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Sickness absence as a prognostic marker for common chronic conditions:

Analysis of mortality in the GAZEL study

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ABSTRACT

Objectives—To determine whether sickness absence is a prognostic marker in terms of mortality among people with common chronic conditions.

Methods—Prospective occupational cohort study of 13 077 men and 4871 women aged 37 to 51 from the National Gas and Electricity Company, France. Records of physician-certified sickness absences over a 3-year period were obtained from employers' registers. Chronic conditions were assessed in annual surveys over the same period. The main outcome measure was all-cause mortality (803 deaths, mean follow-up after assessment of sickness absence, 13.9 years)

Results—In Cox proportional-hazard models adjusted for age, sex, socioeconomic position and co-morbidity, >28 annual sickness absence days vs no absence days was associated with an excess mortality risk among those with cancer (hazard ratio 5.4, 95% CI 2.2 to 13.1), depression (1.7, 1.1 to 2.8), chronic bronchitis/asthma (2.7, 1.6 to 4.6), and hypertension (1.6, 1.0 to 2.6). The corresponding hazard ratios for more than 5 long (>14 days) sickness absence episodes per 10 person-years vs no such episodes were 5.4 (2.2 to 13.1), 1.8 (1.3 to 2.7), 2.0 (1.3 to 3.2) and 1.8 (1.2 to 2.7), respectively. Areas under receiver-operating-characteristics curves for these absence measures varied between 0.56 and 0.73 indicating the potential of these measures to distinguish groups at high risk of mortality. The findings were consistent across sex, age and socioeconomic groups and in those with and without co-morbid conditions.

Conclusion—Data on sickness absence may provide useful prognostic information for common chronic conditions at the population level.

Key words: Sickness absence, mortality, prognosis, working population.

INTRODUCTION

Data on sickness absence are suggested to be a good measure of health in working populations, when health is understood in terms of physical and social functioning.¹⁻³ Associations between sickness absence, chronic conditions and early retirement on medical grounds have been reported in various settings⁴⁻¹² and, recently, three large studies showed that long-term absences are related to future mortality.^{3 13 14} Thus, sickness absence appears to be a predictor of future health in working populations.

There have been repeated calls for increased understanding of prognostic factors that can be used to estimate the chance of recovery from a disease or the chance of unfavourable disease outcomes.¹⁵ We hypothesise that sickness absence may be such a prognostic marker for employees with chronic conditions. The future course of a disease is the net effect of a wide range of factors including premorbid biological disposition, disease severity, co-morbidity, and health-related behaviours, as well as demographic and socioeconomic circumstances. Sickness absence may well capture the full array of diseases employees experience during their job contract and it is also known to be associated with health behaviours, socioeconomic circumstances and other exposures.^{1 16-20}

For chronic conditions of major public health relevance, such as cancer, coronary heart disease and diabetes, mortality is a widely used prognostic outcome. A limitation in previous studies of sickness absence is that they provide little information on whether the level of sickness absence is predictive of death among those with a common chronic condition. If this were the case, sickness absence may prove a useful additional indicator of prognosis for such conditions. We sought to examine this question in the current study. We hypothesised that sickness absence is a good prognostic indicator

because absence records provide day-to-day data on functioning in occupational settings and thus capture the presence of co-morbidity, illness severity, and the effects of risk factors.

METHODS

Study population

We used data from the GAZEL cohort which was established in 1989 and comprised 20,625 employees aged 35-50 from France's national gas and electricity company: Electricité de France-Gaz de France (EDF-GDF).²¹ Since baseline, less than 1% of GAZEL cohort members have been lost to follow-up. In the present study, we included those alive and working for EDF-GDF during 1990-1992 and excluded those who had died, retired or left the company before the 1st January 1993 (n=1390), were non-responders in any of the years 1990-1992 (n=1270), or had missing data on age, sex or socioeconomic position (n=17). Thus, a total of 17 948 participants (13 077 men, 4871 women) aged 37-51 at baseline were included in the analysis.

Sample characteristics

Baseline variables obtained from EDF-GDF records included sex, age and a 3-level employment grade ('high', 'intermediate' and 'low') derived from to the French National Statistics Institute (INSEE

http://www.insee.fr/fr/nom_def_met/nomenclatures/prof_cat_soc/html/L03_N1.HTM).

Assessment of sickness absence

All employees at EDF-GDF are covered by the same sickness insurance scheme entitling them to compensation for work incapacity due to disease or injury. Every sickness-absence episode requires a medical certificate. If a sick-leave spell lasts for more than one year a certificate from an occupational health physician is required every six months. The benefit is the same as ordinary salary and, like the old age pension, is provided by the company. After five years of sickness absence the person is granted a disability pension with benefits that are at the same level as for an old age pension. There is no limit to the duration of a sick-leave spell and persons are not transferred to a disability pension before the end of the five years even if the inability to work is permanent.

