Using "Exposure Prediction Rules" for Exposure Assessment

An Example on Whole-Body Vibration in Taxi Drivers

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Background: It is often difficult and expensive to make direct measurements of an individual's occupational or environmental exposures in large epidemiologic studies.

Methods: In this study, we used information collected in validation studies to develop a prediction rule for assessing exposure in a study with no direct measurement. We established a prediction rule through mixed-effect modeling of direct measurement data and information on observable exposure predictors and their interactions. Specifically, we used 383 measures of whole-body vibration from 247 professional taxi drivers and attempted to quantify vibration exposures for individuals in a large study on low back pain.

Results: Using the "jackknife method," we found that our prediction rule had an acceptably low relative prediction error of 11% (95% confidence interval-10–12%). Implementing the prediction rule would result in measurement errors independent of low back pain and of all identified and observable predictors of whole-body vibration. We applied the predicted levels to compute each person's daily exposure, and found a strong association between the predicted daily whole-body vibration exposure and prevalence of low back pain. This supported the construct validity of the exposure prediction rule.

Conclusions: The predictive and construct validity of our prediction rule suggests that this general statistical approach can be useful in other occupational settings to improve the quality of exposure assessment.

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Exposure assessment remains a major obstacle in both occupational and environmental epidemiology.[1] In environmental studies, it is common to estimate individual exposures from information available at the ecologic level (eg, air monitoring data measured at fixed sites). In the occupational setting, employees who are presumed to have similar workplace exposures are often grouped together, and a crude exposure measure (either qualitative or quantitative) is assigned to each subject in the exposure group (eg, plant workers vs. administrative officers, exposure groups by tasks). This is commonly done without regard to differences in exposures within groups. These approaches can result in unavoidable measurement errors in quantifying individual exposures. As a result, the risk estimates can be distorted, the hypothesis testing could be biased, and the effective sample size is reduced.[2,3] Many epidemiologists have used validation studies to develop analytic methods for correction of bias resulting from exposure measurement errors.[4,5] Direct personal measurement has also been advocated.[6,7] Other methods, including dosimetry algorithms, pharmacokinetic models, and biomarkers, have been proposed to reduce exposure measurement errors in environmental epidemiology.[8]

Although direct measurement of individual exposures seems to be a preferred approach, valid and reliable tools for direct exposure assessment are often not available or practical. Also, most researchers could not afford to take direct exposure measurement from every individual in large epidemiologic studies involving thousands of study subjects. Recently, researchers have begun to address the use of validation studies in epidemiologic research for design efficiency and cost saving.[5,9–11]

In 2000, we initiated the Taxi Drivers' Health Study in Taipei City, Taiwan.[12,13] One research interest of this study was to examine the relation between occupational exposure to whole-body vibration and low back disorders of taxi drivers. Whole-body vibration is an exposure in which mechanical oscillations transmit energy to the body through a supporting system such as a seat or platform. It is a widespread physical hazard of the workplace with an estimated exposure prevalence of 4% to 7% in many industrialized countries.[14]

Both cross-sectional and longitudinal studies have shown a consistent association between long-term occupational exposure to whole-body vibration and low back pain,[15–17] sciatica,[18,19] and herniated lumbar disc.[16,19,20] Although the biologic plausibility of these observations has been supported by biomechanical experiments[21–23] and animal studies,[24–26] uncertainties remain as a result of the lack of exposure data at the individual level.[27,28] Direct and accurate measurement of vibration is an expensive, time-consuming, and demanding process, prompting the search for other approaches.

We describe the development of an exposure prediction rule as a statistical instrument for measuring individual exposures. Specifically, in parallel with the Taxi Drivers' Health Study, we conducted a validation study with detailed exposure assessment on a representative group of taxi drivers.[29] With direct measurement of whole-body vibration, we were able to identify a set of predictors of vibration exposure, including personal factors, vehicle characteristics, and other occupational activities. With this information, we developed prediction rules to quantify personal vibration exposure in a much larger group of taxi drivers enrolled in the main study.

