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Population-Based Exposure-Response Modeling for Hand-Arm Vibration

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Abstract

This thesis is a contribution to the research on the relation between hand-arm vibration exposure and health response research.
Based on a previously published meta-analysis, a pooled analysis of epidemiologic studies on vibration-induced white finger (VWF) in groups of workers who are occupationally exposed to hand-transmitted vibration is performed. Additional selection rules are applied to the studies accepted by the meta-analysis to ensure reliability and comparability. The studies conforming with these provide data on lifetime exposure duration, daily vibration exposure level, and how many members of the population are affected by vibration-induced white finger, i.e. the prevalence in the population. These are linearly interpolated to 10% prevalence to create a model to predict VWF prevalence comparable to the ones included in ISO 5349-1:2001 and the meta-analysis. To this end, the daily vibration exposure, $A(8)$, and the exposure time in years at which 10% of the group of workers are estimated to have developed VWF are employed. The models created from data subsets and the full data set with a regression analysis are compared to the one from the standard and the study that this analysis is based on.
In order to find an interpolation method that emulates the growth of prevalence in a population better than a linear function, data from longitudinal studies are fitted by means of a polynomial regression analysis. This fit is made adaptable by including a factor to represent the hand-transmitted vibration exposure of the respective population. To account for changes in the group of workers an additional parameter is introduced to the polynomial fit. Each of these iterations in developing a generalizable fit is tested on data from longitudinal studies. To make the fit applicable as an interpolation function, the number of fit parameters is reduced to one by relating the exposure factor to the daily vibration exposure, $A(8)$. The resulting model is tested for interpolation on a study that provides data for two groups of workers at two different points in time.
The developed model of the growth of prevalence within a population over time is applied to the data from the pooled analysis. A regression analysis is performed on the resulting data set. The thus created exposure-response model is compared to the ones from the first pooled analysis and the international standard as well as comparable models from other publications to evaluate the influence of the interpolation method and whether the model in ISO 5349-1:2001 over- or underestimates the risk.

Kurzfassung

Diese Dissertation ist ein Beitrag zur Forschung zum Zusammenhang zwischen der Belastung mit Hand-Arm-Vibrationen und der gesundheitlichen Wirkung.
Basierend auf einer veröffentlichten Meta-Analyse wird eine gepoolte Analyse epidemiologischer Studien durchgeführt, die zum vibrationsbedingten vasospastischen Syndrom (VWF) in Gruppen von Arbeitern, die beruflich Hand-Arm-Vibrationen ausgesetzt sind, veröffentlicht wurden. Zusätzliche Auswahlkriterien werden auf die in der Meta-Analyse akzeptierten Studien angewendet, um die Zuverlässigkeit und Vergleichbarkeit sicher zu stellen. Die Studien, die diesen Regeln entsprechen, liefern Daten zur Gesamtbelastungsdauer, zum täglichen Vibrationsbelastungslevel und dazu, wie viele Mitglieder der jeweiligen Population vom vibrationsbedingten vasospastischen Syndrom betroffen sind, also die Prävalenz von VWF. Diese Daten werden linear zu 10% Prävalenz interpoliert, um ein Vorhersagemodel für die VWF-Prävalenz zu erstellen, das vergleichbar zu denen aus der ISO 5349-1:2001 und der Meta-Analyse ist. Hierfür werden der tägliche Vibrationsbelastungswert, $A(8)$, und die Belastungsdauer, bei der geschätzt wird, dass 10% der Arbeitergruppe betroffen sind, in Jahren genutzt. Die Modelle, die mittels einer Regressionsanalyse von dem Datensatz oder Teilsätzen erstellt werden, werden mit denen aus dem Standard und der Studie, auf der diese Analyse basiert, verglichen.
Um eine Interpolationsmethode zu finden, die das Prävalenzwachstum in einer Population besser nachbildet, wird ein Polynom an die Daten von Langzeitstudien mittels einer Regressionanalyse angepasst. Dieser Fit wird durch das Einfügen eines Faktors anpassbar gemacht, der die jeweilige Vibrationsbelastung repräsentiert. Um auch Veränderungen in der Arbeitergruppe widerspiegeln zu können, wird ein weiterer Parameter in das Polynom eingefügt. Jeder dieser Entwicklungsschritte eines verallgemeinerbaren Modells wird an den Daten von Langzeitstudien getestet. Um es für die Interpolation nutzbar zu machen, wird die Anzahl der Fitparameter auf einen reduziert, indem der Belastungsfaktor mit dem täglichen Vibrationsbelastungswert, $A(8)$, in Zusammenhang gebracht wird. Das resultierende Modell wird hinsichtlich seiner Nutzung zur Interpolation an den Daten einer Studie, die Informationen für zwei Gruppen von Arbeitern zu zwei verschiedenen Zeitpunkten beinhaltet, getestet.
Dieses Modell des Prävalenzwachstums innerhalb einer Population im Laufe der Zeit wird an den Daten der gepoolten Analyse angewendet. Wie in der ersten, wird eine Regeressionsanalyse mit den interpolierten Daten durchgeführt. Das so erstellte Belastungs-Wirkungs-Modell wird mit denen aus der ersten gepoolten Analyse, dem Standard und vergleichbaren Modellen aus anderen Veröffentlichungen abgeglichen, um den Einfluss der Interpolationsmethode zu evaluieren, ebenso wie die Frage, ob das Modell in ISO 5349-1:2001 das VWF-Risiko über- oder unterschätzt.

Contents

Chapter 1

Introduction

Exposure to vibration can lead to short-term [37] as well as, if it is prolonged or constantly repeated, lasting physiological effects, whether sensorineural, vascular, or musculoskeletal. These lasting health effects are collectively known as the hand-arm vibration syndrome or HAVS [35]. While the effects of vibration on the nervous system and on the vascular system may influence each other, the respective components of HAVS can develop independently. The present work focuses on the vascular aspect of HAVS. There are several terms for the vascular health issues caused by vibration, such as secondary Raynaud's syndrome or vibration-induced white fingers (VWF) [35].

The pathogenesis, i.e., how VWF develops, is uncertain [35]. Two physical principles can underlie the temporary reduction of blood supply: abnormalities in perfusion pressure or dysregulation and/or abnormalities of the luminal radius of the digital artery. While the development is unclear, Lawson et al. describe that the neurological symptoms of HAVS tend to occur first.

In many countries, the health issues caused by exposure to hand-transmitted vibration are accepted as occupational diseases. The German Association of Occupational Accident Insurance Funds (DGUV) recognizes four occupational diseases related to exposure to hand-transmitted vibration: disorders due to the jolting of pneumatic tools or ones that operate similarly, vibration-induced blood-flow disorder in the hands if it causes incapability of working in the profession that caused the symptoms, carpal tunnel syndrome, and hypothenar and thenar hammer syndrome. The latter two have only been included in the catalog of recognized occupational diseases since 2015. In the case of carpal tunnel syndrome, the DGUV does not distinguished between manual labor and vibration as the underlying cause. The numbers of suspected and accepted cases vary greatly, but all of them are causes for the payment of occupational sickness pensions. The 2020 statistics of DGUV show 10 to 25 new accepted cases of vibration-induced white finger in the years 2005, 2010, 2015, 2019, and 2020 [17]. These numbers only reflect those workers who are affected by VWF severely enough that it forced them to quit the job that had resulted in this occupational disease. Workers with lesser manifestations of VWF are not reflected in this statistic.

Aside from the statistics from occupational accident insurance funds, there are studies that show correlations between vibration exposure and the prevalence of HAVS in groups of workers. Most of these studies focus on workers from one or very few occupations. Palmer et al. conducted a study in which questionnaires were sent out to over 13000 workers and men in the armed forces of Great Britain to evaluate the risk of contracting any symptoms of HAVS based on the respective occupation or source of hand-transmitted vibration [44]. The results obtained from over 5000 responses show that the evaluated jobs are not associated with an equal risk for the vascular and neurological components of HAVS. For VWF, after adjusting for factors such as age, smoking habits, headaches, and perceived tiredness or stress, they found an increased risk for builders and building contractors, carpenters and joiners, motor mechanics, and laborers. For other occupations, high prevalences were found but did not reach statistical significance (welders, bricklayers and masons, plumbers, and farm owners). Furthermore, it was found that the use of all tools correlated with symptoms of HAVS. After adjusting for the use of multiple tools during the work week, the following ones showed an association: hand-guided mowers, concrete breakers, chain saws, jig saws, circular saws, and impact wrenches [44]. The correlation was only statistically significant for the first three. Most studies are done on a single group of workers and hence Palmer et al. stated that there are several occupational groups that are rarely investigated. Overall handheld tools that emit vibration, either electrically or pneumatically powered are considered sources of hand-arm vibration that may lead to VWF or other diseases that are summarized in HAVS. These tools can be percussive or rotary [26].

Working with such handheld tools or machines that emit vibration can cause immediate physiological reactions, but it takes long-term exposure for these to cause lasting health effects. The time it takes to develop symptoms is called the latency [35]. The time from first exposure to the appearance of the first symptoms is often analyzed by means of observing a group prevalence. As described by Lawson et al., the range of latency for vibration-induced white finger was discussed at an international workshop to range from a few months after the beginning of exposure to one year after the exposure to vibration has ended and may span 20 or more years. From the onset of the first symptoms, the prevalence within a population grows with exposure time. Circumstances in which the prevalence decreases, i.e., its reversibility was found to depend on the individual's age, how severe the symptoms had already become, the total duration of exposure to vibration, and the type of handheld vibrating tool or machine used. The primary reference [21] given by Lawson et al. on this subject was unobtainable to the author, which is why only the secondary reference [35] is given here.

How the exposure to vibration affects workers depends on a variety of factors. These may be grouped by factors related to the tool, those related to the operator and those due to the environment and circumstances. Furthermore, in evaluating the effects of vibration exposure, there is another influencing factor which is a number of uncertainties. These may encompass uncertainties in the vibration measurement, as a measurement according to the corresponding standard does not necessarily reflect the vibration workers are exposed to in the field, and the results of the measurement may vary depending on details such as the location of the sensor or the fastening method. Another source of uncertainty is the determination of the daily usage time. Most studies rely on self-reported times, which are known to be affected by recollection bias. Varying working conditions and processes may also be sources of uncertainty when evaluating how hand-transmitted vibration affects workers.
The factors related to the tool include vibration level, frequency content, the time history of the vibration as well as the direction of the vibration [35] (the reference [39] on this given by Lawson et al. was not obtainable prior to the submission of this thesis, but what it is given as a reference for in Lawson et al. is in agreement with [24]). They also encompass tool parameters such as weight, size, and handle shape.
The influencing factors related to the operator are aspects such as the operator's physiology and age, his or her posture while working with vibrating, hand-held tools, his or her expertise in their usage and habits, like smoking [25], as well as pre-existing health conditions. Smoking and alcohol consumption have been found to increase the risks of vascular issues, as well as vibration-induced white finger.
The temperature in the space of work, the duration of usage of the tool, how intermittent this use is, the usage of anti-vibration gloves and the work processes are factors related to

circumstances and the environment that influence the effect of hand-transmitted vibration on a worker. Several studies investigate the difference in VWF case numbers in warm weather regions compared to colder ones. Su et al. [51] found no cases of VWF in a review of studies performed in tropical or subtropical climates, but cases that showed neurological HAVS symptoms and cases of cold fingers, which the authors considered the expression of vascular issues in the warm climate, which illustrates the amount to which temperature as one of these factors can influence the exposure-response relation. [50] showed that the ISO model has not been demonstrated to apply to vibration exposure in tropical climates for the development of VWF.

In an overview of the available literature, Bovenzi found further influencing aspects. The prevalence of the white finger disease with causes other than vibration was found to range from 1.5% to 14% depending on impacting factors such as climate, ethnicity, and working conditions, whereas in populations of workers exposed to vibrations of high magnitudes in northern countries, the prevalence of VWF can reach up to 100% [5]. It was found that there are a number of uncertainties regarding the relation between vibration exposure and VWF: the measures of vibration exposure with regard to magnitude and duration, the employed clinical tests, the healthy-worker effect, and other selection biases due to the nature of cross-sectional studies. With these, this publication makes an addition to the list of influencing factors given by Griffin [24] and Lawson et al. [35] that is concerned with how the data are gathered on the impact of that process. The above-mentioned healthy-worker effect is the description of the tendency that healthy workers remain in a population of workers, while those affected by HAVS are more likely to leave the job which has them exposed to hand-transmitted vibration.

Furthermore, in [5], the exposure-response model included in the ISO 5349 [29] was compared to other published data and was found to both under- and overestimate the time to reach a certain prevalence. The frequency weighting, the lack of data and their reliability, and latency being subjected to a strong recall bias were pointed out as possible reasons. The models from [4] and [8] were compared. It was found that exposures described with the same $A(8)$-value led to different prevalences in the two studies, while there is a similar dependency between the prevalence of VWF and the exposure time in years. This was attributed to other exposure factors that are not included in these three parameters.

This shows the complexity of the relation between exposure to hand-transmitted vibration and health effects. Over the last fifty years, several studies have analyzed the relation between exposure to hand-transmitted vibration and the vibration-induced white finger in one or more groups of workers. Several, both qualitative and mathematical models, are described in Section 2.1. These are then compared to the model included in one of the fundamental standards for hand-arm vibration, ISO 5349-1:2001.

This model and the limits provided in that standard have been questioned in various publications. [18], [19], and [23] found the model to underestimate the risk, while [9], [8], and[33] came to the conclusion that it overestimates the risk of vibration-induced white finger. In a review [5] in the late nineties Bovenzi observed that the studies that claimed over or underestimation by the ISO differed with regard to what tools the workers used respectively and their frequency content. The studies in which workers were exposed to high levels of low-frequency vibration stated that the standard overestimates the risk, while the ones in which there was exposure to vibration with high-frequency components note an underestimation of the risk by the standard.

In the present work, this repeatedly raised question of the validity of the VWF prevalence prediction model in ISO 5349-1:2001 is addressed. The starting point for this is a review of existing exposure-response relations and a pooled analysis. The latter is based on the previously published meta-analysis by Nilsson et al. [43] which offers a preselection of studies that were also used as data sources to create a new exposure-response model within their meta-analysis. From these, a further selection is made and the remaining data are used to create new models. These models are compared to the one from Nilsson et al. and the one from the standard. Furthermore, a model for the growth of prevalence within a group that is exposed to hand-transmitted vibration is developed with the requirement that it can account for latency and for differences in exposures. This model is finally employed in creating another exposure-response model to analyze the influence of different data processing functions. In the final step, it is compared to one of the previously created models, as well as several pre-existing models and the one in the ISO 5349-1:2001.

Chapter 2

Assessment of exposure-response relation for vibration-induced white finger

Exposure-response relations associate, in this case, the vibration as the physical stimulus with the physiological effects in the workers' hands and arms.

For this purpose, epidemiological studies are employed. The present work focuses on two types of studies, longitudinal and cross-sectional studies. In the first, a population is observed repeatedly over a period of time. In the case of a closed cohort, the population remains fixed, no one is leaving or entering the population. For an open cohort, the members of the population may change. In a cross-sectional study, the current state at the time of conducting the study is recorded and therefore provides a snapshot of the workers' health issues, but cannot provide information on their development aside from reports based on each worker's memory [2]. A prevalence reported in a cross-sectional study is hence called a point prevalence. A longitudinal study, or in some cases follow-up studies, provides what is called a period prevalence, as it refers to the prevalence in a population over a certain period of time. These two types of prevalence have to be distinguished from incidence, i.e., the occurrence of new cases.

The measurement and quantification of the vibration emitted by hand-held tools have changed significantly within the last 60 years alongside the measurement equipment. In the current standard ISO 5349-1:2001 [30] a general measurement methodology, frequency weighting, and calculations of vibration levels and exposure values are included. It specifies that the measurement needs to be performed on the tool handle as close to the user's hand as possible in three orthogonal directions with a rigidly mounted sensor, but refers for more details, such as measures that need to be taken for shock vibration measurements, to ISO 5349-2:2001 [31]. It furthermore specifies that the measurement parameter is the frequency-weighted root-mean-square (r.m.s.) acceleration. As most tools and machines emit vibrations in more than one direction and it is assumed that the vibrations in each direction have a similar potential to cause harm, the vibration is therefore evaluated on the basis of a total vibration value

$$a_{hv} = \sqrt{a_{hwx}^2 + a_{hwy}^2 + a_{hwz}^2} \tag{2.1}$$

that combines the frequency-weighted r.m.s. acceleration of each of the three directions a_{hwx}, a_{hwy}, and a_{hwz}.

To evaluate the daily vibration exposure the standard [30] defines the daily exposure time as the duration that vibration enters the hands, T. Combined with the total vibration value a_{hv}, this is used to calculate the daily exposure value

$$A(8) = a_{hv} \cdot \sqrt{\frac{T}{T_0}} = \sqrt{\frac{1}{T_0} \sum_{i=1}^{n} a_{hvi}^2 \cdot T_i} \tag{2.2}$$

with T_0 =8h representing the average duration of a work day. Therefore, $A(8)$ is a frequency-weighted energy equivalent 8h total vibration value that allows for comparisons between exposures of different exposure times and vibration levels [30]. In case a workday includes the usage of more than one tool, the $A(8)$-value is calculated by summing up the individual exposures as included in Equation 2.2 with suffix i.

2.1 Review of exposure-response models and their development

Several studies have related the exposure to hand-transmitted vibration to HAVS in different ways.

2.1.1 Qualitative exposure-response relations

In [52] Taylor et al. analyzed data from populations of chain saw operators, workers using grinders, nobblers, and swagers. The weighted r.m.s. acceleration of their tools and the respective latent interval of each population were plotted against each other. It was found that the latent interval for VWF increased with decreasing acceleration values.

In [40] Miyashita et al. investigated forest workers in Japan and related the total saw operating time to the prevalence of nervous and vascular symptoms as well as muscle and joint issues. These results were compared to those found in a control group of forest workers who were not exposed to vibration. They found a clear correlation between the total operating time and the prevalence of health issues. This publication does not include a mathematical model of the relation between the total operating time and the prevalence and the vibration level of the chain saws is stated to be unknown.

In [53] workers using either rock drills in a mine, chipping hammers on stone or metal in foundries, riveting hammers in a factory, impact wrenches, grinders, or sand rammers in foundries were investigated regarding the experienced symptoms and exposure time. The accelerations were measured for each tool and then compared both among tools and to the levels proposed in the ISO/DIS 5349: 1979 [28] for a daily usage time of 4-8 hours. The symptoms were scored and their weighted summation turned into an index reflecting their severity. For each group of tools and workers, this index was plotted over the total exposure time. Based on the symptoms an index value was defined as the threshold between healthy and injured workers. The total exposure time it took to reach that threshold was then compared between the groups of tools. A mathematical relation was not formed between the index, total exposure time, and measured acceleration.

Futatsuka et al. highlighted the complexity of factors that lead to health issues caused by exposure to hand-arm vibrations [19]. In this study, a pooled analysis of studies of workers in Japan was performed and the authors obtained additional information on vibration and noise levels of the tools used in the respective studies. Using these data, the authors created various exposure-response relations by plotting the weighted acceleration against the prevalence for groups of tools, or for various exposure periods, or against the time before the onset of VWF. While these graphs show a clear relation between the exposure time, the weighted acceleration, and the latency or the prevalence, no mathematical equation representing these is provided in the publication.

In [5] the relation between HAV exposure and various disorders, summed up as HAVS, was investigated. No relation for vibration-induced neuropathy was found. A relation between vibration exposure and bone and joint disorders was questioned. For VWF, like for the other disorders, several studies were reviewed, as well as the model in ISO 5349 [30] and the ones in [4] and [8]. Data from an epidemiologic study were used to compare various measures of exposures in which the ISO frequency-weighted and unweighted acceleration value to a power from 0 to 4 was multiplied by the years of lifetime exposure [5]. A logistic regression analysis achieved the best results for an exposure expression derived from an unweighted acceleration value, but the specific relation was not included. It was concluded that due to a lack of epidemiologic data, a final exposure-response relation could not be determined for VWF.

Griffin et al. combined three of their previous studies and hence obtained HAV exposure data of seven occupational subgroups [25]. They calculated several expressions of vibration exposure from the vibration value and lifetime exposure duration summed up over the tools for each subject varying the power of the weighted and unweighted vibration value from 0 to 4 and adjusted for age and smoking. For all expressions of vibration exposure with its increase an increase in VWF prevalence was found [25], but expressions in which the acceleration value was given a higher weight by means of the power than the exposure time performed worse than those with an equal weight between vibration value and exposure time. This becomes evident in plots of the VWF prevalence over exposure value quintiles for each of the expressions of vibration exposure.

Bovenzi conducted a three-year follow-up study of forestry and stone workers in Italy and comparable unexposed controls [7]. A questionnaire, a medical interview employing color charts, and a cold provocation test were used to diagnose VWF. The application of two different sets of criteria for diagnosing VWF and Raynaud's phenomenon respectively were analyzed. The vibration was measured according to ISO 5349-1:2001. Various measures of cumulative dose, other than those suggested in the standard were calculated from the unweighted as well as the frequency-weighted acceleration, relating different powers of acceleration to the exposure time. A clear difference between the two diagnostic sets of criteria was found in the prevalence and incidence observed in the exposed workers and the controls. A logistic regression analysis showed a clear relation between most of the employed measures of cumulative vibration dose and the prevalence or incidence of VWF. The relation between the total operating time in hours and the prevalence of VWF was more significant than the years of employment. The statistical analysis showed that the combination of the cumulative vibration dose and the exposure time gave the best prediction of VWF. Furthermore, it was found that unweighted accelerations used to calculate the dose predicted VWF better than the weighted ones and that the higher powers resulted in better predictions than the lower powers of the acceleration.

