

Does sickness absence due to psychiatric disorder predict cause-specific mortality? A 16-year follow-up of the GAZEL occupational cohort study.

Maria Melchior, Jane Ferrie, Kristina Alexanderson, Marcel Goldberg, Mika Kivimaki, Archana Singh-Manoux, Jussi Vahtera, Hugo Westerlund, Marie Zins, Jenny Head

► **To cite this version:**

Maria Melchior, Jane Ferrie, Kristina Alexanderson, Marcel Goldberg, Mika Kivimaki, et al.. Does sickness absence due to psychiatric disorder predict cause-specific mortality? A 16-year follow-up of the GAZEL occupational cohort study.. American Journal of Epidemiology, Oxford University Press (OUP), 2010, 172 (6), pp.700-7. 10.1093/aje/kwq186 . inserm-00511645

HAL Id: inserm-00511645

<https://www.hal.inserm.fr/inserm-00511645>

Submitted on 25 Aug 2010

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Original Contribution

Does Sickness Absence Due to Psychiatric Disorder Predict Cause-specific Mortality? A 16-Year Follow-up of the GAZEL Occupational Cohort Study

Maria Melchior*, Jane E. Ferrie, Kristina Alexanderson, Marcel Goldberg, Mika Kivimaki, Archana Singh-Manoux, Jussi Vahtera, Hugo Westerlund, Marie Zins, and Jenny Head

* Correspondence to Dr. Maria Melchior, Centre de Recherche en Épidémiologie et Santé des Populations/UMRS-1018, Épidémiologie des Déterminants Professionnels et Sociaux de la Santé, Inserm, Hôpital Paul-Brousse, Bâtiment 15/16, 16 avenue Paul Vaillant-Couturier, 94800 Villejuif, France (e-mail: maria.melchior@inserm.fr).

Initially submitted January 17, 2010; accepted for publication May 18, 2010.

Mental disorders are a frequent cause of morbidity and sickness absence in working populations; however, the status of psychiatric sickness absence as a predictor of mortality is not established. The authors tested the hypothesis that psychiatric sickness absence predicts mortality from leading medical causes. Data were derived from the French GAZEL cohort study ($n = 19,962$). Physician-certified sickness absence records were extracted from administrative files (1990–1992) and were linked to mortality data from France's national registry of mortality (1993–2008, mean follow-up: 15.5 years). Analyses were conducted by using Cox regression models. Compared with workers with no sickness absence, those absent due to psychiatric disorder were at increased risk of cause-specific mortality (hazard ratios (HRs) adjusted for age, gender, occupational grade, other sickness absence—suicide: 6.01, 95% confidence interval (CI): 3.07, 11.75; cardiovascular disease: 1.84, 95% CI: 1.10, 3.08; and smoking-related cancer: 1.65, 95% CI: 1.07, 2.53). After full adjustment, the excess risk of suicide remained significant (HR = 5.13, 95% CI: 2.60, 10.13) but failed to reach statistical significance for fatal cardiovascular disease (HR = 1.59, 95% CI: 0.95, 2.66) and smoking-related cancer (HR = 1.31, 95% CI: 0.85, 2.03). Psychiatric sickness absence records could help identify individuals at risk of premature mortality and serve to monitor workers' health.

absenteeism; cause of death; depression; longitudinal studies; mental disorders; mortality; work

Abbreviations: CI, confidence interval; EDF-GDF, Electricité de France-Gaz de France; HR, hazard ratio; ICD-9, *International Classification of Diseases*, Ninth Revision; ICD-10, *International Statistical Classification of Diseases and Related Health Problems*, Tenth Revision.

In industrialized nations, mental disorders affect 30%–50% of individuals during their lifetime and are one of the leading causes of morbidity (1). These disorders are especially frequent in adults of working age, and, in addition to being a source of great suffering for those affected and those close to them, they often lead to impaired functioning (2), lost productivity (3), and premature death (4–6).

Research from population studies has shown that only a minority of individuals with mental disorders seek medical care (7, 8) or are absent from work (9). Among the employed, psychiatric sickness absence indicates the presence of severe mental health difficulties and predicts future risk

of poor health (10), disability pension due to mental disorders (11), and mortality (12, 13). However, to our knowledge, the association between psychiatric sickness absence and specific causes of death has been examined in only a single investigation based on the British Whitehall II study. The authors reported an association between psychiatric sickness absence and mortality due to cardiovascular causes and all cancers; however, because of low statistical power, they were not able to examine other frequent causes of death such as specific cancer types and suicide (12). Thus, current knowledge regarding the relation between sickness absence due to psychiatric disorder and patterns of mortality

is incomplete. Thorough documentation of patterns of cause-specific mortality associated with psychiatric sickness absence can help improve understanding of the population impact of mental disorders and establish psychiatric sickness absence as an indicator of later health outcomes.