We obtained computerised sickness-absence records from 1 January 1990 to 31 December 1992. These records included the first and last dates of all absences. For each employee, we computed the total number of sickness-absence days and classified this based on the distribution into categories of 0, 1-28 (four weeks), and >28 days annually. We also computed for each employee the number of sickness-absence episodes of 1-7 days, 8-14 days, and >14 days (long absence episodes). These indices of sickness absence were further categorised by frequency, as in previous studies.³

Assessment of chronic conditions

Prevalent common chronic conditions, known to predict mortality, were derived from the annual GAZEL questionnaires for 1990, 1991 and 1992 using a checklist of common chronic conditions; cancer, diabetes, depression, chronic bronchitis or asthma, coronary heart disease (CHD) or cerebrovascular disease, and chronic hypertension. Participants were deemed to all the conditions checked in any of the three surveys.

Mortality follow-up

Follow-up for all-cause mortality from 1st January 1993 - 25th February 2007 used data from the EDF-GDF human resources department and the retirement fund services. This provides comprehensive mortality tracing for all participants resident in France and those who have emigrated but receive a pension from EDF-GDF.

Statistical methods

Each participant was followed either until death, or to the end of the study period. We calculated Cox proportional-hazard models to examine the associations of sickness absence and chronic conditions with mortality. Hazard ratios and their 95% confidence intervals (CI) were adjusted for age, sex and employment grade. Associations between sickness absence and mortality were additionally adjusted for chronic conditions. Those with no sickness absence or free from the chronic condition of interest were used as the reference. To confirm that observed associations were not confounded by an excess rate of sickness absence shortly before death, in a subsidiary analysis, we excluded those employees who died during the first five years and started mortality follow-up from 1st January 1998. We calculated receiver-operating characteristic (ROC) curves and their respective areas under the curve (AUCs) to further assess the ability of sickness absence to predict mortality.²² AUCs and 95% CI were used to test the null hypothesis that the theoretical AUC is 0.5. The status of sickness absence as a long-term prognostic factor for mortality was studied in analyses confined to participants with chronic conditions. For each chronic condition the AUC is used to examine the ability of sickness absence measures to distinguish between persons with poor vs good prognosis. ROC statistics were calculated with Stata 9.1 (Stata

Corp, College Station, Texas, USA) and all other analyses with the SAS, version 9.1.3 statistical software (SAS Institute, Cary, USA).

RESULTS

Population characteristics

The mean age of the 13 077 men and 4871 women was 45.0 (SD 3.4, range 37-51) years in 1990. Twenty-five percent were in a high employment grade, 57% intermediate grade and 18% low grade. Between 1990 and 1992, we identified a total of 620 405 sickness-absence days. These came from 32 583 sickness-absence episodes in 53 807 person-years.

According to the annual surveys 1990-1992, 3-year prevalence of cancer was 1.2%; diabetes 2.4%; depression 14.4%; chronic bronchitis or asthma 9.0%; CHD or cerebrovascular disease 3.5%; and hypertension 13.1%. In total, 22.3% of participants had at least one chronic condition and 7.1% more than one condition. During the mean follow-up period of 13.9 (SD 1.5, range 0.008-14.2) years from 1993 to 2007, 803 (4.6%) participants died.

Chronic conditions and mortality

All chronic conditions are associated with increased mortality. The hazard ratios (95% CI) from Cox models adjusted for age, sex and employment grade are: 5.23 (3.76-7.29) for cancer; 1.43 (1.00-2.05) for diabetes; 1.49 (1.24-1.80) for depression; 1.77 (1.45-2.15) for chronic bronchitis or asthma; 2.07 (1.59-2.70) for CHD or cerebrovascular disease; and 1.46 (1.22-1.74) for chronic hypertension. The AUCs vary between 0.51 (95% CI 0.50-0.51) for diabetes and 0.53 (95% CI 0.52-0.54) for chronic bronchitis/asthma and hypertension.

