p> <p>4.4. Cumulative exposure associated with neurosensory symptoms (OR=5.7-17.3)</p> <p>4.7 VPT at varying testing frequencies significantly associated with cumulative exposure.</p> <p>4.9 Impulse HTV associated with neurosensory symptoms but not vascular, MSD or CTS.</p> <p>4.1, 4.3, 4.5 Current level of exposure correlated positively with vascular, neurosensory, CTS and MSD.</p>
Sauni et al (2009)[160]	4.1 4.3 4.5 4.7	<p>Type Epidemiological cross-sectional Cohort study of 530 members of metal workers union in Finland chosen at random from 2500 members</p> <p>Population 285/530 Finnish metal workers responded to questionnaire. 133 of this reporting some symptoms attended clinical examination.</p> <p>Outcome definition Specific criteria for VWF and CTS stated. VWF cases staged for vascular and sensorineural SWS. 24 cases of VWF, 12 cases of CTS, Comprehensive questionnaire and clinical assessments by physician including Cold provocation test (50% decrease in FSBP = abnormal), ENMG, grip strength test, pinch force tests, dexterity test, two point discrimination, VPT to ISO 130911-1:2001. Exclusion of other pathologies by physicians. After this diagnostic battery, 24 new cases of HAVS and 12 new cases of CTS were identified</p>	<p>4.1, 4.5 Exposure time did not differ between VWF /CTS cases and others, but cumulative exposure indices (taking account of vibration intensity and duration) were significantly different</p> <p>4.3 All workers with VWF also had sensorineural symptoms.</p> <p>4.7 Statistically significant reduction in grip for VWF patients</p> <p>4.7 VPTs significantly different at 31.5, 63 and 500Hz in VWF patients</p>

Ref	Matrix ID/para number	Study	Outcomes
		<p>Exposure assessment cumulative exposure index, I, based on vibration magnitudes from database and exposure times from questionnaire.</p> $I = \sum Ai(8)^2 \text{ years d}$ <p>Where A(8)= average daily exposure, years = exposure time in years and d = annual exposure time in days.</p> <p>Analysis SPSS t-test or χ^2 tests to compare groups, logistic regression adjusted for age and smoking. Mann-Whitney used to compare differences in cumulative exposure indices and exposure time.</p>	
Sauni R at al (2010) [117]	4.1 4.3 4.7	<p>Type: epidemiological cross sectional</p> <p>Population: 285/530 Finnish metal workers responded to questionnaire. 133 of this reporting some symptoms attended clinical examination..</p> <p>Outcome definition: EQ-5D as quality of life measure</p> <p>Exposure assessment: cumulative exposure index, I, based on vibration magnitudes from database and exposure times from questionnaire.</p> $I = \sum Ai(8)^2 \text{ years d}$ <p>Where A(8)= average daily exposure, years = exposure time in years and d = annual exposure time in days. Used in tertiles.</p> <p>Analysis: Mann-Whitney, Kruskal –Wallis, multivariate analyses with ANCOVA for ED-5D to adjust for age.</p>	<p>4.7 Inverse relationship between EQ-5D and cumulative exposure index, but no decrement from middle (6,800-25,000 $m^2.d.s^{-4}$) to upper tertile of exposure (>25,000 $m^2.d.s^{-4}$). Data suggests cumulative exposure higher in those with CTS, and dose response relationship for musculoskeletal symptoms categorised by tertiles and cumulative exposure index</p> <p>4.1 Exposure time did not differ between VWF /CTS cases and others, but cumulative exposure indices (taking account of vibration intensity and duration) were significantly different</p> <p>4.3 All workers with VWF also had sensorineural symptoms.</p> <p>4.7 Statistically significant reduction in grip for VWF patients</p> <p>4.7 VPTs significantly different at 31.5, 63 and 500Hz in VWF patients.</p>
Starck J (1984) [161]	4.1 4.8	<p>Type Experimental study</p> <p>Exposure assessment ISO 5349 A(4) exposures and</p>	<p>4.1, 4.8 Impulse analysis of vibrations provides additional data to explain, the observed incidence of vibration induced white fingers</p>