In the present study, we examined the association between psychiatric sickness absence and mortality over a follow-up period of 16 years among public-sector employees in France who participated in the GAZEL cohort study. A previous study based on this cohort showed that psychiatric sickness absence predicts the risk of all-cause mortality (13). In the present investigation, our aim was to extend that prior finding by testing associations between psychiatric sickness absence and specific causes of death.

MATERIALS AND METHODS

Study population

The GAZEL cohort was established in 1989 and comprises employees of France's national gas and electricity company, Electricité de France-Gaz de France (EDF-GDF). At baseline, 20,625 workers (15,011 men and 5,614 women) aged 35–50 years were included. The study uses an annual questionnaire to collect data on health, lifestyle, individual, familial, social, and occupational factors. Additional individual data are obtained from various sources within and outside EDF-GDF. Further details of the GAZEL study can be found elsewhere (14). The GAZEL study received approval from the national commission overseeing ethical data collection in France (Commission Nationale Informatique et Liberté).

Measures

Sickness absence. The exposure in this study was all medically certified sick-leave spells exceeding 7 days in a 3-year study period from January 1, 1990, to December 31, 1992. We chose to focus on medically certified sickness absences a) to enhance comparability of our study findings with prior research, b) because the validity of the diagnoses is probably higher than for self-certified sick-leave spells, and c) because such spells have been shown to be a good global measure of health (13, 15, 16). Diagnoses for medically certified sickness absence spells were coded by company physicians by using an abridged version of the *International Classification of Diseases*, Ninth Revision (ICD-9) (17). For the present study, diagnoses for these spells were categorized into psychiatric (ICD-9 chapter 5, codes 290–319) or nonpsychiatric (all other ICD chapters) (10). To be included in a particular diagnostic category, participants had to have at least one sickness absence spell of more than 7 days with that diagnosis during the 3-year exposure window. Dichotomous variables were derived for psychiatric sickness absence spells (0 spells, ≥ 1 spells) and for nonpsychiatric sickness absence spells (0 spells, ≥ 1 spells). During the 3-year exposure window, participants could have several sickness absence spells with different diagnoses; that is, each individual could have both psychiatric and nonpsychiatric sickness absence spells. Because

diagnosis was missing for some spells, a further dichotomous variable was derived for sickness absence spells with missing diagnoses (0 spells with missing diagnosis, ≥ 1 spells with missing diagnosis).

Mortality. Mortality data were obtained from EDF-GDF company records. The causes of death, recorded by France's national registry of deaths (Inserm CépiDC), were linked to GAZEL records for the period January 1, 1993–December 31, 2008. Underlying diagnoses were coded by using ICD-9 up to December 31, 1998 (17) and ICD-10 beginning January 1, 1999 (18). We distinguished deaths due to cancers (ICD-9 codes 140–208, ICD-10 codes C00–C97), cardiovascular causes (ICD-9 codes 390–459, ICD-10 codes I00–I99), and external causes (ICD-9 codes E800–E999, ICD-10 codes V01–X84). Among cancer deaths, we distinguished smoking-related cancers, as in previous studies (oral cavity: ICD-9 codes 140–141 and 143–149, ICD-10 codes C00–C06 and C09–C14; esophagus: ICD-9 code 150, ICD-10 code C15; pancreas: ICD-9 code 157, ICD-10 code C25; respiratory and intrathoracic organs: ICD-9 codes 160–163, ICD-10 codes C30–C34 and C38; and urinary tract: ICD-9 codes 188–189, ICD-10 codes C64–C68) (19). Among deaths due to external causes, we determined suicide (ICD-9 codes E950–E959, ICD-10 codes X60–X84). We selected these subgroups because they represent leading causes of death in France (20) and constitute the largest mortality groups in the GAZEL study.

Covariates. Analyses were adjusted for factors associated with premature mortality (12), that is, demographic characteristics and health behaviors measured at study baseline: age (35–40 years, 41–45 years, or 46–50 years), gender (female or male), marital status (divorced/separated/widowed or married/living with a partner), tobacco smoking (nonsmoker or smoker), and alcohol consumption (in number of drinks of alcohol/day (units): none; moderate (women: ≤ 3 , men: ≤ 4); or heavy (women: ≥ 4 , men: ≥ 5)). Occupational grade in 1989 (low: manual worker or clerk, intermediate: technician or administrative associate professional, or high: engineer or manager) was available from EDF-GDF company records.

