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Which work-related characteristics are most strongly associated with common mental disorders? : A cross-sectional study

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ABSTRACT

OBJECTIVES: Studies exploring work-related risk factors of common mental disorders (CMD) such as major depressive disorder (MDD), generalized anxiety disorder (GAD) or alcohol abuse have generally focused on a limit set of work characteristics. We study, for the first time in a primary care setting, simultaneously multiple workplace risk factors of CMD.

METHOD: We use data from a representative study of working individuals recruited among 2,027 patients of 121 representative general practitioners (GP) in the Nord - Pas-de-Calais region in France (April-August 2014). CMD were assessed using the MINI (Mini International Neuropsychiatric Interview). Six emergent worked-related factors were explored (work intensity, emotional demands, autonomy, social relationships at work, conflict of values, and insecurity of work). Several covariates were considered (patient's, GP's and contextual characteristics). To study the association between workplace risk factors and CMD (MDD; GAD; alcohol abuse) multilevel logistic or Poisson regression models adjusted for covariates were performed.

RESULTS: Among study participants, 389 (19.1%) had current MDD, 522 (25.8%) current GAD and 196 (9.7%) current alcohol abuse. In multivariable analyses adjusted for covariates, MDD/GAD was significantly associated with work intensity (RR=1.16 [1.06 - 1.27]), emotional demands (RR=1.24 [1.13 - 1.35]) and social relations at work (RR=0.78 [0.70 – 0.87]); alcohol abuse was associated with social relations at work (OR=1.31 [1.04 - 1.65]) and autonomy (OR=0.79 [0.64 – 0.98]).

CONCLUSIONS: Several workplace factors are associated with CMD among working individuals seen by a GP. These findings confirm the role of organizational characteristics of work as a correlate of psychological difficulties above and beyond other sources of risk.

Key terms: mental health; primary care; workplace factors

STRENGTHS AND LIMITATIONS OF THE STUDY

- Cross-sectional study design
- Study of occupational factors related to common mental disorders among working adults in primary care with a standardized diagnostic tool in a large sample
- The study was conducted in the Nord – Pas-de-Calais region in France, one of the poorest in France thus, this could lead to a high level of psychological disorders
- Selective participation of general practitioners (GP) that may have caused a larger selection of patient of patient with psychological disorders. However GPs were selected to be representative of the region GPs and a random procedure to define patients included in the study limits this bias

1 INTRODUCTION

Individuals who are part of the labour force are generally in better health,[1] however work can also have negative effects on somatic and psychosocial health. Work-related diseases have been described and among them, common mental disorders (CMD) such as anxiety, depression and alcohol abuse are the most frequent after musculoskeletal disorders.[2] Work-related CMD are responsible for most of sickness absence and long-term work incapacity.[3] The association between work and CMD is bidirectional: work is a risk factor of poor mental health[4] but the presence of CMD can also influence job performance and well-being.[5 6] Several others risk factors of CMD are already known, even if associations vary from the different disorders. Sociodemographic risk factors include being divorced or widowed, having a low educational level, older age, sex.[7-9] Genetic factors[10] and personal or family history of chronic disease or psychiatric disease are also well-known.[11] Environmental factors (social and material deprivation…) were described and show that individuals with low socio economic status had higher risk of depression.[7 8]

Three main theoretical models have been proposed to explain relations between work characteristics and health. First, Karasek[12] proposed that keys to health are psychological demands, decision latitude and social support. Second, Siegrist[13] proposed that the subjectively ascertained effort-reward balance is what matters most. These two models are the gold standard to study psychosocial risk at work and have a good predictive value but they lack some dimensions to well describe the psychosocial environment at work at the individual level. A third model addressing the role of organizational justice developed by Elovainio allowed interpersonal comparison.[14] Several studies evaluate the impact of work using these theoretical models.[4 15 16] In synthesis, the risk of mental disorders is greater when there is high job demands, low job control, high effort-reward imbalance or low organizational justice. As work organization is evolving, others psychosocial factors described as “emergent factors” appear in the recent studies[17-20]: Workers experiencing high job insecurity or role conflict seem also to have a higher levels of CMD.[17 18] Few studies uses validated diagnostic interviews and many studies investigated separately the diagnosis of MDD (most explored), of GAD and alcohol abuse (less explored).[4 21 22] We aimed to assess the

association between GAD, MDD and alcohol abuse in a primary care setting, using validated diagnostic interviews and combining classical and emergent psychosocial work factors simultaneously that have not often been studied in literature even less in a population of individuals consulting their general practitioner (GP).

We conducted our research in a primary care setting. Indeed, persons with CMD are frequently treated by GP either initially or throughout treatment.[23 24] In primary care, the prevalence levels of CMD are therefore high, ranging from 3%[18] to 25% for anxiety disorders,[9 23-26] 6%[9] to 25% for depression[7 23-26] and 2%[24] to 11% for alcohol abuse.[23 24] This makes it important to elucidate work related factors of mental health difficulties in this particular population, considering also several covariates, at the patient's level, at the GP's level and contextual characteristics.

2 METHODS

2.1 Design and Study population

Heracles is a cross-sectional study conducted between April and August 2014 among working individuals consulting a primary care physician in the Nord - Pas-de-Calais region in the North of France. The number of subjects needed and the set-up of the study have previously been described[27]. Briefly, we aimed to include 2 000 patients via their GP. Participating GP's were asked to include randomly a maximum of 24 patients who were actively employed and aged 18 to 65 years regardless of the reason of their appointment.

This study was conducted by the Sentinelles network,[28] part of the INSERM-Paris Sorbonne University research unit UMR-S 1136. This research group has a standing authorization from the French independent administrative authority protecting privacy and personal data (CNIL), n°471 393 to conduct research among GPs and their patients.

2.2 Data collection

After their regular appointment, GPs interviewed their patients for the purposes of the study. Study questionnaires included information on:

2.2.1 Measurement of common mental disorders

CMDs were measured using a standardised diagnostic interview: the Mini International Neuropsychiatric Interview (MINI). The MINI is a structured clinical interview that enables the diagnosis of psychiatric disorders based on the Diagnosis and Statistical Manual of Mental Disorders, fourth edition (DSM-IV).[29]

In this study, three different diagnoses were ascertained: Major Depressive Disorder (MDD) (during the preceding 2 weeks), Generalised Anxiety Disorder (GAD) (during the preceding 6 months), and alcohol abuse (during the preceding 12 months).