Sauni et al. studied the prevalence of all components of HAVS in a population of Finnish metalworkers [46] to analyze the relation between hand-arm vibration exposure and health symptoms. All workers who responded to a questionnaire to have been exposed to hand-arm vibration and to show symptoms of HAVS were clinically examined and took another comprehensive questionnaire. The vibration exposure was evaluated based on the information provided by the participants on which tools they had used and whether or not these were percussive. The European Union's hand-arm vibration Good practice guide [27], a Swedish database [54] or measurements of the Finnish Institute of Occupational Health served as sources for the vibration acceleration values. From this, a hand-arm vibration index was calculated relating the $A(8)$-value of each tool with the years of exposure and the annual exposure time in days. While they found the risk of VWF to increase with increasing HAV index [46] no mathematical relation was created within this study.

To evaluate the exposure-response relation for hand-arm vibration in a tropical climate Su et al. performed a cross-sectional study including forestry workers and workers from an automobile manufacturing plant in Malaysia [50]. The workers were assessed by means of a questionnaire carried out by an occupational physician as well as several tests, such as finger skin temperature and finger vibrotactile perception threshold, in a controlled environment. Vibration measurements were done for every worker on his respective tool used on a typical workpiece in a process as close to their day-to-day work as possible while adhering to the specifications in ISO 5349-2 [31]. Three different measures of dose were calculated: the lifetime vibration dose as described in [25], the total operating time as specified by [41], and the cumulative exposure index that includes the $A(8)$-value, the usage hours per day, and the number of workdays per year as suggested by Sauni et al. in [46]. It was found that while there were cases of numbness, tingling, or finger coldness, no white fingers were reported. A clear relation between the prevalence of neurological symptoms and the lifetime vibration dose and the cumulative exposure index, but not the total operating time was found.

2.1.2 Mathematical exposure-response relations

Griffin highlighted how uncertainties in or lack of knowledge regarding vibration measurement or how the various vibration parameters influence the development of health issues in workers affect the determination of an exposure-response relation or exposure limits in [24]. By means of a pooled analysis of sixteen epidemiological studies from 1946 to 1980 and a regression analysis an exposure-response relation was determined based on the logarithm of the frequency-weighted acceleration V was formed. The latent interval L was found to relate to the acceleration as $L = 9.34 \cdot V^{-0.36}$ with a correlation coefficient of 0.53 (i.e., a coefficient of determination of 0.28). Due to a lack of definitions, it was suggested that it would be better to describe the prevalence of VWF as a function of exposure time. Therefore, a pooled analysis including 21 data points was performed using logarithmic and arcsine transformations and regression analysis. This provided $P = 0.5 \cdot (1 + sin(22 \cdot ln(V) - 55))$ as the relation between the prevalence P and the mean frequency weighted acceleration V with a correlation coefficient of 0.56 (i.e., a coefficient of determination of 0.31). It is furthermore highlighted that the lack of standardization of the measurement and of the term latent interval as well as the low number of studies providing both vibration data and information on the latent interval and the prevalence cause difficulties in determining exposure-response relations.

In [13] Brammer conducted a pooled analysis of epidemiological studies published prior to 1980. These were filtered on the basis of selection rules to ensure reliability and comparability as best as possible. For the model only studies on populations were considered in which only one tool exposing the workers to vibration was used. This enabled the author to assume that all workers within each population all workers essentially performed the same task throughout a workday. The selection of studies comprised 7 populations. From their data a model relating the exposure time before the onset of finger blanching, i.e. the mean latency interval $\bar{t}_{LI}$, to the dominant, single axis, r.m.s. frequency-weighted acceleration a_k on the basis that the development of VWF in a population when considered as a function of exposure duration by is modeled by a normal distribution. The equation for the 50 percentile, to represent the average response is the following

$$\bar{t}_{LI} = \frac{78.7}{a_k^{1.07}} \tag{2.3}$$

with a standard deviation of $s = 0.01 + 0.46 \cdot \bar{t}_{LI}$. This model was tested on data from studies published after 1980 and it was found that their data deviated somewhat from the model. This was concluded to be likely due to the difference in daily usage time which was not factored into the model.

In [11] studies of VWF in forestry workers from a similar time period were analyzed. Brammer performed statistical tests on their data and found the number of years of employment that involve working with power tools emitting vibration to be an acceptable measure for VWF to first develop. Three exposure-response relations were formulated, which included the latent interval, i.e., the time for the first symptoms of VWF to appear. The third of these relates the average latent interval, t_{LI} of a population to the average vibration the members were exposed to. The latter was described as a_K, the frequency-weighted, r.m.s. component acceleration of the one tool or industrial process that the members of the population operated during their full-time employment. Using a least-squares best fit, a simple power curve, relating the latent interval and the acceleration a_K, was determined.

In [12], a method was described for predicting the exposure time to reach a given prevalence from a_K and s that are described above. The method first involved calculating t_{LI} and then using it to determine s (from $s = 0.01 + 0.46 \cdot \bar{t}_{LI}$).
The prevalence of VWF as a function of group exposure time in this model is represented by a cumulative normal distribution. So the exposure time of the population group to reach a given prevalence, $D_{y,P}$, can be derived from the value of the standard normal variable, z, corresponding to the desired cumulative probability, i.e., $D_{y,z} = t_{LI} + sz$ [12].
Values of $D_{y,P}$ for prevalences of 10, 20, 30, 40 and 50% were included in Annex A of ISO 5349:1986 for the operation of hand-held tools or machines throughout the workday. Values for the exposure time to reach 10% prevalence in a population group exposed for 8h near-daily to hand-transmitted vibration, $D_{y,10}$, are given in the revised version of the international standard, ISO 5349-1:2001. They are the same as those for 10% prevalence in the original standard, ISO 5349:1986, as it is assumed that the changes to the calculation of daily exposure in the new standard lead to no net change in the prediction.
These values and the underlying model created by Brammer are referred to as the "ISO model" or "model from the standard" in this dissertation.

Bovenzi et al. analyzed the exposure-response relation for stone workers exposed to hand-transmitted vibration compared to an unexposed control group in Italy [4]. The workers underwent a questionnaire by an occupational physician and their symptoms were rated according to the Stockholm Workshop Scale [22]. The vibration measurement was performed on a representative number of tools according to ISO 5349. A clear relation between the prevalence of VWF and vibration exposure was found. A regression analysis related the prevalence of VWF P to the $A(8)$-value and the exposure time D_y:

$$P = 2.792 \cdot (A(8))^{0.5} \cdot (D_y)^{0.5} (\%) \tag{2.4}$$

showing that the prevalence increases proportionally with the square root of either of them.

In [8] the prevalence of VWF in forestry workers in Italy was studied and compared to an unexposed control group. VWF was diagnosed through subjective reports and medical tests and its severity was staged, forming a differential diagnosis. The vibration of the chain saws was measured in three orthogonal directions, from which the frequency-weighted r.m.s. acceleration was determined as well as the eight-hour energy equivalent frequency-weighted acceleration $A(8)$. By means of logistic regression, a model was formed:

$$P = 0.354 \cdot (A(8))^{1.05} \cdot (D_y)^{1.07} (\%) \tag{2.5}$$

that relates the prevalence of VWF P to the $A(8)$-value and the total duration of exposure D_y in years. The analysis of the prevalence, exposure time, and $A(8)$-value showed that the prevalence increased in a nearly linear manner to either the $A(8)$-value or the exposure time when the respective other stayed constant.

Nilsson et al. [43] conducted a meta-analysis of publications from 1945 to the beginning of 2016 accessible on the databases PubMed and Science Direct. The 4336 identified studies were first screened by abstract and resulted in 294 studies assessed as eligible for full-text screening. The screening criteria were based on the PRISMA guidelines [36]. Out of these studies, 41 were accepted by the authors and 28 were used in their analysis. The reasons for omission for the 13 studies varied from the usage of the same study population to the aim of comparing an unexposed and an exposed group regarding one specific clinical outcome, to only describing the prevalence in vibration-exposed individuals. Among other analyses, the authors interpolated the gathered data linearly to 10% prevalence and performed a regression analysis.

2.1.3 Comparison of models

Out of all these exposure-response relations, there are few that have been constructed in a format that is comparable to the one described in the standard. All the similar ones are displayed in Figure 2.1. Next to the model from ISO 5349-1:2001, the one from Nilsson et al. [43] is shown. Furthermore, the models described in [4] and [8] were transformed to the same format as the model from the standard. For this purpose, the prevalence was set to 10% and the equation rearranged to read

$$D_{y,10} = \left(\frac{10}{2.793 \cdot A(8)^{0.5}} \right)^{\frac{1}{0.5}} \tag{2.6}$$

for [4] and

$$D_{y,10} = \left(\frac{10}{0.356 \cdot A(8)^{1.05}} \right)^{\frac{1}{1.07}} \tag{2.7}$$

for [8] to allow a direct comparison.

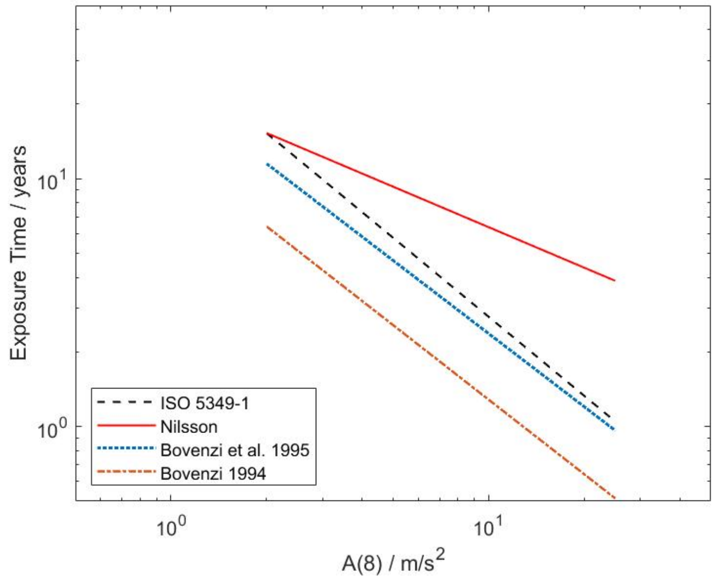

Figure 2.1: All models that share a comparable format to the one in ISO 5349-1:2001 (black dashed line) are shown. The red line shows the one from Nilsson et al. [43], the blue line represents the transformed model from Bovenzi et al. [8], and the orange line is the transformed model from Bovenzi [4]. The latter and the one from Nilsson et al. deviate the most from the model from the standard. The one from [4] runs parallel to the ISO model but much lower, while the model from [43] shows the same starting point but a very different slope.

While the models described in [4] and [8] can be transformed into the same format as the ones from the standard [30] and Nilsson et al. [43], they differ significantly from them as they were constructed from one population whereas the latter were constructed from the data of multiple populations. The model from [8] runs only slightly below the one from the standard. The model from Nilsson et al. predicts that higher $A(8)$-levels and longer exposure times are needed to reach 10% prevalence, whereas the model from [4] assumes much lower values for both to reach that prevalence.

2.2 Pooled analysis and exposure-response models

2.2.1 Pooled analysis

A pooled analysis on the basis of the meta-analysis by Nilsson et al. [43] is performed in the present work. Its steps are depicted in Figure 2.2.

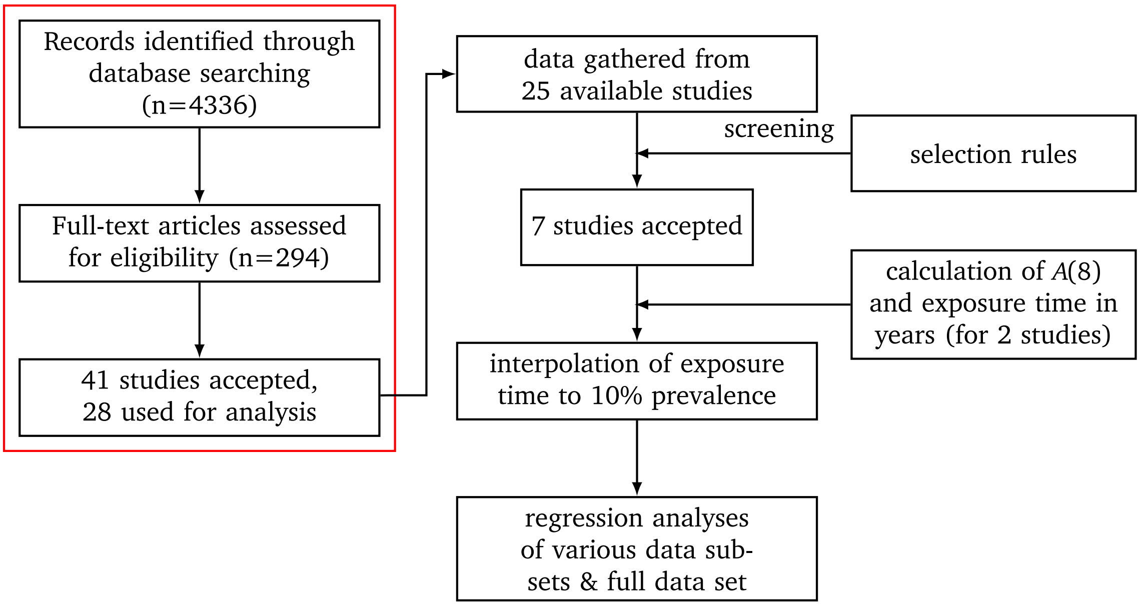

Figure 2.2: Flowchart of pooled analysis. The red box frames the key steps performed in the meta-analysis by Nilsson et al. [43] that constitute as the basis for the present work. On the right-hand side, the steps of the pooled analysis are displayed.

The selection of studies by Nilsson et al. was based on the PRISMA guidelines [36]. This provides a data set with the least selection bias. Out of the 28 studies used for the analysis by Nilsson et al., 25 are available for the present analysis. From all of these, the data on the groups of workers, their respective lifetime exposures, the prevalences of VWF, the used tools, and the resulting $A(8)$-values, as well as the methods employed to evaluate the health of the workers, diagnose VWF and measure the vibration are collected. Further selection rules are introduced to ensure comparability and compliance with the standard ISO 5349-1:2001 (cf. Table 1 [47]).

Five of these focus on the vibration measurement. The first rule ensures that the vibration values provided in each included publication are comparable and suitable to evaluate the model included in the standard by requiring the acceleration measurement at a surface in contact with the hand that vibrates in three mutually orthogonal directions in the frequency range from 5.6 to 1400 Hz while avoiding an instrument overload and DC shifts. All these are specifications in the international standard ISO 5349. For the same purpose, the frequency weighting described in the same standard is to be applied to the measured vibration according to Rule 2. Rules 3 through 5 address how the vibration exposure is to be determined and reported according to ISO 5349-1:2001. From the previously measured frequency-weighted accelerations, the mean value of their vector sum is to be calculated (Rule 3) and used to determine the daily time-averaged vibration energy normalized to the duration of a typical workday, 8 h (Rule 4). If the day-to-day operations comprise more than one source of vibration, the exposures are to be indicated by the sum of time-averaged vibration energies of all involved exposures normalized according to Rule 4 as defined in ISO 5349-1:2001.

Rules 6 through 11 focus on the epidemiologic data. The sixth rule aims to avoid bias in the studied population by demanding that all workers or an unbiased selection of those whose full-time work involves them being exposed to hand-transmitted vibration on a near-daily basis be included. This population has to consist of thirty or more vibration-exposed members. In each study, an effort must have been made to eliminate any worker from Raynaud's disease that is not caused by vibration. Part of this is the necessity to include information that the first episode of finger blanching appeared after starting to be exposed to hand-arm vibration due to their profession (Rule 7, cf. Table 1 [47]). Rule 8 requires the studies to base the diagnosis of VWF on the medical history as well as a clinical assessment. Including a reference to the Stockholm Workshop Scale or the Taylor-Pelmear stages of VWF is optional. These two rules are supposed to ensure that the reported prevalence is not falsified by other cases of Raynaud's phenomenon than VWF. Therefore, if Rules 7 and/or 8 are not fulfilled, it must be assumed that the reported raw prevalence contains workers who show symptoms unrelated to vibration. To make up for this surplus in prevalence, Rule 9 demands the point prevalence of finger blanching in a control group to be deducted. Such a control group comprises persons with a lifestyle and type of work in common with the population but who are not exposed to vibration. To avoid extrapolation and the increase in the potential error that it entails, Rule 10 requires the prevalence in the population group to be 10% or greater. In case Rule 9 applies, this still has to be the case after the prevalence of the control group is removed. According to the final rule, the average lifetime duration the population was exposed to reach the reported point prevalence of VWF must be provided. This is commonly done in years.

Due to these selection rules the number of studies accepted in the present analysis is reduced to seven. Out of these five provided the prevalence, exposure time, and vibration data in the format required. For one study [15], the $A(8)$-value is calculated from the measured vibration spectra provided in the publication. For [6], the exposure time was given in a total number of usage hours and hence is converted into the mean group lifetime exposure in years, D_y:

$$D_y = \frac{t_{exposed}}{T} : N_{workdays\,per\,year} \tag{2.8}$$

with $t_{exposed}$ as the hours of usage, T as the hours of usage per work day [47]. $N_{workdays\,per\,year}$ is calculated from the average number of workdays per year for the years and country in which the study had been conducted, reduced by the number of vacation days and the average amount of sick days.

2.2.2 Exposure-response models

As the models in [30] and [43] estimate the exposure time at which 10% of a population are affected by VWF at a given $A(8)$-value, the lifetime exposures given in the accepted epidemiologic studies are interpolated to 10% prevalence.

To enable a comparison to the model by Nilsson et al. linear interpolation is used first. Later, a prevalence development model, which is described in Section 2.3, is employed to interpolate the selected data.

The data are grouped by the amount of calculation necessary to transform the values provided in the studies into the format needed for the models and by the number of tools used by the respective group of workers. This results in three data sets. One set contains the data from those studies that provided the prevalence, the lifetime exposure in years, and the $A(8)$-value as well as from [15]. One set contains only the data from the three studies in which the workers used only one tool. The final data set contains the data from all studies.

On each of these data sets a regression analysis is performed in [47]. For this purpose, the same function type as in the model in ISO 5349-1:2001 is used

$$D_{y,10} = a \cdot A(8)^b \tag{2.9}$$

which relates the lifetime exposure at which 10% prevalence occur, $D_{y,10}$, with the respective $A(8)$-value. a and b are two numerical fit parameters.

In addition to the regression line, 95-percentile confidence intervals are produced by the analysis for each of the parameters. These result in 95-percentile confidence curves, which represent the most likely region for the exposure-response relation.

2.3 Modeling the development of prevalence

The progression of the prevalence of a disease in a population over time is of interest to assess the risk after a certain amount of exposure or within a certain age group or to give an estimate of how much of a population will be affected in the future. Hence, the World Health Organization (WHO) has provided several models over the years.

2.3.1 WHO model

In a publication from 2003, a model provided by the World Health Organization called DisMod II [1] is described. It is based on the relation between the number of healthy, diseased, and dead people at a certain age and linking them through the incidence of a certain disease, remission from that disease, and case fatality.
It makes use of the interdependency of all the considered variables and therefore allows the usage of a variety of different input and output variable combinations. The model, for example, allows calculating the prevalence of a disease within an age group by means of a set of differential equations on the basis of several different possible combinations of these input parameters: incidence, remission, case fatality, relative risk for total mortality, duration of illness, and mortality due to the disease. One possible example of the usage of the model is given in [1] for asthma.

