ORIGINAL ARTICLE

Occupational and other risk factors for hand-grip strength: the Honolulu-Asia Aging Study

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Background: In certain occupations, including farm work, workers are exposed to hazardous substances, some of which are known to be toxic to the nervous system and may adversely affect muscle strength. Measurement of hand-grip strength may be useful for detecting neurotoxic exposure.
Methods: The authors studied 3522 participants of the Honolulu Heart Program and the Honolulu-Asia Aging Study to determine whether occupational exposures to pesticides, solvents, and metals assessed at exam I (1965–68) are associated with hand-grip strength at exam IV (1991–93) and change in hand-grip strength over 25 years. Correlation, analysis of variance and covariance, and linear regression were used to evaluate the associations.
Results: At exam IV, participants ranged in age from 71–93 years; mean hand-grip strength was 39.6 kg at exam I and 30.3 kg at exam IV. Over 25 years, the decline in hand-grip strength was an average of 8–9 kg for all exposures. Hand-grip strength was inversely associated with age and glucose but directly associated with cognitive function, BMI, and haemoglobin level. No other exposures were associated with hand-grip strength.
Conclusion: This study did not provide evidence that occupational exposure to pesticides, solvents, and metals adversely affected hand-grip strength in this population, but confirmed other important associations with hand-grip strength.

In certain occupations, including farm work, workers are exposed to hazardous substances, some of which are known to be toxic to the nervous system.[1–3] Measurement of hand-grip strength may be useful in detecting neurotoxic exposure. Decline in hand-grip strength predicts increased disability and mortality in older individuals.[4–6]

Certain pesticides, solvents, and metals cause inhibition of cholinesterase enzymes with resultant decrease in levels of the neurotransmitter, acetylcholine.[7–10] Decreased levels of acetycholine in the brain result in deficits in learning and memory, and poor muscle function.[11] Some solvents (for example, hexane) can also inhibit glycolysis in the neurons causing thining and retraction of the myelin sheath.[12] Manganese reduces dopamine levels in the brain causing parkinsonian symptoms.[13] Therefore, these occupational exposures may affect hand-grip strength via a neurotransmitter or a dopaminergic mechanism.

Several studies have explored the association between occupational pesticide exposure and neurological outcomes,[1 2 14] but only a few have investigated and related pesticide exposure to decreased hand-grip strength.[15 16] Laboratory and population based studies have shown that exposure to solvents produce neurotoxic effects including loss of strength in the arms and hands.[17 18] High manganese exposure can cause various motor symptoms,[19] and occupational exposure to mercury compounds can cause hand and arm tremors.[20–22] Other factors, such as age, cognitive function, body mass index (BMI), mid-upper arm circumference, muscle mass, and hand circumference have also been shown to be related to hand-grip strength.[23–26]

The main objective of this study is to investigate the association of occupational exposures to pesticides, solvents, and metals (iron, manganese, or mercury) with hand-grip strength and decline in hand-grip strength over time.

MATERIALS AND METHODS

Study population

This study used data from the Honolulu Heart Program (HHP) and the Honolulu-Asia Aging Study (HAAS). The HHP began in 1965 as a prospective study of cardiovascular disease and stroke in Japanese-American men living on Oahu, and the HAAS was started in the same cohort in 1991 to investigate cognitive decline and other conditions of aging. Informed consent was obtained from the study participants and the study was approved by an institutional review committee. Detailed descriptions of the methods have been previously published.[27] Briefly, these men, all non-institutionalised, were identified through Selective Service records from World War II and located through searches of telephone, business, and state agency records. Approximately 66% of the participants had jobs involving manual labour: craftsmen (for example, cranemen, bulldozer operators), farmers, labourers, operatives (for example, delivery men, welders), and service workers; 7.8% were in professional occupations (for example, chemist, agricultural scientist, chemical engineer); 9% were clerks; 7.6% were managers; 7.3% were salesmen; and 2% were technicians.

Several exams have been conducted to date. Exam I took place during 1965–68 and included 8006 men who were between the ages of 45 and 68 years; exam II (1968–70) included 7498 men; exam III (1971–74) included 6860 men; and exam IV (1991–93) included 3845 men who were between the ages of 71 and 93 years. In the first exam,

Abbreviations: BMI, body mass index; CASI, Cognitive Abilities Screening Index Instrument; HAAS, Honolulu-Asia Aging Study; HHP, Honolulu Heart Program; MMSE, Mini-Mental State Examination; NIOSH, National Institute for Occupational Safety and Health; PEL, permissible exposure limit; PPE, personal protection equipment self-administered questionnaires were completed by each subject and physical examinations were also performed. At subsequent exams, participants were re-interviewed and re-examined. Participants who were diagnosed with Parkinson's disease (n = 61) and stroke (n = 113) before exam IV were excluded from these analyses; two men had both diagnoses. After these 172 exclusions, 7834 men were available for this analysis at exam I, and 3673 at exam IV. The two main outcomes of the study were hand-grip strength at exam IV and decline in hand-grip strength between exams I and IV. Among the 3673 men at exam IV, 151 had no available information on hand-grip strength at exam IV. Three of the men who had available information on hand-grip strength at exam IV did not have such information available at exam I. Analyses were conducted on 3522 men who had available information on hand-grip strength at exam IV, and 3519 men who had information on decline in hand-grip strength.