Sickness absence and mortality

Associations between the sickness-absence measures and mortality are presented in table 1. After adjustment for age, sex and socioeconomic position, a high number of sickness-absence days (defined as more than 28 days per person-year) vs no sickness-absence days is associated with a 2.65-fold excess mortality, the corresponding hazard ratio for a high number of sickness absence episodes lasting >14 days (defined as 5+ episodes per 10 person-years) being 2.10. Both these associations remain after adjustment for all chronic conditions. Excluding participants who died in the first 5 years of follow-up (n = 206) reduces these associations, but they remain statistically significant. Rates for absence episodes lasting 1-7 or 8-14 days are weaker predictors of mortality. Thus, subsequent analyses are confined to the total number of sickness-absence days and the number of long absence episodes (>14 days). These measures are not redundant to each other: 396 (2.2%) participants were in the high category for absence days, 594 (3.3%) in the high category for long absence episodes, and 1255 (7.0%) in the high category for both.

As an indication of the generalisability of these absence measures, taking >28 sickness-absence days annually is associated with excess mortality in men (age- and employment-grade-adjusted hazard ratio 2.91, 95% CI 2.33-3.63) and women (1.64, 0.99-2.65), in those below (3.07, 2.18-4.33) and above (2.45, 1.90-3.04) the age of 45 years, and in the low (4.01, 2.60-6.19), intermediate (2.35, 1.80-2.93) and high (1.71, 0.79-3.69) employment grades. Corresponding hazard ratios for having >5 long absence episodes per 10 person-years varied between 1.56 and 2.65. All p-values for interactions between the two sickness-absence measures and age, sex or grade exceeded 0.05.

TABLE 1--The association between various measures of sickness absence and mortality, the GAZEL study.*

Measure of sickness absence	No. (%) of participants	No. of deaths	Hazard ratio (95% CI), adjusted for		
			Age-, sex-, and grade (A)	A + chronic conditions† (B)	B excluding first 5 years of follow-up
Total number of sickness-absence days (per person-year)					
0	7189 (40.1)	285	1.00	1.00	1.00
>0-28	9102 (50.7)	357	1.02 (0.88-1.20)	0.96 (0.82-1.13)	0.96 (0.80-1.15)
>28	1657 (9.2)	161	2.65 (2.16-3.24)	2.08 (1.68-2.58)	1.59 (1.22-2.07)
Number of sickness-absence episodes 1-7 days (per 10 person-years)					
0	9891 (55.1)	425	1.00	1.00	1.00
1-10	5987 (33.4)	271	1.07 (0.92-1.25)	1.01 (0.86-1.18)	1.00 (0.84-1.20)
>10	2070 (11.5)	107	1.30 (1.04-1.62)	1.13 (0.90-1.42)	1.04 (0.79-1.36)
Number of sickness-absence episodes 8-14 days (per 10 person-years)					
0	13386 (74.6)	559	1.00	1.00	1.00
1-5	3036 (16.9)	151	1.22 (1.01-1.46)	1.13 (0.94-1.35)	1.11 (0.90-1.38)
>5	1526 (8.5)	93	1.52 (1.21-1.91)	1.28 (1.02-1.62)	1.30 (0.99-1.71)
Number of sickness-absence episodes >14 days (per 10 person-years)					
0	13107 (73.0)	509	1.00	1.00	1.00
1-5	2992 (16.7)	149	1.30 (1.08-1.56)	1.20 (1.00-1.45)	0.99 (0.79-1.24)
>5	1849 (10.3)	145	2.10 (1.73-2.54)	1.70 (1.40-2.08)	1.36 (1.07-1.74)

*Sickness absence was measured across years 1990-1992. Chronic conditions were requested in 1990, 1991 and 1992. Follow-up for mortality was from 1993 to 2007.

†Cancer, diabetes, depression, chronic bronchitis or asthma, CHD or cerebrovascular disease, and chronic hypertension entered as separate variables in the model.

Sickness absence and disease prognosis

Taking >28 sickness-absence days annually is associated with an increased risk of death in specific groups, such as those suffering from cancer, depression, chronic bronchitis or asthma, and in participants with hypertension, the age-, sex- and grade-adjusted hazard ratios varying between 2.0 and 4.9 (table 2). Further adjustment for co-morbidity strengthens this association among the cancer patients, reduces the association among those with chronic bronchitis/asthma or hypertension, and has little effect among those with depression; in all cases the association remains statistically significant. Findings for taking >5 long absence episodes per 10 person-years and subsequent mortality are largely similar to those for the number of sickness absence days (table 3). Both these measures of sickness absence are less consistently associated with mortality in patients with diabetes, CHD or cerebrovascular disease.

According to the AUC statistics (tables 2 and 3), the total number of sickness-absence days discriminates mortality risk for all chronic conditions, except diabetes and CHD/cerebrovascular disease. The AUC statistic is particularly good at distinguishing poor vs good prognosis for cancer (AUC 0.73, 95% CI 0.63-0.82). Again the findings for the number of long absence episodes largely replicate these results, except that long absence episodes are able additionally to predict mortality for those with CHD or cerebrovascular disease.