In [3] the predecessor of DisMod II was used on data from five Dutch general practitioner networks on four chronic diseases to evaluate the consistency of incidence and prevalence rate estimates. These networks collect and provide morbidity and healthcare information to monitor population health. Their data have been found to differ from each other, which is largely attributed to the methods with which incidence was distinguished from prevalence as these networks either reported episodes of care or episodes of disease and there can be multiple episodes of care in one of disease. Therefore, Boshulzen et al. also analyzed how this difference affected the differences in morbidity outcomes between the considered networks. The evaluated prevalence and incidence rates could only be consistent if the prevalence presented as a credible function of incidence as influx and mortality as outflux, i.e. it may be assumed that the disease process was stable over time.
Two different approaches were chosen to estimate the incidence and prevalence for the entire Dutch population using the data from all five networks as a basis. The first only calculated the simple mean over all networks of the reported incidence and prevalence which are age- and sex-standardized. The second employed a multi-level model to fit the data, within which

one step is to use 3^{rd}-order polynomials to account for age and the interaction of age and sex [3].
To check the consistency of the prevalence and incidence values reported by each of the networks, the number of prevalent cases was projected onto an assumed population of newborns. Then that network's incidence and mortality data were applied to that population. The resulting prevalence was then compared to the one originally reported by that network in all groups of gender and age. Hereinafter, the predecessor model of DisMod II, DisMod, was fitted employing all data on morbidity and mortality reported by each of the networks to estimate prevalence and incidence rates. Due to a lack of information in several of the networks, the data on mortality and institutionalization, i.e. people leaving the respective network with a high likelihood of dying soon, were used from only the largest network. These network-specific standardized estimates of the incidence and prevalence rates were finally combined into overall estimates. The overall tendency is that the estimates from the simple model were slightly lower than those determined with a simple mean due to the influence of the largest network.
The comparison of the observed incidence and prevalence rates with the estimates from the assumed population showed great consistency overall except for older ages, in which the observed rates were somewhat lower for one of the analyzed diseases. There was good overall consistency for another disease and for the other two, it was lower. In these latter cases, the consistency varied between the networks. One of the reasons for the deviations was stated to be the underestimation of mortality throughout the networks. The misclassification of incidence cases as prevalent cases greatly influenced the modeling.
The more complex estimation approach including DisMod was more robust regarding the incidence rates, but also showed differences between the observed and the estimated data and still reflected the influence of misclassification of cases to a certain extent. The largest discrepancies were found for osteoarthritis of the knee, which is attributed to the disease being protracted and therefore results in fewer visits with a general practitioner. Another issue discovered by the authors is that the consistency of the disease process over time may not always be a valid assumption as the incidence of diabetes has multiplied over a 20-year period.[3]

In [16] the prevalence of hearing loss was modeled using DisMod-MR 2.1, which is a Bayesian meta-regression tool. In this study prevalence, incidence, and years lived with disability are considered. The input data were gathered by means of systematic reviews of epidemiological, population-representative surveys. All reviews were filtered based on criteria regarding the diagnosis and type of hearing loss as well as how population-representative they were. Some of the data had to be transformed using meta-regressions to resolve differences in the reporting or classification of hearing loss.
DisMod-MR 2.1 was run separately for three different severities of hearing loss including a covariate that represents a summary measure of fertility, education, and gross domestic product [16]. Rescaling of all models resulted in the prevalence rates summing up to one for each age, year, sex, and location. Another five DisMod models for severe hearing loss, later rescaled to the prevalence of a hearing loss of a specific severity, another that accounted for hearing aid coverage, and one that investigated the proportion of hearing loss that was accredited to age-related or other factors were run. Uncertainties were included in these models.
The results were grouped based on the Healthcare Access and Quality Index and WHO region. Hearing loss prevalence forecasts were produced. Age-specific prevalence rates for 1990 to 2015 in five-year intervals and for 2019 served as input data to the regression. The year, WHO region, and age were used as predictors. A term to account for the interaction

between year and region was included as well as a cubic spline for age. Coefficients from gender-specific regression analyses were used for the prediction of prevalence rates in the years 2030, 2040, and 2050, accounting for the forecasted population in each WHO region. A significant increase from 1990 to 2019 in both prevalence and years lived with disability was found. Both prevalence and years lived with disability were highest for low values of the Healthcare Access and Quality Index. The results show hearing loss to be the most severe in infants and kids up to the age of five and in adults of 50 years and older. The cause of hearing loss was found to change with age. The authors list as one of the main limitations of this study the sparsity of data, having used 113 survey sources in 54 countries [16]. Another issue mentioned is that, in many cases, hearing loss is not reported together with the underlying cause.

All versions of this WHO model require data typically unavailable for VWF and do not allow for parameters such as exposure time or vibration levels as input parameters. The models, though well-tested, are therefore not an option for the present purpose. The studies described above however do show that the progression of a disease over time or age can be modeled based on various input parameters. One of them included a polynomial to approximate the progression with age. They also presented some of the challenges of creating a model from actual health data, such as a lack of data or the variability between reported data.

2.3.2 Hockey Stick Model and Probit Analysis

Another model for prevalence estimations is the hockey stick regression method which is critically reviewed as a method of estimating safe dosage by Yanagimoto and Yamamoto in [55] and used in studies like the one by Lamm et al. on the risks of low-dosage of arsenic in relation to cancer [34]. According to Yanagimoto and Yamamoto, the method was introduced in 1973 by Hasselblad et al. for safe maximum exposure estimation. It is a regression analysis employing segmented curves that got its name from the shape of the resulting curve. The hockey stick model assumes prevalence to remain constant at a certain value β_0 until a specific level of exposure or dosage x_0 is reached. After that exposure is exceeded a linear increase in prevalence is supposed. β_0 describes "a spontaneous or baseline response which is caused by background stimuli" [55], i.e., the value present in an unexposed group. The main objective is finding a decent estimator of the threshold value x_0. Usually, both of the lines involved in this segmented model are estimated at the same time by means of the constrained least-square method.

In [55], the hockey stick model is compared to the probit model which assumes the response of an individual to a dose to be represented by a random variable that has a distribution dependent on the standard normal distribution function. It employs the baseline value β_0 and two parameters, as used for the hockey stick regression method too. While the hockey stick model always presents with a sharp edge, the probit model is a continuous line that unlike the hockey stick model shows a curved increase.

Yanagimoto's and Yamamoto's comparison of the two models showed issues for both. x_0, the intersection point of the two segments included in the hockey stick method, was found to not necessarily signify a threshold for a safe dose without additional physiological proof. On the other hand, the continuous curve of the probit model was stated to not make a safe dose obvious due to its shape and continuous form and hence required the introduction of a risk level. [55]

The authors also stated the common usage of polynomial regression models, which were not applicable to the problems analyzed in their study. Contrary to both models considered by Yanagimoto and Yamamoto, such an approach appears to meet the criteria of this study.

2.3.3 HAV prevalence model

In the present work, the model has to fulfill not only the requirement of fitting exposure-prevalence data but also needs to be invertible in order for it to be used as an interpolation function later on. Hence the information regarding the common course of such curves and suitable mathematical approaches, as described above, is used to model the development of the prevalence of VWF in a population over time.

All data sets, available to the author, of point and period prevalence show a latency until the first cases of VWF appear in a population. This is followed by an increase of varying slope and saturation after some exposure time at a prevalence below 100%. A polynomial function of the form

$$P = \sum_{i=1}^{n} a_i \cdot D_y^i \tag{2.10}$$

is assumed to fit this s-shaped curve with the prevalence P, i numerical parameters a_i and the exposure time D_y, similar to what was described in [3]. An exemplary period prevalence data set from [42] is fit with polynomial functions of the 3^{rd}- to the 6^{th}- order. These fits are compared regarding their general quality and especially regarding their representation of the development of prevalence within the region from 5%-15% [49], as the model is intended to be used to interpolate epidemiologic data to 10% to create an exposure-response model [48]. The best fit, a 4^{th}-order polynomial, is later shown to be generalizable.

The variation in the experienced exposure of some population groups over time is accounted for by means of an exposure factor $expF(D_y)$ introduced to the generalizable model of the prevalence development

$$P = expF(D_y) \cdot (\sum_{i=1}^{4} a_i \cdot D_y^i) \tag{2.11}$$

that enables both time-varying and time-invariant vibration exposures to be represented [49]. This is necessary as some tools, such as chain saws underwent notable changes in the vibration they emitted, while it remained fairly constant for others. This is tested by fitting further period prevalence data sets from [20] using the values a_1 to a_4 from the generalizable model and adapting only $expF(D_y)$. As the vibration of the tools used in the study changed over the time within which the prevalence data were collected, $expF(D_y)$ is a function over time. The shape of that function is based on the provided information on the changes in the vibration measured on the handle. Allowing for numerical parameters in the $expF(D_y)$-function to be adapted, the generalizable model is fit to these data sets [49].
Most studies employed in Sections 3.1 and 3.3 provide point instead of period prevalences. The generalizable model is adapted to account for the possible changes through which the point prevalence is differentiated from period prevalence. While the changes may be represented by introducing numerical parameters that change the values of a_1 to a_n, it is assumed that the changes due to people leaving and joining the population can be represented by

adding a_1' in

$$P = expF(D_y) \cdot ((a_1 + a_1') \cdot D_y + \sum_{i=2}^{4} a_i \cdot D_y^i) \tag{2.12}$$

to change only a_1 in the generalizable model [49].
The study by Futatsuka and Ueno [20] from which the period prevalence data sets are used to apply Equation 2.11, provided a point prevalence data set for each of the period prevalence data sets. Using the fitted exposure factor from each of the latter, Equation 2.12 is fitted to each of the point prevalence data sets by adapting a_1'.

In the publications that are used as data sources in the two papers summarized in Sections 3.1 and 3.3 one point prevalence for a certain exposure time was reported per studied population. Therefore, the number of parameters that need to be fitted in the generalizable model has to be reduced. Fitting the generalizable model to the period prevalence data sets shows that the data can be modeled well when the exposure factor follows roughly the changes in the acceleration measured on the tool handle. Hence, the exposure factor, $expF$, is related to the measure of vibration exposure, which in the studies used in two of the publications (Sections 3.1 and 3.3) is $A(8)$. The exposure factor is calculated as

$$expF(D_y) \approx \left(\frac{A(X, D_y)}{A(X)_{ref}}\right)^q \tag{2.13}$$

with $A(X, D_y)$ as either the 4h energy equivalent, frequency weighted, dominant component acceleration or 8h energy equivalent, frequency weighted, vector sum vibration value of the population of interest [49]. $A(X)_{ref}$ is either the $A(4)$-value given in the study from which the data was sourced to create the generalizable model [42] or correstponding $A(8)$-value.

By fitting the two point prevalence data points of stone workers from a study by Bovenzi [7] with the generalizable model combined with Equation 2.13 the exponent q is determined. Combining Equations 2.12 and 2.13 give

$$P = \left(\frac{A(8)}{A(8)_{ref}}\right)^q \cdot ((a_1 + a_1') \cdot D_y + \sum_{i=2}^{4} a_i \cdot D_y^i) \tag{2.14}$$

in which a_1 to a_4 are the parameters of the generalizable model and only q and a_1' are adaptable parameters [49]. The value for q from this regression analysis is rounded to one decimal figure.

The study by Bovenzi [7] was done on a group of stone workers and a group of forest workers and contained two point prevalences for both. To test the model with the previously determined value for q it is included in Equation 2.14. For both groups of workers in [7] only the second point prevalence value is assumed to be known and the generalizable model with the q-value and a_1' as an adaptable parameter is used to interpolate from that data point as well as linear interpolation. These two interpolations are compared regarding how well they estimate the second point prevalence reported for each of the groups of workers.

2.4 Evaluation of exposure assessment

In the present work, the main focus is to analyze the model currently included in the standard ISO 5349-1:2001. This goal entailed that several aspects have been accepted for these analyses. One element in which this becomes evident are the selection rules. Another is the usage of the $A(8)$-value and measuring the exposure time in years.

There have been several approaches to alternative evaluations of exposure and the various influencing factors. Due to how the data are reported in the studies employed here, it is not straightforward to apply these different formulations or include further influencing factors in an exposure-response relation.

2.4.1 Alternative measures of exposure

One of the approaches was published in 2003. Griffin et al. performed an analysis of different measures of cumulative exposures to hand-transmitted vibration in relation to VWF. To this end, the data from three previous studies of the authors on dockyard workers, forestry workers, and quarry and stone workers were employed. In all of these, information on medical and employment history, on development and level of VWF, and the vibration exposure was gathered from all included workers [25], though not in all studies in an identical but similar manner.
Unlike the studies included in the present work, in all three studies used by Griffin et al., the tool operating time was asked for in hours per day, days per year, and the total number of years [25] for each tool and worker separately allowing more flexibility in calculating measures of exposure. The total duration operating time was determined for each individual and tool in hours and referred to as lifetime operating duration or lifetime exposure duration. For workers affected by VWF, no matter the severity, the years of exposure were also calculated at the time of the respective study as well as latency. The vibration measurements were done in accordance with ISO 5349, though not in all cases the version from 2001.
In [25], measures of exposure are referred to as vibration doses and constructed as

$$dose = \sum_i [{a_i}^m \cdot t_i] \tag{2.15}$$

with a_i as the weighted or unweighted acceleration magnitude and t_i as the exposure duration for tool i [25]. This dose calculation with $m = 2$ corresponds to the $A(8)$ calculation in ISO 5349-1:2001 with regard to the power relation between acceleration and exposure time. Furthermore, equivalent root-mean-square acceleration magnitudes were determined by

$$a_{h(eq,T)} = \left[\frac{\sum_i a_i^2 \cdot t_i}{\sum_i t_i} \right]^{\frac{1}{2}} \tag{2.16}$$

for each subject and both weighted and unweighted acceleration magnitudes [25].
In a statistical analysis, all different measures of vibration and exposure time were compared in logistic regression analyses. Both, vibration magnitude and exposure duration, were shown to be significant predictors of the likelihood of VWF to varying degrees. Total operating hours were found to serve better in predicting VWF than years of exposure. Unweighted acceleration emerged as a slightly better predictor than weighted acceleration. Logistic regression models showed that all formulations of dose correlated with the prevalence of VWF and with the different stages of VWF, out of which the one for $m = 1$ that gives equal weight to the acceleration magnitude and the lifetime exposure duration performed the best. Using an unweighted acceleration led to improved predictions as well. A dose calculation with $m = 0$

showed to give better results than those with higher orders of m.

Another approach was presented by Sauni et al. in 2009 [46] in a study on Finnish metalworkers. A postally administered questionnaire on HAVS symptoms and HAV exposure served as the selection tool for the study population. Workers reporting signs of HAVS were examined clinically. The vibration perception threshold was measured for each of them. Used tools and exposure durations were provided by the subjects, and vibration magnitudes were gathered from European databases. Exposure time was asked for as hours per day, days per week, and months per year.
The daily exposure was calculated as $A(8)$. This was then employed in determining a HAV index describing the total exposure as

$$I = \sum A_i(8)^2 \cdot years \cdot d \tag{2.17}$$

with $A_i(8)$ as the average daily exposure to tool i, $years$ as the exposure time in years and d as the annual exposure time in days [46].
Like in [25] a logistic regression model was employed in the statistical analysis and adjustments were made for age and smoking. Their analysis showed a good correlation between the HAV index and VWF and for the diseases summed up as HAVS as well. It was also found that the current level of exposure to hand-transmitted vibration correlated positively with the prevalence of VWF [46].

2.4.2 Evaluation of influencing factors

Aside from studies on alternatives to the $A(8)$-value and exposure time in years as measures of exposure, there have been several studies on other aspects listed in the Introduction as influencing factors, such as frequency weightings, body posture, or climate. Some of these are described below.

Brammer and Pitts presented frequency weighting adapted for the evaluation of VWF in 2012 [14]. Based on previous studies that analyzed the frequency-dependency of the vascular response to hand-arm vibration exposure, a primary frequency range was chosen. These frequencies were deemed most noxious, appeared to cause an equal response, and were consistent with biodynamic models. Due to a lack of data on the change in the response to vibration exposure outside of this range and inconclusive results in prior studies comparing different courses for the subsiding in the weighting, for frequency ranges outside of the primary one, a decay of 12 dB per octave as employed in ISO 5349-1:2001 was used. The trial frequency ranges were then constructed by choosing different upper and lower frequency limits separately. The vibration data were gathered either from previous studies on VWF after working with certain power tools or from, at the time of this publication, unpublished work from Brammer and Pitts. All of these had to show similar prevalence and latency in the studied groups of a minimum group size and the tools had to emit vibrations with differing frequency characteristics to allow for a comparison of the trial frequency weightings. A further requirement to make a comparison possible is that all individuals within a studied group had essentially the same exposure, i.e., the same task and the same type of tool. Depending on the available data, the weighting was applied to either the dominant axis vibration or on all three orthogonal components, both expressed in one-third octave bands. The tools and machines included in the analysis were rock drills, chainsaws, pavement breakers, and motorcycles. These exhibited vibrations with different spectra and a dominant axis to various

extend.
An equation, originally constructed using the frequency weighting in the standard, relating the latency in a group to the frequency-weighted acceleration and the daily exposure time was employed. The ratio of this equation for one group to the equation of another group was stated to equal the ratios of their respective latencies, which equals approximately one for groups with roughly the same latencies. After a minor simplification of the employed equation to account for uncertainties due to the usage of different frequency weightings, this ratio was defined as a relative risk ratio on which basis the trial frequency weightings were evaluated.
The relative risk was then compared for different upper frequency limits for rock drill operators versus chain saw users due to their similarities in prevalence and latency and the differences in the vibration spectra of the tools at the higher frequencies. In the process, the relative risk predictions were found to be very sensitive to fairly fine details in the vibration spectra of the tools and therefore influenced by a shift in the upper cut-off frequency.
The influence of the lower frequency limit was analyzed on the basis of workers using pavement breakers and postmen on motorcycles. This was done for those upper limits that appeared to yield the best predictions for VWF.
The results of these separate analyses were combined to determine the frequency weighting for developing VWF [14]. There was a certain ambiguity in both frequency limits, leading the authors to present a range for each. A comparison to a weighting derived from a biodynamic analysis of the energy entering the exposed fingers and from an analysis of epidemiologic data [45] showed that the range presented was similar to both. At low frequencies, the weighting from Brammer and Pitts falls in between the other two, but all three are in agreement about the primary frequency range. This was considered a further indicator that the frequency weighting in the ISO 5349-1:2001 is not well suited for predicting VWF and a weighting like those compared in the final step is likely to be an improvement on that.
On this basis, a frequency weighting was included in the ISO/TR 18570:2017 [32]. In [10], Bovenzi et al. used data from one of their previous cross-sectional epidemiologic studies and different frequency weightings including the one in the ISO/TR 18570:2017 to evaluate the risk of vascular disorders after exposure to hand-transmitted vibration. In the epidemiologic study, over 200 vibration-exposed forestry and stone workers and over 100 controls were investigated by means of a questionnaire and clinical tests. Measurements on the tools were done in accordance with the international standard ISO 5349-1:2001. The r.m.s. value was calculated for the unweighted acceleration and for the weighted one using the weighting W_h from the ISO 5349-1:2001 and the W_p from the technical report. The $A(8)$-value was determined using both weighted root-mean-square acceleration values. To estimate a threshold for the vascular component of the HAVS a vibration exposure value

$$E_{p,d} = \sqrt{\sum_{i=1}^{n} (a_{pvi})^2 \cdot T_i} \tag{2.18}$$

was calculated as advised in the ISO/TR18570 with a_{pvi} as the the W_p frequency-weighted r.m.s. acceleration of the ith operation using tool i and T_i as the time of said operation in seconds [10].
As expected the W_p weighted acceleration values were greater than the ones determined in accordance with ISO 5349-1:2001. The difference became most evident for those tools that emitted shock-like vibrations with great magnitudes in the high-frequency range of the acceleration spectra. The exposure value $E_{p,d}$ and the $A(8)$-value with both weightings were greater for the stone workers. Relative risk and risk differences were found to be significantly increased for the stone workers.
Statistical analyses of exposure-response relations showed that while $A(8)$ calculated with

both frequency weightings significantly associated with the prevalence of VWF, the one calculated with W_p was found to be a better predictor for both groups of workers [10].

In a recent contribution to The 15th International Conference on Hand-Arm Vibration, it is highlighted that many of the factors influencing the transmission of vibration into the hand and arm of a tool operator and its effect have not been addressed in exposure-response relations despite already being recognized as such also in Annex D of ISO 5349-1:2001 [38]. On-body measurements are being presented as one possible solution to allow for vibration measurements that can fairly easily be done on-site without interrupting work processes and therefore being able to account for different workpiece materials, postures, and work processes. Maeda et al. also name the possibility of notifying the user when exposure limits are being approached as an advantage of such on-body measurements. In the study [38] the measurements are done on the wrist. To account for the changes due to the transmission an equation is proposed that relates the estimated vibration on the tool handle that was measured on the wrist to the frequency-weighted acceleration measured according to ISO 5349-1:2001. In a study comparing vibration values from measurements on the wrist and the tool handle to temporary vibration perception threshold shifts were determined for different postures during tool operation. These were found to be predicted better by the on-wrist measured vibration values than those determined in accordance with ISO 5349-2:2001 on the tool handle. The authors point out that the on-body measurement can account for differences in grip and push forces as well as body posture, which all have been found to influence the vibration entering the hand-arm system of the user immensely, while the on-tool measurement cannot account for changes in the coupling between tool handle and user.
This highlights why in the present work, the analyzed relation is intentionally referenced as an exposure-response relation as the vibration exposure can only be determined with some uncertainty and the actual dose of vibration entering a worker's hand is unknown in current analyses.

Chapter 3

Summary of Achievements

This chapter contains the summaries of the main scientific achievements that are reported in detail in the publications attached in Appendix A.1. The papers included in this thesis have undergone full peer-review. They have been published in international journals ([47], see Sec. 3.1; and [48] see Sec.3.3) or are still under review ([49], see Secs. 3.2).

3.1 Inferences from a published meta-analysis of population groups

The corresponding paper [47] entitled "Exposure–response relation for vibration-induced white finger: inferences from a published meta-analysis of population groups" is enclosed in Appendix 1.

Summary

Using the selection of epidemiologic studies from the meta-analysis by Nilsson et al. [43] as data sources the question whether the model in the standard [30] needs improvement and whether the model by Nilsson et al. [43] delivers the latter were addressed.
To ensure comparability and compatibility with the standard and minimize potential errors, further selection rules were introduced. The selected data were grouped based on the amount of calculation needed to transform them into the format needed to create the models and on the number of tools used by the workers who partook in the respective study. A regression analysis was performed on all data sub-sets producing a regresssion curve of the same type as the model from the standard and 95-percentile confidence intervals.
As more data were included, the regression curve approached the line representing the model from the standard [30]. The 95-percentile intervals always include the latter, but not the model from Nilsson et al. [43]. The curve utilizing the data from the three single tool studies differed from the models created with data including studies in which one or multiple power tools and machines were used. A comparison of the raw data from the studies with the models from the standard [30], by Nilsson et al. [43] and from the present analysis, pointed towards potential issues in the method of evaluating vibration exposure in ISO 5349-1:2001 [30] and suggested its model delivers a conservative prediction.

Contribution

This work originated from a discussion with A. J. Brammer at the beginning of the pandemic, in which A. J. Brammer pointed out to me the meta-analysis by Nilsson et al. [43]. I gathered the studies used in it and the data from them and under remote assistance by A. J. Brammer developed further selection rules for the data. I grouped the data and performed the analyses and wrote the bulk of the manuscript for publication with additions from A. J. Brammer. Finally, A. J. Brammer and S. Marburg reviewed the manuscript in detail.