Assessment of occupational exposures

Occupational exposure information collected during exam I was used in these analyses. Participants were asked questions about their present and usual occupation, and the age that they started and finished working in these occupations.

Three industrial hygienists from the National Institute for Occupational Safety and Health (NIOSH) independently assessed the potential for pesticide, metal, and solvent exposure in each reported occupation and reached a consensus. They created four levels of exposure to the agent indicating a score of 0 for no potential of exposure, 1 for low exposure, 2 for medium exposure, and 3 for potential of high exposure.[14] The "high" classification was assigned to those occupation/industry pairings judged to have significant exposures that were frequently well above analytically detectable concentrations and were at least occasionally near or greater than the OSHA permissible exposure limits (PELs), if a PEL existed. A "high" score meant that the industrial hygienists were confident that the industry/occupation pairing would frequently have exposure to the agent. The "medium" exposure classification was assigned to those occupation/industry pairing judged to involve tasks with detectable exposures to the selected agents, but which were considered to usually be below the OSHA PELs. The "low" exposure classification was assigned to those industry/occupation pairings judged to occasionally have undetectable exposures to the selected agents but which would rarely approach the OSHA/PEL. A "0" score indicated that workers in the industry/occupation pairing were believed to have little potential exposure to the agent. The scores not only reflected the industrial hygienists' view of the intensity of exposure, but also their confidence that jobs in these industries would have exposure to these agents.

Although information was collected on present and usual jobs, usual job was used primarily to determine to which industry occupation group a worker should be assigned to determine his exposure. A cumulative (intensity) score was obtained by multiplying the appropriate levels of exposure (0, 1, 2, 3) by the number of years exposed. If exposure to the agents was not obtained in the usual job but was obtained in the present job, the exposure received from the present job was used in calculating the exposure intensity score. All occupational exposures refer to intensity scores at exam I. Exposures were used as continuous variables or categorised into four levels, 0, 1–39, 40–79, and ⩾80, and for mercury, 0, 1–20, 21–30, ⩾31. The cutpoints were selected to allow for sufficient sample sizes in each group.

Assessment of outcomes

Hand-grip strength was measured in kilograms (kg) using the Smedley Hand Dynamometer (Stoelting Co, Wood Dale, IL, USA) during exams I and IV.[28] While seated, the participant extended his arm in front of him on the table and gripped the dynamometer. The width of the handle was adjusted to allow the second phalanx to rest against the inner stirrup of the dynamometer. After verbal encouragement to exert maximum effort, the participant was allowed three attempts, with brief pauses, for each hand alternately. The maximum hand-grip strength was chosen for analyses. Decline in hand-grip strength was calculated by subtracting hand-grip strength at exam IV from hand-grip strength at exam I. Hand-grip strengths at exams I and IV and decline in hand-grip strength were categorised into quartiles.

Assessment of covariates

Body mass index was calculated as weight (kg) divided by height (m^2). A physical activity index was created and is described in detail in Burchfiel *et al*.[29] This index was calculated by multiplying the number of activity hours spent in a 24 hour period (hours were summed across activities) by a weighting factor. The activity levels were basal (for example, sleeping or reclining), sedentary (for example, sitting, standing), slight (for example, casual walking), moderate (for example, carpentry, gardening), and heavy (lifting, shoveling). The weighting factors were based on the estimated oxygen consumption, in litres per minute, required to perform the relevant activities and are 1.0, 1.1, 1.5, 2.4, and 5.0 respectively. Coffee consumption was obtained from the questions (a) "How often do you drink coffee?" (categorised as almost never, once or less a day, twice a day, 3× or more a day), and (b) "How many 4 oz cups do you drink?" Smoking and alcohol history were analysed as pack-years of smoking and number of ounces of alcoholic beverages (wine, beer, and spirits) consumed per month. Alcohol consumption was converted to grams per month. At exam I, blood specimens were collected one hour after participants ingested a 50 g glucose load and analysed for glucose level (mg/100 ml). At exam IV, blood haemoglobin level was assessed. Participants reported the number of years of education. Beginning at exam IV, the Cognitive Abilities Screening Index Instrument (CASI) was used to assess cognitive function.[30] The CASI provides quantitative assessment on attention, concentration, orientation, short term memory, long term memory, language abilities, visual construction, list generating fluency, abstraction, and judgment, and has a score range of 0 (poor) to 100 (excellent). The CASI is considered more sensitive to differences in diagnosis and to variations in cognitive impairment than the other most commonly used cognitive instrument Mini-Mental State Examination (MMSE).[31]