2.2.2 Work's factors

We used a national French questionnaire proposed by experts in the field based on the international scientific literature and after auditioning Robert Karasek and Johannes Siegrist.[19] It combines questions measuring demand - control – social support developed in Karasek's model[12] (2 questions about decision latitude, 4 questions about psychological demands and 2 questions about social support) ; questions measuring effort/reward balance in Siegrist's model[13] (3 questions about reword and one question about overinvestment), and questions about organizational justice from Moorman's questionnaire,[30] questions from the Copenhagen Psychosocial Questionnaire[31] and from the General Nordic Questionnaire for Psychological and Social Factors at Work[32] or from WOrking Conditions and Control Questionnaire (WOCCQ)[33]. Overall, twenty items explore six different areas (Appendix 1): 1) five for the first area related to work intensity and duration (contradictory orders, excessive amounts of work, too much to think about at work, difficulties in balancing work and family life, time needed for work), 2) six items for the second area concerning emotional demands (contacts with customers/beneficiaries, contact with people in distress, conflicts with customers/beneficiaries, the need to hide emotions, fear, exposure to aggressions), 3) two items for the third area concerning autonomy (limited possibility of decision, full and well employment of skills), 4) three items for the fourth area relating quality of social work relations (full-recognition of the work, support from colleagues, support from superior), 5) two items for the fifth area concerning ethical conflicts (possibility to make a work of quality, doing disapproved things) 6) and two items in the last area about insecurity of work (ability to work until retirement, fear of losing job). For four of these items (public contact at work, contact with people in distress, contradictory order, ability to work until retirement) the response was "yes" or "no" and for the other factors the response were "always"/"often"/"sometimes"/"never".

2.2.3 Covariates

Patient's characteristics

We considered already know risk-factors of CMD[7].

- Past somatic or psychiatric problems;

- Sociodemographic (age, gender, family status, family income, level of education);
- Occupational grade[34], they were classified in three groups: blue (farmer/manual worker), pink (technician/associate professional/clerk/service worker) and white collars (manager/professional);[35]
- Company size;
- Job instability: a recombined variable of type of contract

Primary care characteristics[36]

- Reason of medical appointment (somatic, psychological, chronic disease management);
- Sociodemographic (age, gender);
- Practice characteristics (size of practice; easiness with psychological distress issues; opportunity to collaborate with mental health specialists).

Contextual characteristics (by proximity area)

Contextual characteristics have been shown to be associated with CMD in primary care[7 8]

- Psychiatrists, psychologist and GPs density;
- Social deprivation (loneliness, single parenthood, widowhood/divorce) and material deprivation (unemployment, income, level of not graduated)[37 38].

2.3 Statistical Analyses

Socio demographic characteristics of all patients were described and associations between these covariates with GAD, MDD and alcohol abuse were studied using the Chi-square test. Covariates associated with the outcomes with $p<0.2$ were included in the multivariate analysis.

A value was attributed to each answer of the twenty questions regarding occupational factors. Those factors were regrouped according to the 6 dimensions defined in the Gollac report and in order to be able to compare each dimension a Z-score was calculated for each dimension.[19] In bivariate analysis the dimensions were classified high if the score was above the third quartile and low if not, in multivariable models they were used as continuous variable. To study the association between

occupational factors and alcohol we performed multilevel logistic regression models with patient as level one and geographical area as level two. For GAD/MDD we used multilevel Poisson regression models because, given the high prevalence of these problems, logistic regression overestimates relative risks. GAD/MDD or alcohol abuse were the dependent variables and the six occupational factors were the exposition variables. The models were adjusted for each exposition variable and for other covariates that were associated with GAD/MDD or alcohol abuse in a multivariable logistic/Poisson regression model excluding occupational factors. Age, sex and occupational grade were included directly in the adjustment variable.

All analyses were performed using GNU R software version 3.1.1. (lme4 package).

3 RESULTS

3.1 Participation and description of the population

Of the 1 000 GPs contacted by mail, 185 accepted to participate (response rate= 18.5%) and 121 completed the study (Figure 1). Participating GPs were more likely to be male (sex ratio=1.82), and to be 50 years or older; they were disseminated throughout the Nord - Pas-de-Calais region (Table 1). Participating GPs were representative of the other GPs in the Nord - Pas-de-Calais region in term of geographical localisation, age and practice and years.

Participating GPs recruited 2 027 patients among which 389 (19.1%) had MDD, 522 (25.8%) GAD and 196 (9.7%) alcohol abuse. Patients were mostly female (53.6%) aged 42.3 years (sd 10.6) on average, mainly living with a partner (76.2%). Patients were pink collar in 60.1% of cases (clerk/service workers and technician/associate professional), 61.3% had graduated from high school and 30.2% had been unemployed in the past. Among participants, 21.0% came to see their GP for psychological reasons (Table 1). Characteristics of patient with MDD, GAD or alcohol abuse are presented in table 2.

The study response rate was 80%: 41 GPs filled a non-respondent form for 495 patients who refused to participate. Non-respondents did not differ from participants in term of age (p= 0.47) and sex (p=0.23). Comparing with the data of the National Health Insurance for working age patient consulting a GP, participants were older (p<0.01) and were similar for sex distribution (p=0.08).

Table 1: Description of the study population, Héraclès study, France, 2014

	N	%
Work Characteristics		
Work intensity		
High	437	21.6
Low	1588	78.3
Emotional demands		
High	476	23.5
Low	1549	76.4
Autonomy		
High	598	29.5
Low	1427	70.4
Conflict of values		
High	685	33.8
Low	1340	66.1
Social relationships at work		
High	688	33.9
Low	1337	66.0
Insecurity		
High	565	27.9
Low	1460	72.0
Covariates		
Patient Characteristics		
Age group		
[18-35]	597	29.5
[36-50]	872	43.1
[51-65]	552	27.3
Occupational grade		
Blue collar	273	13.9
Pink collar	1185	60.1
White collar	513	26.0
Educational level		
< High school degree	780	38.7
≥ High school degree	1238	61.3
Family status		
Lives alone	481	23.8
Lives with a partner or parents	1543	76.2
Household income (in €)		
[0-3.000]	491	30.6
3.000 +	1112	69.4
Number of worker in the company		
1 to 5	361	18.4
6 to 25	490	25.0
26 to 250	420	21.5
250 +	687	35.1
Past psychiatric problems		
Yes	189	9.8
No	1735	90.2
Past somatic problems		
Yes	559	28.9
No	1373	71.1

Table 1: *(continued)*

	N	%
Purpose of consultation with GP		
Somatic		
Yes	1331	65.7
No	696	34.3
Psychological		
Yes	425	21.0
No	1602	79.0
Chronic disease management		
Yes	313	15.4
No	1714	84.6
Past unemployment		
Yes	613	30.2
No	1414	69.8
Job instability		
Yes	522	33.0
No	1061	67.0
GPs characteristics		
GP's gender		
Male	1364	67.3
Female	663	32.7
GP's age		
[18-39]	194	9.6
[40-49]	626	30.9
[50-59]	832	41.0
60 +	375	18.5
Size of practice population		
0-500	211	11.2
5000 - 1000	993	52.5
1000- 1500	433	22.9
1500+	253	13.4
Easiness with Mental health problems		
High	1600	82.6
Low	338	17.4
High opportunity to work with mental health specialists		
High	1036	52.4
Low	941	47.6
Contextual characteristics		
Social deprivation		
High	552	27.2
Low	1475	72.8
Material deprivation		
High	850	41.9
Low	1177	58.1
Density of psychiatrist		
High	1569	77.4
Low	458	22.6
Density of psychologist		
High	1554	76.7
Low	473	23.3
Density of GP		
High	1525	75.2
Low	502	24.8

3.2 MDD, GAD and alcohol abuse and related work factors

Bivariate analysis

In bivariate analyses, sex was significantly associated with the two outcomes with higher disorders within women for GAD and MDD, for alcohol abuse where men were more affected. Family status, the number of workers in the company, past psychiatric problems, consultation for psychiatric, somatic or chronic diseases and job insecurity were also significantly associated with the two outcomes. Occupational grade, education level and past unemployment were significantly associated ($p<0.01$) with only alcohol abuse with higher rate for blue collars, patients who experienced unemployment in the past and individuals with an education level lower than a high school degree. Age and household income were only associated with MDD/GAD.