Statistical analyses

Our study was based on all GAZEL participants who were alive and actively working on January 1, 1990 ($n = 20,539$). For 19,962 of the study participants (97.2%), complete data were available on mortality and all covariates. To test the hypothesis that psychiatric sickness absence predicts cause-specific mortality, our study outcome, we used Cox regression models, after verifying that the proportional hazards hypothesis was met. In all analyses, we systematically controlled for sickness absence, with nonpsychiatric and missing diagnoses as dichotomous variables to ensure that the associations observed were net of the effect of sickness absence due to other reasons. First, we studied the association between sickness absence spells from 1990 to 1992 and cause-specific mortality from 1993 to 2008 adjusting for age, gender, and occupational grade. Second, we further adjusted the analysis for marital status, tobacco smoking status, and alcohol use. Third, using 15 imputations, we

Table 1. Mortality Rates (1993–2009) According to Spells of Psychiatric Sickness Absence of >7 Days (1990–1992) and Covariates in the French GAZEL Cohort Study

	No.	%	With ≥1 Psychiatric Sickness Absences in 1990–1992		Deaths in 1993–2008	
			No.	%	No.	%
Total participants	19,962				1,144	5.7
Sickness absence, 1990–1992 ^a						
0 Spells	11,830	59.3			591	5.0
≥1 Spell with a psychiatric diagnosis	1,294	6.5			111	8.6
≥1 Spell with a nonpsychiatric diagnosis	6,549	32.8			460	7.0
≥1 Spell with a missing diagnosis	2,460	12.3			162	6.6
Age group, years						
36–40	2,119	10.6	277	13.1	55	2.6
41–45	10,405	52.1	602	5.8	527	5.1
46–50	7,438	37.3	415	5.6	562	7.6
Sex						
Men	14,604	73.2	560	3.8	971	6.7
Women	5,358	26.8	734	13.7	173	3.2
Occupational grade						
High	3,931	19.7	463	11.8	298	7.6
Medium	11,383	57.0	730	6.4	636	5.6
Low	4,648	23.3	101	2.2	210	4.5
Marital status						
Married/living with partner	17,766	89.0	1,028	5.8	970	5.5
Single/divorced/separated/widowed	2,196	11.0	266	12.1	174	7.9
Tobacco smoking status						
Nonsmoker	14,262	71.4	831	5.8	612	4.3
Smoker	5,712	28.6	463	8.1	535	9.3
Alcohol use						
None	519	2.6	79	15.2	45	8.7
Moderate	17,546	87.9	1,089	6.2	894	5.1
Heavy	1,897	9.5	126	6.6	205	10.8

^a Sickness absence groups are not mutually exclusive because participants may have spells in more than one category.

imputed missing values for absence diagnoses and checked that results obtained by using this method were similar to complete case analyses. The multiple imputation analysis was conducted in STATA version 10.1 software (Stata Corporation, College Station, Texas), and all other analyses were performed with SAS version 9.1 statistical software (SAS Institute, Inc., Cary, North Carolina).

RESULTS

Over the 16-year follow-up period (mean, 15.5), there were 1,144 deaths (173 women and 971 men). As shown in Table 1, during the 3-year exposure window, 6.5% of study participants had at least one spell of sickness absence due to psychiatric disorder ($n = 1,294$). Overall, workers

who took psychiatric sickness absence were young, were female, worked in a low-grade occupation, lived without a partner, smoked tobacco, and abstained from alcohol. We found no evidence of statistical interactions between sickness absence and gender; therefore, our analyses controlled for gender rather than stratifying.

Workers with sickness absence due to psychiatric disorder had an increased risk of all-cause mortality (hazard ratio (HR) adjusted for age, gender, occupational grade, and sickness absence due to other diagnoses = 1.70, 95% confidence interval (CI): 1.38, 2.08). Similarly, mortality risk was also elevated for workers with sickness absence for nonpsychiatric reasons (HR = 1.31, 95% CI: 1.16, 1.49).

Table 2 shows associations between psychiatric sickness absence and specific causes of mortality. Adjusting for age, gender, occupational grade, and sickness absence due to

Table 2. Diagnosis-specific Spells of Sickness Absence (1990–1992)^a and Cause-specific Mortality (1990–2008) in the French GAZEL Cohort Study ($n = 19,962$)^b