Statistical methods

Where appropriate, *t* tests were conducted on the main exposure variables and other covariates with hand-grip strength at exam IV and decline in hand-grip strength. Comparisons of means and adjusted means of the main outcomes by exposure categories were assessed by analysis of variance and analysis of covariance.[32] The covariates adjusted for were age, BMI, physical activity, blood glucose, smoking, CASI score, education, haemoglobin level, arthritis, forearm fracture, participant's orientation, diabetes medication, manual labor, and baseline hand-grip strength. Linear regression models were used to obtain the parameter estimates and to assess the significance of trends between the exposures and main outcomes, and covariates and main outcomes. Covariates were chosen for the final models based on a priori knowledge of their associations with the exposures and the outcomes and/or on their associations with the exposures and outcomes during these analyses. All analyses were conducted using the SAS system, version 8.02.[33]

Table 1 Characteristics of study participants, Honolulu Heart Program and Honolulu Asia Aging Study, 1965–68 (exam I) and 1991–93 (exam IV)

Covariates	n	Range	Median	Mean	SD
Exam I					
Age (years)	3522	46–68	52.0	52.6	4.7
BMI (kg/m^2)	3520	14.9–39.9	23.9	23.9	2.9
Physical activity	3505	25.6–65.5	31.8	32.8	4.7
Coffee intake (4 oz cup portions)	3522	0–38	3.0	3.4	3.2
Glucose (mg/dl)	3510	49–671	142.0	151.1	47.7
Alcohol intake (g/month)	3518	0–6055.5	35.6	340.1	602.9
Smoking (pack-years)	3507	0–147	18.0	21.4	22.9
Hand-grip strength (kg)	3519	11–63	39.0	39.6	6.1
Exam IV					
Age (years)	3522	71–93	77.0	77.7	4.6
BMI (kg/m^2)	3453	12.3–39.3	23.5	23.4	3.2
CASI score	3520	0–100	86.9	83.5	13.9
Education (years)	3522	1–24	10.0	10.5	3.2
Haemoglobin (g/dl)	3380	5.9–20.4	14.9	14.9	1.4
Hand-grip strength (kg)	3522	0–55	30.0	30.3	6.8
Decline in hand-grip strength (kg) between exams I and IV	3519	−12 to 38	9.0	9.3	5.8
Arthritis		%			
No	2859	83.6			
Yes, current: under medical care	223	6.5			
Yes, current: not under medical care	261	7.6			
Yes, present only in the past	79	2.3			
Fracture of forearm		%			
No	3351	95.5			
Yes	158	4.5			

RESULTS

At exam IV, the mean age of participants was 77.7 years (range 71–93 years) and participants obtained a mean CASI score of 83.5 (<74 considered "low cognitive function") (table 1). Participant's hand-grip strength was lower at exam IV (mean = 30.3 kg) than at exam I (mean = 39.6 kg). Analyses were also conducted to better characterise participants with very low hand-grip strength values (that is, ⩽10 kg). At exam IV, four men had a hand-grip strength value of 0 kg. Compared with men who had hand-grip strength >10 kg, men who had hand-grip strength values ⩽10 (n = 29, 0.8%) were significantly older (mean = 83.5 *v* 77.7 years), had a significantly lower BMI (mean = 20.7 *v* 23.4 kg/m^2), were significantly less physically active (mean = 27.6 *v* 30.9), had significantly lower cognitive test scores (mean CASI score = 34.8 *v* 83.9), and were significantly more likely to be anaemic (haemoglobin mean = 12.5 *v* 14.9 g/dl). A higher proportion of persons with weaker hand-grip strength reported that they had arthritis (37.5% *v* 14.0%). Between exams I and IV, a decrease in hand-grip strength was experienced by the majority of participants (95.5%); the others experienced an increase or no change (3% and 1.5% respectively) (data not shown). Among participants whose hand-grip strength increased at exam IV compared to exam I, the majority were younger (87% ⩽54 years) at baseline compared with those whose hand-grip strength did not increase at follow up.

The prevalence of occupational exposure based on a participant's usual job ranged from 7.1% for pesticides to 51.7% for solvents (table 2). Years of exposure varied widely

Table 2 Occupational exposure characteristics for study participants, Honolulu Heart Program, 1965–68.

