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ABSTRACT

Introduction In view of the debate about biomechanical and toxic factors in Dupuytren's disease, we aimed to describe its relationship with certain occupational factors and alcohol intake and smoking.

Method Subjects in the French GAZEL cohort answered a questionnaire in 2012 included self-reported Dupuytren's disease, such as disabling Dupuytren's disease (including surgery). In 2007, self-assessed lifetime occupational biomechanical exposure was recorded (carrying loads, manipulating a vibrating tool, climbing stairs), as well as alcohol intake, smoking and diabetes mellitus. Analyses were performed on high alcohol intake, smoking and duration of relevant work exposure, stratified by gender for both outcomes.

Results A total of 13,587 subjects answered the questionnaire in 2012 (73.7% of the questionnaire sent) and constituted the sample (10,017 men and 3,570 women, aged from 64 to 73 years; mean age for men 68 years and for women 65 years). Among men age, diabetes, heavy drinking and over 15 years of manipulating a vibrating tool at work were significantly associated with Dupuytren's disease; except for diabetes, the association with these factors was stronger for disabling Dupuytren's disease (or surgery). Among the 3,570 women included, 160 reported Dupuytren's disease (4.5%). The number of cases in the group of women was too low to reach conclusions, although the findings seemed similar for age, diabetes and vibration exposure.

Conclusion In this large French cohort study, Dupuytren's disease in men was associated with high levels of alcohol consumption and exposure to hand-transmitted vibration. It is likely that the same applied to women.

ARTICLE SUMMARY

- The longitudinal study confirmed that Dupuytren's disease in men was associated with high levels of alcohol consumption and exposure to hand-transmitted vibration in this large French cohort study, adjusted for age and diabetes.

- Although this is one of the first studies to analyze risk factors for women, the number of cases was too small to draw conclusions, though they appeared similar.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The study had limitations: self-reported diagnosis, possible residual confounding (genetic factors mainly).

- Strengths of our study came from the longitudinal design, the relatively large size of the cohort, women included.

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Dupuytren's disease is characterized by chronic contracture of the (fourth and fifth) fingers of the hand toward the palm, usually accompanied by thickening of the palmar skin.[1] It has a clear genetic background.[2–4]

Since its description by Guillaume Dupuytren in 1831 following Henry Cline Sr. and Sir Astley Cooper, there has been controversy regarding biomechanical work exposure which might contribute to the development of this disorder.[5] An exhaustive review and a meta-analysis was conducted to address this controversy, and concluded that there is good evidence of an association between vibration exposure and Dupuytren's disease.[6,7] However, recent opinion still considers that occupational exposure, including vibration, is not a risk factor for Dupuytren's disease in manual workers.[1,8,9] These authors argued there are still conflicting results and that evidence is based only on two longitudinal studies. The roles of alcohol consumption and smoking are also a matter of debate,[9,10] although one large longitudinal study found a clear relationship between such exposure and Dupuytren's disease.[11]

We used data from the GAZEL cohort study to describe the prevalence of Dupuytren's disease, and to analyze its association with certain risk factors, including exposure to vibration, alcohol intake and smoking.

METHODS

Population

The GAZEL cohort is made up of employees of Electricité de France (EDF) and Gaz de France (GDF), the French national utility for energy production and distribution. The company employs workers in various trades and of different socioeconomic status. At baseline in 1989, the cohort included 20,625 volunteers and 18,428 followed, men then aged

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40–50 and women 35–50 years. In January of each year since then, the participants have completed a general self-administered questionnaire about their lifestyle, health, and occupational situation.[12]

In the present study, we included only the subjects who answered the 2012 GAZEL questionnaire (which included a question about Dupuytren's disease).

Potential risk factors

Information on gender and age (at 2012), was collected through the general questionnaire. Occupational risk factors were assessed in the 2007 questionnaire. Data on nine different types of biomechanical exposure were available, including the number of years of exposure during their working lives. In this study of Dupuytren's disease, we analyzed the potential role of manipulating a vibrating tool. As information about forceful activity was not available, carrying loads was considered to be a proxy for forceful work and was also taken into account. Climbing stairs, an irrelevant exposure for Dupuytren's disease, was also used as a 'control exposure' to check the lack of relationship. For these variables, three categories were considered for men based on duration of exposure: i.e. never exposed, exposed but for less than 15 years, and exposed for 15 years or more. In the view of the number of exposed women in the cohort, the exposure for women was only considered as yes or no. In addition, at inception of the cohort in 1989, a 'yes or no' question about manipulating vibrating tools was also available, and computer work was used as control exposure.

Data for alcohol consumption were available for each year since 1992, and three categories were also considered on the basis of the distribution observed. Only heavy drinkers were taken into account based on the results of a previous study:[13] less than 3 glasses aday of any alcohol, 3 to 4 glasses of wine or beer, and 5 or more glasses of wine/beer or 3 glasses or more of spirits a day. If a subject had increased his alcohol consumption between 1992 and

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2012, the highest category was taken into consideration. Data on smoking had been collected at inception in 1989 and grouped in three categories and: nonsmoker or former smoker, 1 to 20 cigarettes/cigars or pipes, over 20 cigarettes/cigars or pipes per day. As for alcohol consumption, the highest smoking category was taken into consideration, if the subject had increased consumption during the study period.

Diabetes mellitus was self-reported every year fron 1989.

Outcomes

When assessed in 2012, a specific question on Dupuytren's disease was asked: " 1) Have you ever had Dupuytren's disease (thickening of the palmar skin, nodes or contracture of the fourth fingers of the hand)? ; 2) if yes, do you have any limitation from it? 3) Have you had surgery for it?".

We considered two outcomes, i.e. Dupuytren's disease (yes or no) based on the answer to the first question; and a three category variable: no Dupuytren's disease (reference), Dupuytren's disease without surgery and without limitations, Dupuytren's disease with surgery or limitation.

Analyses

Univariate and multivariate analyses were stratified on gender for both outcomes. For the multinomial regression model, all the variables were included, except 'control exposure' variables. Statistical Analysis Software was used for all statistical analyses (SAS, v9.3, SAS Institute Inc, Cary, NC, USA). Associations were considered statistically significant if the p-value was less than 0.05.

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RESULTS

The 13 587 subjects who answered the GAZEL questionnaire in 2012 constituted the sample (10,017 men and 3,570 women). The participation rate was 73.7% (18,428 questionnaires sent in 2012). Subjects were aged from 59 to 73 years (mean age 68 years for men and 65 years for women).

Of the 10,017 men included, 839 reported Dupuytren's disease (8.4%), including 342 who reported surgery or limitations (3.4%). Age, diabetes mellitus, heavy drinking and over 15 years of manipulating a vibrating tool at work were significantly associated with self-reported Dupuytren's disease, with a dose-effect relationship (Table 1). Similar results were found when a yes/no question was used at the inception of the cohort in 1989. As expected, none of the 'control exposure' variables were associated with Dupuytren's disease. Reported durations of exposure of carrying loads and smoking habits were not found to be associated with Dupuytren's disease. The associations were stronger when considering disabling Dupuytren's disease (or surgery) than for Dupuytren's disease without reported surgery or disability (Table 2). Figure 1 show a clear dose effect in relation to duration of exposure, with a 5 year step.

Of the 3,570 women included, 160 reported Dupuytren's disease (4.5%), including 78 who reported surgery or limitations (2.2%). Associations were found to be weak and questionable, although age, diabetes and vibration exposure were still significant (Tables 3 and 4); however, only small numbers of women were in the heavy drinking and occupationally exposed groups.

DISCUSSION

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The study confirmed that Dupuytren's disease in men was associated with high levels of alcohol consumption and exposure to hand-transmitted vibration in this large French cohort study, adjusted for age and diabetes, whereas smoking habits and other types of occupational exposure were not. Although this is one of the first studies to analyze risk factors for women, the number of cases was too small to draw conclusions, though they appeared similar.

The study had various limitations. The diagnosis was self-reported, without confirmation of any physical examination by a physician. However, Dupuytren's disease is easily diagnosed, with no major differential diagnoses. The lack of confirmation possibly led therefore to an underestimation of the disorder, but this was probably limited considering that the prevalence of this disorder in the study was comparable with information available for the same age category in the general population.[9] A possible residual confounding effect should also be discussed: information regarding genetic factors, such as family history of Dupuytren's disease, hand trauma, epilepsy and anticonvulsant drug intake, that are considered to be associated with Dupuytren's disease, was not available. However, an association between these factors and vibration exposure and alcohol intake seems unlikely.

One of the strengths of our study is the relatively large size of the cohort. Since we had only one measure of Dupuytren's disease in 2012, i.e. the number of reported cases of Dupuytren's disease, we studied factors associated with prevalent cases. However, assessment of work exposure five years before evaluation of the outcome, and the regular evaluation of alcohol intake and smoking throughout the follow-up period enabled us to be confident about the associations observed, that were confirmed by information collected at inception, i.e. 23 years before.

One important finding was confirmation of the association between alcohol consumption in men with Dupuytren's disease, with a dose-response relationship.[11,13,14] The association with reported limitations (or surgery) was interesting because this has been described many times by clinicians but never reported in large cohort studies.[1] Diabetes seemed to be related to the occurrence of Dupuytren's disease and not with limitations in men, but interestingly was associated with limitations in women. Smoking and heavy smoking were not found to be associated with Dupuytren's disease, which was unexpected considering the possible ischemic etiology of Dupuytren's disease and some recent studies.[11,14] Lack of relationship was possibly due to the limited number of very heavy smokers (61 men and 26 women smoked 2 packs/day or more).

In terms of occupational exposure, only vibration was found to be related to Dupuytren's disease. Previous studies have showed that high cumulative work exposure to vibration (intensity x duration) was associated with Dupuytren's disease.[13,15–18] Although exposure to vibration during working life was self-reported, it corresponded to specific exposure with a probably low memory effect. Hand-vibration transmitting tools in our cohort were mostly screw tools, common drills and (infrequently) pneumatic drills, where strenuous hand grip increase vibration damage. The role of high levels of vibration exposure is plausible, especially as a result of the local hypoxia and chronic ischemia hypothesized in Dupuytren's contracture.[4] Similar magnitudes of strength of association found in published studies support the plausibility of a causal relationship.[7] Carrying loads was studied because, with some tasks, such exposure is associated with manual work, and heavy forceful exposure during the working life was not available in the GAZEL cohort. However, no relationship was found here.