Sickness Absence Category	Cancer (611 Deaths)		Cardiovascular Causes (186 Deaths)		Suicide (53 Deaths)		Other External Causes (61 Deaths)		Other Causes (210 Deaths)	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
<i>Models Adjusted for Age, Gender, Occupational Grade, and Sickness Absence due to Other Diagnoses</i>										
0 Spells	1.00		1.00		1.00		1.00		1.00	
≥1 Spell with a psychiatric diagnosis	1.03	0.74, 1.43	1.84	1.10, 3.08	6.01	3.07, 11.75	1.60	0.62, 4.12	3.16	2.15, 4.64
≥1 Spell with a nonpsychiatric diagnosis	1.33	1.13, 1.58	1.54	1.13, 2.09	1.11	0.62, 1.99	1.35	0.78, 2.32	1.14	0.85, 1.52
≥1 Spell with a missing diagnosis	1.04	0.82, 1.32	1.26	0.83, 1.90	0.76	0.32, 1.81	0.78	0.33, 1.85	1.44	1.00, 2.06
<i>Models Adjusted for Age, Gender, Occupational Grade, Sickness Absence due to Other Diagnoses, Marital Status, Tobacco Smoking, and Alcohol Use</i>										
0 Spells	1.00		1.00		1.00		1.00		1.00	
≥1 Spell with a psychiatric diagnosis	0.91	0.66, 1.27	1.59	0.95, 2.66	5.13	2.60, 10.13	1.36	0.52, 3.54	2.55	1.73, 3.76
≥1 Spell with a nonpsychiatric diagnosis	1.33	1.12, 1.57	1.53	1.12, 2.07	1.10	0.61, 1.97	1.34	0.78, 2.31	1.11	0.83, 1.49
≥1 Spell with a missing diagnosis	0.99	0.78, 1.26	1.21	0.80, 1.82	0.71	0.30, 1.69	0.75	0.32, 1.77	1.33	0.93, 1.91

Abbreviations: CI, confidence interval; HR, hazard ratio.

^a Sickness absence groups are not mutually exclusive because participants may have spells in more than one category; results for each diagnostic category were therefore adjusted for the other 2 diagnostic categories.

^b Cox regression models.

other diagnoses, we found that workers with sickness absence due to psychiatric disorder were at elevated risk of death from suicide (HR = 6.01, 95% CI: 3.07, 11.75), other causes (HR = 3.16, 95% CI: 2.15, 4.64), and cardiovascular disease (HR = 1.84, 95% CI: 1.10, 3.08). After we additionally adjusted for marital status, tobacco smoking status, and alcohol use, these hazard ratios were reduced for suicide (fully adjusted HR = 5.13, 95% CI: 2.60, 10.13), other causes (fully adjusted HR = 2.55, 95% CI: 1.73, 3.76), and cardiovascular disease (fully adjusted HR = 1.59, 95% CI: 0.95, 2.66). Our results were unchanged after excluding 17 participants who had had sickness absence spells due to psychotic disorder. In parallel, mortality risk was also elevated for workers with sickness absence due to nonpsychiatric reasons (fully adjusted—cardiovascular disease: HR = 1.53, 95% CI: 1.12, 2.07, cancer: HR = 1.33, 95% CI: 1.12, 1.57). Results obtained when we imputed missing sickness absence data were similar to those for the complete case analysis.

Distinguishing different cancer types (Table 3), we found that workers with sickness absence due to psychiatric disorder were at elevated risk of dying from a smoking-related cancer (HR adjusted for age, gender, occupational grade, and sickness absence for other diagnoses = 1.65, 95% CI: 1.07, 2.53). This excess risk was reduced after further adjusting for marital status, tobacco smoking, and alcohol use (fully adjusted HR = 1.31, 95% CI: 0.85, 2.03). In further analyses, the association between psychiatric sickness absence and smoking-related cancer mortality was stronger for very long absence spells (≥15 days): the fully adjusted hazard ratio was 1.63 (95% CI: 1.01, 2.62) (not shown). To rule

out the possibility that the association between psychiatric sickness absence and smoking-related cancer mortality reflected misinterpretation of early cancer symptoms (tiredness, weight loss), we verified that the association held after excluding the first 2 years of follow-up (fully adjusted HR = 1.63, 95% CI: 0.95, 2.76). Additionally, workers who took sickness absence due to nonpsychiatric diagnoses also had an elevated, yet somewhat smaller risk of smoking-related cancer mortality (fully adjusted HR = 1.36, 95% CI: 1.06, 1.74) and an elevated risk of non-smoking-related cancer mortality (fully adjusted HR = 1.26, 95% CI: 1.00, 1.59).

DISCUSSION

Main findings

We found that study participants who were absent from work for at least 7 days due to psychiatric disorder had a 6-fold excess risk of suicide, 3.2-fold excess risk of death from other causes, 1.8-fold excess risk of cardiovascular death, and 1.7-fold excess risk of dying from smoking-related cancer. The association between psychiatric sickness absence and mortality risk was attenuated after adjusting for workers' marital status and health behaviors, but it remained statistically significant for suicide and for death from other causes.