METHODS

Study Population

Study protocols were approved by the Human Subjects Committee of the Harvard School of Public Health and the Institutional Review Committee of the Liberty Mutual Research Institute for Safety. Informed consents were obtained for every subject participating in the measurement of whole-body vibration. Details in study design, sampling scheme, and measurement protocols have been reported elsewhere.[29] In brief, we recruited potential subjects from several large cab companies, taxi cooperatives, cab service radio stations, and local unions. Study subjects were men who were registered and currently active professional taxi drivers in Taipei City, and were operating vehicles made by Toyota, Nissan, Honda, or Ford. These 4 manufacturers made approximately 85% of all Taiwan taxis. To get a representative sample of drivers for the validation study, potential participants were grouped into categories of vehicle characteristics (manufacturers, years of make, and engine sizes). We used a stratified sampling scheme to select the drivers and their vehicles. Two hundred ninety-two male drivers were sampled, of whom 247 (85%) completed the scheduled driving tasks, contributing a total of 432 measurements of whole-body vibration.

Measurement of Vibration and Covariates

All drivers were asked to complete preselected driving tasks with driving conditions representing different types of rides (vacant vs. with passengers, short vs. long) assigned to random destinations. We measured the frequency-weighted vertical acceleration over drivers' seat surface in accordance with the ISO 2631–1:1997 methods.[30] At the end of the WBV measurement, each driver was interviewed briefly by the same researcher on occupational history, driving time profiles, and history of low back pain. Information on driver's age, professional seniority, vehicle manufacturer, year of make, and engine size was taken from the records on registered licenses, whereas information on the average days of driving per month and average daily driving duration were obtained either from driving diary recording (if available) or self-report. Weight and height information was also gathered from self-report and cross-validated through available medical records.[12,13] For each of the 247 vehicles, we also took measures on the wheelbase length, tire width, and degree of seat inclination.

Statistical Analysis

Mixed-effect models were used to identify potential predictors of vibration. For the comparison between nested models, the mean structures were determined by likelihood ratio tests based on standard maximal log likelihood. Their corresponding variance–covariance structures were determined by likelihood ratio tests based on restricted maximal log likelihood. In constructing the mixed-effect models, we first determined the best-fit "base model," which included the random subject effect, fixed effects of the 3 sampling factors (manufacturer, year of make, and engine size), and the fixed effect of average driving speed. Speed was included in the base model because we found its essential influence on vibration intensity in a pilot study carried out in the Boston area. A covariate was defined as a potential predictor of vibration if estimate of its fixed effect was significant at a 0.20 level when entering the base model.

Prior Knowledge of Vibration Predictors

In the earlier work on exposure assessment,[29] we identified a set of predictors of whole-body vibration. Average driving speed had a quadratic–linear relation with vibration levels. Vibration was less with large engine size ($\geq$ 1600 cc), long wheelbase, broad tire width, driver's weight and seniority, whereas the use of a seat surface cushion was a predictor of higher vibration exposure. Vibration levels also varied by time of the day (across traffic periods) and differed by automobile manufacturers.

Development of Predictive Mixed-Effect Models

We developed the prediction rule for vibration exposure based on the 383 WBV measurements with complete data information (out of the 432 measurements) collected from these 247 drivers. We excluded 18 that were missing measures of vibration as a result of transient instrument failure and another 31 for which measurement duration was not recorded.

Only observable regressors were used for prediction. We disregarded information from predictors that could not be collected in the large main study. Given the eligible potential predictors, we constructed the following mixed model that includes main effects only:

$$Y_{ij} = \beta_0 + \beta_1(speed)_{ij} + \beta_2(speed)_{ij}^2 + \beta_{3-5}(manufacturers)_i + \beta_{6-7}(engine\ size)_i + \beta_{8-10}(year\ of\ make)_i + \sum \beta_k X_{ijk} + b_{0i} + e_{ij} \quad (1)$$

where Y_{ij} denotes measured vibration level and e_{ij} the error term of j^{th} measurement in subject i, b_{0i} is the random intercept, and β_k is the estimate of fixed effect of covariate X_{ijk}.