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In addition to the well-established genetic factors, and despite the limitations discussed, this study emphasized the roles of occupational hand-transmitted vibration exposure and alcohol consumption in Dupuytren's disease. The question of compensation in some cases following documented high levels of exposure should be reviewed, as should improvement of working conditions with a view to prevention.

DATA SHARING

There is no additional data available

AUTHORS CONTRIBUTION

All authors contributed significantly to the manuscript and approved the final version. MZ, MC and MG involved in the data collection, improved the analyses, comment the manuscript. AD initiate the work, performed the main analyses and draft the manuscript. ZM, CD and AL discussed the project, improved the analyses, comment the manuscript.

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COMPETING INTEREST: None to declare.

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	N (total)	n	%	Odds ratio (univariate analyses)	Odds ratio (multivariate analysis)*
Age²				**1.03 [1.01; 1.06]**	**1.03 [1.00; 1.06]**
Diabetes					
No	8581	692	8.06	1	1
Yes	1436	147	10.24	**1.30 [1.08; 1.57]**	**1.31 [1.07; 1.60]**
*Smoking habits (pack/day)** *					
Non-smoker (or former smoker)	6055	488	8.06	1	1
Smoker < 1	2670	229	8.58	1.07 [0.91; 1.26]	1.05 [0.88; 1.24]
Smoker ≥1	1246	117	9.39	1.18 [0.96; 1.46]	1.05 [0.83; 1.32]
*Drinking habits (glass/day)** *					
<3	2551	174	6.82	1	1
3or 4 glasses of wine /beer	4864	411	8.45	**1.26 [1.05; 1.52]**	**1.22 [1.01; 1.48]**
≥5 glasses of wine/beer or ≥3 glasses of spirits	2577	249	9.66	**1.46 [1.19; 1.79]**	**1.36 [1.10; 1.69]**
Carrying loads (assessed in 2007), number of years of exposure					
No	6812	565	8.29	1	1
1 to 15 years	1026	89	8.67	1.05 [0.83; 1.33]	0.95 [0.74; 1.22]
>15 years	1393	129	9.26	1.13 [0.92; 1.38]	0.91 [0.71; 1.16]
Climbing stairs (assessed in 2007), number of years of exposure					
No	7281	618	8.49	1	
1 to 15 years	810	63	7.78	0.91 [0.69; 1.19]	
>15 years	1147	102	8.89	1.05 [0.85; 1.31]	
Manipulating vibrating tools (assessed in 2007), number of years of exposure					
No	7630	614	8.05	1	1
1 to 15 years	772	76	9.84	1.25 [0.97; 1.60]	1.25 [0.95; 1.65]
>15 years	781	88	11.27	**1.45 [1.15; 1.84]**	**1.52 [1.15; 2.02]**
Carrying loads (assessed in 1989)					
No	8888	737	8.29	1	
Yes	1129	102	9.03	1.10 [0.88; 1.36]	
Manipulating vibrating tools (assessed in 1989)					
No	9278	760	8.19	1	
Yes	739	79	10.69	**1.34 [1.05; 1.71]**	
Computer work (assessed in 1989)					
No	5270	444	8.43	1	
Yes	4747	395	8.32	0.99 [0.86; 1.14]	

Table 1. Univariate and multivariate analyses of Dupuytren's disease (yes versus no) and available factors assessed in the previous period in men.

Data in bold: p<0.05) ,* model included all variables shown, **maximum consumption reached, ² age as continuous variable, OR associated with an increase of one unit

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	N (total)	n	%	Dupuytren's disease without limitations or surgery Odds ratio (univariate analyses)	Odds ratio (multivariate analysis)*	n	%	Dupuytren's disease with limitations or surgery Odds ratio (univariate analyses)	Odds ratio (multivariate analysis)*
Age²	10017	496	4.95	1.01 [0.98; 1.04]	1.00 [0.97; 1.04]	343	3.42	**1.07 [1.03; 1.11]**	**1.07 [1.03; 1.11]**
Diabetes									
No	8581	405	4.72	1	1	287	3.34	1	1
Yes	1436	91	6.34	**1.38 [1.09; 1.74]**	**1.41 [1.10; 1.82]**	56	3.90	1.19 [0.89; 1.60]	1.18 [0.87; 1.59]
Smoking habits (pack/day)**									
Non-smoker (or former smoker)	6055	292	4.82	1	1	196	3.24	1	1
Smoker < 1	2670	132	4.94	1.03 [0.83; 1.27]	1.04 [0.83; 1.30]	97	3.63	1.13 [0.88; 1.45]	1.06 [0.81; 1.37]
Smoker ≥1	1246	68	5.46	1.15 [0.88; 1.51]	1.06 [0.79; 1.43]	49	3.93	1.23 [0.90; 1.70]	1.04 [0.74; 1.46]
Drinking habits (glass/day)**									
<3	2551	103	4.04	1	1	71	2.78	1	1
3 or 4 glasses of wine /beer	4864	264	5.43	**1.37 [1.08; 1.73]**	**1.32 [1.03; 1.68]**	147	3.02	1.11 [0.83; 1.47]	1.09 [0.81; 1.47]
≥5 glasses of wine/beer or ≥3 glasses of spirits	2577	125	4.85	1.24 [0.95; 1.62]	1.12 [0.84; 1.50]	124	4.81	**1.78 [1.32; 2.40]**	**1.71 [1.25; 2.33]**
Carrying loads (assessed in 2007), number of years of exposure									
No	6812	350	5.14	1	1	215	3.16	1	1
1 to 15 years	1026	48	4.68	0.91 [0.67; 1.25]	0.88 [0.63; 1.22]	41	4.00	1.27 [0.90; 1.79]	1.06 [0.73; 1.52]
>15 years	1393	61	4.38	0.86 [0.65; 1.14]	0.79 [0.56; 1.09]	68	4.88	1.56 [1.18; 2.07]	1.08 [0.76; 1.52]
Climbing stairs (assessed in 2007), number of years of exposure									
No	7281	358	4.92	1		260	3.57	1	
1 to 15 years	810	42	5.19	1.05 [0.75; 1.45]		21	2.59	0.72 [0.46; 1.13]	
>15 years	1147	58	5.06	1.03 [0.78; 1.37]		44	3.84	1.08 [0.78; 1.50]	
Manipulating vibrating tools (assessed in 2007), number of years of exposure									
No	7630	377	4.94	1	1	237	3.11	1	1
1 to 15 years	772	38	4.92	1.02 [0.72; 1.43]	1.05 [0.72; 1.52]	38	4.92	**1.62 [1.14; 2.30]**	**1.56 [1.07; 2.29]**
>15 years	781	40	5.12	1.07 [0.77; 1.50]	1.20 [0.81; 1.78]	48	6.15	**2.05 [1.49; 2.82]**	**1.98 [1.34; 2.91]**
Carrying loads (assessed in 1989)									
No	8888	437	4.92	1		300	3.38	1	
Yes	1129	59	5.23	1.07 [0.81; 1.42]		43	3.81	1.14 [0.82; 1.58]	
Manipulating vibrating tools (assessed in 1989)									
No	9278	453	4.88	1		307	3.31	**1**	
Yes	739	43	5.82	1.23 [0.89; 1.69]		36	4.87	**1.51 [1.06; 2.16]**	
Computer work (assessed in 1989)									
No	5270	262	4.97	1		182	3.45	1	
Yes	4747	234	4.93	0.99 [0.83; 1.19]		161	3.39	0.98 [0.79; 1.22]	

Table 2. Univariate and multivariate analyses of Dupuytren's disease (without limitations or surgery, with limitations or surgery, compared with reference class: no Dupuytren's disease) and available factors assessed in the previous period in men.

Data in bold: p<0.05,* model included all variables shown, **maximum consumption reached, ² age as continuous variable, OR associated with an increase of one unit

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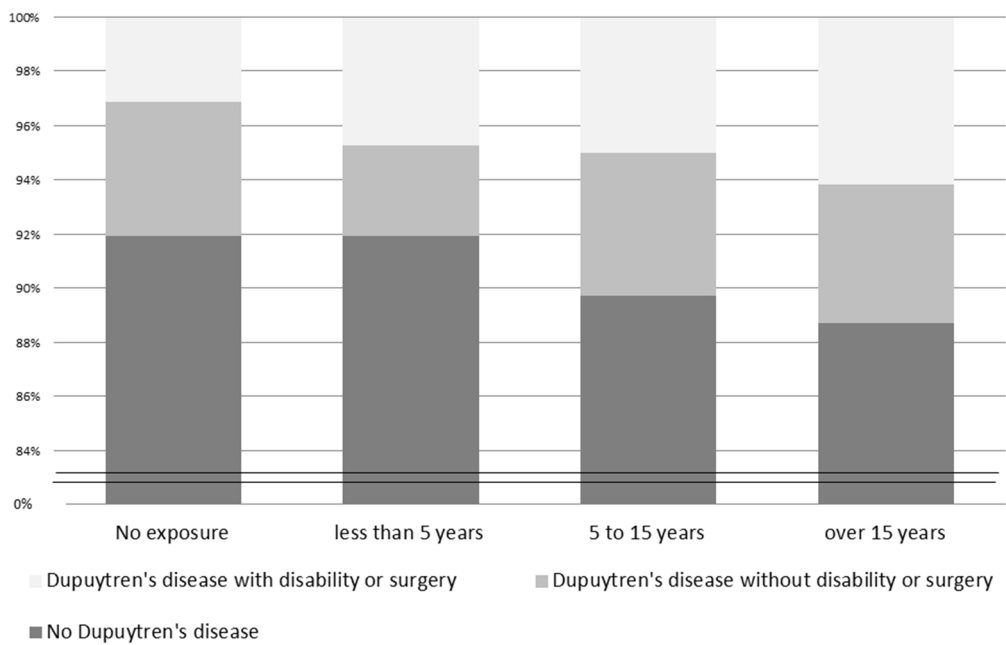|	N (total)	n	%	Odds ratio (univariate analyses)	Odds ratio (multivariate analysis)*
Age²	3570	160	4.48	**1.05 [1.01; 1.09]**	**1.05 [1.01; 1.10]**
Diabetes					
No	3252	140	4.31	1	1
Yes	318	20	6.29	**1.49 [0.92; 2.42]**	**1.71 [1.04; 2.81]**
*Smoking habits (pack/day)**					
Non-smoker (or former smoker)	2626	115	4.38	1	1
Smoker < 1	711	34	4.78	1.10 [0.74; 1.62]	1.16 [0.76; 1.77]
Smoker ≥1	187	8	4.28	0.98 [0.47; 2.03]	0.96 [0.43; 2.11]
*Drinking habits (glass/day)**					
<3	2423	103	4.25	1	1
3or 4 glasses of wine /beer	843	39	4.63	1.09 [0.75; 1.59]	0.83 [0.54; 1.27]
≥5 glasses of wine/beer or ≥3 glasses of spirits	271	17	6.27	1.51 [0.89; 2.56]	1.17 [0.64; 2.12]
Carrying loads (assessed in 2007)					
No	2995	131	4.37	1	
Yes	151	11	7.28	1.72 [0.91; 3.25]	
Climbing stairs (assessed in 2007)					
No	3024	137	4.53	1	
Yes	116	6	5.17	1.15 [0.50; 2.66]	
Manipulating vibrating tools (assessed in 2007)					
No	3163	142	4.49	1	1
Yes	4	2	50.0	**21.28 [2.98; 152.19]**	**17.17 [2.35; 125.62]**
Carrying loads (assessed in 1989)					
No	3433	153	4.46	1	
Yes	137	7	5.11	1.15 [0.53; 2.51]	
Manipulating vibrating tools (assessed in 1989)					
No	3555	159	4.47	1	
Yes	15	1	6.67	1.53 [0.20; 11.67]	
Computer work (assessed in 1989)					
No	885	39	4.41	1	
Yes	2685	121	4.51	1.02 [0.71; 1.48]	