Regarding GP characteristics, GPs gender and opportunity to work with mental health specialist was associated with the two outcomes. Size of practice population was associated only with MDD/GAD.

Most of the contextual variables studied were not associated with our study outcomes, except for material deprivation, density of psychiatrists and psychologists which were significantly associated with MDD/GAD. To the contrary, work characteristics were almost all significantly associated with the two outcomes except insecurity and autonomy which were not associated with alcohol abuse (Table 2).

Table 2: Association between common mental disorders (major depressive disorders (MDD), generalised anxiety disorders (GAD) and Alcohol abuse) and covariates, Héraclès study, France, 2014 (Chi-square test)

	MDD/GAD (n=648)		Alcohol (n=196)	
	N (%)	p	N (%)	p
Work Characteristics				
Work intensity		**<0.01**		**0.01**
High	232 (52.8)		58 (13.3)	
Low	416 (26.2)		138 (8.7)	
Emotional demands		**<0.01**		**<0.01**
High	262 (54.9)		73 (15.3)	
Low	386 (24.9)		123 (7.9)	
Autonomy		**<0.01**		0.48
High	158 (26.4)		53 (8.9)	
Low	490 (34.3)		143 (10.0)	
Conflict of values		**<0.01**		**<0.01**
High	335 (48.8)		90 (13.1)	
Low	313 (23.3)		106 (7.9)	
Social relationships at work		**<0.01**		**0.03**
High	103 (15.0)		52 (7.6)	
Low	545 (40.7)		144 (10.8)	
Insecurity		**<0.01**		0.14
High	242 (42.8)		64 (11.3)	
Low	406 (27.8)		132 (9.0)	
Covariates				
Patient Characteristics				
Age group		**0.03**		0.24
[18-35]	172 (28.8)		48 (8.0)	
[36-50]	306 (35.1)		87 (10.0)	
[51-65]	169 (30.6)		60 (10.9)	
Sex		**<0.01**		**<0.01**
H	266 (28.3)		140 (14.9)	
F	382 (35.2)		56 (5.2)	
Occupational grade		0.32		**<0.01**
Blue collar	79 (28.9)		53 (19.4)	
Pink collar	386 (32.6)		86 (7.3)	
White collar	152 (29.6)		50 (9.7)	
Educational level		0.13		**<0.01**
< High school degree	266 (34.1)		98 (12.6)	
≥ High school degree	381 (30.8)		97 (7.8)	
Family status		**0.01**		**<0.01**
Lives alone	471 (30.5)		63 (13.1)	
Lives with a partner or parents	177 (36.8)		133 (8.6)	
Household income (in €)		**0.03**		0.30
[0-3.000]	184 (37.5)		53 (10.8)	
3.000 +	353 (31.7)		100 (9.0)	
Number of worker in the company		**0.03**		**<0.01**
1 to 5	108 (29.9)		51 (14.1)	
6 to 25	183 (37.3)		53 (10.8)	
26 to 250	138 (32.9)		43 (10.2)	
250 +	203 (29.5)		45 (6.6)	
Past psychiatric problems		**<0.01**		**<0.01**
Yes	108 (57.1)		30 (15.9)	
No	516 (29.8)		150 (8.6)	
Past somatic problems		0.82		0.84
Yes	185 (33.1)		53 (9.5)	
No	445 (32.4)		136 (9.9)	

p: Chi-square test

Table 2: *(continued)*

	MDD and GAD (n=648)		Alcohol (n=196)	
	N (%)	p	N (%)	p
Purpose of consultation with GP				
Somatic		**<0.01**		**0.04**
Yes	335 (25.2)		115 (8.6)	
No	313 (45.0)		81 (11.6)	
Psychological		**<0.01**		**<0.01**
Yes	312 (73.4)		61 (14.4)	
No	336 (21.0)		135 (8.4)	
Chronic disease management		**<0.01**		**<0.01**
Yes	75 (24.0)		46 (14.7)	
No	573 (33.4)		150 (8.8)	
Past unemployment		0.57		**<0.01**
Yes	202 (33.0)		80 (13.1)	
No	446 (31.5)		116 (8.2)	
Job instability		**<0.01**		**<0.01**
Yes	229 (43.9)		70 (13.4)	
No	400 (27.5)		118 (11.1)	
GPs Characteristics				
GP's gender		**<0.01**		**<0.01**
Male	375 (27.5)		152 (11.1)	
Female	273 (41.2)		44 (6.6)	
GP's age		0.13		0.14
[18-39]	72 (37.1)		18 (9.3)	
[40-49]	190 (30.4)		49 (7.8)	
[50-59]	254 (30.5)		95 (11.4)	
60 +	132 (35.2)		34 (9.1)	
Size of practice population		**<0.01**		0.06
0-500	79 (37.4)		18 (8.5)	
5000 - 1000	295 (29.7)		82 (8.3)	
1000- 1500	136 (31.4)		47 (10.9)	
1500+	104 (41.1)		34 (13.4)	
Easiness with Mental health problems		0.21		0.48
High	500 (31.3)		155 (9.7)	
Low	118 (34.9)		28 (8.3)	
High opportunity to work with mental health specialists		**<0.01**		**0.05**
High	345 (36.7)		103 (9.9)	
Low	286 (27.6)		86 (9.1)	
Contextual characteristics				
Social deprivation		0.32		0.87
High	167 (30.2)		52 (9.4)	
Low	481 (32.6)		144 (9.8)	
Material deprivation		**<0.01**		0.74
High	306 (36.0)		85 (10.0)	
Low	342 (29.1)		111 (9.4)	
Density of psychiatrist		**0.02**		0.97
High	522 (33.3)		45 (9.8)	
Low	126 (27.5)		151 (9.6)	
Density of psychologist		**0.05**		0.10
High	515 (33.1)		36 (7.6)	
Low	133 (28.1)		160 (10.3)	
Density of GP		0.06		0.88
High	505 (33.1)		50 (10.0)	
Low	143 (28.4)		146 (9.6)	

p: Chi-square test

Multivariable analysis

All occupational factors were associated with our two study outcomes in unadjusted analysis. In adjusted analyses, patients reporting high levels of work intensity (RR=1.16 [1.06 - 1.27]; p<0.01) and emotional demands (RR=1.24 [1.13 - 1.35]; p<0.01) had a higher risk of MDD/GAD whereas patient with high social relations at work had lower risk to have MDD/GAD (RR=0.78 [0.70 – 0.87]; p<0.01).

Regarding alcohol abuse, social relations at work were associated with higher risk (OR=1.31 [1.04 - 1.65]; p=0.02) and higher autonomy was protective (OR=0.79 [0.64 – 0.98]; p=0.04) (Table 3).