Ref	Matrix ID/para number	Study	Outcomes
		<p>measurements of impulse indices of vibration signals.</p> <p>Analysis Expected latency periods for vibration induced white fingers, computed according to the ISO 5349 draft</p>	
Starck et al (1990)[162]	4.1 4.8	<p>Type Meta analysis of 1 longitudinal and 4 cross sectional studies.</p> <p>Population 5 groups of vibration exposed workers. 76 forest workers, 12 pedestal grinders, 16 stone workers, 171 shipyard workers & 5 platers</p> <p>Outcome definition VWF Self-administered questionnaire. No details of scoring techniques etc.</p> <p>Exposure assessment Vibration measurements to ISO 5349 to obtain the A(4) daily exposure. Measurements also made on the wrist. Measurements of the impulsiveness of the vibration were also made using the crest factor.</p> <p>Analysis Comparison of predicted and observed prevalences and latency of VWF</p>	<p>4.1, 4.8 The best agreement between predicted and measured latencies and prevalences was for forest workers. The worst was for pedestal grinders.</p> <p>4.8 Effects of vibration exposure were under-estimated for pedestal grinders but over-estimated for other hand tools except chain saws. The authors consider that ISO5349 is not considering high peak values of the vibration signal.</p>
Su et al (2012) [163]	4.1 4.3	<p>Type: Systematic review of literature relating to HAVS in tropical and subtropical countries.</p>	<p>4.1 ISO 5349 exposure –response relationship for vascular HAVS is not applicable in tropical countries.</p> <p>4.3 Prevalence of neurological symptoms ranged from 18% to 68% in tropical environment.</p> <p>4.3 There is a need to produce a dose response curve for neurological symptoms.</p> <p>4.1 Finger coldness (as a reported symptom rather than quantified measurement) may be a surrogate for vascular disorder in a tropical environment.</p>
Su et al	4.3	<p>Type: Epidemiological, cross-sectional study of construction</p>	<p>4.3, 4.5 Significant increase in PR ratios with log LVD for tingling</p>

Ref	Matrix ID/para number	Study	Outcomes
(2011)[89]	4.5 4.7	workers Population: Malaysian construction workers n=243 using concrete breakers, impact drills & grinders Outcome definition: Purdue pegboard, temperature discrimination, monofilaments, 2-point discriminator: all assessed as normal/abnormal. Symptoms of blanching, tingling numbness, MSD of the upper extremity. Exposure assessment: Vibration measurements according to ISO5349 and A(8) calculations. Lifetime vibration dose (LVD) according to Griffin (2003) Analysis: largely group comparisons- low-moderate versus high exposure groups.	& numbness in fingers, MSD in upper limbs, neck, finger coldness, Tinel's & Phalen's tests. 4.7 Prevalence of abnormal dexterity (PP test), temperature sensation & light touch sensation higher in high LVD exposure group compared with low-moderate exposure. 4.3, 4.5 Simple regression analysis of total LVD and numbness/tingling/hand grip weakness, finger coldness, abnormal Tinel's/Phalen's were related to trend of LVD'
Sutinen (2006) [64]	4.1 4.3 4.5	Type Epidemiological PS- cross-sectional & cohort study. Population 11 cross-sectional studies 1976-1995 in Finish forestry workers Cohort (internal) 52 forestry workers studied 1976-1995. Chain saws only. Outcome definitions, by medical history VWF by well-demarcated blanching after exclusion of primary Raynaud's, Numbness classified if persistent and troublesome, clinical examination, Jamar hand grip and other upper extremity tests. Exposure assessment –vibration measurements on front & rear handles for a representative chain saws over the project time-frames. Self-reporting of daily tool use. Lifetime dose calculated from summation of A(8) days (frequency-weighted) and years of exposure. Analysis logistic linear or logistic binary regression used.	4.1 In cohort study Lifetime dose significantly related to VWF (p<0.001, after age adjustment and taking into account smoking status 4.3 Lifetime dose did not explain numbness (p=0.36), but associated with upper extremity MSDs. 4.5 Right rotator cuff syndrome related to lifetime dose and age 4.1, 4.3 In cohort study the number of subject with active VWF fell 1976-1995, with only 1 new case, while the prevalence of numbness increased 23% to 40%. Similar results from X-sectional studies.
Tasker (1986)[78]	4.1 4.8	Type Cross sectional study of British gas employees Population 895 vibration exposed workers and 546 meter readers (controls)	4.1 Results showed no relation between VWF (as reported) and use of vibratory tools.