Table 3. Univariate and multivariate analyses of Dupuytren's disease (yes versus no) and available factors assessed in the previous period in women.

Data in bold: p<0.05,* model included all variables shown, **maximum consumption reached, ² age as continuous variable, OR associated with an increase of one unit

	Dupuytren's disease without limitations or surgery				Dupuytren's disease with limitations or surgery			
N (total)	**n**	**%**	**Odds ratio (univariate analyses)**	**Odds ratio (multivariate analysis)***	**n**	**%**	**Odds ratio (univariate analyses)**	**Odds ratio (multivariate analysis)***
Age² 3570	82	2.30	1.04 [0.98; 1.09]	1.04 [0.98; 1.10]	78	2.18	**1.06 [1.01; 1.12]**	**1.07 [1.01; 1.13]**
Diabetes								
No 3252	75	2.31	1	1	65	2.00	1	1
Yes 318	7	2.20	0.97 [0.45; 2.13]	1.18 [0.53; 2.61]	13	4.09	**2.09 [1.14; 3.83]**	**2.27 [1.22; 4.24]**
Smoking habits (pack/day)**								
Non-smoker (or former smoker) 2626	62	2.36	1	1	53	2.02	1	1
Smoker < 1 711	16	2.25	0.96 [0.55; 1.67]	0.99 [0.54; 1.82]	18	2.53	1.26 [0.73; 2.16]	1.36 [0.76; 2.41]
Smoker ≥1 187	3	1.60	0.68 [0.21; 2.19]	0.78 [0.24; 2.55]	5	2.67	1.32 [0.52; 3.35]	1.15 [0.41; 3.27]
Drinking habits (glass/day)**								
≤3 2423	51	2.10	1	1	52	2.15	1	1
3 or 4 glasses of wine /beer 843	23	2.73	1.30 [0.79; 2.14]	1.06 [0.60; 1.87]	16	1.90	0.89 [0.50; 1.56]	0.63 [0.33; 1.20]
≥5 glasses of wine/beer or ≥3 glasses of spirits 271	8	2.95	1.43 [0.67; 3.05]	1.30 [0.57; 3.00]	9	3.32	1.58 [0.77; 3.25]	1.04 [0.46; 2.39]
Climbing stairs (assessed in 2007)								
No 3024	69	2.28	1		68	2.25	1	
Yes 116	2	1.72	0.76 [0.18; 3.14]		4	3.45	1.54 [0.55; 4.31]	
Manipulating vibrating tools (assessed in 2007)								
No 3163	70	2.21	1	1	72	2.28	1	1
Yes 4	1	25.00	**21.57 [1.93; 240.79]**	**18.69 [1.61; 216.66]**	1	25.00	**21.00 [1.88; 234.10]**	**15.87 [1.36; 184.70]**
Carrying loads (assessed in 1989)								
No 3433	78	2.27	1		75	2.18	1	
Yes 137	4	2.92	1.29 [0.47; 3.59]		3	2.19	1.01 [0.31; 3.24]	
Manipulating vibrating tools (assessed in 1989)								
No 3555	81	2.28	1		78	2.19	1	
Yes 15	1	6.67	2.99 [0.39; 23.05]		0	0.00	0.00 [0.00; I]	
Computer work (assessed in 1989)								
No 885	20	2.26	1		19	2.15	1	
Yes 2685	62	2.31	1.02 [0.61; 1.70]		59	2.20	1.02 [0.61; 1.73]	

Table 4. Univariate and multivariate analyses of Dupuytren's disease (without limitations or surgery, with limitations or surgery, compared to reference class: no Dupuytren's disease) and available factors assessed in the previous period in women.

Data in bold: p<0.05,* model included all variables shown, **maximum consumption reached, ² age as continuous variable, OR associated with an increase of one unit

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Proportion of Dupuytren's disease depending duration of vibration exposure in the working life (5 year step).
254x190mm (96 x 96 DPI)

Association between work exposure, alcohol intake, smoking and Dupuytren's disease in a large cohort study (Gazel) =>STROBE Statement

	Item No	Recommendation	YES/NO
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Yes
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Yes
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Yes
Objectives	3	State specific objectives, including any prespecified hypotheses	Yes
Methods			
Study design	4	Present key elements of study design early in the paper	Yes
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Yes
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Yes
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Yes
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Yes
Bias	9	Describe any efforts to address potential sources of bias	Yes
Study size	10	Explain how the study size was arrived at	N/A (multipurpose cohort)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Yes
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Yes
		(*b*) Describe any methods used to examine subgroups and interactions	Yes
		(*c*) Explain how missing data were addressed	N/A
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Yes
		(b) Give reasons for non-participation at each stage	No
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	Yes

			confounders	
			(b) Indicate number of participants with missing data for each variable of interest	Yes
			(c) Summarise follow-up time (eg, average and total amount)	Yes
Outcome data	15*	Report numbers of outcome events or summary measures over time	Yes
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Yes
		(*b*) Report category boundaries when continuous variables were categorized	Yes
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Yes
Discussion			
Key results	18	Summarise key results with reference to study objectives	Yes
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Yes
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Yes
Generalisability	21	Discuss the generalisability (external validity) of the study results	Yes
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Yes

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Association between work exposure, alcohol intake, smoking and Dupuytren's disease in a large cohort study (Gazel)

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Association between work exposure, alcohol intake, smoking and Dupuytren's disease in a large cohort study (Gazel)

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ABSTRACT

Introduction In view of the debate about biomechanical and toxic factors in Dupuytren's disease, we aimed to describe its relationship with certain occupational factors, alcohol intake and smoking.

Method Subjects in the French GAZEL cohort answered a questionnaire in 2012 including self-reported Dupuytren's disease (yes/no), and as disabling Dupuytren's disease (including surgery). In 2007, self-assessed lifetime occupational biomechanical exposure was recorded (carrying loads, manipulating a vibrating tool, climbing stairs), as well as alcohol intake, smoking and diabetes mellitus. Analyses were performed on high alcohol intake, smoking and duration of relevant work exposure, stratified by gender for both outcomes.

Results A total of 13,587 subjects answered the questionnaire in 2012 (73.7% of the questionnaire sent) and constituted the sample (10,017 men and 3,570 women, aged from 64 to 73 years; mean age for men 68 years and for women 65 years). Among men age, diabetes, heavy drinking and over 15 years of manipulating a vibrating tool at work were significantly associated with Dupuytren's disease; except for diabetes, the association with these factors was stronger for disabling Dupuytren's disease (or surgery). Among the 3,570 women included, 160 reported Dupuytren's disease (4.5%). The number of cases in the group of women was too low to reach conclusions, although the findings seemed similar for age, diabetes and vibration exposure.

Conclusion In this large French cohort study, Dupuytren's disease in men was associated with high levels of alcohol consumption and exposure to hand-transmitted vibration. It is likely that the same applied to women.

ARTICLE SUMMARY

- The longitudinal study confirmed that Dupuytren's disease in men was associated with high levels of alcohol consumption and exposure to hand-transmitted vibration in this large French cohort study, after adjustment for age and diabetes.

- Although this is one of the first studies to analyze risk factors for women, the number of cases was too small to draw conclusions, though associations appeared similar to those observed in men.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The study had limitations: self-reported diagnosis, possible residual confounding (genetic factors mainly).

- Strengths of our study came from the longitudinal design, the relatively large size of the cohort, women included.

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Dupuytren's disease is characterized by chronic contracture of the fourth and fifth fingers of the hand toward the palm, usually accompanied by thickening of the palmar skin.[1] It has a clear genetic background.[2–4]

Since its description by Guillaume Dupuytren in 1831 following Henry Cline Sr. and Sir Astley Cooper, there has been controversy regarding biomechanical work exposure which might contribute to the development of this disorder.[5] An exhaustive review and a meta-analysis was conducted to address this controversy, and concluded that there is good evidence of an association between vibration exposure and Dupuytren's disease.[6,7] However, some authors still consider that occupational exposure, including vibration, is not a risk factor for Dupuytren's disease in manual workers.[1,8,9] These authors argued there are still conflicting results and that evidence is based only on two longitudinal studies. The role of alcohol consumption and smoking are also a matter of debate,[9,10] although one large longitudinal study found a clear relationship between such exposure and Dupuytren's disease.[11]

We used data from a large cohort study to describe the prevalence of Dupuytren's disease, and to analyze its association with certain risk factors, including exposure to vibration, alcohol intake and smoking.