3.2 Modeling prevalence development in a population group exposed to vibration

The respective paper [49] with the title “Modelling prevalence development in a population group exposed to vibration, and noise: Application to hand-transmitted vibrations” is referenced in Appendix 1.

Summary

This work proposed models for the development of vibration-induced white finger due to habitual exposure to vibration based on long-term data. The usage of these is intended to enable the interpolation of the prevalences that were observed in different population groups to a common, desired value, as it was originally done linearly in [47].
To this aim, a polynomial fit to prevalence-time data recorded in a population group was made adaptable to various groups with different exposures by including a factor that represented the exposure rate, $expF(D_y)$. To account for further exposure-specific conditions and changes of members of the population group the numerical parameter a_1' was added.
A representative data set recorded in a population group, in which the members remained constant and hence delivered period prevalence data, was fitted by a 4^{th}-order polynomial. This model with the same polynomial coefficients fitted further period prevalence data sets when only $expF(D_y)$ was adjusted. Adding the numerical parameter a_1' allowed the model to fit several point prevalence data sets. Emplying the data from a study that provides two point prevalences for one group of workers gathered a few years apart the factor that represented the exposure rate was related to the $A(8)$-value of that group of workers. The determined equation for $expF(D_y)$ was tested on another data set consisting as well of two point prevalence values. The 4^{th}-order polynomial with the calculated $expF(D_y)$ and adapting only a_1' fit that data set well.

Contribution

The idea for this work stemmed from discovering the interpolation of prevalence to be one of the issues needing to be addressed to check or improve the validity of the exposure-response model in the standard. The approach was developed with A. J. Brammer. The models were created and tested by me under remote assistance of A. J. Brammer. The majority of the manuscript for publication was edited and added to by A. J. Brammer. It was reviewed critically by A.J. Brammer and S. Marburg before publication.

3.3 Effect of Different Methods for Predicting Prevalence

The corresponding paper [48] titled “Exposure-Response Relation for Vibration-Induced White Finger: Effect of Different Methods for Predicting Prevalence” is attached in Appendix 1.

Summary

This pooled analysis on VWF employed the same selection of epidemiologic studies as in [47], summarized in Section 3.1, to evaluate the exposure-response relation and the influence of the model of prevalence development used. To this end, the different prevalences of VWF reported by the epidemiologic studies at the respective cumulative lifetime exposures are interpolated to 10% prevalence linearly, as done in [47], and by means of the polynomial model introduced in [49]. Regression analyses were performed on the calculated data points to construct exposure-response relations for the time at which 10% of a population group was estimated to be affected by VWF, $D_{y,10}$, whose members were subjected to a daily vibration exposure that was described by the 8-h, frequency-weighted, energy-equivalent acceleration sum, $A(8)$, as specified in ISO 5349-1:2001 [30].
The regression analyses resulted in good fits both for the linearly and polynomially interpolated data sets. The increase in the $D_{y,10}$-values when polynomial interpolation is employed shifts the 95-percentile confidence intervals to slightly higher values compared to the ones gathered from the linearly interpolated data set. To mitigate the uncertainty in the precision of the polynomial interpolation the results of both interpolation methods were equally considered. Combining both 95-percentile confidence intervals was assumed to define the most likely range for the exposure-response relation. This region mostly encloses the relation specified in the standard [30] at its lower boundary.
A regression line, by definition, lies in the middle of the data points and therefore may not present a conservative prediction. Hence, the use of the lower 95-percentile confidence interval as an exposure-response relation is proposed as it is likely to deliver a conservative estimate for $D_{y,10}$ for $A(8) > 4\frac{m}{s^2}$. Additionally, the methods for evaluating exposure as currently defined in the international standard [30, 31] need to be reconsidered to resolve the remaining inconsistencies.

Contribution

This work is the application of the work in [49] to the data used in [47] to evaluate the effect of the interpolation using a model that represents the development of prevalence better. The calculations and regresssion analyses for the models were done by me. The evaluation of the results and writing of the manuscript was done in close cooperation with A. J. Brammer. The manuscript was reviewed carefully by A.J. Brammer and S. Marburg.

Chapter 4

Conclusion

In addressing the question of the accuracy of the model in ISO 5349-1:2001 three analyses have been conducted and included here. A pooled analysis based on the meta-analysis by Nilsson et al. [43] was performed [47]. The list of studies deemed suitable from the latter was screened further to ensure comparability of the data and concurrence with ISO 5349-1:2001. This screening resulted in a reduction in the number of studies used in the analysis to 7 from 25. This highlights the lack of data available as already mentioned in [5] and [14]. This is in great part owing to the fact that studies on the exposure either do not report the health response or do not fulfill all criteria applied here to ensure reliability and comparability, and similarly, studies on the health effects tend to either lack information on the vibration the subjects had been exposed to or its measurement or reporting has not been done in accordance with ISO 5349-1:2001. The selection rules applied in [47] furthermore resulted in all but one study originating from the same research group in Italy. Though this was an unintended result of the screening of the studies, it consequently does not allow for the deduction of any conclusions regarding climate as an influencing factor and whether the model in the ISO standard applies to groups of workers in cold climates versus tropical climates. Due to the reporting of the data in the studies, it is not straightforward to apply the frequency weighting for vascular issues after exposure to hand-transmitted vibration and evaluate its influence on the model.

Despite the lack of variety in the origin of the data, they appear to be somewhat scattered, only the few data points from studies in which workers only used one tool or machine seem to align. With just three such studies, no statistical analysis is possible to compare the model including only such single tool studies and the one including all. All models created from either data subsets or the full data set in [47] run below the one from Nilsson et al. [43]. The model that stems from the regression analysis of all data points is closest to the one from the standard. The confidence intervals in all cases at least mostly enclose the model from ISO 5349-1:2001, but hardly ever the one from Nilsson et al. The analysis of the unprocessed data in Figure 4 in [47] shows that all data points lie above the model from ISO 5349-1:2001, but also that they do not appear to group by similar prevalence at certain exposures. These results do not allow determining the validity of the model in the standard but reveal several issues that need to be addressed in the process.

One of these is addressed in the second publication included here [49]. In the first publication to allow for direct comparison to the model in Nilsson et al. [43] the method for prevalence interpolation to 10% has been replicated. Observing the growth of prevalence in a population shows though that it does not progress linearly with the start of exposure. It rather reflects the mean latency and only shows an increase after a certain amount of time. And finally, prevalence is found to saturate after a certain time. This curve shape is not reflected by linear interpolation and hence is addressed in the second publication [49].

A model of VWF prevalence growth after hand-transmitted vibration exposure has been created with the aim to use it to interpolate prevalence data. Hence, data from longitudinal studies are employed to determine a polynomial to fit prevalence growth in a group of workers. A 4^{th}-order polynomial is found to fit the data. Including a factor to account for differences in exposure between populations, $expF(D_y)$ allows fitting the polynomial to data of different groups of workers from another study. All of those fits are done on period prevalence data, while the interpolation is done on point prevalence data. Hence in the next step, an additional parameter, a_1' is included in the polynomial to account for any changes in the members of the population or exposure as they are present in an open cohort. Including a factor for the exposure and the parameter a_1' results in two unknowns that need to be fitted. These are too many unknowns to be fitted if only one point prevalence data point is known, as is the case for the studies used in the analyses in [47] and[48]. In order to reduce the number of unknowns, the exposure factor is related to the $A(8)$-value of the respective study. A test of the thus resulting polynomial is tested on data from a study that includes two prevalence values for two points in time for the same population by interpolating from the later prevalence value. It is shown that the polynomial interpolation predicts the earlier prevalence value better than linear interpolation.

This invertible and adaptable polynomial is then used for interpolation on the data from the first pooled analysis. The resulting data are employed in a regression analysis like in [47] to create a new exposure-response model and evaluate the influence of the interpolation. To this end, the model is then compared to the model from the first analysis. A shift to higher exposure times is found in the interpolated prevalence data, compared to the linearly interpolated ones. Furthermore, the data appears somewhat split into two main groups, the smaller one includes all data from studies in which workers only used one tool and two data points in which few tools were used. These present lower in Figure 2 in [48] than the rest. The fit is found to be good, though the r^2-value is slightly lower than in [47]. The confidence interval of the model created from polynomially interpolated data is found at slightly higher exposures than the one from [47].

As there still is some uncertainty in the interpolation method due to a lack of data on which it could be developed, it is chosen to consider the models from both analyses as equal. The combined area of these two confidence intervals includes the ISO model placing it in the most likely region for an exposure-response relation. As a regression line by definition runs through the data points and does not present a lower limit, using the lower limit of the confidence interval as an exposure-response relation appears as a valid and prudent measure.

The present analyses show several issues. The lack of data has become evident in the pooled analyses and the study in which the polynomial prevalence growth model is developed. Furthermore, show the differences between studies in which workers used one or multiple tools and the clustering of the unprocessed data at different prevalences in Figure 4 in [47] and Figure 3 in [48] show that the evaluation of daily exposure by means of the $A(8)$-value may not work equally well for the exposure to the vibration of multiple tools compared to that involving a single tool. Both the evaluation of the daily exposure time and the lifetime exposure may cause issues as they tend to be subjected to recollection bias. An issue that could not be addressed in the present work is the frequency weighting. Analyzing the influence of the frequency weightings included in ISO 5349-1:2001 and ISO/TR 18570:2017 on the models appears as a good next step, though to this end studies that report the vibration data in a format that allows the application of different weightings or single tool studies that would allow the conversion of the vibration value from one frequency weighting to the other by means of a factor are needed. Another next step would be to extend the data set beyond the one from the meta-analysis by Nilsson et al. [43] to include more recent data and diversify the sources of the employed data.

In conclusion, it is found that the model in ISO 5349-1:2001 presents a conservative prediction and the over- and underestimation stated by several studies cannot be confirmed. The analyses show issues in exposure evaluation that need to be addressed in order to either confirm the model in the standard or create a revised one.

Appendix A

Appendix 1

Publication #1 [47]
The included publication #1 was accepted by the "International Archives of Occupational and Environmental Health" on the 17^{th} of February 2023 and published on the 28^{th} of March 2023:
Scholz, M.F., Brammer, A.J. & Marburg, S. Exposure–response relation for vibration-induced white finger: inferences from a published meta-analysis of population groups. Int Arch Occup Environ Health 96, 757–770 (2023). https://doi.org/10.1007/s00420-023-01965-w

Publication #2 [49]
The referenced publication #2 was submitted to "Acta Acustica" on the 20^{st} of March 2023 and is still under review at the point of the submission of this thesis:
Scholz, M.F., Brammer, A.J. & Marburg, S. Modelling prevalence development in a population group exposed to vibration, and noise: Application to hand-transmitted vibration. Submitted to Acta Acustica (2023).

Publication #3 [48]
The referenced publication #3 was accepted by the "Annals of Work Exposures and Health" on the 11^{th} of September 2023 and published on 20^{th} of September 2023:
Scholz, M.F., Brammer, A.J. & Marburg, S. Exposure-Response Relation for Vibration-Induced White Finger: Effect of Different Methods for Predicting Prevalence. Ann Work Exposures Health 67 (9), 1069-1080 (2023). https://doi.org/10.1093/annweh/wxad050

Publication #2 [49] is still under revision at the time of the publication of this thesis and hence is only referenced.
Publication #3 [48] only appears as a reference in the thesis due to copyright.

International Archives of Occupational and Environmental Health
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ORIGINAL ARTICLE

Exposure–response relation for vibration-induced white finger: inferences from a published meta-analysis of population groups

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Abstract

Purpose It is questioned whether the exposure–response relation for the onset of vibration-induced white finger (VWF) in ISO 5349-1:2001 needs to be revised based on the epidemiologic studies identified by Nilsson et al. (PLoS One https://doi.org/10.1371/journal.pone.0180795, 2017), and whether the relation they derive improves the prediction of VWF in vibration-exposed populations.

Methods A pooled analysis has been performed using epidemiologic studies that complied with selection rules and reported a VWF prevalence of 10% or more, and exposure constructed according to the provisions of ISO 5349-1:2001. The lifetime exposures at 10% prevalence were calculated for various data sets using linear interpolation. They were then compared to both the model from the standard and that developed by Nilsson et al.

Results Regression analyses reveal excluding extrapolation to adjust group prevalences to 10% produce models with 95-percentile confidence intervals that include the ISO exposure–response relation but not that in Nilsson et al. (2017). Different curve fits are obtained for studies involving daily exposure to single or multiple power tools and machines. Studies with similar exposure magnitudes and lifetime exposure durations but markedly different prevalences are observed to cluster.

Conclusions A range of exposures and $A(8)$-values is predicted within which the onset of VWF is most likely to occur. The exposure–response relation in ISO 5349-1:2001, but not that proposed by Nilsson et al., falls within this range and provides a conservative estimate for the development of VWF. In addition, the analyses suggest that the method for evaluating vibration exposure contained in ISO 5349-1:2001 needs revision.

Keywords Hand-arm vibration · Vibration white finger · Exposure–response relation · Prevalence

Introduction

The onset of vibration-induced white finger (VWF) in workers operating power tools or machines is a subject of considerable interest for establishing occupational exposure limits. Guidelines have been proposed from epidemiologic studies and incorporated into regulations and standards. A continuing debate has focused on the accuracy of the guidelines in an annex of the international standard for hand-transmitted vibration, ISO 5349-1:2001 (2001), which are based on an exposure–response model developed by Brammer (1982b). In a recent comprehensive meta-analysis, Nilsson et al. (2017) have analyzed data published over the last 70 years, and used a documented selection of studies to create a new model for predicting a 10% prevalence of VWF in persons whose hands are occupationally exposed to vibration. The predictions of this risk assessment model differ substantially from those contained in ISO 5349-1:2001. The model proposed by Nilsson et al. predicts a longer time at a given exposure rate to reach 10% prevalence of VWF. Here, the question is raised if the model in the standard indeed needs to be revised to account for the information in the recent meta-analysis. Clearly, an accurate prediction based on an appropriate evaluation of vibration exposure is needed to protect workers from damage to the vascular, neurological and musculo-skeletal systems of their hands and to construct meaningful national regulations and legislation. Only if the effects of exposure are assessed correctly is it possible to

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create work environments and schedules that balance productivity with the health and safety of workers.

There have been several attempts to relate occupational exposure of the hands to vibration to the development of VWF (Bovenzi 1994; Bovenzi et al. 1995; Bovenzi 1998a, 2010b; Brammer 1982a, 1986; Futatsuka et al. 1984; Griffin 1982; Griffin et al. 2003; Miyashita et al. 1982; Nilsson et al. 2017; Sauni et al. 2009; Su et al. 2013; Taylor et al. 1975a; Tominaga 1982). These range from ad hoc to population distribution driven models employing regression analyses of selected epidemiological studies of workers to logistic regression models for assessing the odds ratios associated with different methods for estimating daily and lifetime exposures. There are also models for longitudinal studies.

It is evident from this body of work that establishing a relation between vibration exposure and the development of vascular or neurological disturbances in the hand encounters several difficulties. These relate to the measurement of vibration at the hands and determining the exposure to it, ergonomic factors such as hand force and grip, and posture, individual susceptibility (including biological, environmental and climatic factors) and relying on information given by participants concerning their signs, symptoms and work history. Furthermore, different measures of exposure, such as the lifetime vibration dose (Griffin et al. 2003), cumulative exposure index (Sauni et al. 2009) or total operating time (Miyashita et al. 1982) provide alternate and not always compatible metrics for evaluating or predicting the harm from vibration exposure. In addition, most exposures have been in a temperate climate and there are relatively few in a tropical climate. It is well known that low temperatures can cause fingers to whiten and hence vascular spasms are more likely to occur in hands affected by VWF than when in a near-tropical climate (Futatsuka et al. 2005; Su et al. 2013).

An analysis of the relative weight to apply to the magnitude of vibration at a surface in contact with the hands compared to the lifetime exposure duration found that a better prediction of the health effects could be obtained by applying the same power to the total exposure time as to the vibration magnitude, in contrast to the method contained in ISO 5349-1:2001 (Griffin et al. 2003). The authors related this to the calculation not distinguishing between exposures accumulated over a day and those over several years. Also, Griffin et al. found that using an unweighted acceleration resulted in a better prediction of VWF than if the frequency-weighted acceleration recommended in the ISO standard was used. However, recent work has shown that a more nuanced approach is needed to specify a frequency weighting for at least the vascular component of hand-arm vibration syndrome (HAVS) (Brammer and Pitts 2012). Studies have also reported that the relation between vibration exposure and the development of VWF contained in the international standard both underestimates or overestimates the risk in different population groups (Bovenzi et al. 1988, 1995; Bovenzi 1998a, 2012; Engström and Dandanell 1986; Futatsuka et al. 1984; Gerhardsson et al. 2020; Keith and Brammer 1994; Starck et al. 1990; Tominaga 1990; Walker et al. 1985).

In light of these findings and the availability, for the first time, of a comprehensive, systematic meta-analysis identifying studies conducted over the last 70 years relating occupational exposure to vibration to the development of VWF, it would appear both imperative and timely to reassess the suitability of the international standard for the purpose for which it was designed. Accordingly, the purpose of this contribution may be summarized in two objectives. The first is to examine whether the exposure–response relation for the onset of VWF contained in ISO 5349-1:2001, including the method for calculating exposure, needs to be revised based on the results of epidemiologic studies included in the recent meta-analysis by Nilsson et al. (2017). The second is to consider whether the exposure–response relation proposed by Nilsson et al. (2017) improves the prediction of VWF in vibration-exposed population groups. Answers to these questions could imply a need to revise not only the model contained in the standard, but also the methods for evaluating exposure. Such revisions would influence implementation of regulations limiting workplace vibration exposure and machinery vibration emission in many countries that are dependent on the standard, with immediate health and economic consequences.

In this study, the approach chosen by Nilsson et al. (2017) is replicated with modifications to create models to predict the prevalence of 10% VWF in a population group for a given vibration exposure, as described in the Methods. In common with Nilsson et al. (2017), the models assume that the ongoing health risk can be represented on a group basis by a measure of the group's mean daily exposure. Hence, all variability in human response arising from physical, ergonomic, biodynamic and individual factors, including susceptibility and work practices, must be expressed by other model parameters, which are here subsumed by the prevalence. The models are constructed using the procedures for estimating daily and lifetime exposures contained in the international standard. They are then described in the Results with both the exposure–response relation from the standard and that developed by Nilsson et al. (2017). The relation of the three models to the epidemiologic data are analyzed in the Discussion, together with the limitations of the study, to address whether the model in ISO 5349-1:2001 needs revision and if the model created by Nilsson et al. (2017) is an improvement on that in the standard.

Methods

The meta-analysis performed by Nilsson et al. (2017) consisted of a systematic review of original scientific papers published in English in refereed journals. Screening of the literature was initially done by abstract followed by an evaluation of 294 articles against pre-determined criteria established to evaluate overall "quality", from which 52 were judged to be of sufficient quality for inclusion in the analysis. The criteria involved are described in detail in the Annex of Nilsson et al. (2017). Out of these 41 contained data concerning Raynaud's phenomenon.

An overview of the data from all publications judged acceptable by Nilsson et al. (2017) was first created, including the methods of exposure measurement and clinical evaluation used in the various studies. These data were then further screened by the selection rules introduced here (Table 1) to reduce heterogeneity and so ensure compatibility with the objectives of the present study. Hence for the purposes of the present pooled analyses, hand-transmitted vibration had to have been measured in accordance with the requirements of the international standard in effect at the time of the study (ISO 5349:1986 1986, or ISO 5349-1:2001 2001). This is ensured if the first five conditions in Table 1 are fulfilled. Regarding epidemiologic data, studies of VWF are to be included in the analyses if they satisfy conditions 6–11. These rules are designed to ensure that groups are comparable and only those are included in which white fingers are caused by vibration. For example, rule 7 states that the first episode of finger blanching should occur at a fingertip after commencing occupational exposure to hand-transmitted vibration, which is a typical characteristic that distinguishes VWF from white fingers caused by unrelated disease or other factors (Taylor and Pelmear 1975b). Furthermore, as argued in Brammer (1982a), the population group size has to be considered when evaluating such data, as small groups may not be representative of a larger population. It was found there that consistency in the data analysis was obtained for a minimum group size of thirty persons, which is included here in rule 6. The selection rules are intended to enable a simple binary decision between whether or not to include the results of a study in the analyses. However, there were a few studies that may or may not comply with all selection rules on which judgments had to be made concerning the reliability of the data.