	Pesticide	Solvent	Metal	Manganese	Mercury
	n (%)	n (%)	n (%)	n (%)	n (%)
Usual job exposure					
None (0)	3267 (92.9)	1699 (48.3)	2076 (59.0)	2789 (82.3)	3001 (85.4)
Low (1)	37 (1.1)	1096 (31.2)	1027 (29.2)	396 (11.7)	444 (12.6)
Medium (2)	11 (0.3)	231 (6.6)	212 (6.0)	32 (0.9)	71 (2.0)
High (3)	201 (5.7)	490 (13.9)	201 (5.7)	170 (5.0)	0 (0)
Total	3516	3516	3516	3387	3516
Years of exposure					
0	3194 (90.7)	1480 (42.1)	1913 (54.4)	2827 (80.3)	2952 (83.8)
1–15	95 (2.7)	378 (10.7)	275 (7.8)	127 (3.6)	84 (2.4)
16–30	159 (4.5)	912 (25.9)	689 (19.6)	351 (10.0)	274 (7.8)
⩾31	73 (2.1)	749 (21.3)	642 (18.2)	215 (6.1)	211 (6.0)
Total	3521	3519	3519	3520	3521
Intensity score*					
Zero	3266 (92.9)	1699 (48.3)	2076 (59.1)	2788 (82.3)	2891 (85.4)
Low	64 (1.8)	1145 (32.6)	1039 (29.6)	392 (11.6)	157 (4.6)
Medium	119 (3.4)	484 (13.8)	318 (9.1)	147 (4.3)	195 (5.8)
High	66 (1.9)	187 (5.3)	82 (2.3)	59 (1.7)	143 (4.2)
Total	3515	3515	3515	3386	3386

*Categories for mercury intensity scores are 0, 1–20, 21–30, ⩾31; categories for the four other intensity scores are 0, 1–39, 40–79, ⩾80. Intensity score = usual job exposure × years of exposure.

among the five agents; for example, only 6.6% of the men had worked >15 years with pesticides, whereas 47.2% of the men had worked a similar duration with solvents.

Mean age and levels of physical activity tended to increase in general with increasing occupational exposure intensity scores (data not shown). The opposite was true for cognitive functioning and years of education. Pack-years of smoking were not associated with any of the exposures. The relations between these covariates and hand-grip strength at exam I, hand-grip strength at exam IV, and hand-grip strength between exams I and IV are described in tables 3–5. Information on all of the covariates, except CASI score, education, and haemoglobin levels, were collected at exam I. There were significant monotonic increases in the mean values of BMI, coffee consumption, CASI score, years of education, and haemoglobin levels as hand-grip strength at exam IV increased. In contrast, there were significant, general decreases in mean values of age, physical activity, glucose level, alcohol consumption, and smoking with increasing hand-grip strength at exams I and IV. Larger declines in hand-grip strength between exams I and IV were observed with older mean ages, lower mean CASI score, and fewer mean years of education.

We created a dichotomous variable for manual labour. *t* test analyses showed no difference in the mean values of hand-grip strength, and inclusion of this variable in the full multivariate models of tables 6 and 7 did not influence the results. The mean hand-grip strength of men who were anaemic (that is, haemoglobin 5.9–13.5 g/dl) was 26.2 kg, compared with 31.2 kg ($p<0.001$) for non-anaemic men. The mean hand-grip strength for persons who were taking diabetic medication (28.7 kg) was significantly lower than for those who were not on such medication (30.3 kg; $p = 0.018$). There was no difference in hand-grip strength between persons who did and did not have a fracture of the forearm ($p = 0.238$), but there was a significant difference between those who reported no arthritis and those who were currently under medical care for arthritis (30.5 kg *v* 28.8 kg; $p = 0.001$).

At the end of the interview session, the interviewer was asked "Did the participant seem oriented and did he seem to understand the questions and instructions?" For persons who, based on interviewer's assessment, appeared disoriented, the mean hand-grip strength was significantly weaker (22.1 kg) than for those who seemed well oriented (30.9 kg) and those about whom the interviewer was uncertain (26.3 kg), $p<0.001$. Persons who were assessed to be well oriented had significantly lower mean intensity exposure scores to pesticides (19.7 *v* 24.7, $p = 0.006$), solvents (30.9 *v* 36.4, $p = 0.019$), and metals (24.8 *v* 28.7, $p = 0.005$) when compared to men whose orientation was evaluated as poor or uncertain. The mean exposures for manganese and mercury were also lower for the well oriented men but the differences were not statistically significant (data not shown). General orientation of the participant and use of diabetes medication were assessed as potential confounders with no resultant effect on the association, so they were excluded from the final models.

The significant decreasing trend seen with pesticide and solvent exposure in the univariate model disappeared after adjustment for coffee consumption, physical activity, BMI, glucose, cognitive function (CASI score), education, haemoglobin, arthritis, forearm fracture, and hand-grip strength at exam I (table 6). None of the other occupational exposures showed statistically significant associations with hand-grip strength in the fully adjusted model.