Study strengths and limitations

Our study has several strengths. First, we studied an occupational cohort of 19,962 workers employed in a variety

Table 3. Diagnosis-specific Spells of Sickness Absence (1990–1992) and Smoking-related Cancer Mortality (1990–2008) in the French GAZEL Cohort Study ($n = 19,962$)^a

Sickness Absence Category	No. of Participants	Smoking-related Cancers ^b (279 Deaths)			Non-smoking-related Cancers (332 Deaths)		
		No. of Deaths	HR	95% CI	No. of Deaths	HR	95% CI
<i>Models Adjusted for Age, Gender, Occupational Grade, and Sickness Absence due to Other Diagnoses</i>							
0 Spells	11,830		1.00			1.00	
≥1 Spell with a psychiatric diagnosis	1,294	24	1.65	1.07, 2.53	316	0.65	0.39, 1.09
≥1 Spell with a nonpsychiatric diagnosis	6,549	116	1.41	1.10, 1.81	128	1.28	1.01, 1.61
≥1 Spell with a missing diagnosis	2,460	39	1.10	0.78, 1.56	42	0.98	0.70, 1.36
<i>Models Adjusted for Age, Gender, Occupational Grade, Marital Status, Tobacco Smoking, Alcohol Use, and Sickness Absence due to Other Diagnoses</i>							
0 Spells	11,830		1.00			1.00	
≥1 Spell with a psychiatric diagnosis	1,294	24	1.31	0.85, 2.03	316	0.63	0.38, 1.06
≥1 Spell with a nonpsychiatric diagnosis	6,549	116	1.36	1.06, 1.74	128	1.26	1.00, 1.59
≥1 Spell with a missing diagnosis	2,460	39	1.03	0.72, 1.45	42	0.96	0.69, 1.34

Abbreviations: CI, confidence interval; HR, hazard ratio.

^a Cox regression models.

^b Smoking-related cancers include oral cavity: *International Classification of Diseases*, Ninth Revision (ICD-9) codes 140–141 and 143–149, *International Statistical Classification of Diseases and Related Health Problems*, Tenth Revision (ICD-10) codes C00–C06 and C09–C14; esophagus: ICD-9 code 150, ICD-10 code C15; pancreas: ICD-9 code 157, ICD-10 code C25; respiratory and intrathoracic organs: ICD-9 codes 160–163, ICD-10 codes C30–C34 and C38; urinary tract: ICD-9 codes 188–189, ICD-10 codes C64–C68.

of blue-collar and white-collar jobs. Second, we had a 16-year longitudinal follow-up (1992–2008) with a high rate of participation (approximately 75% in each yearly survey) and low loss of participants during follow-up (less than 1% since 1989). Third, sickness absence data were collected from administrative records (21), that is, independently of workers' health status. Fourth, cause-specific mortality data were obtained from a register.

However, we also acknowledge potential limitations. First, the GAZEL cohort comprises middle-aged workers employed by a large national company who tend to be healthier than the total working population from which they were drawn (22, 23), raising the question of generalizability of our findings. Comparisons with other epidemiologic cohorts such as the British Whitehall II study show similar patterns of sickness absence (24) and mortality (12), suggesting that the strength of the association between psychiatric sickness absence and mortality will hold in other settings in France as well as in other countries.

Second, underlying medical diagnoses were missing for 10.6% of sickness absence spells because company physicians did not have a chance to establish the medical cause of absence before the person returned to work. Because of the nondifferential distribution of missing data and its low frequency, this is an unlikely source of major bias for our results. To limit the influence of missing data on our findings, we included a “missing diagnosis” category in our analyses. Additionally, we found similar results when using

a multiple imputation method. A related issue is that, because of stigma and frequent somatic comorbidities, psychiatric disorders may be underreported on sickness absence certificates. However, it is unlikely that company physicians would code a sickness absence as being due to a psychiatric disorder if that were not the case. Thus, the bias caused by misclassification is likely to have attenuated, rather than inflated, the association between sickness absence and mortality (25).

Third, we did not take into account sickness absence spells that occurred after the 3-year sickness absence exposure period, which may have led to underestimation of associations between sickness absence and mortality. However, an advantage of limiting our sickness absence measure to a 3-year exposure period is that we were able to investigate whether sickness absence predicts cause-specific mortality early on.

The association between all-cause sickness absence and overall and cause-specific mortality has been reported previously (13, 16, 26–30). Yet, to our knowledge, the excess mortality risk for workers absent from work due to psychiatric disorder has been reported in only 4 investigations, 2 of which were conducted in a single study population (12, 13, 28, 30), and the excess risk of cardiovascular and cancer mortality has been reported in only 1 investigation (12). Therefore, our results extend prior research by showing that workers absent from work due to psychiatric disorder also appear at high risk of dying from suicide and smoking-related cancer.

Sickness absence as a predictor of mortality risk

Our findings are consistent with past research showing that individuals with a psychiatric disorder are at high risk of dying from several medical conditions (5, 6, 31). In our study, psychiatric sickness absence predicted a 6-fold increase in the risk of suicide. This figure is consistent with 7.7-fold higher mortality from suicide for employees with medically certified sickness absences in the Finnish Public Sector Study (26). Among individuals who suffer from psychiatric disorders, particularly mood disorders such as depression, those absent from work may have especially severe symptoms involving thoughts and behavior, which put them at high risk of suicide (5, 6, 31).