The exposure–response relation in ISO 5349-1:2001 predicts the mean time exposed (in years) to a daily exposure characterized by the 8-h energy-equivalent averaged acceleration, $A(8)$, for the prevalence of VWF in a population group to reach 10%, where

Table 1 Selection rules used to determine the reliability of the data provided by the studies and hence their usage in this pooled analysis (rules 1–5: measurement of vibration, 6–11: epidemiologic data)

Selection rule number	Rule
1	The acceleration of a vibrating surface in contact with the hand is to be determined in up to three mutually orthogonal directions specified by ISO 5349 at frequencies from 5.6 to 1400 Hz, with avoidance of instrument overload and DC shifts
2	Vibration is to be filtered to de-emphasize the contribution from frequencies above 16 Hz by the frequency weighting in ISO 5349
3	Exposures are to be computed from the mean value of the frequency-weighted vector sum of acceleration components (ISO 5349-1 2001)
4	Exposures are to be characterized by the daily time-averaged vibration energy normalized to a reference time of 8 h (ISO 5349-1 2001)
5	Exposures consisting of daily operations involving more than one source of vibration are to be expressed by the sum of the time-averaged vibration energies of the different exposures per ISO 5349-1:2001. The sum is to be normalized as in rule 4
6	The population group must consist of all, or an unbiased selection of, workers whose full-time occupation involves near-daily exposure to hand-transmitted vibration. Thirty or more vibration-exposed persons must be included in the study
7	A documented attempt has been made to exclude persons suffering from primary Raynaud's disease or causes of secondary Raynaud's phenomenon other than vibration, and include information that the first episode of finger blanching occurred at a fingertip after commencing occupational exposure to vibration
8	The diagnosis of VWF has been based on medical history and clinical assessment with or without reference to the Stockholm Workshop Scale for vascular disorders or the Taylor–Pelmear stages of VWF
9	In the absence of the information in 7 and/or 8, the raw point prevalence in the exposed population group must be assumed to contain persons with signs not associated with vibration. Compensation for the observed excess prevalence may be obtained by removing the point prevalence of finger blanching recorded in a control group with similar lifestyle and engaged in equivalent work but unexposed to vibration
10	A minimum of 10% of the population group must be diagnosed with VWF or, for studies not in compliance with 7 and/or 8, 10% in excess of the prevalence recorded in a control group
11	The mean lifetime duration of exposure to reach the point prevalence of VWF determined in a population group must be reported (commonly in years)

$$A(8) = a_{hv} \cdot \sqrt{\frac{T}{T_0}} = \sqrt{\frac{1}{T_0}\sum_{i=1}^{n} a_{hvi}^2 \cdot T_i}. \tag{1}$$

In this equation, T_0 is the reference time for calculating the daily exposure, which is 8 h in ISO 5349-1:2001 in order to represent a conventional workday. The earlier version of the standard employed a reference time of 4 h, but this is not applied to data here. T is the time the users were exposed to the frequency-weighted vibration total value, a_{hv}. For daily exposures involving a variety of power tools or machines, each used for different times during a workday, the component exposures are summed as in Eq. 1 for n tools or machines, where T_i, is the time of exposure to the ith tool or machine with vibration total value of a_{hvi}.

Now the point prevalence of VWF recorded in all epidemiologic studies included in the analyses was not 10%. Thus, in order to examine the accuracy of the ISO prediction, the exposure duration at the point in time of each study at which 10% of the population would have been affected by VWF needs to be determined. For this purpose, the method used in Nilsson et al. (2017), which assumes a linear increase in prevalence of Raynaud's phenomenon with time, is also used here. But in order to keep the error as low as possible, extrapolation is avoided and only interpolation allowed. Consequently, only data for those population groups that had a prevalence of 10% or more when the epidemiologic study was conducted are included in the analyses.

Furthermore, a zero prevalence of VWF at zero duration lifetime exposure to vibration needs to be assumed in order to reconstruct the lifetime exposure for 10% prevalence. This implies that the observed prevalence of VWF contains no individuals with signs and symptoms from causes other than vibration exposure, which is the reason for selection rules 7, 9 and 10 (Table 1). Rule 7 requires a differential diagnosis to rule out other causes for white finger for cases observed in a given study. If there is doubt surrounding the origin of the white fingers reported, rule 9 requires an unexposed control group to be a part of each study to enable the raw prevalence to be adjusted. An adjustment is only made in the analyses described here if the authors were not convinced that the conditions contained in the rules had been met.

Most of the studies used in Nilsson et al. (2017) involved population groups that operated more than one vibrating power tool or machine per workday: hence exposures to multiple tools are included as long as rule 5 is satisfied, with $A(8)$ calculated according to Eq. 1.

In addition to estimating the exposure time at 10% point prevalence, in some cases more calculation was needed in order to have data in the format needed for the models. Chatterjee et al. (1978) did not provide an $A(8)$-value, but published vibration spectra from which it could be calculated. Numerical values were recovered from the spectra in the graphs showing the measured vibration. Using these a frequency-weighted spectrum was determined. In addition, the a_{hv}-value was calculated by forming the vector sum of the acceleration components according to Eq. 2 (from ISO 5349-1:2001) and inserting it into Eq. 1:

$$a_{hv} = \sqrt{a_{hwx}^2 + a_{hwy}^2 + a_{hwz}^2} \tag{2}$$

The other study for which additional calculations were needed to reduce heterogeneity was that by Bovenzi (1998b). Here, the lifetime exposure is given in total hours of tool or machine usage. Thus, it needs to be converted into the corresponding exposure in years in order to be usable in the models. Therefore, the number of workdays was estimated from statistics for the average number of workdays per year from 1965 to 1994 in the country concerned (The Workingdays Team 2021). Twenty statutory vacation days as well as the average number of sick days derived from WHO statistics were deducted from this number to estimate the average number of days actually worked annually (World Health Organization 2021). These workdays were then used to calculate the lifetime exposure in years:

$$D_y = \frac{t_{\text{exposed}}}{T_0} \div N_{\text{workdays per year}}. \tag{3}$$

In this equation, D_y is the time the workers were exposed given in years, t_{exposed} is the total hours of tool or machine usage and T_0 equals 8 h. The division of t_{exposed} by T_0 gives the total number of workdays the users were exposed. Dividing this by the average number of days worked per year, $N_{\text{workdays per year}}$, enables D_y to be estimated.

These calculations, together with linear interpolation of the point prevalence, produced a data set of mean group lifetime exposures in years to reach 10% prevalence for the corresponding $A(8)$-values. This data set was then analyzed using a regression analysis. Hence, the following power function was used, which also has the same form as the model employed in the standard ISO 5349-1 (2001):

$$D_{y,10} = a \cdot A(8)^b, \tag{4}$$

where $D_{y,10}$ is the mean cumulative lifetime exposure of the population group to reach a 10% prevalence of VWF, and a and b are best-fit numerical parameters to the data. This process was done first with the data for which $A(8)$ values were reported, or calculated using Eqs. 1 and 2, and no additional calculations except interpolation to 10% prevalence were needed. Then the data that required further calculations were added stepwise, by including those with values for $A(8)$ estimated using Eq. 3. In addition, studies using only a single power tool or machine were analyzed separately. In all cases, no limitation on daily exposure duration was set.

The objectives of this study are achieved by interpreting the results of the regression analyses. Particular attention is paid to the gradient of the relations, b, and the goodness of fit of the models to the data (coefficient of determination, r^2). In addition, 95-percentile confidence intervals for the functional relations are presented, i.e., the intervals delineate the range of relations with form given by Eq. 4 that are compatible with the data. The confidence intervals thus provide tests for the accuracy of the model included in the international standard and provide information on whether the exposure–response relation proposed by Nilsson et al. (2017) improves prediction of the development of VWF in vibration-exposed population groups.

Results

Studies deemed reliable by Nilsson et al. (2017) for evaluating the development of VWF and available to the present authors are listed in Table 2. The reason for exclusion from the analyses is given, and whether an $A(8)$-value was provided for the group's exposure. The last two columns indicate whether and what further processing of the data was required, and if an adjustment to the reported prevalence of VWF in the population group was needed.

The decision on inclusion or exclusion of a study was based on the selection rules in Table 1. Yet, as stated in the method section, not all studies fit into this binary framework. For example, according to the description of the measurement procedure in Chatterjee et al. (1978), no use of a mechanical filter was reported despite measuring the vibration of percussive tools. This omission would exclude

Table 2 Studies considered usable by Nilsson et al. (2017) with the reason if used or not in the analyses, whether an $A(8)$-value is provided, whether further processing of the data is needed to get the $A(8)$-value or the exposure time needed for the model

Study	Included	Reason for in-/exclusion	A(8) provided	Further processing and method
Bovenzi et al. (1980)	No	No acceleration value(s)	No	–
Bovenzi et al. (1985)	No	No mechanical filter	No	–
Bovenzi et al. (1988)	No	No $A(8)$	No	–
Bovenzi (1994)	Yes	–	Yes	No
Bovenzi et al. (1995)	Yes	–	Yes	No
Bovenzi (1998b)	Yes	–	Yes	Yes, see Eq. 3
Bovenzi et al. (2000)	No	Less than 30 vibration-exposed persons	Yes	–
Bovenzi et al. (2005)	No	Less than 10% prevalence	Yes	–
Bovenzi (2008)	Yes	–	Yes	No
Bovenzi et al. (2008)	Yes	–	Yes	No
Bovenzi (2010a)	Yes	–	Yes	No
Bovenzi (2010b)	No	Same data as Bovenzi (2010a)	Yes	–
Burström et al. (2010)	No	No acceleration value(s), less than 10% prevalence when control group considered	No	–
Hagberg et al. (2008)	No	Exposure data incompatible with present analyses	No	–
Nilsson et al. (1989)	No	No $A(8)$	No	–
Brubaker et al. (1987)	No	No $A(8)$	No	–
Chatterjee et al. (1978)	Yes	Vibration spectra show no evidence of distortion due to lack of mechanical filter during measurement	No	Yes, see Eqs. 1 and 2
Letz et al. (1992)	No	Measures of vibration produced different acceleration value(s)	No	–
Palmer et al. (1998)	No	No acceleration value(s), no control group	No	–
Walker et al. (1985)	No	No acceleration value(s), less than 10% prevalence when control group considered	No	–
Mirbod et al. (1992)	No	Vibration measurement method, no unexposed control group	No	–
Mirbod et al. (1994)	No	Vibration measurement method	No	–
Yamada et al. (1995)	No	No $A(8)$	No	–
Tominaga (1994)	No	No $A(8)$, less than 10% prevalence when control group considered	No	–
Su et al. (2013)	No	No white fingers	No	–

the study according to the selection rules. However, the authors provide vibration spectra for the power tools from which it can be seen at low frequencies there is no spurious increase in acceleration with decreasing frequency (i.e., no evidence of distortion introduced by the transducer, commonly referred to as a “DC-Shift”), and hence no evidence of perturbed acceleration values. For these reasons the study is included in the analyses.

The data from the studies marked as included in Table 2 are listed in Table 3 and plotted in Figs. 1, 2, 3 and 4. Figures 1, 2 and 3 show the mean lifetime exposure to reach 10% point prevalence of white fingers in a vibration-exposed population group, $D_{y,10}$, as a function of the daily exposure expressed by $A(8)$. The model from ISO 5349-1:2001 is included in all the figures as a dashed black line. The model created by Nilsson et al. (2017) is plotted as a continuous red line. The best fit to the data is shown by the continuous blue line, and the thick blue lines display the 95-percentile confidence intervals for the regression.

Table 4 contains details of each model and the parameters of the regression analyses. The table identifies the data sources for each model and how the data were processed. The data from each study were given equal weight in all models. Values of r^2 and parameters a and b of each regression analysis are given. In the studies included in the analyses shown in Figs. 2 and 4 workers used one or more of the following tools or machines: chipping hammers, straight grinders, rock drills, hand cutters, rock breakers, angle grinders, light stone hammers, chain saws, caulking tools, impact wrenches, nut runners, scaling hammers, hand-held

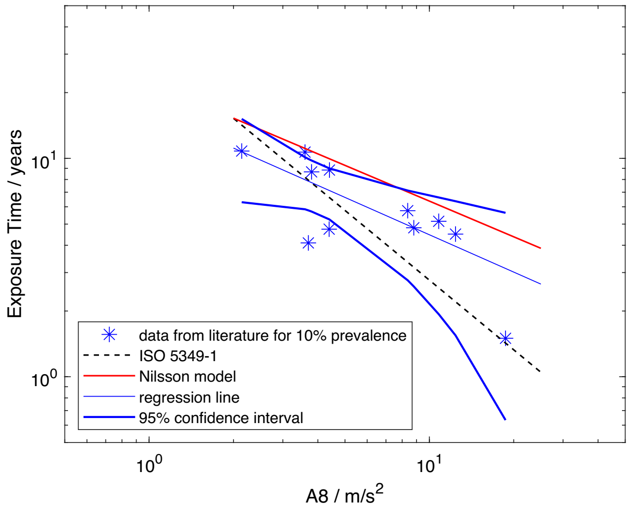

Fig. 1 Model 1: predicted mean lifetime exposures versus $A(8)$ to reach 10% point prevalence of VWF for data set (stars), regression line for model 1 (continuous blue line), model from Nilsson et al. (2017) (red line), exposure–response relation from ISO 5349-1:2001 (dashed black line), and 95-percentile confidence intervals for model 1 (thick blue lines) (color figure online)

Table 3 Tools used, $A(8)$-values, mean group exposure times D_y, population size and point prevalences derived from the publications, and the interpolated exposure times to 10% point prevalence $D_{y,10}$. All data for male workers

Study	$A(8)/\frac{m}{s^2}$	Tools used	D_y/years	Population Size	Prevalence / %	$D_{y,10}$ / years
Bovenzi (1994)	8.4	Rock breakers, rock drills, angle grinders, light stone hammers	17.4	570	30.2	5.76
Bovenzi (1994)	12.4	Rock breakers, rock drills	18.3	145	40.7	4.50
Bovenzi (1994)	2.1	Angle grinders	14.9	188	13.8	10.80
Bovenzi (1994)	10.8	Angle grinders, light stone hammers	18.9	237	36.7	5.15
Bovenzi et al. (1995)	4.4	Chain saws, AV chain saws	11.1	222	23.4	4.74
Bovenzi (1998b)	1.9	Selection from: caulking tools, chipping hammers, impact wrenches, nut runners, scaling hammers, hand-held grinders and polishers	17.9	132	12.1	14.79
Bovenzi (1998b)	4.2		17.8	65	23.1	7.71
Bovenzi (1998b)	1.7		21.5	140	15.0	14.33
Bovenzi (1998b)	8.3	Selection from: rock drills, road breakers, hammer drills, stone ham- mers, hand-held grinders and polishers	24.6	41	36.6	6.72
Bovenzi (1998b)	4.7		15.0	31	51.6	2.91
Bovenzi (1998b)	4.1	Chain saws, brush saws	9.1	165	23.0	3.96
Bovenzi (2008)	3.7	Chain saws, AV chain saws	10.9	128	26.6	4.10
Bovenzi et al. (2008)	4.4	Brush saws, chain saws, grinders, polishers, inline hammers	16.0	216	18.1	8.84
Bovenzi et al. (2008)	3.6	Brush saws, chain saws	15.8	183	14.8	10.68
Bovenzi et al. (2008)	8.8	Grinders, polishers, inline hammers	17.5	33	36.4	4.81
Bovenzi (2010a)	3.8	Brush saws, chain saws, grinders, polishers, inline hammers	15.0	249	17.3	8.67
Chatterjee et al. (1978)	18.7	Percussive drills	7.5[a]	42	50.0	1.50

[a]Median group exposure time

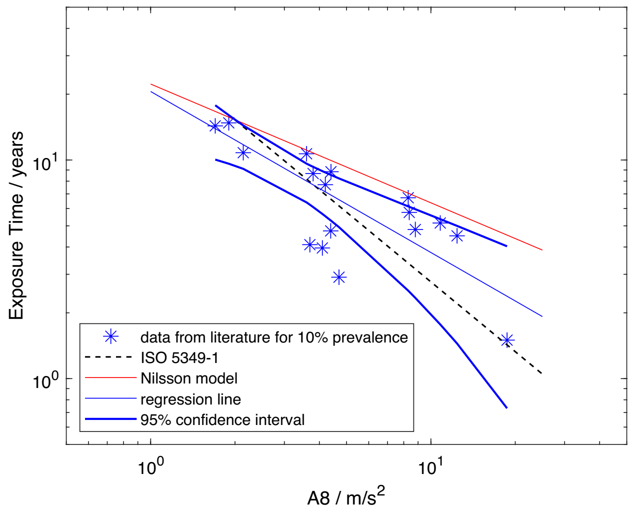

Fig. 2 Model 2: predicted mean lifetime exposures versus $A(8)$ to reach 10% point prevalence of VWF for data set (stars), regression line for model 2 (continuous blue line), model from Nilsson et al. (2017) (red line), exposure–response relation from ISO 5349-1:2001 (dashed black line), and 95-percentile confidence intervals for model 2 (thick blue lines) (color figure online)

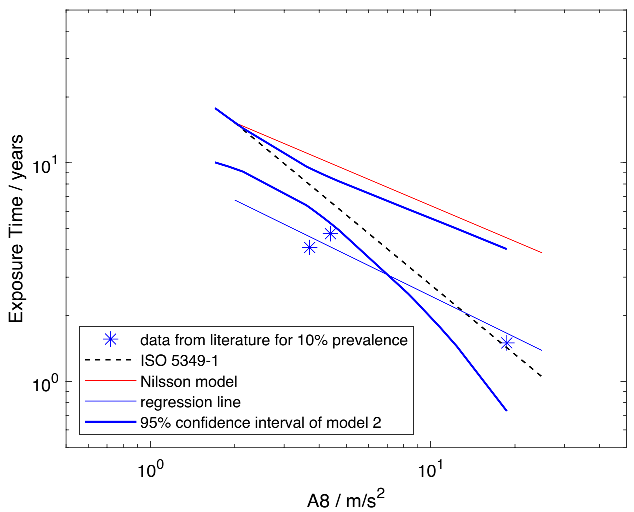

Fig. 3 Model 3: predicted mean lifetime exposures versus $A(8)$ to reach 10% point prevalence of VWF for studies in which workers only used one power tool throughout the workday (stars), regression line for model 3 (continuous blue line), model from Nilsson et al. (2017) (red line), exposure–response relation from ISO 5349-1:2001 (dashed black line), and 95-percentile confidence intervals for model 2 (thick blue lines) (color figure online)

grinders, polishers, road breakers, hammer drills, and brush saws.

Figure 1 shows the data set for which values of $A(8)$ were provided by the authors of the studies, as well as the data point from Chatterjee et al. (1978) in which the $A(8)$ value was derived from the component frequency spectra of the power tools. It can be seen from the figure that data are available for a broad range of frequency-weighted accelerations (from approximately $A(8) = 1.5–20\frac{\mathrm{m}}{\mathrm{s}^2}$), and lifetime exposures (from approximately 1.5 to 11 years). The data are scattered somewhat along the line of the model from the standard, a majority above and some below, while the line of the Nilsson et al. (2017) model lies above all data points. However, the regression line from model 1 runs roughly parallel to the latter and intersects the dashed line representing the ISO model at a value of $A(8)$ of about $3.7\frac{\mathrm{m}}{\mathrm{s}^2}$. The 95-percentile lines, representing between them the most likely region in which the "true" relation between the lifetime exposure to reach 10% prevalence of VWF and $A(8)$, include most data points and the ISO model (dashed black line). The red line representing the model from Nilsson et al. (2017) lies mostly outside the most probable region in which the "true" relation is expected to be found, and is intersected by the limit of one of the confidence intervals.

The results for model 2 are shown in Fig. 2. Here, the data from Bovenzi (1998b) for which additional calculations were needed to estimate $A(8)$ are added to the data from the previous figure. The combined data set appears to be as scattered as that in Fig. 1. However, the slope of the regression line has shifted towards that of the model from the standard. From Table 4 the gradients are now -0.74 and -1.07, respectively. As in Fig. 1, all the data points are below the red line that represents the model developed by Nilsson et al. (2017). The 95-percentile lines continue to enclose the ISO curve, but enclose fewer of the data points than previously. Thus the confidence intervals now define a smaller region in which the "true" relation between exposure and the development of VWF is predicted to occur. This is reflected in the coefficient of determination, which has increased from 0.60 to 0.69 indicating that more of the variability has been captured by the model. No attempt has been made to further reduce the variability by introducing confounding variables or co-factors as none are considered in the ISO or Nilsson et al.'s (2017) models. The red line representing the Nilsson et al. (2017) model now lies further outside the most probable region in which the "true" relation is expected, but is still intersected by one of the confidence intervals.

There are three studies in which workers used only one power tool each workday in the meta-analysis of Nilsson et al. (2017) that can be included here. The data for these are shown in Fig. 3. With the low number of such studies, the possibilities for analysis are limited, but they can be fitted by a curve specified by Eq. 4. However, it lies far below the model in Nilsson et al. (2017), while the data points are closer to the model in the standard. Reference to Table 4 reveals that the gradient for model 3 is close to that for model 1, namely -0.63 versus -0.57. However, there is a difference in a-values between model 3 and all the other models (viz., 10.4 versus 16.5 and 20.6). This difference

Table 4 Details of models including processing, r^2-value for the regression analysis where applicable, fit parameters, and sources of the data included in each model [b for the model in ISO 5349:2001 is – 1.07 (Brammer 1982a)]

Model	1	2	3	Original data
Figure	1	2	3	4
Raw prevalence adjusted to 10%	Yes	Yes	Yes	No
Unedited data sorted by prevalence	No	No	No	Yes
r^2	0.60	0.69	–	–
Fit parameter a	16.5	20.6	10.4	–
Fit parameter b	– 0.57	– 0.74	– 0.63	–
Data sources	Bovenzi (1994), Bovenzi et al. (1995), Bovenzi (2008), Bovenzi et al. (2008), Bovenzi (2010a), Chatterjee et al. (1978)	Bovenzi (1994), Bovenzi et al. (1995), Bovenzi (1998b), Bovenzi (2008), Bovenzi et al. (2008), Bovenzi (2010a), Chatterjee et al. (1978)	Bovenzi et al. (1995), Bovenzi (2008), Chatterjee et al. (1978)	Bovenzi (1994), Bovenzi et al. (1995), Bovenzi (1998b), Bovenzi (2008), Bovenzi et al. (2008), Bovenzi (2010a), Chatterjee et al. (1978)

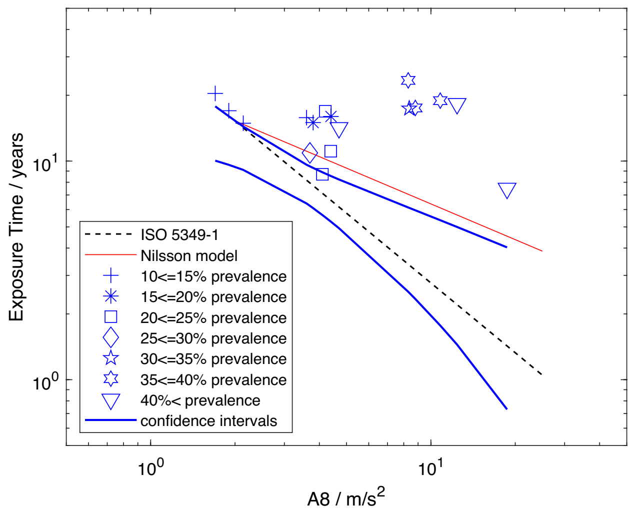

Fig. 4 Mean exposure times versus $A(8)$ reported in studies included in model 2 stratified by 5% prevalence intervals (see legend for symbols), all data points above exposure–response model from ISO 5349-1:2001 (dashed black line) and above or intersect the upper limit of the 95-percentile confidence interval of model 2 (thick blue lines), but not above model from Nilsson et al. (2017) (red line); note some data points with different prevalences cluster (color figure online)

results in the regression line for model 3 falling partly outside the confidence intervals of model 2, which, from the data accepted here from the Nilsson et al. (2017)'s meta-analysis, define the most probable region in which the "true" relation between exposure and the development of 10% VWF prevalence is predicted to occur.