TABLE 2--The association between mean annual number of sickness absence days across years 1990-1992 and mortality during 1993-2007 for employees with chronic conditions, the GAZEL study.

Sub-population	Number of sickness-absence days			
	No. of absence days per person-year	No. of participants (No. of deaths)	Age-, sex-, and grade-adjusted hazard ratio (95% CI)	Age-, sex-, grade-, and co-morbidity adjusted hazard ratio (95% CI)
Cancer	0	45 (4)	1.00	1.00
	>0-28	95 (7)	0.96 (0.28-3.30)	1.01 (0.29-3.51)
	>28	69 (26)	4.85 (1.66-14.14)	5.92 (1.98-17.76)
	AUC* (95% CI):	0.73 (0.63-0.82)		
Diabetes	0	140 (7)	1.00	1.00
	>0-28	227 (15)	1.26 (0.50-3.17)	1.24 (0.49-3.12)
	>28	64 (9)	2.68 (0.93-7.78)	2.35 (0.75-7.37)
	AUC* (95% CI):	0.60 (0.50-0.70)		
Depression	0	552 (30)	1.00	1.00
	>0-28	1433 (57)	0.83 (0.53-1.29)	0.80 (0.51-1.25)
	>28	591 (54)	1.99 (1.26-3.16)	1.74 (1.10-2.78)
	AUC* (95% CI):	0.56 (0.51-0.61)		
Chronic bronchitis or asthma	0	479 (25)	1.00	1.00
	>0-28	891 (56)	1.26 (0.78-2.03)	1.24 (0.77-2.00)
	>28	238 (37)	3.30 (1.93-5.64)	2.69 (1.56-4.64)
	AUC* (95% CI):	0.60 (0.55-0.65)		
CHD or cerebrovascular disease	0	168 (16)	1.00	1.00
	>0-28	300 (23)	0.77 (0.40-1.46)	0.75 (0.39-1.44)
	>28	152 (21)	1.36 (0.70-2.64)	1.25 (0.64-2.43)
	AUC* (95% CI):	0.54 (0.47-0.63)		
Hypertension	0	766 (45)	1.00	1.00
	>0-28	1263 (71)	1.01 (0.69-1.48)	0.96 (0.65-1.40)
	>28	329 (38)	2.15 (1.36-3.38)	1.61 (1.00-2.60)
	AUC* (95% CI):	0.56 (0.51-0.60)		

*AUC (area under receiver-operating-characteristic curve) of >0.5 indicates ability of the measure to distinguish groups at risk of mortality.

TABLE 3--The association between the number of long (>14 days) sickness absence episodes during 1990-1992 and mortality during 1993-2007 for employees with chronic conditions, the GAZEL study.

Sub-population	Number of sickness-absence episodes >14 days			
	No. of episodes per 10 person-years	No. of participants (No. of deaths)	Age-, sex-, and grade-adjusted hazard ratio (95% CI)	Age-, sex-, grade-, and co-morbidity adjusted hazard ratio (95% CI)
Cancer	0	92 (7)	1.00	1.00
	1-5	57 (10)	2.63 (1.00-6.92)	2.56 (0.96-6.87)
	>5	60 (20)	4.68 (1.96-11.15)	5.43 (2.24-13.14)
	AUC* (95% CI)	0.69 (0.61-0.78)		
Diabetes	0	282 (18)	1.00	1.00
	1-5	69 (2)	0.42 (0.10-1.82)	0.42 (0.10-1.82)
	>5	80 (11)	2.09 (0.94-4.67)	1.86 (0.78-4.44)
	AUC* (95% CI)	0.56 (0.46-0.67)		
Depression	0	1386 (63)	1.00	1.00
	1-5	545 (23)	1.04 (0.64-1.68)	1.03 (0.63-1.66)
	>5	645 (55)	2.02 (1.39-2.92)	1.84 (1.27-3.15)
	AUC* (95% CI)	0.57 (0.52-0.62)		
Chronic bronchitis or asthma	0	1060 (58)	1.00	1.00
	1-5	284 (25)	1.61 (1.01-2.59)	1.49 (0.93-2.40)
	>5	264 (35)	2.46 (1.59-3.80)	2.01 (1.28-3.15)
	AUC* (95% CI)	0.60 (0.55-0.65)		
CHD or cerebrovascular disease	0	340 (25)	1.00	1.00
	1-5	136 (16)	1.64 (0.87-3.10)	1.53 (0.80-2.92)
	>5	144 (19)	1.69 (0.92-3.11)	1.42 (0.76-2.65)
	AUC* (95% CI)	0.58 (0.51-0.64)		
Hypertension	0	1556 (82)	1.00	1.00
	1-5	438 (33)	1.52 (1.01-2.28)	1.44 (0.96-2.17)
	>5	364 (39)	2.21 (1.49-3.28)	1.75 (1.16-2.65)
	AUC* (95% CI)	0.58 (0.53-0.62)		

*AUC (area under receiver-operating-characteristic curve) of >0.5 indicates ability of the measure to distinguish groups at risk of mortality.