Over a 25 year period, the decline in hand-grip strength was an average of 8–9 kg regardless of exposure (table 7). After full risk factor adjustment, the mean decline in hand-grip strength with all exposures was similar to the unadjusted mean values.

DISCUSSION

Pesticide and solvent exposure at work at exam I were associated with diminished hand-grip strength 25 years later; however, the association disappeared after risk factor adjustment. Our results disagree with the results of a case-control study, where persons occupationally exposed to a variety of volatile organic solvents had significant impairment of motor functions such as hand-grip strength.[17] That study had a much smaller sample size ($n = 57$) than ours.

In a case-control study that evaluated the effects of acute organophosphate pesticide poisonings on hand grip and pinch strength, subjects who were severely and moderately poisoned with this agent showed significantly weaker hand-grip strength compared with controls.[15] These authors also reported that men who were severely poisoned with these neuropathic agents had large and significant deficits in hand-grip strength at the first examination, which worsened considerably at the second examination.[16] The men recovered part of their strength at the third examination, but they remained significantly weaker than the controls. High levels of pesticide exposure, such as those obtained through chemical disasters, are more likely to cause symptoms that would require the need for hospitalisation (for example, hypersalivation, chest tightness due to bronchoconstriction).[8] More moderate exposures cause subtle abnormalities, some of which may be evident only through neurological examination.

Additional findings in our study include independent associations between several variables and hand-grip strength. Results from analysis of variance showed general decreases in the mean values of age and glucose, and increases in BMI, CASI scores, and haemoglobin levels with increasing hand-grip strength. Older men and men with higher BMI at baseline (who also had higher initial grip strength) were also more likely to experience steeper declines in hand-grip strength. Reasons for these findings are unclear, yet similar results were also reported elsewhere.[34] Adjustment for physical activity and education (separately) did not alter the direct association between BMI and decline in hand-grip strength. Desrosiers and colleagues[34] suggested that because the women in their study were initially weaker than the men, they lost less grip strength. However, this reasoning is not substantiated because another study found greater grip strength declines for women than for men.[35] It is also possible that participants with higher BMI may have been more prone to develop medical conditions over the 25 year period causing a more rapid loss of hand-grip strength. The inverse relation of hand-grip strength with age has been reported in several studies.[23 25 34 36] Certain indicators of mental and nutritional status may affect hand-grip strength.[24 38] For example, depressed mood has been associated with a decrease in hand-grip strength. In our study, information on depression was available for a limited subset, but sample sizes were insufficient to allow for meaningful analyses. Pennix and colleagues[38] investigated the association between anaemia and several markers of physical functioning among elderly persons in Italy. Anaemic persons had significantly lower hand-grip strength than those without anaemia. Our findings were consistent with that of Pennix and colleagues, but anaemic persons did not show a greater adverse effect on hand-grip strength from any occupational exposure.

Decline in hand-grip strength is predictive of increased disability and mortality in older individuals. Previous results from the HAAS found that persons who exhibited lower hand-grip strength at baseline and lower body weight, in all

Table 3 Mean levels and univariate regression coefficients of participant characteristics at exam I by hand-grip strength (kg) at exam I

	Levels of hand-grip strength in kg at exam I					
	11–36 (n = 1054)	37–39 (n = 713)	40–44 (n = 1050)	⩾45 (n = 702)	Coeff/SE	p for trend*
Age (years)	54.7 (5.3)	52.6 (4.5)	51.8 (4.1)	50.7 (3.5)	−0.437/0.020	<0.001
Physical activity	33.1 (4.3)	32.8 (4.8)	32.8 (4.8)	32.7 (4.8)	−0.004/0.002	0.062
Coffee consumption (4 oz cups)	3.2 (3.1)	3.4 (3.4)	3.4 (3.1)	3.7 (3.5)	0.1515/0.031	<0.001
Glucose (mg/dl)	149.7 (46.2)	153.1 (48.7)	151.9 (47.8)	150.1 (48.9)	−0.002/0.002	0.464
BMI (kg/m^2)	23.1 (3.0)	23.8 (2.8)	24.0 (2.7)	24.9 (2.7)	0.531/0.034	<0.001
Alcohol intake (g/month)	344.4 (623.8)	319.1 (567.3)	336.6 (590.6)	359.9 (625.4)	0.0001/0.001	0.906
Smoking (pack-years)	21.4 (24.1)	22.1 (23.5)	20.6 (21.7)	21.9 (22.5)	0.0021/0.004	0.634

* p for trend obtained from linear regression models (unadjusted).
n changes slightly for each variable.
Coeff, parameter estimate from linear regression models; SE, standard error (note: the regression coefficients were unadjusted).