Finally, the original, unedited data from the studies used in the analyses are plotted in Fig. 4 according to the reported point prevalences, which have been divided into ranges (e.g., from 10 to ≤ 15%, 15 to ≤ 20%, etc.), and identified by different symbols. As already noted, all the studies included here have a prevalence of 10% or more. Hence, all the data points should be on or above a line that represents a model predicting 10% prevalence. This is the case for the dashed black line portraying the model from ISO 5349-1:2001, but not for the red line showing the model from Nilsson et al. (2017). The data can also be seen to lie above or intersect the upper 95-percentile confidence limit from model 2 (thick blue line), confirming that the confidence interval associated with this model does define a range of exposures within which VWF is expected to occur at a prevalence of 10% or less.

Close inspection of Fig. 4 reveals that data points with different prevalences cluster (i.e., some different shaped symbols appear close together), implying unresolved issues remain in the method for calculating vibration exposure specified in the standard. The prevalences in these clusters range in one case from 10% to over 40% and in another from 30% to over 40%. The single tool studies included in this study can be found as the triangle on the very right in Fig. 4 as well as the square just above the continuous red line representing the model from Nilsson et al. (2017) and the diamond on the latter. As their raw prevalences were 23.4% (square), 26.6% (diamond) and 50% (triangle), it would be expected that they would lie at increasing "distance" in time or $A(8)$ from a line representing a 10% prevalence of VWF. This is at least roughly the case for the model from ISO 5349-1:2001, but less so for the model of Nilsson et al. (2017).

Discussion

A pooled analysis has been performed of studies identified as most likely to contain reliable data in a recent meta-analysis conducted by Nilsson et al. (2017). Additional selection rules have been introduced to control heterogeneity of the exposure data reported in different studies, which has been further reduced by re-calculating the lifetime exposure for studies in which a different metric was used from that employed here. Linear interpolation to a mean group prevalence of 10% has been used to reduce heterogeneity of the VWF point prevalences reported in different studies.

The PRISMA guidelines (Liberati et al. 2009) were followed in the meta-analysis, with publications screened by abstract first. Out of the originally 4335 publications obtained by the literature search, 4041 were discarded. The authors did not give reasons for this high number of excluded studies. The remaining 294 publications were screened in full-text. Of these, 41 were deemed usable for an analysis of Raynaud's phenomenon from exposure to vibration, as already noted, and another 11 studies were used to examine other health effects. The remaining 242 were excluded for reasons such as the aim of the study not being to evaluate the risk of HAVS, missing data on exposure or duplicate publishing of data. The chosen publications were then evaluated by a list of criteria designed to establish the risk of bias and hence the overall scientific "quality" of each study. The criteria weighted the subjective description of signs and symptoms, investigational methodology, differential diagnosis and staging of signs and symptoms. The weightings were not, however, incorporated in their derivation of the exposure–response model. For this the data from all studies included in the meta-analysis were deemed usable. By means of linear interpolation and extrapolation the mean exposure time at which there was a 10% prevalence of Raynaud's phenomenon was determined. This was plotted versus the respective $A(8)$-value. Then a further analysis was performed to create a predictive model.

Our analyses accepted the data sources believed by Nilsson et al. (2017) to contain low bias, and so avoided bias associated with the selection of studies by the present authors, but with some changes. Studies were screened using an additional set of selection rules introduced here to confirm the reliability of the data and compliance with the methods for evaluating vibration exposure in the international standards (Table 1), and only those complying with both Nilsson et al.'s and these rules were included in the models. Furthermore, the calculation of the mean exposure time at 10% point prevalence was limited to interpolation, hence all studies with a raw prevalence of less than 10% were excluded from the models described here.

The reasons for the exclusion of extrapolated data from the analyses can be seen from Fig. 5. This diagram exemplifies the estimation of the mean lifetime exposures necessary for two notional population groups to reach 10% prevalence VWF, to illustrate the limitations of extrapolation for the type of models developed here. One notional population group had a prevalence of 25% VWF when the mean exposure of the group was 15 years, and the second a prevalence of 4% when the mean exposure was 8 years. The example requires interpolation for the former population group and extrapolation for the latter.

The limitations of extrapolation may be illustrated by introducing uncertainty into the knowledge of the prevalence. In Fig. 5, the limitation takes the form of uncertainty concerning the magnitude of the observed, or raw, prevalence in each population group. This could arise, for example, from misdiagnosis, from subjects providing erroneous or misleading information (information bias), or from individuals being absent from the group at the time of a (cross-sectional) study. For the example in Fig. 5, the perturbation in the raw prevalence is taken to be ±0.5% (i.e., an error involving one person in a population of 100 vibration-exposed individuals). The consequent uncertainty in the exposure durations estimated for 10% prevalence is shown by the thick horizontal blue line for interpolation and red line for extrapolation. Clearly, linear extrapolation to 10% prevalence from an observed prevalence below 10% introduces uncertainty of substantial magnitude into the estimated 10% prevalence compared to that introduced by linear interpolation.

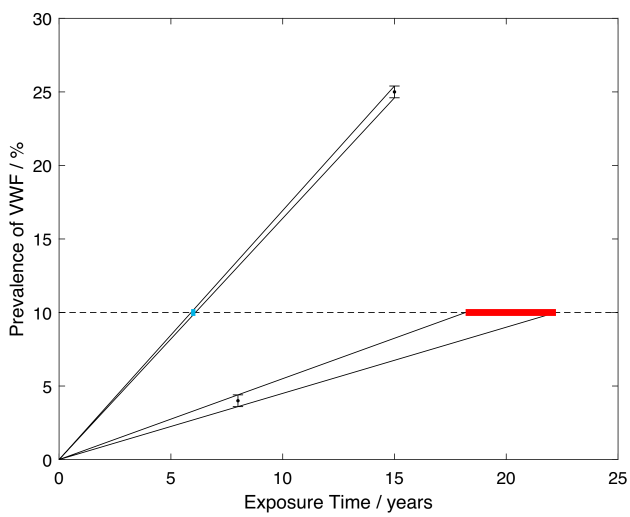

Fig. 5 Two notional studies with equal uncertainties in prevalence (black circles with error bars), linear interpolation and extrapolation including uncertainties to 10% prevalence (black lines), effect of uncertainties on estimation of exposure time at which 10% prevalence occurs (blue—interpolation, red—extrapolation) (color figure online)

Comparing Figs. 1 and 2 to the analysis by Nilsson et al. (2017) reveals that using only interpolation eliminated data points from the models with mean lifetime exposures of 50 years, and more (see their figure 17). Such mean group lifetime exposure durations are highly unlikely for any occupation, and can only be obtained by some form of extrapolation. Hence, for the reasons described, extrapolation can be expected to introduce errors in the models with the inclusion of every data point so obtained. Even excluding studies with prevalence below 10%, the data are scattered (see, for example, Fig. 2). The model from Nilsson et al. (2017) is located above all data points and is not generally included within the 95-percentile confidence intervals for models 1 and 2. Hence it is not considered a probable fit to these data. This is believed to result primarily from the inclusion of extrapolated data in Nilsson et al.'s model. In contrast, the model from the international standard lies within the 95-percentile in both Figs. 1 and 2 and, as more data are included in the analysis, the closer the regression line approaches that in ISO 5349-1:2001. While the confidence intervals alone cannot confirm the validity of the model employed in ISO 5349-1:2001, neither can they confirm the need for its revision.

When reliable data are selected for assessing the risk of developing VWF, Fig. 4 demonstrates that the ISO model provides a conservative prediction for the occurrence of 10% prevalence of VWF in a population group, as all data points lie above the line representing the model. This implies more exposure than depicted by the model in the ISO standard is needed to reach VWF prevalences of 10% or more. Furthermore, the 95-percentile confidence interval for 10% prevalence of model 2 lies below or intersects all data points in Fig. 4 and does not generally include the model from Nilsson et al. (2017), yet encloses the model from ISO 5349-1:2001. As the interval identifies the region within which the exposure–response relation most probably lies and where the prevalence is expected to be 10% or, from data deemed reliable, less, it supports the conclusion that the prediction of the model from the standard is conservative. Yet, if the methods for evaluating vibration exposures contained in ISO 5349-1:2001 were generally applicable to all power tools and machines, and working conditions, the distribution of the data in Fig. 4 should be such that prevalence increases with increasing $A(8)$ or lifetime exposure. However, data points with different prevalences and similar values of $A(8)$ cluster, as already observed, implying that at least one parameter in the construction of the vibration exposure (e.g., Eq. 1) needs to be revised or an additional factor or confounder taken into account.

In considering the need for revision, it is important to distinguish between the exposure–response relation in ISO 5349-1:2001 and the methods for estimating the exposure. The former came from the model developed by Brammer (1982a, b). This considered epidemiologic studies involving workers whose full-time occupations involved near-daily, day-long operation of a single power tool or machine and produced the dashed line in Figs. 1, 2, 3 and 4 that was subsequently adopted by the ISO for their standard. No adjustment was made for the different daily durations of exposure occurring in different occupations. Methods for quantifying the daily exposure to hand-transmitted vibration were formulated independently from the model by the architects of ISO 5349-1:2001, and have not been modified in the analyses reported here. These include: (1) the specification of an equinoxious contour for exposure to vibration at different frequencies [i.e., a frequency weighting; the ISO 5349 frequency weighting was employed in Brammer (1982a, b)]; (2) the relative importance of the frequency-weighted acceleration and the daily duration of exposure in constructing the daily exposure; and (3) the combination of exposures to different power tools or machines during a workday. The combination of daily exposures to construct a lifetime exposure also needs to be considered. None of these factors has yet been taken into account in the models developed here, and each may have an effect on the resulting prediction.

The analyses reported here do provide insight into one of the factors influencing the quantification of exposure, namely the combining of exposures to different power tools or machines during a workday. According to the standard, when multiple tools are used during a working day, the measured exposure to each can be summed to obtain an overall daily exposure, expressed by the $A(8)$-value, according to Eq. 1. The ISO exposure–response model is based on epidemiologic studies involving use of only one power tool or machine per day, as already noted, while the meta-analysis by Nilsson et al. (2017) contains only three such studies. In consequence, it is not possible to develop statistical inferences from these data. Nevertheless, it does appear by comparing the regression lines in Figs. 2 and 3 (or values for a and b of model 2 with those for model 3 in Table 4) that the exposure–response relation for daily exposures using only single power tools or machines may deviate from that for daily exposures involving multiple power tools or machines constructed using Eq. 1. This implies the need to reconsider the calculation of daily exposures when multiple power tools or machines are used during a workday.

While the clustering of data in Fig. 4 also suggests that the method for combining exposures during a workday in Eq. 1 needs to be reconsidered, the scatter of data points when all prevalences have been adjusted to the same value suggests that broader reconsideration of the method for calculating exposure may be necessary (see Figs. 1, 2). Inspection of the values for the coefficient of determination in Table 4 reveals that the inclusion of additional epidemiologic studies (i.e., model 1 → 2) increased r^2 from 0.60 to 0.69. The welcome, though modest, improvement in fit to the regression line is far short of that obtained in an analysis involving only exposures to single power tools during a workday ($r^2 = 0.82$) (Brammer 1982a). This last-mentioned analysis employed selection rules similar to those in Table 1, but only included studies in which the prevalence of VWF was 50%, or greater.

The origin of the data scatter in Figs. 1 and 2 cannot be deduced from the results of the analyses presented here, but suggests that any re-appraisal of the calculation of daily exposure will require reconsideration of at least the other primary factor in its specification, namely the vibration magnitude(s). The apparent limitations of the frequency weighting employed in the international standard for assessing the harmful effects of hand-transmitted vibration have been well documented (Bovenzi 2012; Brammer and Pitts 2012; Griffin et al. 2003). ISO has recently published a Technical Report that contains a frequency weighting specifically for assessing the risk of developing VWF, based on the analysis of Brammer and Pitts (2012) (ISO/TR 18570 2017). Also, the time history of exposures, and in particular the impulsiveness that characterizes the vibration of impact tools, will need to be considered in future evaluations of exposure–response relations (Starck and Pyykkö 1986; Starck et al. 1990).

The models derived here, as well as the model described by Nilsson et al. (2017), suffer from several limitations. Perhaps the most consequential is the estimation of the group mean lifetime exposure to reach 10% prevalence. The prevalence of VWF in a population group as exposure proceeds can be expected to follow a probability distribution dependent primarily on factors defining the health hazard to individuals and the number of persons in the group, combined with the changes in group membership. As the case definition of VWF is binary in nature, the period prevalence could be expected to approximately follow a cumulative normal distribution in a cohort with no change in membership, provided that there are a sufficient number of persons in the population group (ensured here by selection rule #6, Table 1). Deviations from the anticipated distribution will result from persons entering and leaving the population group as exposure continues as well as changes in the daily exposure (e.g., from changes in work practices and in power tools or machines), with the magnitude of the deviations depending on these factors. However, the essential curvilinear form of the relation between point prevalence and exposure time can be expected to be maintained. Hence, linear interpolation, as used here and by Nilsson et al. (2017), will likely tend to underestimate the lifetime exposure to 10% prevalence, and may render fortuitous the inclusion of the ISO prediction within the 95-percentile confidence intervals for the models. Consequently, future analyses will have to consider other methods of interpolation.

Another consideration is the correct identification of Raynaud's phenomenon due to vibration. Selection rules #7 to #9 (Table 1) have been introduced here to provide a common framework for assessing the epidemiologic data considered to contain low bias by Nilsson et al. (2017). The unintentional inclusion of individuals with signs and symptoms from causes other than vibration exposure in the observed prevalence also tends to underestimate the lifetime exposure to 10% prevalence by linear interpolation.

An additional consideration is determining the usage times for each power tool or machine used during a workday, and hence compiling a reasonable estimate of the daily exposure for the population group from observation or workers' recollections. Clearly, with more power tools and machines used daily, and with normal day-to-day variations in work, this task multiplies, and the uncertainty in the daily exposure will increase.

A further limitation of our study arises from all but one of the publications employed in the analyses being conducted by one research group in a single country (Italy). This outcome of the process developed for selecting studies to include in the models was fortuitous. The selection rules were finalized before their application to any study was considered. Nevertheless, our results are subject to possible author bias and limited geographical applicability.

Nilsson et al. (2017) rated each study included in their meta-analysis based on a numerical score to assess the risk of bias, Of the 41 studies deemed acceptable for consideration of the development of VWF, the studies conducted by Bovenzi and co-workers used to construct our models were ranked from 2nd to 17th, with an average ranking of 8th (most reliable data ranked #1). Thus, there is little doubt that the studies are of high quality, and so are unlikely to contain significant author bias of a nature to invalidate their inclusion in a pooled analysis.

Reports of environmental conditions that precipitate episodic finger blanching have focused on a wide range of cool or cold temperatures as, for example, experienced in the United Kingdom or the continental USA, with the trigger mechanism also involving central body temperature, metabolic rate, vascular tone and emotional state (Taylor and Pelmear 1975b; Hamilton 1918). That VWF is repeatedly reported in Italy with its moderate climate would suggest that vibration-induced vascular disturbances are to be expected in countries at similar or increased latitudes. According to Nilsson et al. (2017), VWF has been reliably documented to have occurred in Canada, Finland, Italy, Japan, Korea, Sweden, The Netherlands, the United Kingdom, and the USA (see their Table 1). The fact that the international standard places no geographical restriction on the application of its exposure–response relation is further evidence that the primary causative agent is believed to be vibration rather than environmental, ethnic, or lifestyle factors peculiar to a single country (ISO 5349-1 2001). The question of the universality of the vascular response to vibration, rather than the response being specific to a given country, has also been considered (Brammer 1978). It was reasoned that the introduction and adoption world-wide of one-man chain saws with similar technology in the late 1950s and early 1960s (Lee and Acres 2020), and hence vibration, should lead to similar latencies of VWF in population groups of forest workers if the primary causative agent were vibration. In fourteen studies of full-time chain saw operators published between 1964 and 1971, the mean latency for finger blanching was found to be 3.6 ± 1.0 years (mean ± standard deviation, SD). The short latency together with the small SD are suggestive of a vascular response that differs little between the countries in which the studies were conducted, which included Australia, Czechoslovakia, England, New Zealand, Scotland, and Tasmania in addition to many of the countries listed above. Thus our analyses are likely to be broadly applicable. However, the apparent absence of vibration-induced vasospasms being observed in a tropical climate has already been noted (Futatsuka et al. 2005; Su et al. 2013).

Conclusions

Regression analyses have shown that excluding data points obtained by extrapolation and from studies failing the selection rules developed here changed the model for developing a 10% prevalence of VWF in a vibration-exposed population group from that proposed by Nilsson et al. (2017). Furthermore, it has been shown that without these data points the models derived here are closer to the model in the international standard, ISO 5349-1:2001. Hence, while the analyses cannot confirm the validity of the exposure–response relation in ISO 5349-1:2001, neither can they confirm the need for its revision. However, the analyses do confirm that the exposure–response relation proposed by Nilsson et al. (2017) does not improve the prediction of the prevalence of VWF in vibration-exposed population groups.

The range of exposures within which VWF is predicted to occur at prevalences of 10% or less has been derived in the form of a 95-percentile confidence interval. The model proposed by Nilsson et al. (2017) generally falls outside this interval and hence cannot be considered a fit to the epidemiologic data. In contrast, the ISO model is found to fall within the confidence interval and, as more studies are included in the models constructed here, the best fit to the data tends toward the ISO model although it still differs considerably in gradient.

The results of this study also suggest that the ISO model provides a conservative prediction for the development of 10% prevalence of VWF in a population group. They also reveal that the present method for evaluating vibration exposure contained in the international standard needs revision. Specifically, the models imply the need to revise the calculation of daily exposure when multiple power tools or machines are used during a workday. In future studies, alternate formulations of the vibration magnitude as well as predictive models that better represent the development of the prevalence of VWF in a group of workers will be needed. And, finally, the data set will need to be expanded beyond the studies deemed usable in the meta-analysis by Nilsson et al. (2017), by including those not found by the search engines they used and those published since their meta-analysis was performed and in languages other than English.

Thus, at this time, we do not recommend changes to either the calculation of exposure or the exposure–response relation in ISO 5349-1:2001 (ISO 5349-1 2001) until further analyses of the issues identified here have been completed.

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Exposure–response relation for vibration-induced white finger: effect of different methods for predicting prevalence

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Abstract

A pooled analysis of vibration-induced white finger (VWF) in population groups of workers has been performed using the results of a published meta-analysis as source material (Nilsson T, Wahlström J, Burström L. Hand-arm vibration and the risk of vascular and neurological diseases a systematic review and meta-analysis. PLoS One. 2017:12(7):e0180795. https://doi.org/10.1371/journal.pone.0180795). The methods of data selection follow those described previously by Scholz et al. (in Scholz MF, Brammer AJ, Marburg S. Exposure-response relation for vibration-induced white finger: inferences from a published meta-analysis of population groups. Int Arch Occup Environ Health. 2023a:96(5):757–770. https://doi.org/10.1007/s00420-023-01965-w) to enable comparison with the results of the present work. The analyzed epidemiologic studies contain different prevalences of VWF observed after different durations of employment involving exposure to the vibration of power tools and machines. These prevalences are transformed to 10% prevalence by either linear or polynomial (i.e. "*S*"-shaped curvilinear) interpolation in order to compare with the exposure–response relation contained in the relevant international standard (ISO 5349-1:2001). An exposure–response relation is constructed using regression analysis for the time (in years) to reach 10% prevalence in a population group, when subjected to a daily vibration exposure calculated according to the procedures specified in the standard, $A(8)$. Good fits to the data are obtained when polynomial and linear prevalence interpolation is used. The 95-percentile confidence intervals (CIs) of the exposure–response relation predicted by polynomial prevalence interpolation lie at somewhat larger lifetime exposures than those obtained by linear prevalence interpolation. Uncertainty in the precision of polynomial prevalence interpolation is mitigated by giving equal weight to linear interpolation when interpreting the results. When the 95-percentile CIs of the exposure–response models obtained by linear and polynomial prevalence interpolation are used to define the most probable exposure–response relation, the resulting common range of values includes the ISO exposure–response relation. It is proposed that an exposure–response relation for the onset of VWF derived from a regression analysis is specified in terms of the lower limit of its CI. Hence, when exposure measures are constructed according to the ISO standard and equal weight is given to the results of the 2 methods for interpolating prevalence described here, the ISO exposure–response relation would be considered to provide a conservative estimate for a 10% prevalence of VWF to develop in a population group, at least for $A(8) > 4$ m/s^2. It thus remains the relation to use for assessing exposure to hand-transmitted vibration in the workplace. Additional research is needed to resolve inconsistencies in the ISO method for calculating daily exposures.