Our findings also indicate that psychiatric sickness absence confers a nearly 2-fold risk of cardiovascular mortality, which was just below statistical significance in our fully adjusted analysis. This finding is in line with evidence suggesting that common mental disorders such as depression increase the likelihood of cardiovascular risk factors (32, 33), disease (33–35), and mortality (5, 33, 36). This association probably reflects multiple mechanisms including behavioral characteristics (tobacco smoking, poor diet, lack of physical activity) (33, 37); increased social isolation (38); poor overall health (33, 39); as well as biologic risk factors (including dysregulation of the hypothalamic-pituitary axis, disturbance in heart rate variability, malfunction of blood clotting processes, heightened inflammatory immune response, and obesity) (38).

The excess risk of cancer mortality among workers with psychiatric sickness absence has been reported previously in the Whitehall II cohort study (12); our data further suggest that this association is driven by smoking-related cancer deaths. Importantly, this finding held even after excluding the first 2 years of follow-up, implying that it is not solely a reflection of early cancer symptoms (tiredness, weight loss) being interpreted as signs of psychological distress.

The excess risk of smoking-related cancer mortality was just below the statistically significant level in our fully adjusted analyses, which may reflect the small number of cases but also the influence of covariates that we adjusted for—mainly, tobacco smoking. Nevertheless, it is important to note that, even in the fully adjusted analysis, the risk of death from smoking-related cancer was elevated (HR = 1.31). Smoking could mediate the relation between psychiatric disorder and cancer, and the presence of psychiatric disorder may predict poor cancer prognosis, which could reflect at least 3 mechanisms: 1) a propensity for cancers with a poor prognosis, such as smoking-related tumors, among individuals with psychiatric disorder; 2) an impaired ability to seek medical help, resulting in delayed diagnosis (5); and 3) reduced adherence to medical treatment (40). Data on cancer stage at diagnosis and on medical treatment are not available for GAZEL study participants, but future research should examine the relation between psychiatric disorder and cancer prognosis in greater detail.

Overall, our estimates are concurrent with findings from population-based studies that reported increased risks of suicide and cardiovascular mortality for individuals with

common psychiatric disorder such as depression and anxiety (5, 31). Evidence regarding the relation between common mental disorders and cancer mortality is less conclusive; however, our finding of an association with smoking-related cancer is broadly in agreement with those findings reported for depression and subsequent risk of smoking-related cancer in the most recently conducted meta-analysis (summary relative risk = 1.4, 95% CI: 0.9, 2.2) (41) and is consistent with a recent report of an increased risk of lung cancer death in relation to depression (42). Thus, sickness absence due to psychiatric disorder appears to be a valid indicator of mental disorder.

We also found that sickness absence due to nonpsychiatric diagnoses confers an increased risk of death from cancer (smoking and nonsmoking related) and cardiovascular disease. In other words, the association between sickness absence and cardiovascular mortality appears to be observed regardless of the underlying cause of absence. However, for suicide, cancer death, and other causes of death, the association varies depending on the underlying medical diagnosis. This finding implies that information on medical causes of sickness absence can be of value to researchers and public health professionals interested in predicting cause-specific mortality.

Conclusions

Psychiatric sickness absence from work appears to be a valid indicator of future mortality risk. Individuals absent from work because of psychiatric disorder may be an appropriate target for interventions aiming to reduce the burden of premature mortality due to suicide, cardiovascular disease, and smoking-related cancer. For instance, to detect individuals at risk of suicide, occupational health services could put in place special follow-up for those who experience psychiatric sickness absence. Moreover, psychiatric sickness absence records, often routinely available, could be useful in monitoring workers' mental health.

ACKNOWLEDGMENTS

Author affiliations: INSERM UMRS 1018, Epidemiology of Occupational and Social Determinants of Health, Villejuif, France (Maria Melchior, Marcel Goldberg, Archana Singh-Manoux); Université Versailles-Saint-Quentin, UMRS 1018, Villejuif, France (Maria Melchior, Marcel Goldberg, Archana Singh-Manoux); Department of Epidemiology and Public Health, University College London Medical School, London, United Kingdom (Jane E. Ferrie, Mika Kivimaki, Archana Singh-Manoux, Jenny Head, Hugo Westerlund); Division of Insurance Medicine, Department of Clinical Neuroscience, Karolinska Institute, Stockholm, Sweden (Kristina Alexanderson, Hugo Westerlund); Department of Public Health, University of Turku and Turku University Hospital and Finnish Institute of Occupational Health, Turku, Finland (Jussi Vahtera); Stress Research Institute, Stockholm University, Stockholm, Sweden (Hugo Westerlund); and CETAF-RPPC, INSERM UMRS 1018,

Epidemiology of Occupational and Social Determinants of Health, Villejuif, France (Marie Zins).