METHODS

Population

The GAZEL cohort is made up of employees of Electricité de France (EDF) and Gaz de France (GDF), the French national utility for energy production and distribution (GAZEL stands for GAZ and ELectricité). The company employs workers in various trades and of different socioeconomic status. At baseline in 1989, the cohort included 20,625 volunteers,

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men then aged 40–50 and women 35–50 years, and 18,428 are still followed up. In January of each year since then, the participants have completed a general self-administered questionnaire about their lifestyle, health, and occupational situation.[12]

In the present study, we included only the subjects who answered the 2012 GAZEL questionnaire (which included a question about Dupuytren's disease).

Potential risk factors

Information on gender and age (in 2012), was collected through the general questionnaire. Occupational risk factors were assessed in the 2007 questionnaire. Data on nine different types of biomechanical exposure were available, including the number of years of exposure during their working lives (carrying loads, bending trunk, drive a vehicle, kneeling, climbing stairs, climbing ladder, working with arm over the shoulder, carrying load on the shoulder, manipulating a vibrating tool). In this study of Dupuytren's disease, we analyzed the potential role of manipulating a vibrating tool. As information about forceful activity was not available, carrying loads was considered to be a proxy for forceful work and was also taken into account. Climbing stairs, an irrelevant exposure for Dupuytren's disease, was also used as a 'control exposure' to check the lack of relationship. For these variables, three categories were considered for men based on duration of exposure: i.e. never exposed, exposed but for less than 15 years, and exposed for 15 years or more. In view of the number of exposed women in the cohort, the exposure for women was only considered as yes or no. In addition, at inception of the cohort in 1989, a 'yes or no' question about manipulating vibrating tools was also available, and computer work was used as control exposure.

Data for alcohol consumption were available for each year since 1992, and three categories were also considered on the basis of the distribution observed. Only heavy drinkers were taken into account based on the results of a previous study:[13] less than 3 glasses a day of any

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alcohol, 3 to 4 glasses of wine or beer, and 5 or more glasses of wine/beer or 3 glasses or more of spirits a day. If a subject had increased his alcohol consumption between 1992 and 2012, the highest category was taken into consideration. Data on smoking had been collected at inception in 1989 and grouped in three categories : nonsmoker or former smoker, 1 to 20 cigarettes/cigars or pipes, over 20 cigarettes/cigars or pipes per day. As for alcohol consumption, the highest alcohol-intake category was taken into consideration if the subject had increased consumption during the study period.

Diabetes mellitus was self-reported every year from 1989.

Outcomes

In 2012, a specific question on Dupuytren's disease was asked: " 1) Have you ever had Dupuytren's disease (thickening of the palmar skin, nodes or contracture of the fourth finger of the hand)? ; 2) if yes, do you have any limitations because of it? 3) Have you had surgery for it?".

We considered two outcomes, i.e. Dupuytren's disease (yes or no) based on the answer to the first question; and a three category variable: no Dupuytren's disease (reference), Dupuytren's disease without surgery and without limitations, Dupuytren's disease with surgery or limitations.

Analyses

Univariate and multivariate analyses were stratified on gender for both outcomes. For the multinomial regression model, all the risk factors previously described were included, except 'control exposure' variables. Statistical Analysis Software was used for all statistical analyses

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(SAS, v9.3, SAS Institute Inc, Cary, NC, USA). Associations were considered statistically significant if the p-value was less than 0.05. Odds ratios (OR) and their 95% confidence intervals were computed.

Authorization from the appropriate ethics committee was obtained (« Comité Consultatif National d'Ethique pour les Sciences de la Vie et de la Santé »).

RESULTS

The 13 587 subjects who answered the GAZEL questionnaire in 2012 constituted the sample (10,017 men and 3,570 women). The participation rate was 73.7% (18,428 questionnaires sent in 2012). Subjects were aged from 59 to 73 years (mean age 68 years for men and 65 years for women).

Of the 10,017 men included, 839 reported Dupuytren's disease (8.4%), including 342 who reported surgery or limitations (3.4%). Age, diabetes mellitus, heavy drinking and over 15 years of manipulating a vibrating tool at work were significantly associated with self-reported Dupuytren's disease, with a dose-effect relationship (Table 1). Similar results were found when a yes/no question was used at the inception of the cohort in 1989. As expected, none of the 'control exposure' variables were associated with Dupuytren's disease. Reported durations of exposure to carrying loads and smoking habits were not found to be associated with Dupuytren's disease. The associations were stronger when considering disabling Dupuytren's disease (or surgery) than for Dupuytren's disease without reported surgery or disability (Table 2). Figure 1 show a clear dose effect in relation to duration of exposure, using a 5-year step.

Of the 3,570 women included, 160 reported Dupuytren's disease (4.5%), including 78 who reported surgery or limitations (2.2%). Associations were found to be weak, although age,

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diabetes and vibration exposure were still significant (Tables 3 and 4); however, only a small number of women were heavy drinkers or occupationally exposed.

DISCUSSION

The study confirmed that Dupuytren's disease in men is associated with high levels of alcohol consumption and exposure to hand-transmitted vibration in this large French cohort study, after adjustment for age and diabetes, whereas smoking habits and other types of occupational exposure were not. Although this is one of the first studies to analyze risk factors among women, the number of exposed cases was too small to draw any conclusion, although associations appeared similar to those observed in men.

The study had some limitations. The major limitation came from the fact that the diagnosis was self-reported, without any confirmation by physical examination by a physician. In most cases, Dupuytren's disease is easily diagnosed, with no major differential diagnoses, although it might be previous hand trauma, camptodactyly, tendovaginitis stenosans in a fixed flexion position for example. In addition, we considered the 4th digit only.[14] This lack of confirmation may have led to an underestimation of the prevalence of the disorder but it was probably limited, considering that the prevalence of this disorder in our study was comparable with that observed for the same age category in the general population.[9,15] A possible residual confounding effect should also be discussed: information regarding genetic factors, such as family history of Dupuytren's disease, hand trauma, epilepsy and anticonvulsant drug intake, that are considered to be associated with Dupuytren's disease, was not available. However, an association between these factors and vibration exposure and alcohol intake seems unlikely.

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One of the strengths of our study is the relatively large size of the cohort. Since we had only one measure of Dupuytren's disease in 2012, i.e. the number of reported cases of Dupuytren's disease, we studied factors associated with prevalent cases. However, assessment of work exposure five years before evaluation of the outcome, and the regular evaluation of alcohol intake and smoking throughout the follow-up period enabled us to be confident about the associations observed. Those were confirmed by information collected at inception, i.e. 23 years before.

One important finding was confirmation in a large study of the association between alcohol consumption and Dupuytren's disease among men, with a dose-response relationship.[11,13,16] Although we might discuss the arbitrary cut off,[17] the association with reported limitations (or surgery) was a new finding because it has been described by clinicians before, but rarely reported in large cohort studies.[1,18,19] Diabetes seemed to be related to the occurrence of Dupuytren's disease but not with limitations in men. Interestingly, it was associated with limitations in women. Ever smoking and heavy smoking were not found to be associated with Dupuytren's disease, which was unexpected considering the possible ischemic etiology of Dupuytren's disease, and the contrary findings in some recent studies.[11,16] Absence of a relationship could be due to the small number of very heavy smokers (61 men and 26 women smoked 2 packs/day or more).

In terms of occupational exposure, only vibration was found to be related to Dupuytren's disease. Previous studies have shown that high cumulative occupational exposure to vibration (intensity x duration) was associated with Dupuytren's disease.[13,20–23] Although exposure to vibration during the working life was self-reported, it corresponded to a very specific

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exposure, probably with a low memory effect (workers tend to remember correctly this type of precise exposure). Hand-vibration transmitting tools in our cohort were mostly screw tools, common drills and (infrequently) pneumatic drills, where strenuous hand grip increases vibration damage. The role of high levels of vibration exposure is plausible, especially as a result of the local hypoxia and chronic ischemia hypothesized in Dupuytren's contracture.[4] Similar figures for the strength of the association found in published studies support the plausibility of a possible causal relationship.[7] Carrying loads was studied because, with some tasks, such exposure is associated with manual work, and heavy forceful exposure during the working life was not available in the GAZEL cohort. However, no relationship was found here.

In addition to the well-established genetic factors, and despite the limitations discussed, this study emphasized the role of occupational hand-transmitted vibration exposure and alcohol consumption in Dupuytren's disease. The question of compensation in some cases with documented high levels of exposure should be reviewed, as should improvements of working conditions with a view to prevention.

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AUTHORS CONTRIBUTION

All authors contributed significantly to the manuscript and approved the final version. MZ, MC and MG were involved in the data collection, improved the analyses, commented the manuscript. AD initiated the work, performed the main analyses and drafted the manuscript. ZM, CD and AL discussed the project, improved the analyses, commented the manuscript.

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DATA SHARING

No additional data available

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	N (total)	n	%	Odds ratio (univariate analyses, [95% confidence intervals])	Odds ratio (multivariate analysis logistic model, [95% confidence intervals])*
Age²				**1.03 [1.01; 1.06]**	**1.03 [1.00; 1.06]**
Diabetes					
No	8581	692	8.06	1	1
Yes	1436	147	10.24	**1.30 [1.08; 1.57]**	**1.31 [1.07; 1.60]**
*Smoking habits (pack/day)**					
Non-smoker (or former smoker)	6055	488	8.06	1	1
Smoker < 1	2670	229	8.58	1.07 [0.91; 1.26]	1.05 [0.88; 1.24]
Smoker ≥1	1246	117	9.39	1.18 [0.96; 1.46]	1.05 [0.83; 1.32]
*Drinking habits (glass/day)**					
<3	2551	174	6.82	1	1
3or 4 glasses of wine /beer	4864	411	8.45	**1.26 [1.05; 1.52]**	**1.22 [1.01; 1.48]**
≥5 glasses of wine/beer or ≥3 glasses of spirits	2577	249	9.66	**1.46 [1.19; 1.79]**	**1.36 [1.10; 1.69]**
Carrying loads (assessed in 2007), number of years of exposure					
No	6812	565	8.29	1	1
1 to 15 years	1026	89	8.67	1.05 [0.83; 1.33]	0.95 [0.74; 1.22]
>15 years	1393	129	9.26	1.13 [0.92; 1.38]	0.91 [0.71; 1.16]
Climbing stairs (assessed in 2007), number of years of exposure					
No	7281	618	8.49	1	
1 to 15 years	810	63	7.78	0.91 [0.69; 1.19]	
>15 years	1147	102	8.89	1.05 [0.85; 1.31]	
Manipulating vibrating tools (assessed in 2007), number of years of exposure					
No	7630	614	8.05	1	1
1 to 15 years	772	76	9.84	1.25 [0.97; 1.60]	1.25 [0.95; 1.65]
>15 years	781	88	11.27	**1.45 [1.15; 1.84]**	**1.52 [1.15; 2.02]**
Carrying loads (assessed in 1989)					
No	8888	737	8.29	1	
Yes	1129	102	9.03	1.10 [0.88; 1.36]	
Manipulating vibrating tools (assessed in 1989)					
No	9278	760	8.19	1	
Yes	739	79	10.69	**1.34 [1.05; 1.71]**	
Computer work (assessed in 1989)					
No	5270	444	8.43	1	
Yes	4747	395	8.32	0.99 [0.86; 1.14]	

Table 1. Univariate and multivariate analyses of Dupuytren's disease (yes versus no) and available factors assessed in the previous period in men.