Key words: exposure–response relation; hand-arm vibration; prevalence; vibration white finger.

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What's Important About This Paper?

Hand-transmitted vibration is known to cause vibration-induced white finger (VWF). The accuracy of the exposure–response relation within ISO 5349-1:2001 has been repeatedly challenged. The study fitted data from a pooled analysis of epidemiologic studies to create exposure–response relations, and proposed a relation that provides a conservative estimate for 10% prevalence of VWF in a population group at exposures included in the ISO standard and is largely in agreement with the ISO model.

Introduction

Occupational exposure of the hands to vibration is well known to result in a complex of peripheral neurological, vascular, and musculoskeletal signs and symptoms known as the hand-arm vibration syndrome (Lawson *et al.*, 2011). While exposure has been controlled by regulation and legislation based on the international standard describing the measurement and evaluation of human exposure to hand-transmitted vibration (ISO 5349-1, 2001), the accuracy of the exposure–response relation within the standard has been repeatedly questioned (Futatsuka *et al.*, 1984; Walker *et al.*, 1985; Engström and Dandanell, 1986; Starck *et al.*, 1990; Tominaga, 1990; Keith and Brammer, 1994; Bovenzi *et al.*, 1995; Bovenzi, 1998a 2012; Nilsson et al. 2017; Gerhardsson et al. 2020; Scholz et al. 2023a). This relation predicts the time exposed (in years) for a group of workers in a given occupation to reach a 10% prevalence of the vascular component of the syndrome, colloquially known as vibration-induced white finger (VWF), from the magnitude of their daily vibration exposure. It will be referred to here as the ISO exposure–response relation. A recent, comprehensive meta-analysis of epidemiologic studies conducted over the last 70 yr has provided a valuable database with which to establish exposure–response relations in groups of workers experiencing essentially the same vibration exposure (Nilsson et al. 2017). With this information, the accuracy of the ISO exposure–response relation, which is based on an exposure–response model constructed more than 40 yr ago with the limited data available at that time (Brammer 1982a, b), can be assessed against the current state of knowledge.

There have been several exposure–response models proposed in the literature for VWF (Taylor et al. 1975a; Brammer 1982a, b, 1986; Griffin 1982; Miyashita et al. 1982; Tominaga 1982; Futatsuka et al. 1984; Bovenzi 1994, 1998a, 2010b; Bovenzi et al. 1995; Griffin et al. 2003; Sauni et al. 2009; Su et al. 2013; Nilsson et al. 2017; Scholz et al. 2023a). All the models, with the exception of those described by Nilsson et al. (2017) and Scholz et al. (2023a), were developed prior to the meta-analysis conducted by Nilsson et al., and so they could not take advantage of its assessment of the "quality" of the epidemiologic studies published since the end of the Second World War. Scholz et al. (2023a) not only followed the protocol employed by Nilsson et al. (2017) for selecting studies to include in their pooled analysis but also extended it by further selection rules.

Cross-sectional epidemiologic studies of population groups, each of which has involved exposure to the vibration of a different power tool, or tools, and/or machine(s) for a different time, can be expected to present different point prevalences of VWF at the time of the study. To be compatible with the ISO exposure–response relation, it is necessary to establish the mean years of employment in an occupation involving vibration exposure (D_y) for each population group to develop a 10% point prevalence of VWF, $D_{y,10}$. Hence, a method for transforming the prevalences observed in different epidemiologic studies to a common prevalence of 10% is required. The method for reducing this heterogeneity adopted in Nilsson et al. (2017) and Scholz et al. (2023a) was to assume a linear growth of prevalence with exposure time (in years).

The purpose of this contribution is to consider an alternate method for estimating a 10% point prevalence of VWF in population groups from the observed prevalence. This method predicts an "*S*"-shaped growth of prevalence with exposure time, thus allowing for the saturation in prevalence that must ultimately occur (i.e. the prevalence cannot be greater than 100%). The resulting exposure–response relation is compared with that derived using linear interpolation of prevalence in Scholz et al. (2023a). The goal is to establish the sensitivity of the exposure–response relation to the method for estimating a 10% prevalence of VWF. For this reason, the same datasets and general modeling methods employed by Scholz et al. (2023a) are also used here and are summarized in the Methods section. Complete descriptions are to be found in Scholz et al. (2023a). The results of the analysis employing the dataset believed to contain the most reliable information on the point prevalence of VWF in populations of vibration-exposed workers is then presented. The model is compared with the predictions of the corresponding exposure–response model in Scholz et al. (2023a) and with the ISO exposure–response relation to answer questions surrounding its accuracy. The consequent interpretation of the ISO exposure–response relation and uncertainties in the analyses are then discussed, followed by our conclusions. A more extensive discussion of exposure–response relations for VWF and on modeling the change of its prevalence in a population is to be found in Scholz et al. (2023a) and Scholz et al. (2023b), respectively.

Methods

Dataset for pooled analysis

The present work is an extension of the pooled analysis described by Scholz et al. (2023a). It was based on the meta-analysis conducted by Nilsson et al. (2017), who screened 4,335 publications on the hand-arm vibration syndrome on the basis of accepted criteria to reduce bias (Liberati et al. 2009) and used the data from the 25 selected studies to create an exposure–response model. Scholz et al. (2023a) added a further set of selection rules designed to further reduce heterogeneity by (i) ensuring that the vibration measurements and exposures complied with the practices described in the international standard, (ii) confirming persons experiencing white fingers unconnected to vibration exposure were excluded from the prevalence estimate, and (iii) including only studies in which the prevalence of VWF was greater or equal to 10% [see Table 1 of Scholz et al. (2023a)].

Thus, for a study to be included, the daily vibration exposure must be expressed in terms of the 8-h, frequency-weighted, energy-equivalent acceleration sum as defined in the ISO standard, subsequently referred to here as the daily exposure or $A(8)$. Scholz et al. (2023a) also introduced rules to confirm that a differential diagnosis for VWF had been conducted. If in doubt, there was a requirement for the inclusion of a nonexposed control group in the study and consequent adjustment to the reported raw prevalence to account for cases unrelated to vibration exposure. Hence, 2 point prevalences could be established for each population group: zero prevalence VWF at zero exposure time (as all cases unrelated to VWF have been removed from the population) and the observed or adjusted prevalence, as appropriate, at the exposure time at which the cross-sectional study was conducted. This time would usually be the mean duration of employment of group members in the activity involving vibration exposure (in years). Additionally, a minimum group size was established (30 persons). Studies eligible for inclusion in the pooled analysis thus contained the point prevalence of VWF, D_y, and $A(8)$. A dataset was hence formed containing population groups, all of whose members were engaged near-daily in essentially the same activity involving the same daily vibration exposure, either from using a single tool or from using multiple tools and machines (e.g. forestry chain saw operators, miners operating rock drills, factory workers using a combination of power tools, etc.).

While almost all studies accepted into our pooled analysis reported $A(8)$ values, one study required $A(8)$ to be calculated from the provided vibration spectra and daily tool/machine usage time. Another required the lifetime exposure to be converted from the total cumulative hours of usage into estimates of D_y. The studies considered from Nilsson et al. (2017)'s meta-analysis and the decision on their use in the present analysis are reported in Table 2 of Scholz et al. (2023a), and for that reason are not repeated here. The most common reasons for exclusion were that either no $A(8)$ value or data to calculate it were reported or that the measurement methods did not comply with those in the international standard.

Interpolation of prevalence to a common value

The change over time of the prevalence of VWF in a population group, all of whose members are engaged in essentially the same activity to which a common daily vibration exposure can be assigned, is expected to follow an "*S*"-shaped curvilinear function, as shown in Fig. 1A. In this example, the period prevalences from the commencement of an occupation involving vibration exposure recorded at intervals at which D_y ranged from 4 to 36 yr are shown by asterisks. It is assumed based on the design of the study that persons with white fingers from causes other than exposure of the hands to vibration have been excluded from the dataset so that at zero exposure time, the prevalence of VWF is zero. Hence, the *y*-intercept of the prevalence growth function is zero.

Now the outcome of a cross-sectional study is typically a single-point prevalence recorded at the mean group exposure time, D_y. For the purposes of the present discussion, 2 notional examples of such studies taken from the dataset in Fig. 1A are illustrated in Fig. 1B: the study was "conducted" after (i) 26 yr' exposure (red, upper asterisk) and (ii) after 4-yr' exposure (green, lower asterisk). To predict a chosen prevalence, here 10% for comparison with the ISO exposure–response relation, the mean group exposure time at which the point prevalence was reported is linearly interpolated to estimate the time at which 10% prevalence occurs in Scholz et al. (2023a). The interpolation employs the 2 available data points (zero prevalence at zero exposure time and the red asterisk) and is shown by the red line in Fig. 1B. It yields $D_{y,10,i}$= 10 yr for this example. Scholz et al. (2023a) excluded studies in which the observed prevalence was less than 10%, which would have required extrapolation to

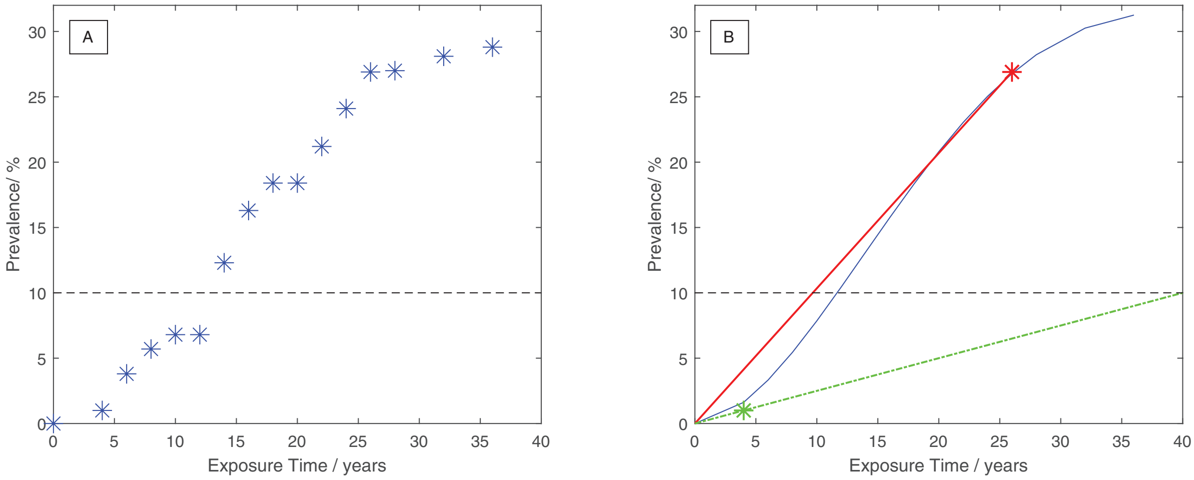

Fig. 1. (A) Example of growth of period prevalence of VWF with accumulating mean exposure time in a population group, D_y (asterisks—data from Nilsson et al. [1989]). (B) Single data point from a notional cross-sectional epidemiologic study of this population group conducted after 26-yr' exposure (red asterisk), with polynomial interpolation (blue, "*S*"-shaped curve), and linear interpolation (red, continuous line) to zero prevalence. Data point from a second notional cross-sectional epidemiologic study of the population group conducted after 4-yr' exposure (green asterisk), with linear extrapolation from zero prevalence through the data point (green, dash-dotted line). The estimated time at which 10% prevalence occurs in this population group, $D_{y,10}$, is for linear interpolation 10 yr, for polynomial interpolation 12 yr, and for linear extrapolation 40 yr.

reach this value and introduced the potential for a substantial error. This is shown by the green line in Fig. 1B and yields $D_{y,10,e'}$= 40 yr for this example of extrapolating the prevalence to 10%.

The use of linear interpolation to estimate $D_{y,10}$ for every study in the dataset is replaced by interpolation using a polynomial model of VWF prevalence growth in a population from Scholz et al. (2023b) for the present analysis, which is shown by the blue curve in Fig. 1B. This prevalence growth function is adapted to each analyzed population group by inserting the respective $A(8)$ value into the following expression for prevalence:

$$P \approx \left(\frac{A(8)}{3.59}\right)^{0.3} \cdot [(0.2985 + a'_1) \cdot D_y + 0.1001 \cdot {D_y}^2 + (-0.003213) \cdot {D_y}^3 + 0.00002886 \cdot {D_y}^4] \quad (1)$$

where P is the point prevalence, D_y is the mean group exposure time in years, and a'_1 is a fitted, nondimensional parameter that accounts for study-specific changes in exposure due to, for example, ergonomic, biodynamic, and environmental factors and changes in group membership over time. The numerical coefficients of D_y are derived from studies that recorded the change in the prevalence of VWF in a population group. They have been shown to provide excellent fits to the (few) studies in which period or point prevalences have been reported at different exposure times (Scholz et al. 2023b). The first part of the equation includes the $A(8)$ value and therefore allows the model to account for different daily vibration exposures.

Hence, for each study in the dataset, the single prevalence obtained in the study combined with the origin is used in a regression analysis to fit Equation 1 by adapting a'_1 for a given $A(8)$. The resulting polynomial is used to determine the exposure time at which the prevalence is 10%.

For the examples in Fig. 1, the estimated exposure times for the population group to reach 10% prevalence are: 10 yr for linear interpolation, as already noted, and 12 yr for polynomial interpolation. While the exposure time at which the prevalence of VWF in this population group was 10% was not recorded, it can be seen from Fig. 1A to have occurred between 12- and 14-yr exposure.

At first sight, $D_{y,10}$ computed using polynomial interpolation might always be expected to be greater than that obtained by linear interpolation, as shown in Fig. 1B. However, the reverse can occur in circumstances such as a rapid increase in prevalence followed by a long plateau during which the cross-sectional study was performed.

Exposure–response models

The exposure–response model of ISO 5349-1 (2001) considers the daily exposure of all members in a population group of vibration-exposed workers, each of whom performs essentially the same activity, to be the same. Hence, all sources of variability between group members (e.g. arising from physical, biodynamic, and individual factors, including biologic susceptibility, work practices, and posture) are subsumed by other model parameters, which in this case is the prevalence. The same assumption underlies the models constructed here and in Scholz et al. (2023a).

The ISO exposure–response relation predicts the relation between $D_{y,10}$ and $A(8)$ at which 10% prevalence of VWF will occur and is believed to apply to all occupations in which vibrating power tools and machines are used. However, the standard states that it is only "provisionally" applicable to repeated shock excitations. For comparison with this relation, an exposure–response model is obtained by means of a regression analysis to obtain the best fit to the dataset. Curves, like those in ISO 5349-1 (2001) and Scholz et al. (2023a), are obtained using

$$D_{y,10} = a \cdot A(8)^{b} \qquad (2)$$

where a and b are the fit parameters. The results of each epidemiologic study are given equal weight in the least-squares curve fit.

Results

Models using polynomial or linear prevalence interpolation

The $A(8)$ and D_y values, the population sizes, and the point prevalences of VWF in the respective studies, as taken from Scholz et al. (2023a), are listed in Table 1. The table, furthermore, contains the linearly and polynomially interpolated exposure times at which it is estimated that 10% prevalence occurs. The fit parameter of the polynomial prevalence interpolation, a'_1, is also shown in that table. For all 17 analyzed groups of workers, the estimated $D_{y,10}$ is greater with polynomial interpolation than with linear. For 2 groups, a'_1 is negative; in 10 cases, it is between 0 and 1, and for 5 groups, it exceeds 1.

To construct an exposure–response relation in the same form as that in the ISO standard, the polynomially interpolated exposure times, $D_{y,10}$, are regressed on the respective $A(8)$ values using Equation (2). In Fig. 2, these data points are shown as asterisks, with daily exposures to single power tools and/or machines as larger and bold asterisks, together with the respective regression analysis.

The regression fit is shown in Fig. 2 as a thin blue line, while the corresponding 95-percentile confidence interval (CI) is displayed by thick blue lines. Figure 2 also contains the ISO exposure–response relation (dashed black line) and the 95-percentile CI lines for

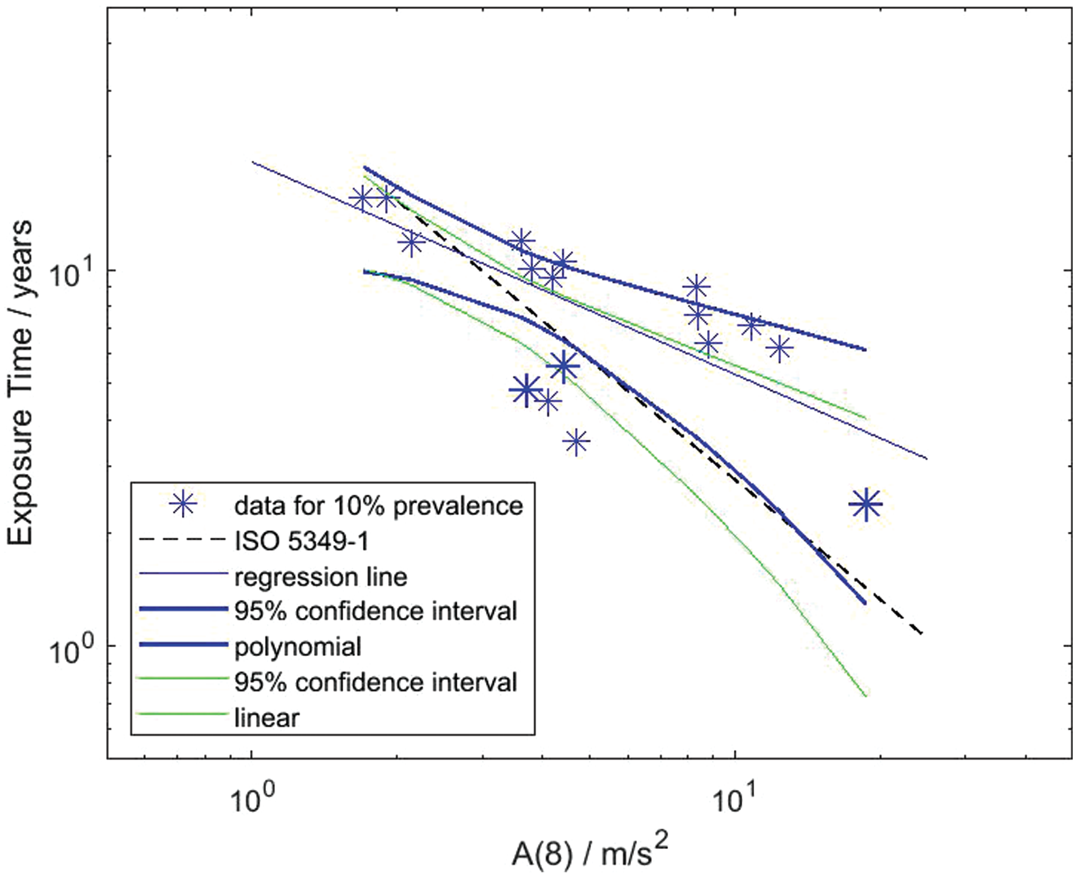

Fig. 2. Exposure–response models in the form employed by ISO 5349-1:2001—$D_{y,10}$ versus $A(8)$. Dataset (asterisks), the single tool studies are indicated by larger and bold asterisks, regression analysis for the model from polynomially interpolated prevalence data (thin blue line), 95-percentile CI curves (thick blue lines), and 95-percentile CI curves of model from linearly interpolated prevalence data (Scholz et al. 2023a, green lines), and ISO exposure–response relation (black dashed line).

the corresponding model using linear interpolation to 10% prevalence (model 2 from Scholz et al. (2023a), green lines).

Comparing models created from linearly and polynomially interpolated prevalences shows that the ISO exposure–response relation is no longer always well within the 95-percentile CIs predicted for 10% prevalence of VWF by polynomial interpolation (see Fig. 2). Rather, the results suggest that it follows the lower limit of the 95-percentile of the model obtained from polynomially interpolated prevalence data for $A(8) > 4$ m/s^2 and deviates from that limit at smaller values of $A(8)$.

In Table 2, the r^2-values and fit parameters a and b of the model from linearly interpolated prevalence data from Scholz et al. (2023a) and the model from polynomially interpolated data are presented, as well as the data sources. The r^2-value of the model created with the polynomially interpolated data points is smaller than that created with linearly interpolated prevalences. The absolute values of both fit parameters of the model created from polynomially interpolated data are also slightly smaller than those from the model in Scholz et al. (2023a).

While the reduction in r^2 might be considered evidence that polynomial interpolation is inferior to linear interpolation for these data, there is an alternative interpretation. Close inspection of the larger and bold asterisks in Fig. 2 reveals an apparent difference in response to daily exposures involving multiple power tools and machines as opposed to single power tools and machines. The larger and bold asterisks representing studies in which single power tools or machines were used daily can be seen not to lie randomly within the datasets as might be expected, but rather all lie below the regression fit to the data. In contrast, the asterisks for studies involving daily exposures to multiple power tools and machines mostly lie above the regression line. This implies that there is a discrepancy between the assessment of daily exposures to single as opposed to multiple power tools and machines by $A(8)$. The former interpretation that polynomial interpolation is inferior to linear interpolation is also at odds with the curvilinear growth in prevalence over time in a population group, as shown in Fig. 1A, which has been observed in other documented studies of the change in prevalence of VWF (see, e.g. Futatsuka and Ueno 1985). The latter interpretation thus appears more likely.