Ref	Matrix ID/para number	Study	Outcomes
		<p>Outcome definition No details of how VWF was assessed in this paper (Ref Walker et al 1985 for details. Positive response to questions in occupational nurse administered questionnaire. No classification of VWF)</p> <p>Exposure assessment Vibration measurements using accelerometers on the handle and in the hand and a laser measuring vibration on the operator's hand</p> <p>Analysis χ^2 tests were used to investigate statistical significance between populations with $p < 0.01$)</p>	<p>4.1 Prevalence was 9.5% in controls and 9.6% in vibration exposed group. When adjusted for age differences it was 12.2%, still not statistically significant. Whereas vibration magnitudes indicate that there should be a much higher prevalence.</p> <p>4.8 Results indicate that the dose response curve in the then ISO/DIS 5349 document over estimates the likely prevalence of VWF for use of machines with low-frequency action.</p>
Theriault et al (1982) [164]	4.1 4.2	<p>Type: Cross sectional study</p> <p>Population: 1540 forestry workers in Quebec</p> <p>Outcome definition: Interviews conducted by medical students, questionnaires completed. 60 random operators underwent detailed medical examination. 57 of 60 cases were confirmed as RP.</p> <p>Exposure assessment: N/a</p> <p>Analysis: Logistic regression identify independent variables</p>	<p>4.1 Prevalence of RP 30.5% among chainsaw workers and 8.7 % among controls. Mean LI to onset was 7.8 ± 5.6 years.</p> <p>4.2 Direct proportional increase in prevalence of RP with no of years use</p> <p>4.1 Strong association with RP and smoking</p>
Tominaga (2005)[122]	4.8	<p>Type Modelling of old experimental data</p> <p>Population pre 1980 data; populations unclear, but subjects chosen for using single type of tool, groups of the former could be formed and >20 subjects within a certain duration range</p> <p>Outcome definition Symptoms of VWF finger numbness/tingling and upper limb pain</p> <p>Analysis Linear multiple regression analysis</p>	<p>4.8 Author suggests a new frequency weighting which better explains the symptoms, but weighting high frequencies relatively higher than ISO5349-1</p> <p>4.8 A new frequency weighting which correlates well with the incidence of VWF (but not numbness and tingling or joint pain) is proposed from the five tested.</p> <p>4.8 More weight should be given to higher frequencies and less weight should be given to lower frequencies than in ISO 5349 weighting</p>
Une et al (1985) [94]	4.1 4.5	<p>Type: cross-sectional study of radiological elbow changes in chainsaw users & road maintenance workers</p>	<p>4.5 Overall scores for changes in chainsaw operators elbows were significantly higher than those of road maintenance workers.</p>

Ref	Matrix ID/para number	Study	Outcomes
		<p>Population: 375 Japanese chainsaw operators and 26 road maintenance workers. The former cohort were sampled to produce 3 groups categorised according to length of chain saw use, age matched to +/-2 years. Road maintenance control group selected (n=26) to age match (n=52) of the chain saw operatives.</p> <p>Exposure assessment: Exposure time in years divided in to 3 groups</p> <p>Outcome measure: left elbow joints X-rayed.</p> <p>Analysis: Chi square analyses aggregating degree of radiological changes</p>	<p>4.1 Chainsaw operators had 57.7% prevalence of RP, road workers had none. While a doubling of RP prevalence in those with 8-12 years exposure compared with 7 years or less, no real investigation of RP prevalence rates versus duration of exposure or severity of RP with exposure.</p> <p>4.5 Tendency for radiological changes to become more pronounced with longer chain use, but differences not significant at 5% level.</p>
Virokannas (1992) [112]	4.7	<p>Type Cross-sectional study of vibration exposed workers and control group</p> <p>Population 77 occupationally (from snow mobiles, hand held tampers and chain saws) exposed workers and 77 controls</p> <p>Outcome definition Measurement of VPTs 16Hz to 500Hz</p> <p>Exposure assessment Lifetime exposures in hours.</p> <p>Analysis Paired t-tests, linear regression to compare association of VPTs with age. ANOVA to evaluate effect of HAV on VPT. VPTs in exposed age-adjusted from data in the controls.</p>	<p>4.7 Age adjusted VPTs at all frequencies were significantly higher in HAV exposed group.</p> <p>4.7 Vibration-induced changes in VPTs start at higher frequencies (~125Hz) and progress to lower frequencies (~31.5Hz)</p> <p>4.7 VWF not significantly associated with VPT when age and vibration were included in the analysis</p>
Virokannas 1995 [113]	4.7 4.11	<p>Type: Epidemiological cross-sectional study</p> <p>Population: 31 railway workers & 32 lumberjacks (7 excluded -2 with polyneuropathy & 5 indicative CTS)</p> <p>Outcome definition: VPT measured at 6 frequencies 16-500 Hz.</p> <p>Exposure assessment: total hours of tool use, by worker interrogation. Mainly tamping machines (railways) and chain saws in forestry. Frequency weighted acceleration ranges for the these two tool categories given:2-4 & 10-14 m.s⁻² in chainsaws and tampers respectively.</p>	<p>4.7 Total exposure in hours had a significant linear correlation with VPT on a logarithmic scale in all railworkers and foresters except at 16Hz. VPT measured at 250 Hz showed maximal effect of vibration. Coefficients of determination (R²) between VPT at 250Hz and duration of exposure were 0.31 & 0.58</p> <p>4.11 Paper quotes frequency weighted (ISO5349) acceleration 2-4 & 10-14 m.s⁻² for chain saws and tamping machines respectively. Rail workers had ~two-fold increase in VPTs compared with foresters, frequency weighted magnitudes were 4 times higher but</p>