Data in bold: p<0.05 ,* model included all variables shown, **maximum consumption reached, ² age as continuous variable, OR associated with an increase of one unit

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				Dupuytren's disease without limitations or surgery		Dupuytren's disease with limitations or surgery			
	N (total)	n	%	Odds ratio (univariate analyses, [95% confidence intervals])	Odds ratio (multivariate analysis logistic model, [95% confidence intervals]))*	n	%	Odds ratio (univariate analyses, [95% confidence intervals])	Odds ratio (multivariate analysis logistic model, [95% confidence intervals]))*
Age²	10017	496	4.95	1.01 [0.98; 1.04]	1.00 [0.97; 1.04]	343	3.42	**1.07 [1.03; 1.11]**	**1.07 [1.03; 1.11]**
Diabetes									
No	8581	405	4.72	1	1	287	3.34	1	1
Yes	1436	91	6.34	**1.38 [1.09; 1.74]**	**1.41 [1.10; 1.82]**	56	3.90	1.19 [0.89; 1.60]	1.18 [0.87; 1.59]
*Smoking habits (pack/day)**									
Non-smoker (or former smoker)	6055	292	4.82	1	1	196	3.24	1	1
Smoker < 1	2670	132	4.94	1.03 [0.83; 1.27]	1.04 [0.83; 1.30]	97	3.63	1.13 [0.88; 1.45]	1.06 [0.81; 1.37]
Smoker ≥1	1246	68	5.46	1.15 [0.88; 1.51]	1.06 [0.79; 1.43]	49	3.93	1.23 [0.90; 1.70]	1.04 [0.74; 1.46]
*Drinking habits (glass/day)**									
<3	2551	103	4.04	1	1	71	2.78	1	1
3 or 4 glasses of wine /beer	4864	264	5.43	**1.37 [1.08; 1.73]**	**1.32 [1.03; 1.68]**	147	3.02	1.11 [0.83; 1.47]	1.09 [0.81; 1.47]
≥5 glasses of wine/beer or ≥3 glasses of spirits	2577	125	4.85	1.24 [0.95; 1.62]	1.12 [0.84; 1.50]	124	4.81	**1.78 [1.32; 2.40]**	**1.71 [1.25; 2.33]**
Carrying loads (assessed in 2007), number of years of exposure									
No	6812	350	5.14	1	1	215	3.16	1	1
1 to 15 years	1026	48	4.68	0.91 [0.67; 1.25]	0.88 [0.63; 1.22]	41	4.00	1.27 [0.90; 1.79]	1.06 [0.73; 1.52]
>15 years	1393	61	4.38	0.86 [0.65; 1.14]	0.79 [0.56; 1.09]	68	4.88	1.56 [1.18; 2.07]	1.08 [0.76; 1.52]
Climbing stairs (assessed in 2007), number of years of exposure									
No	7281	358	4.92	1		260	3.57	1	
1 to 15 years	810	42	5.19	1.05 [0.75; 1.45]		21	2.59	0.72 [0.46; 1.13]	
>15 years	1147	58	5.06	1.03 [0.78; 1.37]		44	3.84	1.08 [0.78; 1.50]	
Manipulating vibrating tools (assessed in 2007), number of years of exposure									
No	7630	377	4.94	1	1	237	3.11	1	1
1 to 15 years	772	38	4.92	1.02 [0.72; 1.43]	1.05 [0.72; 1.52]	38	4.92	**1.62 [1.14; 2.30]**	**1.56 [1.07; 2.29]**
>15 years	781	40	5.12	1.07 [0.77; 1.50]	1.20 [0.81; 1.78]	48	6.15	**2.05 [1.49; 2.82]**	**1.98 [1.34; 2.91]**
Carrying loads (assessed in 1989)									
No	8888	437	4.92	1		300	3.38	1	
Yes	1129	59	5.23	1.07 [0.81; 1.42]		43	3.81	1.14 [0.82; 1.58]	
Manipulating vibrating tools (assessed in 1989)									
No	9278	453	4.88	1		307	3.31	**1**	
Yes	739	43	5.82	1.23 [0.89; 1.69]		36	4.87	**1.51 [1.06; 2.16]**	
Computer work (assessed in 1989)									
No	5270	262	4.97	1		182	3.45	1	
Yes	4747	234	4.93	0.99 [0.83; 1.19]		161	3.39	0.98 [0.79; 1.22]	

Table 2. Univariate and multivariate analyses of Dupuytren's disease (without limitations or surgery, with limitations or surgery, compared with reference class: no Dupuytren's disease) and available factors assessed in the previous period in men.

Data in bold: p<0.05,* model included all variables shown, **maximum consumption reached, ² age as continuous variable, OR associated with an increase of one unit

	N (total)	n	%	Odds ratio (univariate analyses, [95% confidence intervals])	Odds ratio (multivariate analysis logistic model, [95% confidence intervals]))*
Age²	3570	160	4.48	**1.05 [1.01; 1.09]**	**1.05 [1.01; 1.10]**
Diabetes					
No	3252	140	4.31	1	1
Yes	318	20	6.29	**1.49 [0.92; 2.42]**	**1.71 [1.04; 2.81]**
Smoking habits (pack/day)**					
Non-smoker (or former smoker)	2626	115	4.38	1	1
Smoker < 1	711	34	4.78	1.10 [0.74; 1.62]	1.16 [0.76; 1.77]
Smoker ≥1	187	8	4.28	0.98 [0.47; 2.03]	0.96 [0.43; 2.11]
Drinking habits (glass/day)**					
<3	2423	103	4.25	1	1
3or 4 glasses of wine /beer	843	39	4.63	1.09 [0.75; 1.59]	0.83 [0.54; 1.27]
≥5 glasses of wine/beer or ≥3 glasses of spirits	271	17	6.27	1.51 [0.89; 2.56]	1.17 [0.64; 2.12]
Carrying loads (assessed in 2007)					
No	2995	131	4.37	1	
Yes	151	11	7.28	1.72 [0.91; 3.25]	
Climbing stairs (assessed in 2007)					
No	3024	137	4.53	1	
Yes	116	6	5.17	1.15 [0.50; 2.66]	
Manipulating vibrating tools (assessed in 2007)					
No	3163	142	4.49	1	1
Yes	4	2	50.0	**21.28 [2.98; 152.19]**	**17.17 [2.35; 125.62]**
Carrying loads (assessed in 1989)					
No	3433	153	4.46	1	
Yes	137	7	5.11	1.15 [0.53; 2.51]	
Manipulating vibrating tools (assessed in 1989)					
No	3555	159	4.47	1	
Yes	15	1	6.67	1.53 [0.20; 11.67]	
Computer work (assessed in 1989)					
No	885	39	4.41	1	
Yes	2685	121	4.51	1.02 [0.71; 1.48]	

Table 3. Univariate and multivariate analyses of Dupuytren's disease (yes versus no) and available factors assessed in the previous period in women.

Data in bold: p<0.05,* model included all variables shown, **maximum consumption reached, ² age as continuous variable, OR associated with an increase of one unit

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	N (total)	n	%	Dupuytren's disease without limitations or surgery		n	%	Dupuytren's disease with limitations or surgery	
				Odds ratio (univariate analyses, [95% confidence intervals])	Odds ratio (multivariate analysis logistic model, [95% confidence intervals]))*			Odds ratio (univariate analyses, [95% confidence intervals])	Odds ratio (multivariate analysis logistic model, [95% confidence intervals]))*
Age²	3570	82	2.30	1.04 [0.98; 1.09]	1.04 [0.98; 1.10]	78	2.18	**1.06 [1.01; 1.12]**	**1.07 [1.01; 1.13]**
Diabetes									
No	3252	75	2.31	1	1	65	2.00	1	1
Yes	318	7	2.20	0.97 [0.45; 2.13]	1.18 [0.53; 2.61]	13	4.09	**2.09 [1.14; 3.83]**	**2.27 [1.22; 4.24]**
*Smoking habits (pack/day)***									
Non-smoker (or former smoker)	2626	62	2.36	1	1	53	2.02	1	1
Smoker < 1	711	16	2.25	0.96 [0.55; 1.67]	0.99 [0.54; 1.82]	18	2.53	1.26 [0.73; 2.16]	1.36 [0.76; 2.41]
Smoker ≥1	187	3	1.60	0.68 [0.21; 2.19]	0.78 [0.24; 2.55]	5	2.67	1.32 [0.52; 3.35]	1.15 [0.41; 3.27]
*Drinking habits (glass/day)***									
<3	2423	51	2.10	1	1	52	2.15	1	1
3 or 4 glasses of wine /beer	843	23	2.73	1.30 [0.79; 2.14]	1.06 [0.60; 1.87]	16	1.90	0.89 [0.50; 1.56]	0.63 [0.33; 1.20]
≥5 glasses of wine/beer or ≥3 glasses of spirits	271	8	2.95	1.43 [0.67; 3.05]	1.30 [0.57; 3.00]	9	3.32	1.58 [0.77; 3.25]	1.04 [0.46; 2.39]
Climbing stairs (assessed in 2007)									
No	3024	69	2.28	1		68	2.25	1	
Yes	116	2	1.72	0.76 [0.18; 3.14]		4	3.45	1.54 [0.55; 4.31]	
Manipulating vibrating tools (assessed in 2007)									
No	3163	70	2.21	1	1	72	2.28	1	1
Yes	4	1	25.00	**21.57 [1.93; 240.79]**	**18.69 [1.61; 216.66]**	1	25.00	**21.00 [1.88; 234.10]**	**15.87 [1.36; 184.70]**
Carrying loads (assessed in 1989)									
No	3433	78	2.27	1		75	2.18	1	
Yes	137	4	2.92	1.29 [0.47; 3.59]		3	2.19	1.01 [0.31; 3.24]	
Manipulating vibrating tools (assessed in 1989)									
No	3555	81	2.28	1		78	2.19	1	
Yes	15	1	6.67	2.99 [0.39; 23.05]		0	0.00	0.00 [0.00; I]	
Computer work (assessed in 1989)									
No	885	20	2.26	1		19	2.15	1	
Yes	2685	62	2.31	1.02 [0.61; 1.70]		59	2.20	1.02 [0.61; 1.73]	

Table 4. Univariate and multivariate analyses of Dupuytren's disease (without limitations or surgery, with limitations or surgery, compared to reference class: no Dupuytren's disease) and available factors assessed in the previous period in women.