In Fig. 3, the point prevalence data are plotted as reported in the epidemiologic studies, adjusted if necessary to exclude persons with white fingers unconnected to vibration exposure, where the respective point prevalences are encoded in the symbols. The figure includes the ISO exposure–response relation (dashed black line) and the CIs of the current model generated from polynomially interpolated prevalence data (blue thick lines) and of the model generated from linearly interpolated prevalences from Scholz et al. (2023a) (green lines). The 95-percentile CI of the latter almost completely includes the model from the international standard, while the lower CI of the present model lies almost on the ISO model at values of $A(8) >$ 4 m/s^2 as already noted. While the CI from Scholz et al. (2023a) is below almost all data points and only intersects 2 of them (see green curves), the interval from the present study encloses 2 data points and intersects 2. One of the enclosed data points is in the 10–15% prevalence range (cross), and one is between 20% and 25% prevalence (open square). One of the data points on the (blue) line is in the 25–30% prevalence interval (diamond), and the other is in the 10–15% prevalence range (cross).

Figure 3 also shows that 3 of the 4 studies in which the prevalence is in the range of 10–15% lie on, or very close to, the ISO exposure–response relation and one above. There are no studies below the ISO relation, which, if present, would have indicated that the ISO exposure–response relation fails to provide sufficient protection from VWF.

Models that can be compared with the ISO exposure–response relation

A comparison of the ISO exposure–response relation with others for predicting a 10% prevalence of VWF is shown in Fig. 4. It contains the unedited epidemiologic data stratified by point prevalence, as also shown in Fig. 3, and includes those models that are in the same format as the ISO relation or can be converted into it to allow a comparison. In addition to the models already discussed and the ISO exposure–response relation, there is a model by Nilsson et al. (2017) and 2 models by Bovenzi (Bovenzi, 1994), and Bovenzi and co-workers (Bovenzi *et al.*, 1995). The model by Nilsson et al. (2017) is shown by the red line in Fig. 4. The model by Bovenzi (1994) (orange line) was based on one population of stone workers, and the model by Bovenzi et al. (1995) (turquoise line) on one population of forestry workers, which limits their general applicability. They lie below all other models and suggest exposure to vibration is far more hazardous than the other models predict and that working populations have experienced. In contrast, the model from Nilsson et al. (2017) (red line) lies above the data point for one epidemiologic study in which the reported VWF prevalence was in the range of 20–25% and intersects 2 studies with different daily vibration exposures (i.e. different $A(8)$ values), one of which reported a VWF prevalence in the range 25–30% and the other 10–15%. Hence, this model substantially underestimates the risk

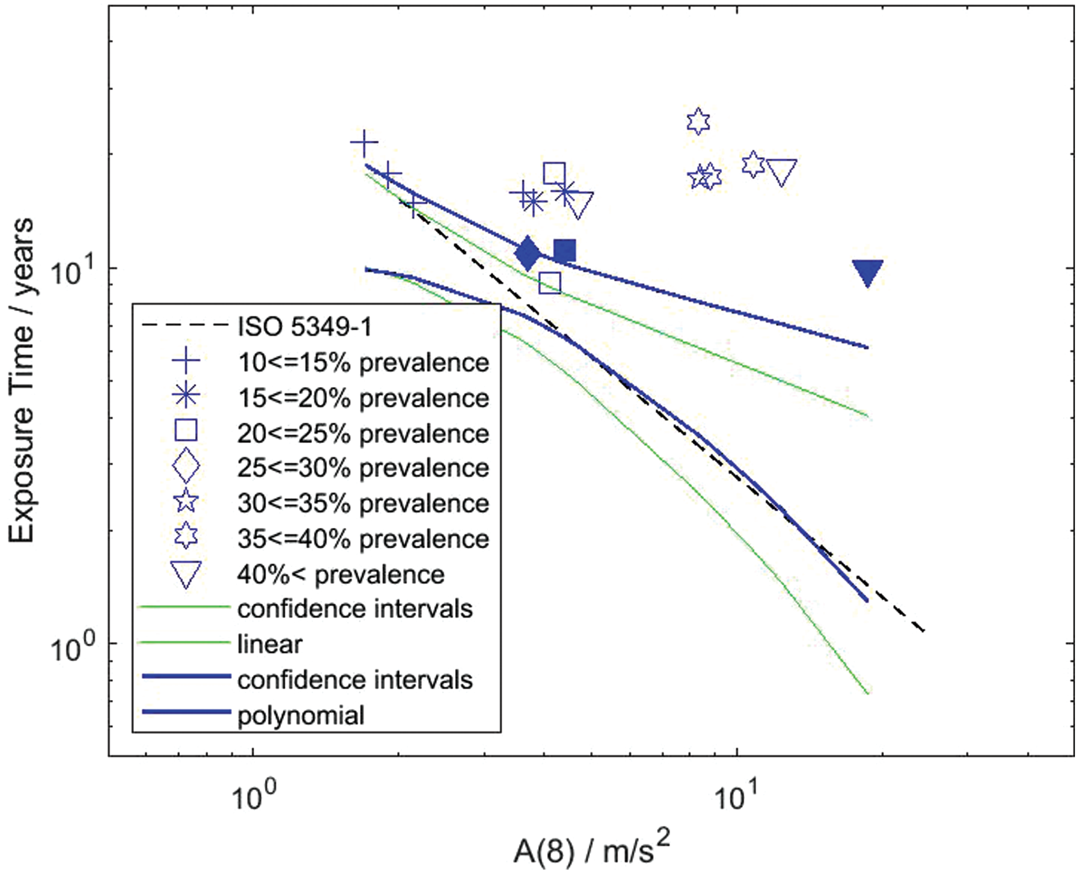

Fig. 3. Point prevalences reported in the used epidemiologic studies, adjusted if necessary to exclude persons with white fingers unconnected to vibration exposure, shown by symbols sorted by prevalence and plotted as D_y versus $A(8)$, data for daily use of single power tools or machines shown by filled symbols, 95-percentile CI curves of model constructed using linearly interpolated prevalence data from Scholz et al. (2023a) (green lines), 95-percentile CI curves from model constructed using polynomially interpolated prevalence data (thick blue lines), and ISO exposure–response relation (black dashed line).

of developing VWF and would not provide protection for workers using vibrating power tools or machines. Both the models in the analyses described here, shown by the blue and green lines, lie below the data points from epidemiologic studies yet lie above the ISO exposure–response relation for $A(8)$ greater than about 3–4 m/s^2. Thus, they neither substantially underestimate nor overestimate the risk of workers developing VWF.

The most apparent difference between the exposure–response models generated from linearly and polynomially interpolated prevalence data is that the latter has a smaller slope than the model from Scholz et al. (2023a) (viz.: −0.74 for linearly, and −0.56 for polynomially interpolated prevalence data—see Table 2). Also, the gradient of the model generated from polynomially interpolated prevalence data is close to that found by correlating the exposure times and $A(8)$ values for 10% prevalence of VWF in the studies included in Nilsson et al. (2017)'s meta-analysis (compare blue and red lines in Fig. 4).

Discussion

The present pooled analysis includes studies with the least bias, according to Nilsson et al. (2017). Their selection was enhanced by our selection rules in Scholz et al. (2023a), which focused on compliance with ISO 5349-1 (2001), on confirming signs and symptoms were associated with vibration exposure, and on studies with more than 10% prevalence. The exclusion of studies by our selection rules reduced the dataset from 25 to 7 studies, of which almost all turned out to originate from the same research group despite the authorship not having been considered in the selection process. Additionally, refraining from extending the dataset allows for a direct comparison between the influences of the 2 methods for interpolating prevalence on the exposure–response relation. The studies accepted by Nilsson et al. (2017), but not used here were most commonly rejected due to the vibration measurement method or lack thereof or lack of a value for $A(8)$, as already noted. A second reason for exclusion was to

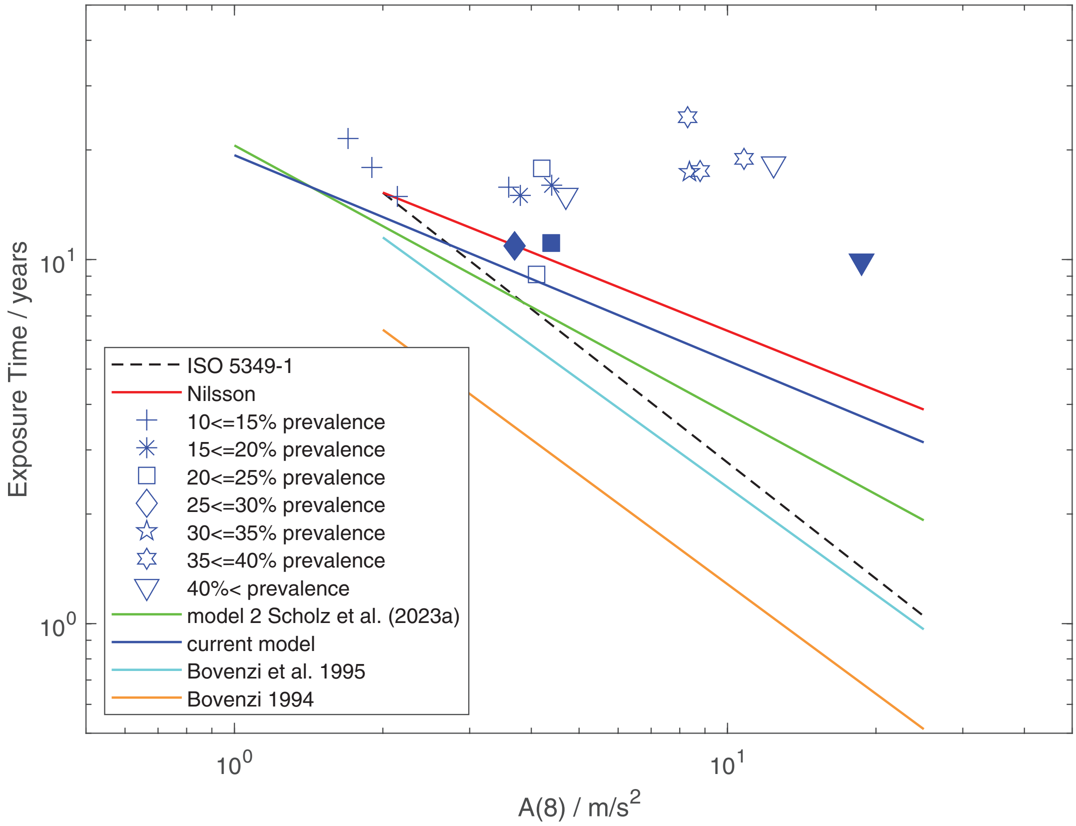

Fig. 4. Exposure–response models predicting 10% point prevalence of VWF plotted as $D_{y,10}$ versus A(8) compared with the prevalence of VWF reported in the included occupational groups, which has been adjusted if necessary to exclude persons with white fingers unconnected to vibration exposure and is shown by a symbol incorporating the magnitude of the prevalence. Data for daily use of single power tools or machines are shown by filled symbols. Model from ISO 5349-1 (2001) (black dashed line), model generated from linearly interpolated prevalence data from Scholz et al. (2023a) (green line), and model generated from polynomially interpolated prevalence data (blue line), model in Bovenzi et al. (1995) based on data from forestry workers (turquoise line), model in Bovenzi (1994) based on data from stone workers (orange line), and model from Nilsson et al. (2017) (red line) .

avoid extrapolated prevalence data in the generation of our exposure–response models. Figure 1 illustrates that the error introduced by extrapolating the observed, or adjusted, prevalence to 10% is greater than that introduced by interpolation. In these examples, linear interpolation underestimates the mean exposure time to reach 10% prevalence by 17%, while linear extrapolation from the prevalence recorded in the population after 4 yr exposure overestimates the exposure time by 233%. The comparatively large error introduced by extrapolating observed prevalences of <10% to 10% is believed to be the reason for the Nilsson et al. (2017) model, which includes studies in which the observed prevalence is less than 10%, underestimating the risk of developing VWF (see the red line in Fig. 4).

While the polynomial function from Scholz et al. (2023b) appears to represent the growth of prevalence in a population better than linear interpolation (e.g. see Fig. 1B), there is still some uncertainty around the magnitude of the exponent (q = 0.3) in Equation 1. Owing to the limited number of studies that provides a point prevalence for a group of workers at more than one exposure time, the exponent was determined from one dataset and tested on the only other independent dataset not used in deriving the polynomial prevalence growth function. Clearly, the availability of more test options would be desirable to reduce uncertainty in the magnitude of the exponent. Also, the large positive values of a'_1 in Table 1 require further investigation, as values of $a'_1 > 1$ substantially increase the growth rate of the prevalence–time function [e.g. see Figure 7a of Scholz et al. (2023b)].

There is one difference in the data used for interpolation between the present analysis and those of Scholz et al. (2023a). The study by Chatterjee et al. (1978) provided a mean and a median value for D_y. Their analyzed population group consisted of workers from 4 different mines. In 2 figures [Figures 5 and 6 in Chatterjee et al. (1978)], the prevalence is plotted separately for the mean and median exposure times. The relation between the median exposure time and prevalence appears to be nearly linear, while that for the mean exposure time shows a pattern that resembles more a curve such as that portrayed in Fig. 1A. Hence,

Table 1. Daily exposures, $A(8)$, and exposure times (in years), D_y, population sizes and point prevalences derived from the publications, both the linearly and polynomially interpolated exposure time to reach 10% prevalence, $D_{y,10}$, and parameter a'_1 from the polynomial interpolation (see Equation 1).

Study	$A(8)$/m/s^2	D_y/ years	Population size	Pre-valence/%	Linear interpol. $D_{y,10}$/ years	Poly. interp. $D_{y,10}$/ years	a'_1
Bovenzi (1994)	8.4	17.4	570	30.2	5.9	7.6	0.396
Bovenzi (1994)	12.4	18.3	145	40.7	4.5	6.2	0.571
Bovenzi (1994)	2.1	14.9	188	13.8	10.8	11.8	0.178
Bovenzi (1994)	10.8	18.9	237	36.7	5.2	7.1	0.427
Bovenzi et al. (1995)	4.4	11.1	222	23.4	4.7	5.6	1.20
Bovenzi (1998b)	1.9	17.9	132	12.1	14.8	15.5	−0.140
Bovenzi (1998b)	4.2	17.8	65	23.1	7.7	9.5	0.282
Bovenzi (1998b)	1.7	21.5	140	15.0	14.3	15.5	−0.111
Bovenzi (1998b)	8.3	24.6	41	36.6	6.7	9.0	0.180
Bovenzi (1998b)	4.7	15.0	31	51.6	2.9	3.5	2.27
Bovenzi (1998b)	4.1	9.1	165	23.0	4.0	4.5	1.73
Bovenzi (2008)	3.7	10.9	128	26.6	4.1	4.8	1.64
Bovenzi et al. (2008)	4.4	16.0	216	18.1	8.8	10.5	0.137
Bovenzi et al. (2008)	3.6	15.8	183	14.8	10.7	12.0	0.0128
Bovenzi et al. (2008)	8.8	17.5	33	36.4	4.8	6.4	0.637
Bovenzi (2010a)	3.8	15.0	249	17.3	8.7	10.1	0.228
Chatterjee et al. (1978)	18.7	9.9	42	50.0	1.5[a]	2.4	2.34

[a]Calculated with a median group exposure time of 7.5 yr.

Table 2. Details of models, including prevalencea interpolation method. The values of r^2 for the regression analyses (Equation 2), fit parameters a and b of the models from Scholz et al. (2023a) and the present analysis, and sources of the data included in each model (N.B. b in ISO 5349-1:2001 is −1.06, a is 31.8).

Source	Scholz et al. (2023a)	Present analysis
Interpolation method	Linear	Polynomial
r^2	0.69	0.56
Fit parameter a	20.6	19.4
Fit parameter b	−0.74	−0.56
Data sources	Bovenzi (1994); Bovenzi et al. (1995); Bovenzi (1998b); Bovenzi (2008); Bovenzi et al. (2008); Bovenzi (2010a); Chatterjee et al. (1978)	

the median value was used for linear interpolation in Scholz et al. (2023a) and the mean exposure time was used in the present analysis. The difference between linear and polynomial interpolation to a prevalence of 10% is from 1.5 to 2.4 yr in this population (see Table 1).

Perhaps, the closest to the "true" exposure–response relation for the onset of VWF that can be obtained from these analyses is to focus on the region common to the 95-percentile CIs identified here by our models. Close inspection of Fig. 3 reveals that there is a small region between the lower blue curve and upper green curve that converges from large $A(8)$ values down to about 3–4 m/s^2, below which the contours diverge. The ISO exposure–response relation lies on the lower boundary of this region (i.e. the boundary defined by the lower blue curve) from large $A(8)$ values to an $A(8)$ value of about 4 m/s^2 before crossing the interval to reach the upper limit (i.e. the green curve) at $A(8)$ = 2 m/s^2. While the ISO exposure–response relation largely remains on the boundary of the region within which the "true" exposure–response relation is believed to occur according to our models, the difference in slope of the relation in the standard from those in the present work is substantial (e.g. see Fig. 4 and values of b in Table 2).

However, regression lines, by their nature, will inevitably over- and underestimate the response to vibration recorded in individual epidemiologic studies. This is clearly evident from the locations of the 10% prevalences predicted for the individual studies (asterisks) relative to the regression line (thin blue line) in Fig. 2 (i.e. the asterisks can be seen to be scattered both above and below the thin blue line). This observation suggests that an exposure–response relation should not be specified in terms of the regression line itself, but perhaps rather in terms of a contour forming the lower limit of the CI defined by the regression analysis. Thus, when exposures are constructed according to the procedures specified by the ISO standard, its exposure–response relation, which mostly falls on the lower limit of the CIs common to both of our models (see Fig. 3), can be considered to provide a conservative estimate for 10% of a vibration-exposed population group to develop VWF, at least for values of $A(8)$ exceeding 4 m/s^2. However, it does not represent the best-fit regression line for such data.

There remain concerns surrounding the methodology adopted for assessing daily vibration exposure in ISO 5349-1:2001. To appreciate these, it is important to distinguish between the ISO exposure–response relation, i.e. the dashed line in Figs 2–4) and the method for calculating the daily exposure, $A(8)$. The former is based on the model by Brammer (1982a, b, 1986), as already noted, while the latter was devised by the architects of ISO 5349-1:2001. The clustering of data points with different prevalences in Figs 3 and 4 (i.e. the closeness of different shaped symbols with similar magnitudes of $A(8)$ and D_y) suggests that the method for calculating daily exposure needs to be reconsidered in order to eliminate this inconsistency. The evaluation of exposure time, both daily and cumulative (i.e. years), also factors in and has mostly been determined on the basis of workers' recollections, which are prone to error. This error is likely to accumulate with the number of power tools or machines used in a workday. It should be noted that the 3 single power tool studies, in which this uncertainty would be expected to be comparatively small, all reported similar mean exposures, D_y, and so are distributed horizontally in Figs. 3 and 4 (shown by filled symbols), with the highest prevalence associated with the largest value of $A(8)$, as would be expected. Another concern is the apparent difference in response to daily exposures involving multiple power tools and machines as opposed to single power tools and machines, as noted above and shown in Fig. 2. However, the frequency weighting may also play a role in the discrepancies. The limitations of the currently employed frequency weighting, which is used both in the Brammer model and in calculating $A(8)$, have been shown by several studies (Griffin et al. 2003; Bovenzi 2012; Brammer and Pitts 2012). An alternate frequency weighting has been introduced that is believed to provide a better fit to the development of VWF from exposure to hand-transmitted vibration (ISO/TR 18570, 2017). And finally, neither these analyses nor the ISO metric for daily exposure differentiate between continuous and transient vibrations, i.e. mechanical shocks, which may also influence the exposure–response relation as well as a factor into inaccuracies in prevalence prediction.

Conclusions

To address questions regarding the validity of the ISO exposure–response relation and the influence of the interpolation method for transforming prevalences to 10%, exposure–response relations have been constructed for the onset of VWF that are applicable generally to persons whose hands are occupationally exposed to vibration. No epidemiologic studies included in the pooled analyses were conducted in tropical climates, so the applicability of the relations to these environments is unknown. A regression analysis shows that a good fit to the data can be obtained when polynomial interpolation is used to transform the prevalences of VWF observed in epidemiologic studies to a common prevalence of 10%, although the gradient of the resulting exposure–response model is somewhat less than that obtained previously by linear prevalence interpolation. The 95-percentile CIs obtained by the regression analysis from polynomially interpolated prevalences lie at somewhat larger lifetime exposures for a given daily exposure than those obtained by the model that is based on linearly interpolated prevalences.

Uncertainty in the precision of polynomial interpolation to 10% prevalence can be mitigated by giving equal weight to linear interpolation in interpreting the results. When the CIs of the models obtained from linearly and polynomially interpolated prevalence data are combined to define the region that includes the most probable exposure–response relation, they almost completely enclose the exposure–response relation contained in the ISO standard. However, the gradient of the ISO exposure–response relation clearly deviates from those found in the present work.

It is proposed that an exposure–response relation should not be specified in terms of a regression line itself, but rather in terms of a contour formed by the lower limit of its CI. Thus, when exposure measures are constructed according to the ISO standard and equal weight is given to the results of the 2 methods for interpolating prevalence described here, its exposure–response relation would be considered to provide a conservative estimate for 10% of a population group to develop VWF, at least for $A(8) > 4$ m/s^2. It thus remains the relation to use for assessing exposure to hand-transmitted vibration in the workplace, although inconsistencies in the ISO method for calculating daily exposures remain to be resolved.

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Conflict of interest statement

The authors declare that they have no known competing interests that could have appeared to influence the work reported in this paper.

Data availability

The research data associated with this article are included within the article.

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