Potential interaction terms, when entering the main effect model (*equation 1),* were defined as being significant at the 0.05 level for the likelihood ratio test based on maximum likelihood, but only 2-way interactions between retained covariates were considered. Predictive mixed-effect models with all possible combinations of potential interaction terms were then built. We determined the best predictive model by minimizing the estimates of error variance using the restricted maximum likelihood method. The presumed predictive mixed-effect model is given as:

$$Y_{ij} = \beta_0 + \beta_1(speed)_{ij} + \beta_2[(speed)_{ij}]^2 + \beta_{3-5}(manufacturers)_i + \beta_{6-7}(engine\ size)_i + \beta_{8-10}(year\ of\ make)_i + \sum \beta_k X_{ijk} + \sum \beta_{kk'}(X_{ijk} * X_{ijk'}) + b_{0i} + e_{ij} \quad (2)$$

where Y_{ij} denotes measured vibration level and e_{ij} the error term of j^{th} measurement in subject i, b_{0i} is the random intercept, β_k is the estimate of fixed effect of *observable* predictor $X_{ijk'}$, and $\beta_{kk'}$ is the coefficient for potential 2-way interaction term between retained covariates X_{ijk} and $X_{ijk'}$ that include speed, sampling factors, and other potential predictors.

Predictive Validity

We evaluated the predictive validity of the "best" predictive mixed-effect model by estimating the mean absolute prediction error (ie, the absolute difference between measured and predicted whole-body vibration given by *equation 2*) and relative prediction error (ie, absolute prediction error divided by the measured whole-body vibration). There can be bias in estimating prediction errors when using regression models that were built, at least partly, on the measurements that we would like to predict. To reduce this bias, all predicted vibration values are given by the jackknife method.[31,32] That is, each time we dropped one subject along with all his measured vibration values, the best prediction model was refit to the rest of data and those coefficients of *equation 2* were updated and used to predict the vibration levels of the dropped-out subject. This procedure was repeated 247 times, and all measured and predicted vibration values were pooled to calculate the means of absolute (in m/s^2) and relative (%) prediction error.

The jackknifed prediction errors provide an estimate of measurement errors that result from using the predictive mixed-effect model to estimate vibration exposure at individual levels. Assuming the efficiency of jackknifing, we performed a multiple linear regression analysis to assess whether these measurement errors depend on the presence of low back pain or other variables.

Computation of Daily Vibration Exposure

We adapted the "energy equivalence principle"[30,33,34] to calculate daily vibration exposure for each subject. The energy absorption power of whole-body vibration is proportional to the square of acceleration.[30,33,34] Under the assumption that human response is related to absorbed vibration energy, the "energy equivalence principle" holds that 2 vibration exposures with different intensities and exposure durations are equivalent when:

$$a_1{}^2 * T_1 = a_2{}^2 * T_2 \quad (3)$$

where a_1 ,a_2 are the vibration accelerations with exposure durations T_1 and T_2.

Therefore, the daily vibration dose is computed as:

$$WBVd_i = \sum (a_{ij}{}^2 * t_{ij}) \quad (4)$$

where $WBVd_i$ is the daily exposure dose of whole-body vibration, a_{ij} is frequency-weighted vibration magnitude (in m/s^2) during traffic period j as predicted from the best predictive model, given the reported average driving speed and other covariates for driver i, and t_{ij} is the duration (in hours) spent in traffic period j for driver i. The computed dose thus has the unit per m^2/s^4-hour.

Construct Validity

We evaluated the construct validity of the exposure prediction rule by testing the hypothesis that there is an association between vibration dose and low back pain. We included low back pain in the analysis only if it was reported as having started after the man became a taxi driver, and it had resulted in medical attention or days away from work.

The crude prevalence odds ratio (POR) of low back pain associated with one unit change in vibration dose was calculated through a simple logistic regression (the base model). We used multiple logistic regression to obtain the adjusted POR estimates. For a covariate to be included in the final model, one of the following was necessary: 1) the covariate had to be a plausible risk factor for low back pain, 2) its entry into the base model caused at least a 10% change of the POR associated with vibration dose, or 3) the *P* value for testing its association with low back pain should be less than 0.20. We used Hosmer-Lemeshow goodness-of-fit test to assess the model fitting.[35]

RESULTS

The predictive mixed-effect models incorporated the following variables: average driving speed, driver's age, professional seniority, daily driving time, body weight, manufacturer, and the year and make and engine size of operating vehicles. We were not able to use the information on length of wheelbase, tire width, and use of seat surface cushion because these data were either not collected or mostly missing in the full study. The best predictive mixed-effect model was determined as:

$$\begin{aligned} Y_{ij} = {} & \beta_0 + \beta_1(speed)_{ij} + \beta_2(speed)_{ij}^{\,2} + \beta_{3-5}(manufacturers)_i \\ & + \beta_{6-7}(engine\ size)_i + \beta_{8-10}(year\ of\ make)_i + \beta_{11}(age)_i \\ & + \beta_{12}(body\ weight)_i + \beta_{13}(traffic\ period)_i \\ & + \beta_{14}(professional\ seniority)_i + \beta_{15}(daily\ driving\ duration)_i \\ & + \beta_{16-17}(speed)_{ij}{*}(engine\ size)_i \\ & + \beta_{18}(body\ weight)_i{*}(professional\ seniority)_i \\ & + \beta_{19}(body\ weight)_i{*}(age)_i \\ & + \beta_{20-21}(speed)_{ij}^{\,2}{*}(year\ of\ make)_i + b_{0i} + e_{ij} \end{aligned} \tag{5}$$

where Y_{ij} denotes measured vibration level and e_{ij} the error term of j^{th} measurement in subject i, b_{0i} is the random intercept, and β_k is the estimate of fixed effect of vibration predictors and interaction terms as indicated.

Analysis of the error estimates e_{ij} from the final predictive mixed-effect model (*equation 5*) showed an approximately normal distribution, supporting the use of mixed-effect modeling. Figure 1 provides the distributions of absolute and relative jackknifed prediction errors. The average absolute prediction error was 0.033 m/s^2 (95% confidence interval [CI] = 0.030–0.037). Ninety-two percent of all predictions had absolute errors less than 0.1 m/s^2. The average relative prediction error was 11% (CI = 10–12%), and 75% of all predictions have relative errors less than 20%.

The multiple regression of jackknifed prediction errors indicated that, as expected, tire width and use of surface cushion were 2 substantial sources of measurement errors. If information on these 2 factors were not available, the vibration exposure tended to be underestimated by 0.016 m/s^2 for those using surface cushion and overestimated by 0.025 m/s^2 for those whose vehicles' tire widths were greater than 165 mm. However, jackknifed prediction errors did not depend on the presence of low back pain, driver's seniority, age, body weight, daily driving time profiles, daily driving distance, and other available vehicle characteristics such as transmission type and fuel sources (natural gases vs. petroleum), year and make, manufacturer, and engine size. Repeating the measurement errors analyses by mixed-effect modeling yielded very similar results.

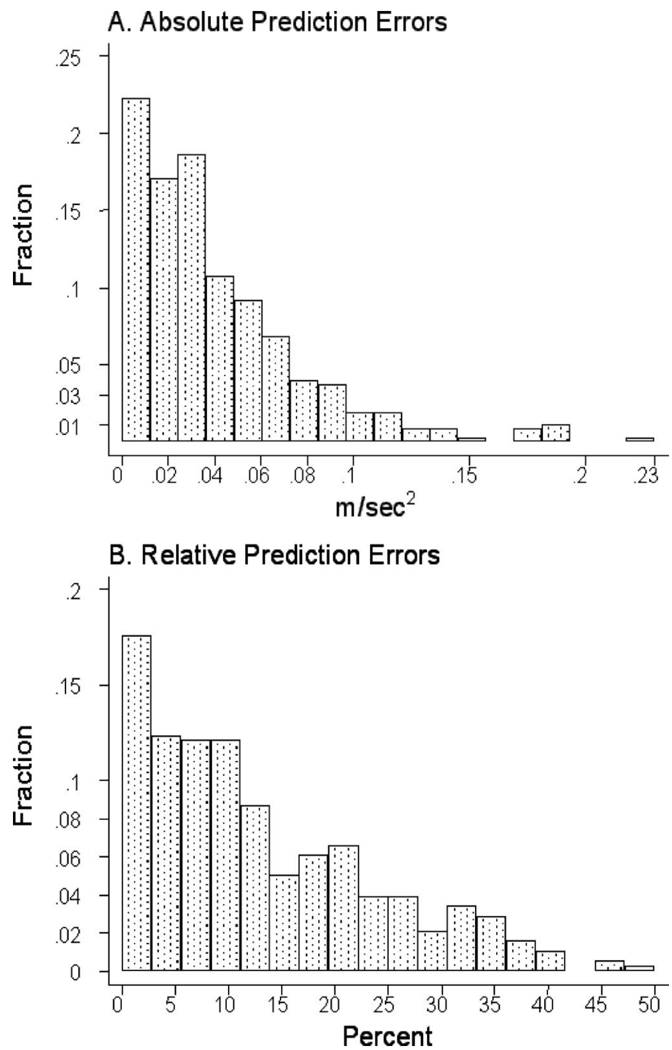

FIGURE 1. Distribution of (**A**) absolute prediction errors (m/s^2) for whole-body vibration and (**B**) relative prediction errors (%) of the predicted values.