Data in bold: p<0.05,* model included all variables shown, **maximum consumption reached, ² age as continuous variable, OR associated with an increase of one unit

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Association between work exposure, alcohol intake, smoking and Dupuytren's disease in a large cohort study (Gazel)

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ABSTRACT

Introduction In view of the debate about biomechanical and toxic factors in Dupuytren's disease, we aimed to describe its relationship with certain occupational factors, ~~and~~ alcohol intake and smoking.

Method Subjects in the French GAZEL cohort answered a questionnaire in 2012 ~~included~~ including self-reported Dupuytren's disease (yes/no), ~~such~~ and as disabling Dupuytren's disease (including surgery). In 2007, self-assessed lifetime occupational biomechanical exposure was recorded (carrying loads, manipulating a vibrating tool, climbing stairs), as well as alcohol intake, smoking and diabetes mellitus. Analyses were performed on high alcohol intake, smoking and duration of relevant work exposure, stratified by gender for both outcomes.

Results A total of 13,587 subjects answered the questionnaire in 2012 (73.7% of the questionnaire sent) and constituted the sample (10,017 men and 3,570 women, aged from 64 to 73 years; mean age for men 68 years and for women 65 years). Among men age, diabetes, heavy drinking and over 15 years of manipulating a vibrating tool at work were significantly associated with Dupuytren's disease; except for diabetes, the association with these factors was stronger for disabling Dupuytren's disease (or surgery). Among the 3,570 women included, 160 reported Dupuytren's disease (4.5%). The number of cases in the group of women was too low to reach conclusions, although the findings seemed similar for age, diabetes and vibration exposure.

Conclusion In this large French cohort study, Dupuytren's disease in men was associated with high levels of alcohol consumption and exposure to hand-transmitted vibration. It is likely that the same applied to women.

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ARTICLE SUMMARY

- The longitudinal study confirmed that Dupuytren's disease in men was associated with high levels of alcohol consumption and exposure to hand-transmitted vibration in this large French cohort study, after adjustedment for age and diabetes.

- Although this is one of the first studies to analyze risk factors for women, the number of cases was too small to draw conclusions, though they associations appeared similar to those observed in men.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The study had limitations: self-reported diagnosis, possible residual confounding (genetic factors mainly).

- Strengths of our study came from the longitudinal design, the relatively large size of the cohort, women included.

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Dupuytren's disease is characterized by chronic contracture of the (fourth and fifth) fingers of the hand toward the palm, usually accompanied by thickening of the palmar skin.[1] It has a clear genetic background.[2–4]

Since its description by Guillaume Dupuytren in 1831 following Henry Cline Sr. and Sir Astley Cooper, there has been controversy regarding biomechanical work exposure which might contribute to the development of this disorder.[5] An exhaustive review and a meta-analysis was conducted to address this controversy, and concluded that there is good evidence of an association between vibration exposure and Dupuytren's disease.[6,7] However, recent opinionsome authors still considers that occupational exposure, including vibration, is not a risk factor for Dupuytren's disease in manual workers.[1,8,9] These authors argued there are still conflicting results and that evidence is based only on two longitudinal studies. The roles of alcohol consumption and smoking are also a matter of debate,[9,10] although one large longitudinal study found a clear relationship between such exposure and Dupuytren's disease.[11]

We used data from the GAZELa large cohort study to describe the prevalence of Dupuytren's disease, and to analyze its association with certain risk factors, including exposure to vibration, alcohol intake and smoking.

METHODS

Population

The GAZEL cohort is made up of employees of Electricité de France (EDF) and Gaz de France (GDF), the French national utility for energy production and distribution (GAZEL stands for GAZ and ELectricité). The company employs workers in various trades and of

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different socioeconomic status. At baseline in 1989, the cohort included 20,625 volunteers, men then aged 40–50 and women 35–50 years, and 18,428 are still followed up, men then aged 40–50 and women 35–50 years. In January of each year since then, the participants have completed a general self-administered questionnaire about their lifestyle, health, and occupational situation.[12]

In the present study, we included only the subjects who answered the 2012 GAZEL questionnaire (which included a question about Dupuytren's disease).

Potential risk factors

Information on gender and age (atin 2012), was collected through the general questionnaire. Occupational risk factors were assessed in the 2007 questionnaire. Data on nine different types of biomechanical exposure were available, including the number of years of exposure during their working lives (carrying loads, bending trunk, drive a vehicle, kneeling, climbing stairs, climbing ladder, working with arm over the shoulder, carrying load on the shoulder, manipulating a vibrating tool). In this study of Dupuytren's disease, we analyzed the potential role of manipulating a vibrating tool. As information about forceful activity was not available, carrying loads was considered to be a proxy for forceful work and was also taken into account. Climbing stairs, an irrelevant exposure for Dupuytren's disease, was also used as a 'control exposure' to check the lack of relationship. For these variables, three categories were considered for men based on duration of exposure: i.e. never exposed, exposed but for less than 15 years, and exposed for 15 years or more. In the view of the number of exposed women in the cohort, the exposure for women was only considered as yes or no. In addition, at inception of the cohort in 1989, a 'yes or no' question about manipulating vibrating tools was also available, and computer work was used as control exposure.

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Data for alcohol consumption were available for each year since 1992, and three categories were also considered on the basis of the distribution observed. Only heavy drinkers were taken into account based on the results of a previous study:[13] less than 3 glasses a day of any alcohol, 3 to 4 glasses of wine or beer, and 5 or more glasses of wine/beer or 3 glasses or more of spirits a day. If a subject had increased his alcohol consumption between 1992 and 2012, the highest category was taken into consideration. Data on smoking had been collected at inception in 1989 and grouped in three categories and: nonsmoker or former smoker, 1 to 20 cigarettes/cigars or pipes, over 20 cigarettes/cigars or pipes per day. As for alcohol consumption, the highest smoking alcohol-intake category was taken into consideration, if the subject had increased consumption during the study period.

Diabetes mellitus was self-reported every year fron from 1989.

Outcomes

When assessed in In 2012, a specific question on Dupuytren's disease was asked: " 1) Have you ever had Dupuytren's disease (thickening of the palmar skin, nodes or contracture of the fourth fingers of the hand)? ; 2) if yes, do you have any limitations from because of it? 3) Have you had surgery for it?".

We considered two outcomes, i.e. Dupuytren's disease (yes or no) based on the answer to the first question; and a three category variable: no Dupuytren's disease (reference), Dupuytren's disease without surgery and without limitations, Dupuytren's disease with surgery or limitations.

Analyses

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Univariate and multivariate analyses were stratified on gender for both outcomes. For the multinomial regression model, all the ~~variables~~ risk factors previously described were included, except 'control exposure' variables. Statistical Analysis Software was used for all statistical analyses (SAS, v9.3, SAS Institute Inc, Cary, NC, USA). Associations were considered statistically significant if the p-value was less than 0.05 ~~and confidence interval at 95% with its odds ratio (OR)~~. Odds ratios (OR) and their 95% confidence intervals were computed.

Authorization from the appropriate ethics committee ~~were~~was obtained (« Comité Consultatif National d'Ethique pour les Sciences de la Vie et de la Santé »).

RESULTS

The 13 587 subjects who answered the GAZEL questionnaire in 2012 constituted the sample (10,017 men and 3,570 women). The participation rate was 73.7% (18,428 questionnaires sent in 2012). Subjects were aged from 59 to 73 years (mean age 68 years for men and 65 years for women).

Of the 10,017 men included, 839 reported Dupuytren's disease (8.4%), including 342 who reported surgery or limitations (3.4%). Age, diabetes mellitus, heavy drinking and over 15 years of manipulating a vibrating tool at work were significantly associated with self-reported Dupuytren's disease, with a dose-effect relationship (Table 1). Similar results were found when a yes/no question was used at the inception of the cohort in 1989. As expected, none of the 'control exposure' variables were associated with Dupuytren's disease. Reported durations of exposure ~~of~~to carrying loads and smoking habits were not found to be associated with Dupuytren's disease. The associations were stronger when considering disabling Dupuytren's disease (or surgery) than for Dupuytren's disease without reported surgery or disability (Table

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2). Figure 1 show a clear dose effect in relation to duration of exposure, ~~with~~ using a 5--year step.

Of the 3,570 women included, 160 reported Dupuytren's disease (4.5%), including 78 who reported surgery or limitations (2.2%). Associations were found to be weak ~~and questionable~~, although age, diabetes and vibration exposure were still significant (Tables 3 and 4); however, only a small number~~s~~ of women were ~~in the heavy drinking and occupationally exposed groups~~ heavy drinkers or occupationally exposed.

DISCUSSION

The study confirmed that Dupuytren's disease in men ~~was~~ is associated with high levels of alcohol consumption and exposure to hand-transmitted vibration in this large French cohort study, after adjust~~ed~~ment for age and diabetes, whereas smoking habits and other types of occupational exposure were not. Although this is one of the first studies to analyze risk factors ~~for~~ among women, the number of exposed cases was too small to draw any conclusion~~s~~, although ~~they~~ associations appeared similar to those observed in men.