Generalisability and long-term prediction of death

Men and women with cancer may have very different risk of death as cancer in women is mainly breast cancer, which has a much better prognosis than lung cancer, a common cause of early death in men of working age in France.²³ In spite of this, there is no sex difference in associations between sickness absence days, long sickness absence episodes and mortality among those with cancer (p for interaction >0.35) or other chronic conditions ($p>0.54$ for diabetes; $p>0.26$ for depression; $p>0.74$ for chronic bronchitis/asthma; $p>0.58$ for CHD/cerebrovascular disease; and $p>0.70$ for hypertension). In the same vein, we found no strong evidence of differences in these associations by age group (p for interaction >0.07) or socioeconomic position ($p>0.37$). Thus, the associations between sickness absence measures and mortality in employees with chronic conditions seem to be generalisable across demographic and socioeconomic groups.

To examine whether sickness absence is a long-term predictor of mortality among employees with chronic conditions, we excluded those who died during the first 5 years of follow-up (table 4). High numbers of sickness absence days and long sickness absence episodes are strongly associated with mortality among employees with cancer and chronic bronchitis/asthma. Among hypertensive employees, the association remains similar to that observed before the exclusions, but due to lower numbers does not reach statistical significance. The magnitude of the association between absence days and mortality is slightly reduced among depressive employees while that of long absence episodes is reduced considerably.

Co-morbidity

Of the participants, 4844 (27.0%) have one chronic condition, 1136 (6.3%) two chronic conditions, 194 (1.1%) three conditions and 26 (0.1%) four conditions. The associations of sickness absence with mortality are not different for participants with one chronic condition compared to those with co-morbidity (i.e., two or more chronic conditions)(table 5).

TABLE 4--The association between sickness absence and mortality for employees with chronic conditions excluding participants who died during the first 5 years of follow-up, the GAZEL study.

Sub-population	Total number of sickness-absence days			Number of sickness-absence episodes >14 days		
	No. of days per person-year	No. of participants (No. of deaths)	Age-, sex-, and grade-adjusted hazard ratio (95% CI)	No. of episodes per 10 person-years	No. of participants (No. of deaths)	Age-, sex-, and grade-adjusted hazard ratio (95% CI)
Cancer	0 >0-28 >28	43 (2) 92 (4) 54 (11)	1.00 1.23 (0.22-6.79) 5.06 (1.10-23.37)	0 1-5 >5	90 (5) 51 (4) 48 (8)	1.00 1.57 (0.42-5.88) 4.68 (1.01-9.62)
Diabetes	0 >0-28 >28	137 (4) 224 (12) 60 (5)	1.00 1.85 (0.58-5.96) 2.82 (0.70-11.42)	0 1-5 >5	277 (13) 69 (2) 75 (6)	1.00 0.57 (0.13-2.57) 1.61 (0.58-4.48)
Depression	0 >0-28 >28	549 (27) 1421 (45) 569 (32)	1.00 0.71 (0.43-1.15) 1.30 (0.77-2.21)	0 1-5 >5	1376 (53) 538 (16) 625 (35)	1.00 0.85 (0.49-1.50) 1.55 (1.00-2.39)
Chronic bronchitis or asthma	0 >0-28 >28	473 (19) 878 (43) 222 (21)	1.00 1.29 (0.75-2.23) 2.56 (1.33-4.91)	0 1-5 >5	1049 (47) 275 (16) 249 (20)	1.00 1.27 (0.72-2.26) 1.76 (1.02-3.02)
CHD or cerebrovascular disease	0 >0-28 >28	165 (13) 293 (16) 144 (13)	1.00 0.65 (0.31-1.36) 1.08 (0.50-2.35)	0 1-5 >5	335 (20) 131 (11) 136 (11)	1.00 1.53 (0.73-3.23) 1.29 (0.61-2.72)
Hypertension	0 >0-28 >28	756 (35) 1248 (56) 311 (20)	1.00 1.06 (0.69-1.63) 1.56 (0.88-2.76)	0 1-5 >5	1540 (66) 428 (23) 347 (22)	1.00 1.36 (0.84-2.18) 1.62 (0.99-2.65)

TABLE 5--The association between sickness absence and mortality for employees with one or more chronic conditions, the GAZEL study.