Table 3: major depressive disorders **(**MDD), generalized anxiety disorders (GAD) and alcohol abuse work-related factors, Héraclès study, France, 2014. Multilevel regression models

	MDD/GAD (n=1782)						Alcohol (n=1776)					
	Unadjusted			Adjusted			Unadjusted			Adjusted		
	RR	CI 95%	P	RR[1]	CI 95%	P	OR	CI 95%	P	OR[2]	CI 95%	P
Work intensity	**1.46**	**[1.35 - 1.57]**	**<0.01**	**1.16**	**[1.06 - 1.27]**	**<0.01**	**1.35**	**[1.17 - 1.57]**	**<0.01**	1.20	[0.98 - 1.46]	0.08
Emotional demands	**1.53**	**[1.43 - 1.64]**	**<0.01**	**1.24**	**[1.13 - 1.35]**	**<0.01**	**1.46**	**[1.27 - 1.68]**	**<0.01**	1.21	[0.98 - 1.48]	0.06
Autonomy	**0.68**	**[0.63 - 0.73]**	**<0.01**	0.94	[0.85 - 1.04]	0.26	**0.70**	**[0.60 - 0.80]**	**<0.01**	**0.79**	**[0.64 - 0.98]**	**0.04**
Conflict of values	**1.45**	**[1.35 - 1.56]**	**<0.01**	1.06	[0.96 - 1.17]	0.26	**1.35**	**[1.17 - 1.55]**	**<0.01**	1.21	[0.97 - 1.50]	0.09
Social relationships at work	**0.61**	**[0.56 - 0.66]**	**<0.01**	**0.78**	**[0.70 - 0.87]**	**<0.01**	**0.81**	**[0.70 - 0.95]**	**0.01**	**1.31**	**[1.04 - 1.65]**	**0.02**
Insecurity	**1.13**	**[1.05 - 1.22]**	**<0.01**	1.03	[0.95 - 1.11]	0.49	**1.14**	**[1.00 - 1.30]**	**0.05**	0.94	[0.80 - 1.12]	0.50

RR : relative risk
OR: odd ratio
[1] Adjusted on : each occupational factors, age, sex, occupational grade, past psychiatric problems, alcohol abuse, material deprivation and GP's gender
[2] Adjusted on : each occupational factors, age, sex, occupational grade, family status, number of person in the company, past psychiatric problems, job instability, education level, past unemployment, GAD and MDD

4 DISCUSSION

4.1 Main results

In our study conducted among a large sample of persons consulting a GP, we found that several work characteristics are associated with mental health. Unfavourable social relations at work are associated with a higher risk of MDD/GAD, but a lower risk of alcohol abuse. High work intensity and high emotional demands at work are associated with a higher risk of MDD/GAD. Finally, low autonomy at work is significantly associated with a higher risk of alcohol abuse.

4.2 Comparison with literature

We confirm, for the first time in primary care, the association between common mental disorders and work social support. This is consistent with data from a cross sectional study conducted in Japan (using the K10 questionnaire to assess depression): higher risk of depressive symptoms for workers with low social support at work (OR=3.8)[39]. It is also coherent with data from a meta-analysis of 17 other studies investigating depressive disorders.[40] Low social support at work is also associated with anxiety disorders as already observed in the population based study of Wang: employees with high stress in social support from superior or co-workers had higher risk of having anxiety disorders for both gender.[41] However, the causal direction of this association cannot be determined due to the cross sectional design of our study. It is possible that low social support increases the risk of having depression or anxiety as it has been shown in different longitudinal studies.[42] Moreover, it is well known that social relations and support (outside or inside work) affect psychological health,[43] but it is also possible that individual with no depression or anxiety disorders have better social support.[43] Finally, the association between GAD/MDD and social support could also be related to negative views of social support when depressed or anxious.[44] For alcohol abuse an inverse association is observed: higher risk associated with high social relationship at work and this result is consistent with results of

a cross sectional study conducted among Canadian workers.[21] It raises question about festive alcohol consumption with colleagues in or outside the company.[45]

Work intensity, or high psychological demand in terms of high working time and intensity was associated with depressive symptoms in the meta-analysis of Theorell (10 studies).[40] The meta-analysis of longitudinal studies of Netterstrom highlights the adverse effect of high psychological demand on the occurrence of depressive disorders.[42] However, this association could also ensue that persons with depressive disorders have distorted views of psychological demands.[44]

High emotional demands at work have already been observed for depressive disorders among women in a population-based nested case-control study of 14,166 psychiatric patients in Denmark (IRR=1.39)[22] or for GAD in the French prospective study SIP (using the same diagnostic tool MINI) (RR=1.66 among workers with high emotional demand[18]). The designs of those two studies argue for the negative effect of high emotional demand on depression and anxiety, but in our cross sectional study the causal attribution is not possible thus it is also possible that people with depression and/or anxiety have a different view towards those demands.[44]

Autonomy appears related to alcohol abuse, as reported in an English prospective study: low decision latitude, which is a part of the autonomy axis in our study, is associated to higher risk of alcohol dependence within women.[46]

We do not confirm the association found earlier between CMD and high job insecurity or conflict of value.[17 18 20]

4.3 Strengths and limitations of the study

Several limitations of our study should be acknowledged.

First, our study was conducted in the Nord - Pas-de-Calais region, i.e. one of the poorest in France with a total 4,000,000 inhabitants. This highly industrialized region during the first half of the 20th century, suffered since 1950 from industrial decline, mines, textile and steel industries gradually closing. Despite the growth of services and some specialized industries (car, rail and glass), levels of education, unemployment (15%), and poverty and health indicators (e.g. life expectancy) are unfavourable. The Nord - Pas-de-Calais region have a low density of GPs (11% less than in France)

and other medical specialities (24% less).[47] Moreover, the study was conducted after the 2008 recession, which has been associated with an increase in the prevalence of common mental health disorders worldwide.[48 49] This could lead to a high level of psychiatric disorders. The prevalence of MDD, GAD and alcohol abuse within patient consulting a GP is respectively 19.1%, 25.8% and 9.7%. This is consistent in the superior limits with studies in primary care ranging prevalence from 6% to 25% for depression, 3% to 25% for anxiety and 2% to 11% for alcohol abuse.[7 9 23-26] Results should be replicated in others areas.

Second, a possible weakness is the selective participation of GPs. GPs who have participated in the study could be especially interested in common mental disorders. This interest may be related to interest of GP itself, but it could also be related to the GPs patient rate of common mental disorders. Therefore, it may cause a larger selection of patient with psychological disorders. However, participation rate were similar to previous studies[24 50] and GP were selected to be representative of the Nord - Pas-de-Calais GPs in term of geographical localisation and therefore limiting this possible bias. Participating GP had similar age, practice and years of practice than all GP in the region. Patient selection should also be considered. However, a random procedure to define patients included in the study limits this bias. Indeed, GPs were asked to include patient following an inclusion schedule that was provided at the start of the study. This allowed us to include patient in different time slots of the week. Moreover a non-respondent form had to be filled by the GPs but we suppose that the filling rate was low because only 41 GPs filled this form and declare that 495 patient were not included. Characteristics of patients included and those not included did not differ in term of age and sex.