The study had ~~various~~ some limitations. The major limitation came from the fact that the diagnosis was self-reported, without any confirmation ~~of any~~by physical examination by a physician. ~~However~~In most cases, Dupuytren's disease is easily diagnosed, with no major differential diagnoses, although it might be previous hand trauma, camptodactyly, tendovaginitis stenosans in a fixed flexion position for example~~.~~, I~~i~~n addition, ~~of~~ we ~~also~~ considered the 4th digit only,[14]. ~~The~~ This lack of confirmation ~~possibly~~ may have led ~~therefore~~ to an underestimation of the prevalence of the disorder~~,~~ but ~~this~~ it was probably limited~~.~~, considering that the prevalence of this disorder in ~~the~~ our study was comparable with

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~~information available~~that observed for the same age category in the general population.[9,15][9] A possible residual confounding effect should also be discussed: information regarding genetic factors, such as family history of Dupuytren's disease, hand trauma, epilepsy and anticonvulsant drug intake, that are considered to be associated with Dupuytren's disease, was not available. However, an association between these factors and vibration exposure and alcohol intake seems unlikely.

One of the strengths of our study is the relatively large size of the cohort. Since we had only one measure of Dupuytren's disease in 2012, i.e. the number of reported cases of Dupuytren's disease, we studied factors associated with prevalent cases. However, assessment of work exposure five years before evaluation of the outcome, and the regular evaluation of alcohol intake and smoking throughout the follow-up period enabled us to be confident about the associations observed., ~~that~~ Those were confirmed by information collected at inception, i.e. 23 years before.

One important finding was confirmation in a large study of the association between alcohol consumption ~~in men with~~and Dupuytren's disease among men, with a dose-response relationship.[11,13,16][11,13,14] Although we might discuss the arbitrary cut off.[17] ~~T~~the association with reported limitations (or surgery) was ~~interesting~~ a new finding because ~~this~~it has been described ~~many times~~ by clinicians before, but ~~never~~ rarely~~slightly~~ reported in large cohort studies.[1,18,19][1] Diabetes seemed to be related to the occurrence of Dupuytren's disease ~~and~~ but not with limitations in men., ~~but i~~Interestingly, it was associated with limitations in women. Ever S~~s~~moking and heavy smoking were not found to be associated with Dupuytren's disease, which was unexpected considering the possible ischemic etiology of Dupuytren's disease. and the contrary findings in some recent studies.[11,16][11,14] ~~Lack~~ Absence of a

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relationship ~~was possibly~~could be due to the ~~limited~~small number of very heavy smokers (61 men and 26 women smoked 2 packs/day or more).

In terms of occupational exposure, only vibration was found to be related to Dupuytren's disease. Previous studies have ~~showed~~ shown that high cumulative ~~work~~ occupational exposure to vibration (intensity x duration) was associated with Dupuytren's disease.[13,20–23][13,15–18] Although exposure to vibration during the working life was self-reported, it corresponded to a very specific exposure, ~~with a~~probably with a low memory effect (workers ~~remind well~~tend to remember correctly this type of precise exposure). Hand-vibration transmitting tools in our cohort were mostly screw tools, common drills and (infrequently) pneumatic drills, where strenuous hand grip increases vibration damage. The role of high levels of vibration exposure is plausible, especially as a result of the local hypoxia and chronic ischemia hypothesized in Dupuytren's contracture.[4] Similar ~~magnitudes of~~figures for the strength of the association found in published studies support the plausibility of a possible causal relationship.[7] Carrying loads was studied because, with some tasks, such exposure is associated with manual work, and heavy forceful exposure during the working life was not available in the GAZEL cohort. However, no relationship was found here.

In addition to the well-established genetic factors, and despite the limitations discussed, this study emphasized the role~~s~~ of occupational hand-transmitted vibration exposure and alcohol consumption in Dupuytren's disease. The question of compensation in some cases ~~following~~ with documented high levels of exposure should be reviewed, as should improvement~~s~~ of working conditions with a view to prevention.

DATA SHARING

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There is no additional data available

AUTHORS CONTRIBUTION

All authors contributed significantly to the manuscript and approved the final version. MZ, MC and MG were involved in the data collection, improved the analyses, commented the manuscript. AD initiated the work, performed the main analyses and drafted the manuscript. ZM, CD and AL discussed the project, improved the analyses, commented the manuscript.

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FOUNDINGS

COMPETING INTEREST: None to declare.

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	N (total)	n	%	Odds ratio (univariate analyses, [95% confidence intervals])	Odds ratio (multivariate analysis logistic model, [95% confidence intervals])*
Age²				**1.03 [1.01; 1.06]**	**1.03 [1.00; 1.06]**
Diabetes					
No	8581	692	8.06	1	1
Yes	1436	147	10.24	**1.30 [1.08; 1.57]**	**1.31 [1.07; 1.60]**
*Smoking habits (pack/day)***					
Non-smoker (or former smoker)	6055	488	8.06	1	1
Smoker < 1	2670	229	8.58	1.07 [0.91; 1.26]	1.05 [0.88; 1.24]
Smoker ≥1	1246	117	9.39	1.18 [0.96; 1.46]	1.05 [0.83; 1.32]
*Drinking habits (glass/day)***					
0	2551	174	6.82	1	1
1 or 4 glasses of wine /beer	4864	411	8.45	**1.26 [1.05; 1.52]**	**1.22 [1.01; 1.48]**
2 glasses of wine/beer or ≥3 glasses of spirits	2577	249	9.66	**1.46 [1.19; 1.79]**	**1.36 [1.10; 1.69]**
Carrying loads (assessed in 2007), number of years of exposure					
No	6812	565	8.29	1	1
1 to 15 years	1026	89	8.67	1.05 [0.83; 1.33]	0.95 [0.74; 1.22]
>15 years	1393	129	9.26	1.13 [0.92; 1.38]	0.91 [0.71; 1.16]
Climbing stairs (assessed in 2007), number of years of exposure					
No	7281	618	8.49	1	
1 to 15 years	810	63	7.78	0.91 [0.69; 1.19]	
>15 years	1147	102	8.89	1.05 [0.85; 1.31]	
Manipulating vibrating tools (assessed in 2007), number of years of exposure					
No	7630	614	8.05	1	1
1 to 15 years	772	76	9.84	1.25 [0.97; 1.60]	1.25 [0.95; 1.65]
>15 years	781	88	11.27	**1.45 [1.15; 1.84]**	**1.52 [1.15; 2.02]**
Carrying loads (assessed in 1989)					
No	8888	737	8.29	1	
Yes	1129	102	9.03	1.10 [0.88; 1.36]	
Manipulating vibrating tools (assessed in 1989)					
No	9278	760	8.19	1	
Yes	739	79	10.69	**1.34 [1.05; 1.71]**	
Computer work (assessed in 1989)					
No	5270	444	8.43	1	
Yes	4747	395	8.32	0.99 [0.86; 1.14]	

Table 1. Univariate and multivariate analyses of Dupuytren's disease (yes versus no) and available factors assessed in the previous period in men.

Data in bold: p<0.05 ,* model included all variables shown, **maximum consumption reached, ² age as continuous variable, OR associated with an increase of one -unit

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	N (total)	n	%	Dupuytren's disease without limitations or surgery		n	%	Dupuytren's disease with limitations or surgery	
				Odds ratio (univariate analyses, [95% confidence intervals])	Odds ratio (multivariate analysis logistic model, [95% confidence intervals])*			Odds ratio (univariate analyses, [95% confidence intervals])	Odds ratio (multivariate analysis logistic model, [95% confidence intervals])
Age²	10017	496	4.95	1.01 [0.98; 1.04]	1.00 [0.97; 1.04]	343	3.42	**1.07 [1.03; 1.11]**	**1.07 [1.03; 1.11]**
Diabetes									
No	8581	405	4.72	1	1	287	3.34	1	1
Yes	1436	91	6.34	**1.38 [1.09; 1.74]**	**1.41 [1.10; 1.82]**	56	3.90	1.19 [0.89; 1.60]	1.18 [0.87; 1.59]
*Smoking habits (pack/day)***									
Non-smoker (or former smoker)	6055	292	4.82	1	1	196	3.24	1	1
Smoker < 1	2670	132	4.94	1.03 [0.83; 1.27]	1.04 [0.83; 1.30]	97	3.63	1.13 [0.88; 1.45]	1.06 [0.81; 1.37]
Smoker ≥1	1246	68	5.46	1.15 [0.88; 1.51]	1.06 [0.79; 1.43]	49	3.93	1.23 [0.90; 1.70]	1.04 [0.74; 1.46]
*Drinking habits (glass/day)***									
<3	2551	103	4.04	1	1	71	2.78	1	1
3 or 4 glasses of wine /beer	4864	264	5.43	**1.37 [1.08; 1.73]**	**1.32 [1.03; 1.68]**	147	3.02	1.11 [0.83; 1.47]	1.09 [0.81; 1.47]
≥5 glasses of wine/beer or ≥3 glasses of spirits	2577	125	4.85	1.24 [0.95; 1.62]	1.12 [0.84; 1.50]	124	4.81	**1.78 [1.32; 2.40]**	**1.71 [1.25; 2.33]**
Carrying loads (assessed in 2007), number of years of exposure									
No	6812	350	5.14	1	1	215	3.16	1	1
1 to 15 years	1026	48	4.68	0.91 [0.67; 1.25]	0.88 [0.63; 1.22]	41	4.00	1.27 [0.90; 1.79]	1.06 [0.73; 1.52]
>15 years	1393	61	4.38	0.86 [0.65; 1.14]	0.79 [0.56; 1.09]	68	4.88	1.56 [1.18; 2.07]	1.08 [0.76; 1.52]
Climbing stairs (assessed in 2007), number of years of exposure									
No	7281	358	4.92	1		260	3.57	1	
1 to 15 years	810	42	5.19	1.05 [0.75; 1.45]		21	2.59	0.72 [0.46; 1.13]	
>15 years	1147	58	5.06	1.03 [0.78; 1.37]		44	3.84	1.08 [0.78; 1.50]	
Manipulating vibrating tools (assessed in 2007), number of years of exposure									
No	7630	377	4.94	1	1	237	3.11	1	1
1 to 15 years	772	38	4.92	1.02 [0.72; 1.43]	1.05 [0.72; 1.52]	38	4.92	**1.62 [1.14; 2.30]**	**1.56 [1.07; 2.29]**
>15 years	781	40	5.12	1.07 [0.77; 1.50]	1.20 [0.81; 1.78]	48	6.15	**2.05 [1.49; 2.82]**	**1.98 [1.34; 2.91]**
Carrying loads (assessed in 1989)									
No	8888	437	4.92	1		300	3.38	1	
Yes	1129	59	5.23	1.07 [0.81; 1.42]		43	3.81	1.14 [0.82; 1.58]	
Manipulating vibrating tools (assessed in 1989)									
No	9278	453	4.88	1		307	3.31	1	
Yes	739	43	5.82	1.23 [0.89; 1.69]		36	4.87	**1.51 [1.06; 2.16]**	
Computer work (assessed in 1989)									
No	5270	262	4.97	1		182	3.45	1	
Yes	4747	234	4.93	0.99 [0.83; 1.19]		161	3.39	0.98 [0.79; 1.22]	

Table 2. Univariate and multivariate analyses of Dupuytren's disease (without limitations or surgery, with limitations or surgery, compared with reference class: no Dupuytren's disease) and available factors assessed in the previous period in men.