This work was supported by an ESRC Research Seminar Series Competition 2007/8 (RES-451-26- 0491); the Swedish Council of Working Life and Social Research (grants 2004-2021 to K. A. and 2007-1143 to H. W.); the National Heart, Lung, and Blood Institute (R01HL036310 to M. K.); the National Institute on Aging (R01AG013196 to A. S. M.; R01AG034454 to A. S.-M. and M. K.); the Academy of Finland (grants 117604, 124271, 124322, and 129262 to M. K. and J. V.); the Finnish Work Environment Foundation to M. K.; a EURYI award from the European Science Foundation to A. S.-M; and an Agence Nationale de la Sante (ANR) grant to M. M. The GAZEL cohort was funded by EDF-GDF and INSER and received grants from the Association de la Recherche sur le Cancer, the Fondation de France, and the French Ministry of Health-IRESP (TGIR Cohortes).

The authors thank EDF-GDF, especially the Service des Etudes Médicales and the Service Général de Médecine de Contrôle and the “Caisse centrale d’action sociale du personnel des industries électrique et gazière.” They also acknowledge the GAZEL cohort study team responsible for data management.

Conflict of interest: none declared.

REFERENCES

- Kessler RC, Angermeyer M, Anthony JC, et al. Lifetime prevalence and age-of-onset distributions of mental disorders in the World Health Organization’s World Mental Health Survey Initiative. *World Psychiatry*. 2007;6(3):168–176.
- Druss BG, Hwang I, Petukhova M, et al. Impairment in role functioning in mental and chronic medical disorders in the United States: results from the National Comorbidity Survey Replication. *Mol Psychiatry*. 2009;14(7):728–737.
- Wang PS, Beck AL, Berglund P, et al. Effects of major depression on moment-in-time work performance. *Am J Psychiatry*. 2004;161(10):1885–1891.
- Harris EC, Barraclough B. Excess mortality of mental disorder. *Br J Psychiatry*. 1998;173:11–53.
- Mykletun A, Bjerkeset O, Dewey M, et al. Anxiety, depression, and cause-specific mortality: the HUNT Study. *Psychosom Med*. 2007;69(4):323–331.
- Hiroeh U, Kapur N, Webb R, et al. Deaths from natural causes in people with mental illness: a cohort study. *J Psychosom Res*. 2008;64(3):275–283.
- Honkonen T, Virtanen M, Ahola K, et al. Employment status, mental disorders and service use in the working age population. *Scand J Work Environ Health*. 2007;33(1):29–36.
- Hämäläinen J, Isometsä E, Sihvo S, et al. Use of health services for major depressive and anxiety disorders in Finland. *Depress Anxiety*. 2008;25(1):27–37.
- Bültmann U, Rugulies R, Lund T, et al. Depressive symptoms and the risk of long-term sickness absence: a prospective study among 4747 employees in Denmark. *Soc Psychiatry Psychiatr Epidemiol*. 2006;41(11):875–880.
- Melchior M, Ferrie JE, Alexanderson K, et al. Using sickness absence records to predict future depression in a working population: prospective findings from the GAZEL cohort. *Am J Public Health*. 2009;99(8):1471–1422.
- Kivimäki M, Ferrie JE, Hagberg 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):915–920.
- Head J, Ferrie JE, Alexanderson K, et al. Diagnosis-specific sickness absence as a predictor of mortality: the Whitehall II Prospective Cohort Study. *BMJ*. 2008;337:a1469. (doi: 10.1136/bmj.a1469).
- Ferrie JE, Vahtera J, Kivimäki M, et al. Diagnosis-specific sickness absence and all-cause mortality in the GAZEL Study. *J Epidemiol Community Health*. 2009;63(1):50–55.
- Goldberg M, Leclerc A, Bonenfant S, et al. Cohort profile: the GAZEL Cohort Study. *Int J Epidemiol*. 2007;36(1):32–39.
- Marmot M, Feeney A, Shipley M, et al. Sickness absence as a measure of health status and functioning: from the UK Whitehall II Study. *J Epidemiol Community Health*. 1995;49(2):124–130.
- Kivimäki M, Head J, Ferrie JE, et al. Sickness absence as a global measure of health: evidence from mortality in the Whitehall II Prospective Cohort Study. *BMJ*. 2003;327(7411):364. (doi:10.1136/bmj.327.7411.364).
- World Health Organization. *International Classification of Diseases. Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death*. Ninth Revision. Geneva, Switzerland: World Health Organization; 1977.
- World Health Organization. *International Statistical Classification of Diseases and Related Health Problems*. Tenth Revision. Geneva, Switzerland: World Health Organization; 1993.
- Davey Smith G, Shipley M, Leon DA. Height and mortality from cancer among men: prospective observational study. *BMJ*. 1998;317(7169):1351–1352.
- Saurel-Cubizolles MJ, Chastang JF, Menvielle G, et al. Social inequalities in mortality by cause among men and women in France. *J Epidemiol Community Health*. 2009;63(3):197–202.
- Alexanderson K, Norlund A. Sickness absence—causes, consequences, and physicians’ sickness certification practice. A systematic literature review by the Swedish Council on Technology Assessment in Health Care. *Scand J Public Health*. 2004;32(suppl 63):256–258.
- Goldberg M, Chastang JF, Leclerc A, et al. Socioeconomic, demographic, occupational, and health factors associated with participation in a long-term epidemiologic survey: a prospective study of the French GAZEL cohort and its target population. *Am J Epidemiol*. 2001;154(4):373–384.
- Goldberg M, Chastang JF, Zins M, et al. Health problems were the strongest predictors of attrition during follow-up of the GAZEL cohort. *J Clin Epidemiol*. 2006;59(11):1213–1221.
- Stansfeld S, Feeney A, Head J, et al. Sickness absence for psychiatric illness: the Whitehall II Study. *Soc Sci Med*. 1995;40(2):189–197.
- Henderson M, Glozier N, Holland Elliott K. Long term sickness absence. *BMJ*. 2005;330(7495):802–803.
- 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):321–326.
- Kivimäki M, Head J, Ferrie JE, et al. Sickness absence as a prognostic marker for common chronic conditions: analysis of mortality in the GAZEL Study. *Occup Environ Med*. 2008;65(12):820–826.