We included 221 drivers for the evaluation of construct validity. Excluded subjects had either missing information on low back pain (n = 7) or a covariate (n = 10), or had already had obvious low back pain before becoming taxi drivers (n = 9). In Table 1, we compare these 221 drivers with those participating in the main study,[12,13] and also cross-referenced this comparison to the nationwide survey statistics.[36] With respect to age, professional seniority, daily driving duration and distance, these 221 drivers are very similar to the refer-

TABLE 1. Characteristics of 221 Drivers Included in the Multiple Logistic Regression Analysis for Evaluating Construct Validity, as Compared With All Drivers in the Main Study and a Reference Population*

Characteristics	Drivers in the Validation Study (n = 221) Mean ± SD	Drivers in the Main Study (n = 1 242) Mean ± SD	Reference* Mean
Age (yrs)	45 ± 8	45 ± 9	44
Body mass index (kg/m^2)	24.7 ± 3.7	24.9 ± 3.6	—
Professional seniority (yrs)	9 ± 7	11 ± 8	9
Average days of driving per month	26 ± 3	26 ± 3	27
Daily driving duration (hrs)	10 ± 2.3	10 ± 2.8	10
Daily driving distance (km)	184 ± 47	169 ± 60	182
Measured vertical vibration† (m/s^2)	0.31 ± 0.06	—	—
Estimated daily vibration dose‡ (m^2/s^4-hr)	1.06 ± 0.32	—	—

*From the Department of Statistics, Ministry of Transportation and Communication, Taiwan.[36]
†Frequency-weighted acceleration in root-mean-square measured at the z-axis over the seat surface.
‡Computed from Equation 4 according to "energy equivalence principle"

ence statistics. Although they had been drivers for a relatively shorter period, the 221 drivers in the current study on average drove for longer distances per day than those in the main study.

The crude prevalence odds ratio of low back pain associated with an increment of daily vibration exposure by each m^2/s^4-hour was 3.7 (CI = 1.5–9.2). After adjusting for age, body mass index, professional seniority, registration type, seat inclination, vehicle engine size, and use of lumbar support, the estimated association was nearly unchanged (3.7; CI = 1.1–12.2). No data were available to adjust for other potential confounders such as smoking, occupational activities (eg, lifting, bending/twisting), and work-related psychosocial factors. The Hosmer-Lemeshow test supported the goodness-of-fit of the multiple logistic regression presented ($P = 0.60$).

DISCUSSION

Our approach to exposure prediction provides an efficient way to assess individual occupational and environmental exposures in large epidemiologic studies. In the illustrated example on whole-body vibration, the information on observable predictors (driver's age, weight, vehicle characteristics, driving distance, and driving time) used in the prediction rule could be gathered efficiently through questionnaire, interview, or driving diary records without measuring vibration in each of the thousands of taxi drivers included in the main study.

The proposed prediction rule for vibration exposure had an acceptable predictive validity as evaluated by the jackknife method. The mean relative prediction error was 10.9% within the vibration exposure levels ranging from 0.17 to 0.55 m/s^2, whereas the vibration meter we used in previous fieldwork[29] had an average instrument error of 4% within the range 0.1 to 1.0 m/s^2. This imperfect result, partially as a consequence of the methods we applied, was not unexpected. Information on some important vibration predictors was missing in the main study. Failing to take into account the between-subject differences in these factors in the predictive models (Equations 2 and 5) could result in substantial prediction error. In our example, had we had not disregarded any information of all identified predictors in the validation study, the average jackknifed prediction error would have been reduced by 33% (from 0.033 m/s^2 to 0.022 m/s^2). Understanding these sources of prediction error resulting from exposure predictors not observable in the main study could encourage researchers to search for external information and evaluate whether the research outcomes depend on these sources of exposure measurement error. When there are nonignorable prediction errors, such additional information about the known error sources in relation to research outcomes could provide more valid statistical inference in the main study.