If we were able to take into account many co-variables (individuals, GPs and contextual), we missed for some important individual variables (as social support outside of work, life events...) we would like to control to study CMD and work-related factors.

Despite these limitations, the results of this study are of interest because they study occupational factors related to CMD (MDD/GAD and alcohol abuse) among working adults in primary care with a standardized diagnostic tool (MINI) in a large sample (n=2 027).[29] However we have to be cautious about these results and further studies in other areas have to be done in order to confirm our findings.

4.4 Conclusion

Our study is one of the first studying simultaneously well-known factors related to the job strain and effort-reward imbalance models and new occupational factors described in recent literature and the first conducted among working individuals in primary care. Results point out the importance of social support at work and different occupational factors that are associated with MDD, GAD and alcohol abuse. These results could be a starting point to apprehend these factors with the patient and to communicate with occupational physician.

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CONTRIBUTORS

Study concept and design: MR, NY, MM, AL, TB, LP. Data analysis and collection: MR, LFC, MM, LP. Drafting of the manuscript: MR. Critical revision of the manuscript: NY, MM, AL. All authors have approved the final manuscript.

COMPETING INTERESTS

All authors declare that they do not have any competing interests and declare independence from the funders.

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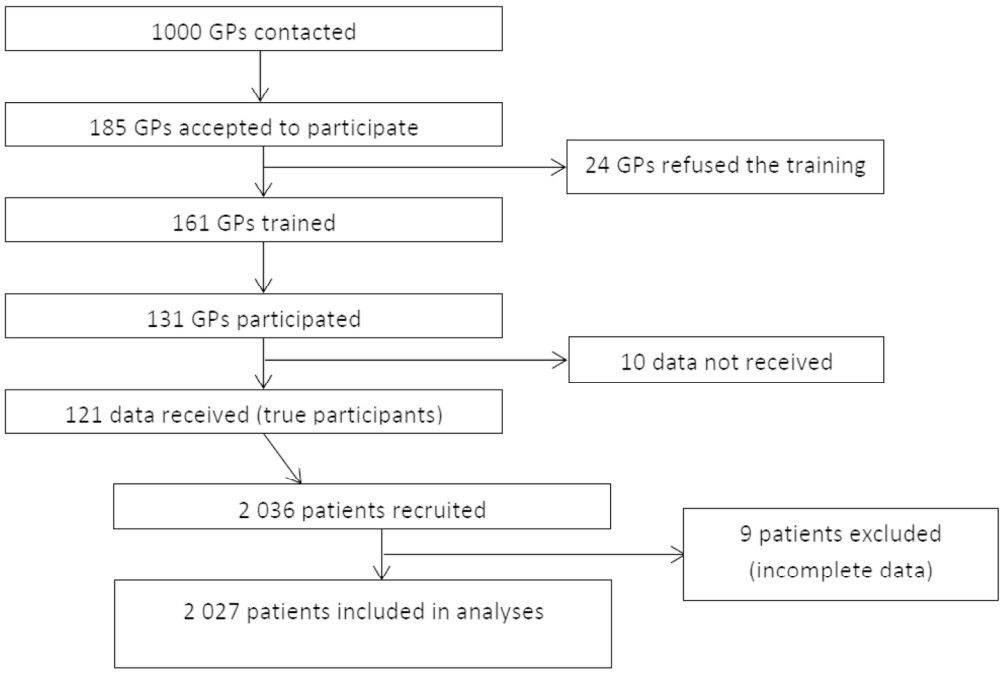
Legends:

Figure 1: Flow chart of participation in the Héraclès study, France, 2014



Flow chart of participation in the Heracles study, France, 2014

154x104mm (300 x 300 DPI)

Appendix 1: Work's factor questionnaire

1) **Work intensity**

- I receive contradictory orders or indication ("Yes"/"No")
- I am asked excessive amounts of work ("Always"/"Often"/"Sometimes"/"Never")
- I have too much to think about at work ("Always"/"Often"/"Sometimes"/"Never")
- I have difficulties in balancing work and family life ("Always"/"Often"/"Sometimes"/"Never")
- I have the time needed to do my work ("Always"/"Often"/"Sometimes"/"Never")

2) **Emotional demands**

- I work in contact with customers/beneficiaries ("Yes"/"No")
- I am in contact with people in distress ("Yes"/"No")
- I have conflicts with customers/beneficiaries ("Always"/"Often"/"Sometimes"/"Never")
- I have to hide my emotions and pretend to be in a good mood ("Always"/"Often"/"Sometimes"/"Never")
- I sometimes experience fear during my work ("Always"/"Often"/"Sometimes"/"Never")
- During my work, I am exposed to physical, verbal, psychological aggressions ("Always"/"Often"/"Sometimes"/"Never")

3) **Autonomy**

- I have very little freedom to decide how I do my job ("Always"/"Often"/"Sometimes"/"Never")
- I can fully employ my skills ("Always"/"Often"/"Sometimes"/"Never")

4) **Conflict of values**

- I have the possibility to make a work of quality ("Always"/"Often"/"Sometimes"/"Never")
- In my work, I have to do disapproved things ("Always"/"Often"/"Sometimes"/"Never")

5) **Social relationships at work**

- My work is fully recognized ("Always"/"Often"/"Sometimes"/"Never")
- I have support from colleagues ("Always"/"Often"/"Sometimes"/"Never")
- I have support from superior ("Always"/"Often"/"Sometimes"/"Never")

6) **Insecurity of work**

- I feel able to do my current job until retirement ("Yes"/"No")
- I work with fear of losing my job ("Always"/"Often"/"Sometimes"/"Never")

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **page 1 and 2**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found - **page 1 and 2**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **page 4 and 5**
Objectives	3	State specific objectives, including any prespecified hypotheses - **page 4 and 5**
Methods		
Study design	4	Present key elements of study design early in the paper - **page 6**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection - **page 6**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants - **page 6**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable – **page 6 to 8**
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 - **page 6 to 8**
Bias	9	Describe any efforts to address potential sources of bias – **page 6**
Study size	10	Explain how the study size was arrived at – **page 6**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why – **page 8 and 9**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **page 8 and 9**
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
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 – **page 10 and figure 1**
		(b) Give reasons for non-participation at each stage – **figure 1**
		(c) Consider use of a flow diagram – **figure 1**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders – **page 10 to 12**
		(b) Indicate number of participants with missing data for each variable of interest
Outcome data	15*	Report numbers of outcome events or summary measures – **page 13**
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 – **page 13 to 17**
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a

		meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives – **page 18**
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 – **page 19 and 20**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence – **page 18 and 19**
Generalisability	21	Discuss the generalisability (external validity) of the study results – **page 20 and 21**
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 – **page 21**

*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 www.strobe-statement.org.

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Which work-related characteristics are most strongly associated with common mental disorders?: A cross-sectional study

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Which work-related characteristics are most strongly associated with common mental disorders? : A cross-sectional study

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ABSTRACT

OBJECTIVES: Studies exploring work-related risk factors of common mental disorders (CMD) such as major depressive disorder (MDD), generalized anxiety disorder (GAD) or alcohol abuse have generally focused on a limited set of work characteristics. We study, for the first time in a primary care setting, simultaneously multiple work-related risk factors of CMD.