Table 4 Mean levels and univariate regression coefficients of participant characteristics at exams I and IV by hand-grip strength (kg) at exam IV

	Levels of hand-grip strength in kg at exam IV					
	0–25 (n = 774)	26–30 (n = 1009)	31–35 (n = 987)	⩾36 (n = 752)	Coeff/SE	p for trend*
Age (years)	56.0 (5.4)	53.1 (4.3)	51.3 (3.8)	50.1 (3.0)	−0.648/0.022	<0.001
Physical activity	33.2 (4.7)	32.9 (4.8)	32.7 (4.6)	32.6 (4.6)	−0.008/0.003	0.002
Coffee consumption (4 oz cups)	3.1 (3.0)	3.3 (3.3)	3.5 (3.3)	3.8 (3.3)	0.1472/0.035	<0.001
Glucose (mg/dl)	154.7 (53.2)	154.3 (50.3)	149.0 (43.0)	146.0 (43.5)	−0.010/0.002	<0.001
BMI (kg/m^2)	23.3 (3.0)	23.9 (2.9)	24.0 (2.7)	24.3 (2.7)	0.271/0.040	<0.001
Alcohol intake (g/month)	358.2 (692.8)	336.6 (575.4)	323.0 (562.7)	348.8 (590.5)	−0.0001/.001	0.487
Smoking (pack-years)	22.5 (24.5)	20.8 (23.1)	20.9 (22.6)	21.8 (21.5)	−0.0050/.005	0.366
CASI score†	73.1 (21.3)	84.3 (10.0)	87.5 (8.4)	88.1 (7.4)	0.226/0.007	<0.001
Education† (years)	9.6 (3.2)	10.5 (3.2)	10.9 (3.2)	11.0 (3.0)	0.332/0.035	<0.001
Haemoglobin† (g/dl)	14.2 (1.6)	14.7 (1.4)	15.1 (1.3)	15.3 (1.2)	1.455/0.078	<0.001

* p for trend obtained from linear regression models (unadjusted).
†Covariates assessed at exam IV.
n changes slightly for each variable.
Coeff, parameter estimate from linear regression models; SE, standard error (note: the regression coefficients were unadjusted).

Table 5 Mean levels and univariate regression coefficients of participant characteristics at exams 1 and IV by decline in hand-grip strength

	Levels of decline in hand-grip strength (in kg)					
	−12–4 (n = 684)	5–8 (n = 958)	9–13 (n = 1142)	⩾14 (n = 735)	Coeff/SE	p for trend*
Age (years)	51.3 (3.9)	52.3 (4.6)	53.0 (4.8)	53.6 (5.1)	0.209/0.021	<0.001
Physical activity	32.7 (4.2)	32.9 (4.5)	32.8 (4.8)	33.1 (5.0)	0.004/0.002	0.074
Coffee consumption (4 oz cups)	3.3 (3.0)	3.5 (3.3)	3.5 (3.4)	3.3 (3.1)	0.0033/0.030	0.915
Glucose (mg/dl)	146.9 (41.6)	148.0 (46.1)	152.6 (49.1)	156.8 (52.2)	0.010/0.002	<0.001
BMI (kg/m^2)	23.4 (2.8)	23.7 (2.8)	24.0 (2.8)	24.4 (2.9)	0.257/0.034	<0.001
Alcohol intake (g/month)	325.7 (553.9)	338.3 (601.0)	328.4 (567.5)	373.7 (696.2)	0.0002/0.001	0.346
Smoking (pack years)	20.2 (21.7)	22.0 (23.1)	21.5 (23.1)	21.7 (23.6)	0.0063/0.004	0.141
CASI score†	86.4 (8.8)	86.0 (8.9)	83.7 (12.3)	77.5 (21.2)	−0.117/0.007	<0.001
Education† (years)	10.7 (3.2)	10.6 (3.1)	10.5 (3.2)	10.3 (3.2)	−0.082/0.031	0.008
Haemoglobin† (g/dl)	15.2 (1.2)	15.0 (1.3)	14.8 (1.4)	14.4 (1.7)	−0.847/0.068	<0.001

* p for trend obtained from linear regression models (unadjusted).
†Covariates assessed at exam IV.
n changes slightly for each variable.
Coeff, parameter estimate from linear regression models; SE, standard error (note: the regression coefficients were unadjusted).

age groups, were more likely to die before the follow up examination.[4 5 28]

There are some limitations in this study. We based our exposure estimates on reported usual or last job held. Therefore, this may not have accurately reflected all the jobs that the participants held over their exposure history. We were not able to adjust for depression, a factor that possibly may have produced bias in this study, weakening or strengthening our associations. Information on non-occupational exposures was not available. Misclassification of environmental exposures is likely to have resulted in non-differential bias, producing weaker associations. The long delay between exposures and outcomes means that exposures could have changed during the follow up period. No information was available on use of personal protective equipment (PPE), a likely effect modifier. It is reasonable to assume that during the earlier decades, none of the participants had access to PPE but this situation could have changed to some extent during the later years.