The other major source of prediction error is the result of the fact that individual exposure prediction was based on fixed effect estimates. When we implemented the jackknife procedure and dropped one subject with all his vibration measures, these observations in effect worked as "surrogated sets" of vibration measures that we would have observed external to the validation sample or collected prospectively. At the same time, the information about the random subject effect on vibration levels (the b_{0i} in Equations 1, 2, and 5) was not used to predict the vibration values of that dropped subject. Because the original goal was to apply the prediction rule to those from whom we would not have direct measurement data, jackknifing on subjects rather on measurements is a valid approach. In the special case that we are interested in making vibration prediction prospectively on this group of

247 drivers, we could use our prior knowledge about random subject-effects to further improve the predictive validity.

The implication of having a significant random subject-effect in a predictive mixed-effect model needs to be noted. In a null model without any exposure predictors, the random subject effect accounts for approximately 58% of total vibration variance. The estimated variance of random subject effect decreases by 48% when the observable WBV predictors and interaction terms are included in the final predictive model, but the random effect b_{0i} in *Equation 5* remained strong. This remaining between-subject exposure variability could result from the unmeasured between-subject or between-vehicle differences in driving behavior, design or performance of the suspension system, or road surface factors. When applying the exposure prediction rule developed from a validation sample with characteristics systemically different from the main study subjects, a significant random-subject effect should alert the researchers to the possibility of systemic or differential bias resulting from unknown sources of between-subject variability.

The analyses of jackknifed prediction errors help to explain other sources of measurement error in prediction of the exposure and help to improve the validity of subsequent statistical inference. Three main implications could be drawn from these analyses. First, our data suggest that the measurement errors in predicting individual vibration intensity are independent of the outcome (low back pain). This implies that, although we are unable to create a perfect predictive instrument, the likelihood of finding an association biased away from null is greatly reduced. Second, the measurement errors do not vary by the known population differences between the main study and the validation study (such as professional seniority and daily driving distance, Table 1). This gives us more confidence in applying the predicted exposure to the main study. Third, knowing that some factors are important sources of measurement error will allow us to apply appropriate statistical methods for bias correction.[4,37]

The applicability of our proposed exposure prediction rule to a target population is demonstrated by its construct validity. Construct validity is concerned with the validity of inferences about unobserved constructs on the basis of presumed indicators under a theoretical framework.[38] One way to establish construct validity is to test hypothesized relationships between the construct of interest (daily whole-body vibration in our case) and the presumed indicator (low back prevalence). If the presumably associated indicator was also the outcome of research interest in the main study, the process of evaluating construct validity could also provide useful information for further bias correction in the main study, assuming that there were no other unadjusted confounding and that the directly measured construct in the validation study is the true "gold standard."

The direct application of our exposure prediction rule for whole-body vibration to other groups of taxi drivers needs cautious consideration. Its unconditional generalizability to other professional drivers is not recommended. Like with any other prediction rules, specific usability of the proposed prediction rule should not be extended beyond the observed ranges of exposure predictors. Difference in the driving conditions (eg, urban vs. rural environment) and vehicle characteristics could change the measured vibration levels. For instance, the observed average driving speed in our validation sample was 20 km/hr, ranging from 5 km/hr to 55 km/hr,[29] largely because driving speed limit is 30 km/hr in metropolitan Taipei and 40 km/hr in most suburban areas. Applying our prediction rule to other settings of taxi drivers where driving at high speed is not uncommon (eg, more traveling on highways for taxi drivers designated to serve airport passengers) could be problematic. The proposed vibration prediction rule obviously has no direct practical use for taxi drivers operating vehicles other than those used for the taxicab business in Taipei or for other professional drivers operating completely different categories of vehicles. Nevertheless, the more general principle of using information on observable predictors to develop a statistical instrument through a validation study is completely transferable to many other occupational settings and environmental studies.

We recognize several other limitations of our study. First, with respect to predictive validity, we evaluated the performance of the proposed WBV prediction rule based on a statistical validation technique, namely the jackknife method, instead of doing external or prospective validation. At this stage, no further data were available for prospective validation. This statistical predictive validity could need to be reconfirmed in a prospective validation sample. Second, although the demonstrated construct validity provided evidence for a likely exposure–response relation between low levels of whole-body vibration and low back pain not described before, by no means is this analysis aimed to be confirmatory. Our statistical inference is restricted by the fact that this is a cross-sectional analysis and that we were not able to collect information on other important confounding factors such as lifting, bending/twisting activities, and psychosocial factors, which are established risk factors for low back pain and could confound the observed association.

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