METHOD: We use data from a representative study of working individuals recruited among 2,027 patients of 121 representative general practitioners (GP) in the Nord - Pas-de-Calais region in France (April-August 2014). CMD were assessed using the MINI (Mini International Neuropsychiatric Interview). Six emergent worked-related factors were explored (work intensity, emotional demands, autonomy, social relationships at work, conflict of values, and insecurity of work). Several covariates were considered (patient's, GP's and contextual characteristics). To study the association between workplace risk factors and CMD (MDD; GAD; alcohol abuse) multilevel Poisson regression models adjusted for covariates were performed.

RESULTS: Among study participants, 389 (19.1%) had current MDD, 522 (25.8%) current GAD and 196 (9.7%) current alcohol abuse. In multivariable analyses adjusted for covariates, MDD/GAD was significantly associated with work intensity (RR=1.16 [1.06 - 1.27]) (absolute risk = 52.8%), emotional demands (RR=1.24 [1.13 - 1.35]) (absolute risk = 54.9%) and social relations at work (RR=0.78 [0.70 – 0.87]) (absolute risk = 15.0%); alcohol abuse was associated with social relations at work (RR=1.25 [1.01 - 1.53]) (absolute risk = 7.6%) and autonomy (OR=0.82 [0.67 – 0.99]) (absolute risk = 8.9%).

CONCLUSIONS: Several workplace factors are associated with CMD among working individuals seen by a GP. These findings confirm the role of organizational characteristics of work as a correlate of psychological difficulties above and beyond other sources of risk.

Key terms: mental health; primary care; workplace factors

STRENGTHS AND LIMITATIONS OF THE STUDY

- Cross-sectional study design
- Study of occupational factors related to common mental disorders among working adults in primary care with a standardized diagnostic tool in a large sample
- The study was conducted in the Nord – Pas-de-Calais region in France, one of the poorest in France thus, this could lead to a high level of psychological disorders
- Selective participation of general practitioners (GP) may have led to an overrepresentation of patients with psychological disorders. However GPs were selected to be representative of the region's GPs and the use of a random procedure to define patients included in the study limits this bias

1 INTRODUCTION

Individuals who are part of the labour force are generally in better health than the unemployed,[1] however work can also have negative effects on somatic and psychosocial health.[2] A study with trained general practitioners (GP) in occupational medicine found that mental health issues are the most frequent disorders attributed to work, after musculoskeletal disorders.[3] They are responsible for most of sickness absence and long-term work incapacity.[4] In France, data from the national health insurance shows that 20% of sickness absence are caused by mental disorders with an increased proportion for long term sickness absence.[5] Mental disorders encountered among employed are mainly “Common Mental Disorders” (CMD), as defined based on epidemiological data by a systematic review and meta-analysis of this literature, as a combination of disorders across the mood, anxiety and substance use disorder (alcohol) spectrum.[6] The association between work and CMD is bidirectional: work has been shown as a risk factor of poor mental health[7] but the presence of CMD can also influence job performance and well-being.[8 9] Several others risk factors of CMD are already known, even if associations vary for the different disorders. Sociodemographic risk factors include being divorced or widowed, having a low educational level, older age, sex.[10-12] Genetic factors[13] and personal or family history of somatic chronic disease or psychiatric disease are also well described in literature.[14] Environmental factors (e.g. social and material deprivation, etc.) were described and show that low socio-economic status was associated with higher rates of depression.[10 11]

Psychosocial factors related to the work environment are of particular interest because they may be more easily prevented than those which results from life events, which are often unavoidable. Three main theoretical models have been proposed to explain relations between work characteristics and mental health. First, Karasek[15] argued that keys to health are psychological demands, decision latitude and social support. Second, Siegrist[16] proposed that the subjectively ascertained effort-reward balance is what matters most. These two models are the gold standard to study psychosocial risk at work and have a good predictive value but they lack some dimensions to well describe the psychosocial environment at work at the individual level and more precisely dimension

about procedural justice in the company. A third model addressing the role of organizational justice developed by Elovainio included interpersonal comparison, that is to say comparison of the response of the company in the same situation for different employees.[17] Several studies evaluate the impact of work on mental health using these theoretical models.[7 18 19] Overall, the risk of mental disorders is higher when there is high job demands, low job control, high effort-reward imbalance or low organizational justice. As work organization is evolving, other psychosocial factors described as "emergent factors" (e.g. insecurity at work, conflict of values, etc.) appear in the recent studies[20-23]: Workers experiencing high job insecurity or role conflict also seem to have a higher levels of CMD.[20] [21]An important systematic meta-review identified three overlapping categories of work-placed risk factors that may contribute to the development of common mental health problems (considering depression and/or anxiety), combining emergent and classical factors and identified with reasonable levels of evidence: imbalanced job design (high job demands, low job control, low social support in work-place, effort-reward imbalance), occupational uncertainty (low job control, low procedural justice, job insecurity, temporary employment status, low social support in work-place) and lack of value and respect in workplace (effort-reward imbalance, procedural justice, temporary employment status, low social support in work-place).[7] This review did not describe precisely CMD (MDD was most explored, GAD less explored[7 24 25] and alcohol abuse should also be explored among CMD) and as reported by the authors, it was based too frequently upon self-reported questionnaires and not validated diagnostic interviews. Moreover, those factors changes over time with modification of the labour market (increased globalization, competition, new forms of work organization, etc). A French study assessed changes in psychosocial work factors between 2006 and 2011 and showed that some psychosocial work factors deteriorated (decision latitude, social support, reward, role conflict and work life imbalance) between 2006 and 2011. It also found that these changes varied according to age, occupation, sector activity and type of contract.[26] The objective of this study is to assess the association between GAD, MDD and alcohol abuse in a primary care setting, using validated diagnostic interviews and combining most psychosocial work-related risk factors in a population of individuals consulting their general practitioner (GP). Combining emergent and classical factors is important in order to identify which are most strongly related to workers' mental

health, this was outlined in the meta-review by Harvey *et al*.[7] We considered that this population is important to explore as people with CMD are frequently treated by GP either initially or throughout treatment.[27 28] In primary care, the prevalence levels of CMD are high, ranging from 3%[21] to 25% for anxiety disorders,[12 27-30] 6%[12] to 25% for depression[10 27-30] and 2%[28] to 11% for alcohol abuse.[27 28] Two studies conducted in the United Kingdom show that a third of patients seeing a GP for work-related reasons had a mental health issue.[3 31] It constitutes a major clinical issue: GPs often have difficulties managing work-related mental health problems, as they often lack negotiation strategies regarding sick leave, communication skills and cooperation with occupational physicians.[32] GPs encounter every type of workers and not only big industrial settings with occupational services. A better understanding of work related factors of mental health is important in order to help GPs to consider specific actions.