Sub-p opulation	Total number of sickness-absence days			Number of sickness-absence episodes >14 days		
	No. of days per person-year	No. of participants (No. of deaths)	Age-, sex-, and grade-adjusted hazard ratio (95% CI)	No. of episodes per 10 person-years	No. of participants (No. of deaths)	Age-, sex-, and grade-adjusted hazard ratio (95% CI)
Employees with one chronic condition	0	1557 (79)	1.00	0	3225 (140)	1.00
	>0-28	2646 (108)	0.89 (0.66-1.19)	1-5	902 (50)	1.39 (1.01-1.93)
	>28	641 (59)	2.23 (1.56-3.18)	>5	717 (56)	2.07 (1.50-2.84)
Employees with two or more chronic conditions (co-morbidity)	0	2767 (22)	1.00	0	695 (50)	1.00
	>0-28	730 (53)	0.97 (0.59-1.61)	1-5	292 (27)	1.36 (0.85-2.18)
	>28	350 (54)	2.13 (1.28-3.55)	>5	369 (52)	2.06 (1.39-3.07)

DISCUSSION

The principal finding of this study is that data on sickness absence may provide important prognostic information for several common conditions of major public health relevance. A high level of sickness absence was associated with a 2- to 5-fold excess mortality among employees with cancer, depression, chronic bronchitis, asthma, and hypertension. This association was robust for two simple measures of sickness absence, the total number of annual sickness-absence days and the number of sickness-absence episodes longer than 14 days. There was no evidence of significant variation in the magnitude or direction of these associations between men and women, young and old employees, those at different levels of the socioeconomic hierarchy, or those with and without co-morbid conditions.

To our best knowledge this is the first systematic examination of sickness absence as a potential tool for the estimation of disease prognosis. Areas under the receiver-operating characteristic curves for sickness absence measures were 0.7 among employees with cancer; 0.6 among those suffering from chronic bronchitis or asthma, and slightly lower for depressive and hypertensive employees (but 95% CIs did not include 0.50). These figures provide moderately strong support for the ability of sickness absence to distinguish individuals at increased mortality risk within specific chronic conditions (area under the curve for a perfect predictor is 1.0). The magnitude of the predictive power is comparable to those of two established, widely-used clinical predictors, the Framingham risk score and the metabolic syndrome in relation to incident coronary heart disease and type 2 diabetes (areas under the curves between 0.6 and 0.7).^{24 25}

Exclusion of deaths from the first five years of follow-up little affected the association between sickness absence and mortality in people with cancer, chronic

bronchitis/asthma and hypertension, but reduced this association in depressive employees. Depression contributes to increased risk of sickness absence but the status of depression may fluctuate over time and thus the association between sickness absence and mortality may be particularly open to effect dilution among depressive employees. The reason why sickness absence is predictive of mortality in the depressed is not clear. Co-morbid chronic diseases seem an unlikely explanation as adjustment for all chronic conditions we studied hardly attenuated the association between sickness absence and mortality in this group. However, unhealthy behaviours, such as smoking, substance abuse and self-harm, are a potential candidate because they contribute to both sickness absence and mortality and there is a considerable variation in such behaviours among the depressed people.²⁶⁻²⁹

We found no attenuation of the sickness absence-mortality association among cancer patients after the effect of other diseases was taken into account. In contrast, this adjustment reduced the association among hypertensive employees and those suffering from chronic bronchitis or asthma. Indeed, prognosis is obviously worse when hypertension is secondary to coronary heart disease, stroke, or diabetes, or when hypertension is combined with depression. Similarly, these and other conditions are likely to contribute to sickness absence and mortality among people with chronic bronchitis or asthma.

Our study on all participants, irrespective of whether they had chronic conditions or not, adds to evidence suggesting that long-term sickness absence can be used as a global measure of health differentials between employees.^{3 4 9 13} With over 800 deaths, this is the largest study of sickness absence, disease and mortality to date and the observed sickness absence-mortality associations in the total cohort are in keeping with results reported in recent smaller-scale studies.^{3 13} Moreover, associations remained after

excluding the first 5 years of follow-up meaning that excess sickness absence shortly before death is unlikely to explain our findings.