By excluding from our study participants who had died by exam IV, we were also excluding those who were older and/or less healthy, and who consequently had weaker hand-grip

Table 6 Unadjusted and adjusted mean hand-grip strength (kg) at exam IV (1991–93) and linear regression coefficients by occupational intensity score categories at exam I (1965–68)

	Unadjusted			Risk factor adjusted*		Risk factor adjusted†	
	n	Mean (SD)	Coeff/SE	Mean (SE)	Coeff/SE	Mean (SE)	Coeff/SE
Pesticide							
Zero	3266	30.3 (6.7)	−0.022/0.007	30.4 (0.1)	−0.0032/0.006	30.4 (0.1)	0.0053/0.005
Low	64	31.2 (7.0)		32.3 (0.7)		31.6 (0.6)	
Medium	119	29.4 (7.9)		30.7 (0.6)		31.1 (0.5)	
High	66	27.6 (5.6)		29.3 (0.7)		30.2 (0.6)	
p for trend		<0.001		0.580		0.275	
Solvent							
Zero	1699	30.3 (6.7)	−0.010/0.004	30.3 (0.1)	−0.0013/0.004	30.4 (0.1)	−0.0026/0.003
Low	1145	30.5 (6.8)		30.7 (0.2)		30.6 (0.2)	
Medium	484	29.9 (7.0)		30.5 (0.3)		30.3 (0.2)	
High	187	29.4 (6.4)		30.2 (0.4)		30.5 (0.4)	
p for trend		0.014		0.730		0.414	
Metal							
Zero	2076	30.3 (6.8)	−0.004/0.005	30.3 (0.1)	0.0065/0.005	30.4 (0.1)	−0.0001/0.004
Low	1039	30.4 (6.6)		30.7 (0.2)		30.5 (0.2)	
Medium	318	30.1 (6.9)		30.9 (0.3)		30.3 (0.3)	
High	82	29.6 (6.7)		30.5 (0.7)		30.5 (0.5)	
p for trend		0.441		0.168		0.984	
Manganese							
Zero	2788	30.3 (6.8)	0.004/0.006	30.4 (0.1)	0.0102/0.005	30.5 (0.1)	0.0038/0.005
Low	392	30.6 (6.9)		31.2 (0.3)		30.9 (0.3)	
Medium	147	30.7 (6.4)		30.9 (0.5)		30.6 (0.4)	
High	59	30.4 (6.8)		31.1 (0.8)		30.8 (0.6)	
p for trend		0.554		0.063		0.409	
Mercury							
Zero	2891	30.3 (6.9)	−0.004/0.011	30.5 (0.1)	0.0022/0.009	30.5 (0.1)	−0.0007/0.008
Low	157	31.1 (6.0)		31.0 (0.5)		30.5 (0.4)	
Medium	195	30.6 (6.5)		30.9 (0.4)		31.0 (0.4)	
High	143	29.8 (6.2)		30.3 (0.5)		30.2 (0.4)	
p for trend		0.700		0.814		0.929	

CASI score, education, and haemoglobin levels were assessed at exam IV; all other covariates were assessed at exam I.
*Adjusted for coffee consumption, physical activity, BMI, glucose, cognitive function (CASI score), education, haemoglobin, arthritis, and forearm fracture.
†Adjusted for coffee consumption, physical activity, BMI, glucose, cognitive function (CASI score), education, haemoglobin, arthritis, forearm fracture, and hand-grip strength at exam I.
Categories for mercury intensity scores are 0, 1–20, 21–30, ⩾31; categories for the four other intensity scores are 0, 1–39, 40–79, ⩾80.
Coeff, parameter estimate from linear regression models; SE, standard error.
p for trend obtained from linear regression models.

strength. Analyses showed that the mean (SD) baseline hand-grip strength of men who were not present at exam IV was about 2 kg lower compared to those who participated in exam IV—37.4 (6.4) versus 39.0 (6.1). Participants who were more likely to be absent at exam IV would also be those who might have been more seriously affected by the occupational exposures. Therefore, a survival bias may be present which would tend to reduce associations if present.