2 METHODS

2.1 Design and Study population

Heracles is a cross-sectional study conducted between April and August 2014 among working individuals consulting a primary care physician in the Nord - Pas-de-Calais region in the North of France. The number of subjects needed and the set-up of the study have previously been described[33]. Briefly, with an estimated prevalence of 20% and to have a precision of 10%, we aimed to include 2,000 patients via their GP. Participating GPs who gave an oral consent to participate, were asked to include randomly a maximum of 24 patients who met the following criteria: being actively employed and aged 18 to 65 years, regardless of the reason of their medical appointment. GPs were selected to be representative of the distribution of GPs in 15 areas of the Nord-Pas-de-Calais region that we studied. GPs had to include the two first patients who met the inclusion criteria in each previously defined time slot. Approximately ¼ of the GPs of the region were contacted to participate, they were selected in a way that was proportional to the distribution of GPs in 15 areas of Nord – Pas-de-Calais region that were studied. GP's had to include the two first patient who met the inclusion criteria in each time slot defined previously with GPs according to their working schedule. Before the appointment the GP gave written information to their patients to inform them about the study and asked them to sign an informed consent.

This study was conducted by the Sentinelles network,[34] part of the INSERM-Paris Sorbonne University research unit UMR-S 1136. This research group has a standing authorization from the French independent administrative authority protecting privacy and personal data (CNIL), n°471 393 to conduct research among GPs and their patients.

2.2 Data collection

Participating GPs received a 15 minute phone training on the use of the questionnaire before the beginning of the study. After their regular appointment, GPs interviewed their patients for the purposes of the study. Study questionnaires included information on:

2.2.1 Measurement of common mental disorders

CMDs were measured using a standardised diagnostic interview: the Mini International Neuropsychiatric Interview (MINI) that was used as a screening tool. The MINI is a structured clinical interview that enables the diagnosis of mental disorders based on the Diagnosis and Statistical Manual of Mental Disorders, fourth edition (DSM-IV).[35]

In this study, three different diagnoses were ascertained: Major Depressive Disorder (MDD) (during the preceding 2 weeks), Generalised Anxiety Disorder (GAD) (during the preceding 6 months), and alcohol abuse (during the preceding 12 months).

Depending on the mental disorders studied, the sensibility of the MINI varied between 83 to 94% (MDD: 94%; GAD: 88%; Alcohol: 83%), the specificity between 72 to 97% (MDD: 79%; GAD: 72%; Alcohol: 97%) and the Kappa concordance coefficient between 0.36 to 0.82 (MDD: 0.73; GAD: 0.36; Alcohol: 0.82). The inter-rater and test-retest reliability measured by Kappa coefficient were good, respectively 0.88 to 1 and 0.76 to 0.93.[36]

2.2.2 Work characteristics

Work characteristics were self-reported by the patient to their GP. We used a national French questionnaire proposed by experts in the field based on the international scientific literature and after auditioning Robert Karasek and Johannes Siegrist.[22] It combines questions measuring demand - control – social support developed in Karasek's model[15] (two questions about decision latitude, four questions about psychological demands and two questions about social support) ; questions measuring effort/reward balance in Siegrist's model[16] (three questions about reward and one question about overinvestment), and questions about organizational justice from Moorman's questionnaire,[37] questions from the Copenhagen Psychosocial Questionnaire[38] and from the

General Nordic Questionnaire for Psychological and Social Factors at Work[39] or from WOrking Conditions and Control Questionnaire (WOCCQ)[40]. Overall, twenty items explore six different areas (Appendix 1): 1) five for the first area related to work intensity and duration (contradictory orders, excessive amounts of work, too much to think about at work, difficulties in balancing work and family life, time needed for work), 2) six items for the second area concerning emotional demands (contacts with customers/beneficiaries, contact with people in distress, conflicts with customers/beneficiaries, the need to hide emotions, fear, exposure to aggressions), 3) two items for the third area concerning autonomy (limited possibility of decision, full and well employment of skills), 4) three items for the fourth area relating quality of social work relations (full-recognition of the work, support from colleagues, support from superior), 5) two items for the fifth area concerning ethical conflicts (possibility to make a work of quality, doing disapproved things) 6) and two items in the last area about insecurity of work (ability to work until retirement, fear of losing job). For four of these items (public contact at work, contact with people in distress, contradictory order, ability to work until retirement) the response was either “yes” or “no” and for the other factors the responses were “always”/”often”/”sometimes”/”never” numbered from 1 to 4. Reliability of the questionnaire was assessed by computing an alpha Cronbach coefficient. This coefficient varied between 0.34 to 0.68. The reliability was lower for ethical conflicts (α=0.34), emotional demands (α=0.44) and higher for work intensity (α=0.48), insecurity of work (α=0.48), autonomy (α=0.65) and social work relations (α=0.68).

2.2.3 Covariates

Patient’s characteristics

We considered already know risk-factors of CMD.[10]

- Past somatic or psychiatric problems;
- Sociodemographic (age, gender, family status, family income, level of education);
- Occupational grade[41], they were classified in three groups: blue (farmer/manual worker), pink (technician/associate professional/clerk/service worker) and white collar workers (manager/professional);[42]

- Company size;
- Job instability: a recombined variable of type of contract

Primary care characteristics[43]

- Reason for medical appointment (somatic, psychological, chronic disease management);
- Sociodemographic (GP's age, GP's gender);
- Practice characteristics (size of practice; comfort with psychological distress issues; opportunity to collaborate with mental health specialists).

Contextual characteristics (by proximity area)

Contextual characteristics have been shown to be associated with CMD in primary care[10 11]

- Psychiatrists, psychologist and GPs density;
- Social deprivation (loneliness, single parenthood, widowhood/divorce) and material deprivation (unemployment, income, level of not graduated);[44 45]
- Geographical area: 15 proximity areas defined by the regional health agency of the Nord – Pas-de-Calais region.

2.3 Statistical Analyses

Some of the covariates were recoded to use fewer categories. For family status, participants living alone or living with parents were grouped into one category. For family income, participants were grouped in two categories: [0-3,000 euros (which corresponds to approximately two times the minimum wage in France) and >=3,000 euros. For educational level, we created two categories: less than a high school degree (no degree, degree below high school) or a degree higher or equal to a high school degree. For age, our continuous variable was studied in three categories based on the distribution 18-35; 36-50; 51-65.

Sociodemographic characteristics of all patients were described and associations between these covariates with GAD, MDD and alcohol abuse were studied using the Chi-square test. Covariates associated with the outcomes with $p<0.2$ were included in the multivariate analysis.

A value was attributed to each answer of the twenty questions regarding occupational factors. Those factors were regrouped according to the 6 dimensions defined in the Gollac report and in order to be able to compare each dimension, a Z-score was calculated for each dimension.[22] A correlation matrix of the different work characteristics was computed and presented in a supplementary file (appendix 2). In bivariate analysis the dimensions were classified as high if the score was above the third quartile and as low if not, in multivariable models they were used as continuous variables. To study the association between occupational factors and alcohol we performed multilevel logistic regression models with patient as level one and geographical area as level two. GAD and MDD were merged into the same variable because of intercorrelation. To study the association between occupational factors and GAD/MDD and alcohol we used multilevel Poisson regression models using a robust error variance procedure (sandwich estimation)[46] with patient as level one and geographical area as level two. Given the high prevalence of these problems, Poisson regression was preferred to logistic regression to avoid overestimating the risk ratios.[47] GAD/MDD or alcohol abuse were the dependent variables and the six occupational factors were the exposition variables. The models were adjusted for each exposition variable and for other covariates that were associated with GAD/MDD or alcohol abuse ($p<0.05$) in a multivariable Poisson regression model excluding occupational factors. Age, sex and occupational grade were included directly in the adjustment variable. Absolute risk within exposed population was computed for each occupational factors.