Data in bold: p<0.05,* model included all variables shown, **maximum consumption reached, ² age as continuous variable, OR associated with an increase of one unit

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	N (total)	n	%	Odds ratio (univariate analyses, [95% confidence intervals])	Odds ratio (multivariate analysis logistic model, [95% confidence intervals])*
Age²	3570	160	4.48	**1.05 [1.01; 1.09]**	**1.05 [1.01; 1.10]**
Diabetes					
No	3252	140	4.31	1	1
Yes	318	20	6.29	1.49 [0.92; 2.42]	**1.71 [1.04; 2.81]**
Smoking habits (pack/day)*					
Non-smoker (or former smoker)	2626	115	4.38	1	1
Smoker < 1	711	34	4.78	1.10 [0.74; 1.62]	1.16 [0.76; 1.77]
Smoker ≥1	187	8	4.28	0.98 [0.47; 2.03]	0.96 [0.43; 2.11]
Drinking habits (glass/day)*					
≤3	2423	103	4.25	1	1
3 or 4 glasses of wine /beer	843	39	4.63	1.09 [0.75; 1.59]	0.83 [0.54; 1.27]
≥5 glasses of wine/beer or ≥3 glasses of spirits	271	17	6.27	1.51 [0.89; 2.56]	1.17 [0.64; 2.12]
Carrying loads (assessed in 2007)					
No	2995	131	4.37	1	
Yes	151	11	7.28	1.72 [0.91; 3.25]	
Climbing stairs (assessed in 2007)					
No	3024	137	4.53	1	
Yes	116	6	5.17	1.15 [0.50; 2.66]	
Manipulating vibrating tools (assessed in 2007)					
No	3163	142	4.49	1	1
Yes	4	2	50.0	**21.28 [2.98; 152.19]**	**17.17 [2.35; 125.62]**
Carrying loads (assessed in 1989)					
No	3433	153	4.46	1	
Yes	137	7	5.11	1.15 [0.53; 2.51]	
Manipulating vibrating tools (assessed in 1989)					
No	3555	159	4.47	1	
Yes	15	1	6.67	1.53 [0.20; 11.67]	
Computer work (assessed in 1989)					
No	885	39	4.41	1	
Yes	2685	121	4.51	1.02 [0.71; 1.48]	

Table 3. Univariate and multivariate analyses of Dupuytren's disease (yes versus no) and available factors assessed in the previous period in women.
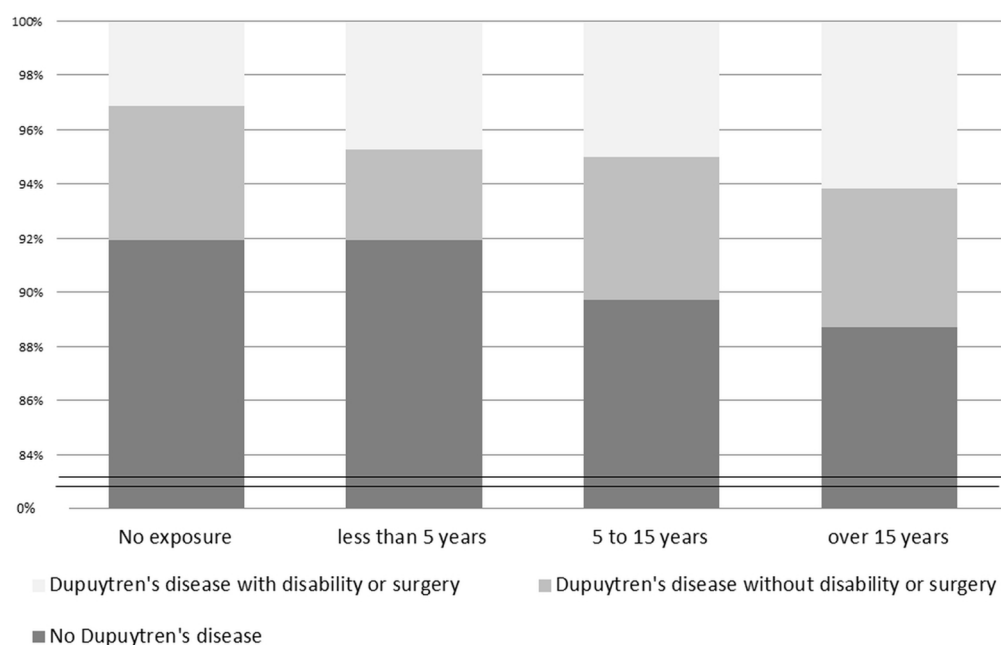
Data in bold: p<0.05,* model included all variables shown, **maximum consumption reached, ² age as continuous variable, OR associated with an increase of one unit

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	N (total)	n	%	Odds ratio (univariate analyses, [95% confidence intervals])	Odds ratio (multivariate analysis logistic model, [95% confidence intervals])*	n	%	Odds ratio (univariate analyses, [95% confidence intervals])	Odds ratio (multivariate analysis logistic model, [95% confidence intervals])*
				Dupuytren's disease without limitations or surgery				Dupuytren's disease with limitations or surgery	
Age²	3570	82	2.30	1.04 [0.98; 1.09]	1.04 [0.98; 1.10]	78	2.18	**1.06 [1.01; 1.12]**	**1.07 [1.01; 1.13]**
Diabetes	3252	75	2.31	1	1	65	2.00	1	1
Yes	318	7	2.20	0.97 [0.45; 2.13]	1.18 [0.53; 2.61]	13	4.09	**2.09 [1.14; 3.83]**	**2.27 [1.22; 4.24]**
Smoking habits (pack/day)**									
Non-smoker (or former smoker)	2626	62	2.36	1	1	53	2.02	1	1
Smoker < 1	711	16	2.25	0.96 [0.55; 1.67]	0.99 [0.54; 1.82]	18	2.53	1.26 [0.73; 2.16]	1.36 [0.76; 2.41]
Smoker ≥1	187	3	1.60	0.68 [0.21; 2.19]	0.78 [0.24; 2.55]	5	2.67	1.32 [0.52; 3.35]	1.15 [0.41; 3.27]
Drinking habits (glass/day)**	2423	51	2.10	1	1	52	2.15	1	1
< 4 glasses of wine /beer	843	23	2.73	1.30 [0.79; 2.14]	1.06 [0.60; 1.87]	16	1.90	0.89 [0.50; 1.56]	0.63 [0.33; 1.20]
≥5 glasses of wine/beer or ≥3 glasses of spirits	271	8	2.95	1.43 [0.67; 3.05]	1.30 [0.57; 3.00]	9	3.32	1.58 [0.77; 3.25]	1.04 [0.46; 2.39]
Climbing stairs (assessed in 2007)	3024	69	2.28	1		68	2.25	1	
Yes	116	2	1.72	0.76 [0.18; 3.14]		4	3.45	1.54 [0.55; 4.31]	
Manipulating vibrating tools (assessed in 2007)	3163	70	2.21	1	1	72	2.28	1	1
Yes	4	1	25.00	**21.57 [1.93; 240.79]**	18.69 [1.61; 216.66]	1	25.00	**21.00 [1.88; 234.10]**	15.87 [1.36; 184.70]
Carrying loads (assessed in 1989)	3433	78	2.27	1		75	2.18	1	
Yes	137	4	2.92	1.29 [0.47; 3.59]		3	2.19	1.01 [0.31; 3.24]	
Manipulating vibrating tools (assessed in 1989)	3555	81	2.28	1		78	2.19	1	
Yes	15	1	6.67	2.99 [0.39; 23.05]		0	0.00	0.00 [0.00; I]	
Computer work (assessed in 1989)	885	20	2.26	1		19	2.15	1	
Yes	2685	62	2.31	1.02 [0.61; 1.70]		59	2.20	1.02 [0.61; 1.73]	

Table 4. Univariate and multivariate analyses of Dupuytren's disease (without limitations or surgery, with limitations or surgery, compared to reference class: no Dupuytren's disease) and available factors assessed in the previous period in women.

Data in bold: $p<0.05$,* model included all variables shown, **maximum consumption reached, ² age as continuous variable, OR associated with an increase of one unit

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Proportion of Dupuytren's disease depending duration of vibration exposure in the working life (5 year step).
119x90mm (300 x 300 DPI)

Association between work exposure, alcohol intake, smoking and Dupuytren's disease in a large cohort study (Gazel) =>STROBE Statement

	Item No	Recommendation	YES/NO
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Yes
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Yes
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Yes
Objectives	3	State specific objectives, including any prespecified hypotheses	Yes
Methods			
Study design	4	Present key elements of study design early in the paper	Yes
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Yes
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Yes
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Yes
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Yes
Bias	9	Describe any efforts to address potential sources of bias	Yes
Study size	10	Explain how the study size was arrived at	N/A (multipurpose cohort)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Yes
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Yes
		(*b*) Describe any methods used to examine subgroups and interactions	Yes
		(*c*) Explain how missing data were addressed	N/A
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Yes
		(b) Give reasons for non-participation at each stage	No
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	Yes

			confounders
			(b) Indicate number of participants with missing data for each variable of interest	Yes
			(c) Summarise follow-up time (eg, average and total amount)	Yes
Outcome data	15*	Report numbers of outcome events or summary measures over time	Yes
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Yes
		(*b*) Report category boundaries when continuous variables were categorized	Yes
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Yes
Discussion			
Key results	18	Summarise key results with reference to study objectives	Yes
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Yes
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Yes
Generalisability	21	Discuss the generalisability (external validity) of the study results	Yes
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Yes

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.