Methodology

Assessment of common chronic diseases based on self-reports is a potential source of misclassification bias. However, according to previous studies, the agreement between self-reports and medical records is high for diabetes (total agreement 97%), hypertension (88%), myocardial infarction (98%), and stroke (98%),³⁰ and 87% of self-reported asthma patients have been verified as having chronic asthma.³¹ Self-reported cancer and depression are likely to be affected by under-reporting, because of the associated stigma or lack of knowledge or denial.³²⁻³⁴ However, as we focussed on those people who did report these conditions there is probably little risk of misclassification in the analysis of prognosis.

We obtained sickness absence from the employers' records, but such data may be difficult to obtain for cohorts with employees from a large number of different workplaces. Previous studies on working populations suggest that the agreement between self-reported and recorded sickness-absence days is generally good and in the Whitehall II study self-reported and recorded data predicted mortality equally well.^{2 14} This suggests that it should be possible to use self-reports of sickness-absence days when absence records are not available. Further research is now needed to confirm the validity of self-reported sickness-absence for specific chronic conditions, as the possibility of using self-reports would simplify the collection of sickness absence data in epidemiological studies of general populations.

Conclusion

Data from a large contemporary cohort of French employees suggest that information on sickness absence may contribute to the estimation of prognosis for common chronic conditions at a population level. Our findings provide a basis for considering increased use of sickness absence in research of prognosis in working populations.

MAIN MESSAGES

High levels of sickness absence were associated with a 2- to 5-fold excess mortality among employees with cancer, depression, chronic bronchitis, asthma, and hypertension.

These associations were generalisable across demographic and socioeconomic groups.

The association between sickness absence and mortality was weaker for those with coronary heart disease or cerebrovascular disease.

POLICY IMPLICATIONS

Data on sickness absence may provide an important prognostic marker for a number of diseases of major public health relevance.

Conflict of interest: None declared.

Contributors: All authors formulated the hypothesis, analysed/interpreted the data and wrote the paper. MK is guarantor for the paper. MZ and MG are the Principal Investigators of the GAZEL study.

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References

1. Marmot M, Feeney A, Shipley M, North F, Syme SL. Sickness absence as a measure of health status and functioning: from the UK Whitehall II study. *J Epidemiol Community Health* 1995;49(2):124-30.
2. Alexanderson K, Norlund A, (Eds.). Sickness absence - causes, consequences, and physicians' sickness certification practices: A systematic review. *Scandinavian Journal of Public Health* 2004;32 (Suppl 63):1-263.
3. Kivimäki M, Head J, Ferrie JE, Shipley MJ, Vahtera J, Marmot MG. Sickness absence as a global measure of health: evidence from mortality in the Whitehall II prospective cohort study. *Bmj* 2003;327(7411):364.
4. Taylor PJ, BurrIDGE J. Trends in death, disablement, and sickness absence in the British Post Office since 1981. *Br J Ind Med* 1982;39(1):1-10.
5. Chevalier A, Luce D, Blanc C, Goldberg M. Sickness absence at the French National Electric and Gas Company. *Br J Ind Med* 1987;44(2):101-10.
6. Borg K, Hensing G, Alexanderson K. Predictive factors for disability pension--an 11-year follow up of young persons on sick leave due to neck, shoulder, or back diagnoses. *Scand J Public Health* 2001;29(2):104-12.
7. Gjesdal S, Bratberg E. Diagnosis and duration of sickness absence as predictors for disability pension: results from a three-year, multi-register based and prospective study. *Scand J Public Health* 2003;31(4):246-54.
8. Kivimäki M, Forma P, Wikstrom J, Halmeenmäki T, Pentti J, Elovainio M, et al. Sickness absence as a risk marker of future disability pension: the 10-town study. *J Epidemiol Community Health* 2004;58(8):710-1.
9. Bambra C, Norman P. What is the association between sickness absence, mortality and morbidity? *Health Place* 2006;12(4):728-33.
10. Lund T, Kivimäki M, Labriola M, Villadsen E, Christensen KB. Using administrative sickness absence data as a marker of future disability pension: The prospective DREAM study of Danish private sector employees. *Occup Environ Med* 2007.
11. Labriola M, Lund T. Self-reported sickness absence as a risk marker of future disability pension. Prospective findings from the DWECS/DREAM study 1990-2004. *Int J Med Sci* 2007;4(3):153-8.