Ref	Matrix ID/para number	Study	Outcomes
		Analysis: linear correlation/regression between VPT and total exposure time	exposure durations were shorter. 4.11 Data suggest that the relationship between the frequency-weighted acceleration and duration of tool use is not of equal weight in causing abnormality in VPT. [ISO5349 and the calculation of A(8) assume that acceleration is of greater weight than duration of tool use]. The presented data suggest that (freq.-weighted acceleration) ² .(duration) is a better fit.
Wagrowska-Koski et al (2011) [87]	4.1	Type: Case series Population: 45 diagnosed patients with symptoms for at least 5 years. Outcome definition: General medical examination, functionality tests of vascular system, vibrotactile tests. Exposure assessment: N/a	4.1 Stage 1 cases appear to be reversible on cessation of exposure, but not for stage 2.
Walker (1985) [165]	4.1	Type Epidemiological cross sectional study Population 905 men in the gas industry using road breakers and 552 men as control group Outcome measures VWF from nurse led questionnaire Exposure assessment Years of exposure	4.1 Prevalence of VWF not statistically different to controls. The linear increase in VWF by categorised (n=5) use of tools from 1-5 years (9.3%) to >21 years (17.8%) was suggested as due to age rather than vibration from age related prevalence in controls
Ye et al (2012) [131]	4.12	Type Experimental Population 14 healthy male volunteers – 12 data sets used Outcome definition. Finger blood flow in the middle and little fingers of both hands using strain gauge plethysmography Exposure assessment N/A Analysis: T-test of paired means and GEE for repeated measures within subject.	4.12 Different repetition rates and peak magnitudes (but the same frequency weighted rms acceleration) caused similar decreases in blood flow implying that the ISO 5349 model is applicable for shock vibration. 4.12 Indicates that use of the rms acceleration is adequate for estimating the effects of shocks, but study limited and more work needed.

A critical review of evidence related to hand-arm vibration syndrome and the extent of exposure to vibration

This report describes a systematic literature review on the nature of the exposure-response relationship between hand-transmitted vibration and the elements of hand-arm vibration syndrome (HAVS), ie the vascular, neurosensory and musculoskeletal components. Annex C of ISO 5349-1:2001 contains an exposure-response relationship for vascular HAVS, yet this review of the literature has not found any strong evidence of a precise quantitative relationship between exposure to vibration and health outcomes, either for vascular or neurosensory HAVS. There is some evidence that suggests possible limited reversibility of vascular HAVS after cessation of exposure. However, the limited evidence concerning neurosensory HAVS does not indicate any reversibility of the condition.

This review indicates that there are a number of unknowns with regard to the exposure-response relationships for HAVS. Despite on-going research in the area of HAVS, quantitative exposure-response relationships for HAVS remain elusive and ill-defined. It has still not been possible to establish if there is a no effect level for vibration exposure, other than the somewhat obvious zero exposure level.

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