A major strength of the study is its prospective design. The sample size is large, thus allowing for adequate power even after stratification. Several factors were available for assessment of confounding. Objective measurements of hand-grip strength were taken with a dynamometer that is known to be accurate and reliable.[39] We excluded persons with clinical diagnoses of PD or stroke by exam IV since their hand-grip ability might have been affected by these conditions. Our study used the best possible method for assessing chronic exposure in an occupational epidemiological study. Exposure assessment methods combined exposures from the usual job (and sometimes from the present job) at exam I with the number of years worked to produce a measure of cumulative exposure. Industrial hygienists used their professional knowledge to develop the assignment of exposures. It is likely that this process benefited the study by minimising misclassification of exposure. To our knowledge, our study was one of the larger studies to investigate pesticide and solvent exposures with hand-grip strength, and the first epidemiological study to investigate associations between occupational exposures to these metals and hand-grip strength.

This study did not provide evidence that cumulative occupational exposure to pesticides, solvents, and metals, after adjustment for other factors, adversely affected hand-grip strength or its change over time. Due to certain limitations, these results should be interpreted with caution. However, consistent with other studies, some factors assessed during mid-life were independently related to hand-grip strength later in life and to the decline in hand-grip strength. Age, smoking, and glucose were inversely related, while education, cognitive function, and haemoglobin (assessed at exam IV), and BMI were directly related to hand-grip strength. In addition, increasing age, smoking, glucose, BMI, and decreasing education, cognitive function and haemoglobin were associated with greater declines in hand-grip strength over time.

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Table 7 Unadjusted and adjusted mean decline in hand-grip strength over 25 years (1965–68 to 1991–93) and linear regression coefficients by occupational intensity score categories at exam IV (1965–68)

	Unadjusted			Risk factor adjusted*		Risk factor adjusted†	
	n	Mean (SD)	Coeff/SE	Mean (SE)	Coeff/SE	Mean (SE)	Coeff/SE
Pesticide							
Zero	3263	9.3 (5.8)	−0.003/0.006	9.3 (0.1)	−0.0121/0.005	9.2 (0.1)	−0.0056/0.005
Low	64	9.2 (6.5)		8.6 (0.7)		8.1 (0.6)	
Medium	119	8.9 (6.5)		8.3 (0.5)		8.6 (0.5)	
High	66	9.4 (4.3)		8.7 (0.7)		9.3 (0.6)	
p for trend		0.621		0.027		0.256	
Solvent							
Zero	1697	9.2 (5.8)	0.004/0.004	9.1 (0.1)	0.0038/0.004	9.2 (0.1)	0.0029/0.003
Low	1144	9.3 (5.9)		9.2 (0.2)		9.1 (0.2)	
Medium	484	9.8 (5.7)		9.6 (0.3)		9.4 (0.2)	
High	187	9.2 (5.9)		9.0 (0.4)		9.2 (0.4)	
p for trend		0.249		0.289		0.360	
Metal							
Zero	2074	9.2 (5.9)	0.006/0.004	9.1 (0.1)	0.0054/0.004	9.2 (0.1)	0.0004/0.004
Low	1038	9.2 (5.6)		9.2 (0.2)		9.1 (0.2)	
Medium	318	10.2 (6.0)		9.8 (0.3)		9.4 (0.3)	
High	82	9.3 (5.9)		9.2 (0.6)		9.2 (0.5)	
p for trend		0.160		0.227		0.916	
Manganese							
Zero	2786	9.3 (5.9)	0.004/0.005	9.2 (0.1)	0.0015/0.005	9.3 (0.1)	−0.0033/0.005
Low	392	9.4 (5.9)		9.1 (0.3)		8.9 (0.3)	
Medium	147	9.5 (5.1)		9.5 (0.5)		9.2 (0.4)	
High	59	9.5 (6.4)		9.2 (0.7)		9.0 (0.6)	
p for trend		0.504		0.778		0.472	
Mercury							
Zero	2889	9.3 (5.9)	0.004/0.009	9.2 (0.1)	0.0030/0.009	9.2 (0.1)	0.0012/0.008
Low	157	9.5 (5.0)		9.7 (0.4)		9.3 (0.4)	
Medium	195	8.7 (5.7)		8.7 (0.4)		8.8 (0.4)	
High	143	9.8 (5.6)		9.5 (0.5)		9.5 (0.4)	
p for trend		0.647		0.726		0.876	

CASI score, education, and haemoglobin levels were assess at exam IV; all other covariates were assessed at exam I.
*Adjusted for coffee consumption, physical activity, BMI, glucose, cognitive score (CASI score), haemoglobin, and education.
†Adjusted for coffee consumption, physical activity, BMI, glucose, cognitive score (CASI score), haemoglobin, education, and hand-grip strength at exam 1.
Decline in hand-grip strength = hand-grip strength at exam I minus hand-grip strength at exam IV.
Categories for mercury intensity scores are 0, 1–20, 21–30, ⩾31; categories for the four other intensity scores are 0, 1–39, 40–79, ⩾80.
Coeff, parameter estimate from linear regression models; SE, standard error.
p for trend obtained from linear regression models.

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