28. Gjesdal S, Ringdal PR, Haug K, et al. Mortality after long-term sickness absence: prospective cohort study. *Eur J Public Health*. 2008;18(5):517–521.
29. Lund T, Kivimäki M, Christensen KB, et al. Socio-economic differences in the association between sickness absence and mortality: the prospective DREAM Study of Danish private sector employees. *Occup Environ Med*. 2009;66(3):150–153.
30. Gjesdal S, Haug K, Ringdal P, et al. Sickness absence with musculoskeletal or mental diagnoses, transition into disability pension and all-cause mortality: a 9-year prospective cohort study. *Scand J Public Health*. 2009;37(4):387–394.
31. Joukamaa M, Heliövaara M, Knekt P, et al. Mental disorders and cause-specific mortality. *Br J Psychiatry*. 2001;179:498–502.
32. Patten SB, Williams JV, Lavorato DH, et al. Major depression as a risk factor for high blood pressure: epidemiologic evidence from a National Longitudinal Study. *Psychosom Med*. 2009;71(3):273–279.
33. Whang W, Kubzansky LD, Kawachi I, et al. Depression and risk of sudden cardiac death and coronary heart disease in women: results from the Nurses' Health Study. *J Am Coll Cardiol*. 2009;53(11):950–958.
34. Hemingway H, Marmot M. Evidence based cardiology: psychosocial factors in the aetiology and prognosis of coronary heart disease. Systematic review of prospective cohort studies. *BMJ*. 1999;318(7196):1460–1467.
35. Rosengren A, Hawken S, Ounpuu S, et al. Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13648 controls from 52 countries (the INTERHEART study): case-control study. *Lancet*. 2004;364(9438):953–962.
36. Carney RM, Freedland KE, Jaffe AS. Depression as a risk factor for coronary heart disease mortality. *Arch Gen Psychiatry*. 2001;58(3):229–230.
37. van Gool CH, Kempen GI, Penninx BW, et al. Relationship between changes in depressive symptoms and unhealthy lifestyles in late middle aged and older persons: results from the Longitudinal Aging Study Amsterdam. *Age Ageing*. 2003;32(1):81–87.
38. Goldston K, Baillie AJ. Depression and coronary heart disease: a review of the epidemiological evidence, explanatory mechanisms and management approaches. *Clin Psychol Rev*. 2008;28(2):288–306.
39. Kamphuis MH, Geerlings MI, Giampaoli S, et al. The association of depression with cardiovascular mortality is partly explained by health status. The FINE Study. *J Affect Disord*. 2009;114(1-3):184–192.
40. Spiegel D, Giese-Davis J. Depression and cancer: mechanisms and disease progression. *Biol Psychiatry*. 2003;54(3):269–282.
41. Oerlemans ME, van den Akker M, Schuurman AG, et al. A meta-analysis on depression and subsequent cancer risk. *Clin Pract Epidemiol Ment Health*. 2007;3:29. (doi:10.1186/1745-0179-3-29).
42. Hamer M, Chida Y, Molloy GJ. Psychological distress and cancer mortality. *J Psychosom Res*. 2009;66(3):255–258.