12. Kivimäki M, Ferrie JE, Hagberg J, Head J, Westerlund H, Vahtera J, et al. Diagnosis-specific sick leave as a risk marker for disability pension in a Swedish population. *J Epidemiol Community Health* 2007;61(10):915-20.
13. Vahtera J, Pentti J, Kivimäki M. Sickness absence as a predictor of mortality among male and female employees. *J Epidemiol Community Health* 2004;58(4):321-6.
14. Ferrie JE, Kivimäki M, Head J, Shipley MJ, Vahtera J, Marmot MG. A comparison of self-reported sickness absence with absences recorded in employers' registers: evidence from the Whitehall II study. *Occup Environ Med* 2005;62(2):74-9.
15. Hemingway H. Prognosis research: why is Dr. Lydgate still waiting? *J Clin Epidemiol* 2006;59(12):1229-38.
16. North F, Syme SL, Feeney A, Head J, Shipley MJ, Marmot MG. Explaining socioeconomic differences in sickness absence: the Whitehall II Study. *Bmj* 1993;306(6874):361-6.
17. Ferrie JE, Head J, Shipley MJ, Vahtera J, Marmot MG, Kivimäki M. BMI, obesity, and sickness absence in the Whitehall II study. *Obesity (Silver Spring)* 2007;15(6):1554-64.
18. Lund T, Labriola M, Christensen KB, Bultmann U, Villadsen E. Physical work environment risk factors for long term sickness absence: prospective findings among a cohort of 5357 employees in Denmark. *Bmj* 2006;332(7539):449-52.
19. Kivimäki M, Vahtera J, Thomson L, Griffiths A, Cox T, Pentti J. Psychosocial factors predicting employee sickness absence during economic decline. *J Appl Psychol* 1997;82(6):858-72.
20. Melchior M, Krieger N, Kawachi I, Berkman LF, Niedhammer I, Goldberg M. Work factors and occupational class disparities in sickness absence: findings from the GAZEL cohort study. *Am J Public Health* 2005;95(7):1206-12.
21. Goldberg M, Blanc M, Chastang JF, Blanc C, Sommer M. The health data base of a nationwide company - its use in epidemiological studies. *J Occup Med* 1982;24(1):47-52.
22. Zweig MH, Campbell G. Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine. *Clin Chem* 1993;39(4):561-77.
23. Melchior M, Berkman LF, Kawachi I, Krieger N, Zins M, Bonenfant S, et al. Lifelong socioeconomic trajectory and premature mortality (35-65 years) in France: findings from the GAZEL Cohort Study. *J Epidemiol Community Health* 2006;60(11):937-44.
24. Wannamethee SG, Shaper AG, Lennon L, Morris RW. Metabolic syndrome vs Framingham Risk Score for prediction of coronary heart disease, stroke, and type 2 diabetes mellitus. *Arch Intern Med* 2005;165(22):2644-50.

25. McNeill AM, Rosamond WD, Girman CJ, Golden SH, Schmidt MI, East HE, et al. The metabolic syndrome and 11-year risk of incident cardiovascular disease in the atherosclerosis risk in communities study. *Diabetes Care* 2005;28(2):385-90.
26. Freedland KE, Carney RM, Skala JA. Depression and smoking in coronary heart disease. *Psychosom Med* 2005;67 Suppl 1:S42-6.
27. Aharonovich E, Liu X, Nunes E, Hasin DS. Suicide attempts in substance abusers: effects of major depression in relation to substance use disorders. *Am J Psychiatry* 2002;159(9):1600-2.
28. Nunes EV, Levin FR. Treating depression in substance abusers. *Curr Psychiatry Rep* 2006;8(5):363-70.
29. Nunes EV, Rounsaville BJ. Comorbidity of substance use with depression and other mental disorders: from Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) to DSM-V. *Addiction* 2006;101 Suppl 1:89-96.
30. Okura Y, Urban LH, Mahoney DW, Jacobsen SJ, Rodeheffer RJ. Agreement between self-report questionnaires and medical record data was substantial for diabetes, hypertension, myocardial infarction and stroke but not for heart failure. *J Clin Epidemiol* 2004;57(10):1096-103.
31. Kauppi P, Laitinen LA, Laitinen H, Kere J, Laitinen T. Verification of self-reported asthma and allergy in subjects and their family members volunteering for gene mapping studies. *Respir Med* 1998;92(11):1281-8.
32. Desai MM, Bruce ML, Desai RA, Druss BG. Validity of self-reported cancer history: a comparison of health interview data and cancer registry records. *Am J Epidemiol* 2001;153(3):299-306.
33. Eaton WW, Neufeld K, Chen LS, Cai G. A comparison of self-report and clinical diagnostic interviews for depression: diagnostic interview schedule and schedules for clinical assessment in neuropsychiatry in the Baltimore epidemiologic catchment area follow-up. *Arch Gen Psychiatry* 2000;57(3):217-22.
34. Metzger MH, Goldberg M, Chastang JF, Leclerc A, Zins M. Factors associated with self-reporting of chronic health problems in the French GAZEL cohort. *J Clin Epidemiol* 2002;55(1):48-59.