All analyses were performed using GNU R software version 3.1.1. (lme4 package).[48 49]

3 RESULTS

3.1 Participation and description of the population

Of the 1,000 GPs contacted by mail, 185 accepted to participate (response rate= 18.5%) and 121 completed the study (Figure 1). Participating GPs were more likely to be male (sex ratio=1.82), and to be 50 years or older; they were disseminated throughout the Nord - Pas-de-Calais region (Table 1). Participating GPs were representative of the other GPs in the Nord - Pas-de-Calais region in term of geographical localisation, age, type and years of practice.

Participating GPs recruited 2,027 patients among which 389 (19.1%) had MDD, 522 (25.8%) GAD and 196 (9.7%) alcohol abuse. Patients were mostly female (53.6%) aged 42.3 years (sd 10.6) on average, mainly living with a partner (76.2%). Patients were pink collar workers in 60.1% of cases (clerk/service workers and technician/associate professional), 61.3% had graduated from high school and 30.2% had been unemployed in the past. Among participants, 21.0% came to see their GP for psychological reasons (Table 1). Characteristics of patient with MDD, GAD or alcohol abuse are presented in table 2.

The study response rate was 80%: 41 GPs filled a non-respondent form for 495 patients who refused to participate. Non-respondents did not differ from participants in term of age (p= 0.47) and sex (p=0.23). Comparing with the data of the National Health Insurance for working age patient consulting a GP, participants were older (p<0.01) and were similar for sex distribution (p=0.08).

Table 1: Description of the study population, Héraclès study, France, 2014

	N	%
Work Characteristics		
Work intensity		
High	437	21.6
Low	1,588	78.3
Emotional demands		
High	476	23.5
Low	1,549	76.4
Autonomy		
High	598	29.5
Low	1,427	70.4
Conflict of values		
High	685	33.8
Low	1,340	66.1
Social relationships at work		
High	688	33.9
Low	1,337	66.0
Insecurity		
High	565	27.9
Low	1,460	72.0
Covariates		
Patient Characteristics		
Age group		
[18-35]	597	29.5
[36-50]	872	43.1
[51-65]	552	27.3
Occupational grade		
Blue collar	273	13.9
Pink collar	1,185	60.1
White collar	513	26.0
Educational level		
< High school degree	780	38.7
≥ High school degree	1,238	61.3
Family status		
Lives alone	481	23.8
Lives with a partner or parents	1,543	76.2
Household income (in €)		
[0-3.000]	491	30.6
3.000 +	1,112	69.4
Number of worker in the company		
1 to 10	361	18.4
11 to 50	490	25.0
51 to 250	420	21.5
250 +	687	35.1
Past psychiatric problems		
Yes	189	9.8
No	1,735	90.2
Past somatic problems		
Yes	559	28.9
No	1,373	71.1

Table 1: *(continued)*

	N	%
Purpose of consultation with GP		
Somatic		
Yes	1,331	65.7
No	696	34.3
Psychological		
Yes	425	21.0
No	1,602	79.0
Chronic disease management		
Yes	313	15.4
No	1,714	84.6
Past unemployment		
Yes	613	30.2
No	1,414	69.8
Job instability		
Yes	522	33.0
No	1,061	67.0
GPs characteristics		
GP's gender		
Male	1,364	67.3
Female	663	32.7
GP's age		
[18-39]	194	9.6
[40-49]	626	30.9
[50-59]	832	41.0
60 +	375	18.5
Size of practice population		
0-500	211	11.2
5000 - 1000	993	52.5
1000- 1500	433	22.9
1500+	253	13.4
Comfort with Mental health problems		
High	1,600	82.6
Low	338	17.4
High opportunity to work with mental health specialists		
High	1,036	52.4
Low	941	47.6
Contextual characteristics		
Social deprivation		
High	552	27.2
Low	1,475	72.8
Material deprivation		
High	850	41.9
Low	1,177	58.1
Density of psychiatrist		
High	1,569	77.4
Low	458	22.6
Density of psychologist		
High	1,554	76.7
Low	473	23.3
Density of GP		
High	1,525	75.2
Low	502	24.8
Geographical area		
Métropole Flandre intérieure	1,035	51.1
Hainault - Cambrésis	333	16.4
Artois - Douaisis	337	16.6
Littoral	322	15.9

3.2 MDD, GAD and alcohol abuse and related work factors

Bivariate analysis (Table 2)

In bivariate analyses, sex was significantly associated with the two outcomes: high levels of GAD and MDD in women and high levels of alcohol abuse in men. Family status, the number of workers in the company, past psychiatric problems, consultation for psychiatric, somatic or chronic diseases and job insecurity were also significantly associated with the two outcomes. Occupational grade, education level and past unemployment were significantly associated ($p<0.01$) with only alcohol abuse with higher rates for blue collar workers, patients who experienced unemployment in the past and individuals with an education level lower than a high school degree. Age and household income were only associated with MDD/GAD.

Regarding GP characteristics, GP gender and opportunity to work with mental health specialist was associated with the two outcomes. Size of practice population was associated only with MDD/GAD.

Most of the contextual variables studied were not associated with our study outcomes, except for material deprivation and density of psychiatrists and psychologists which were significantly associated with MDD/GAD. To the contrary, work characteristics were almost all significantly associated with the two outcomes except insecurity and autonomy which were not associated with alcohol abuse (Table 2).

Table 2: Association between common mental disorders (major depressive disorders (MDD), generalised anxiety disorders (GAD) and Alcohol abuse) and covariates, Héraclès study, France, 2014 (Chi-square test)

	MDD and GAD (n=648)		Alcohol (n=196)	
	N (%)	p (χ2-df)	N (%)	p (χ2-df)
Work Characteristics				
Work intensity		<0.01		0.01
High	232 (52.8)	(111.1 - 1)	58 (13.3)	(7.5 - 1)
Low	416 (26.2)		138 (8.7)	
Emotional demands		<0.01		<0.01
High	262 (54.9)	(149.8 - 1)	73 (15.3)	(21.8 - 1)
Low	386 (24.9)		123 (7.9)	
Autonomy		<0.01		0.48
High	158 (26.4)	(11.6 - 1)	53 (8.9)	(0.6 - 1)
Low	490 (34.3)		143 (10.0)	
Conflict of values		<0.01		<0.01
High	335 (48.8)	(134.4 - 1)	90 (13.1)	(13.5 - 1)
Low	313 (23.3)		106 (7.9)	
Social relationships at work		<0,01		0,03
High	103 (15.0)	(137.2 - 1)	52 (7.6)	(4.9 - 1)
Low	545 (40.7)		144 (10.8)	
Insecurity		<0,01		0,14
High	242 (42.8)	(41.8 - 1)	64 (11.3)	(2.2 - 1)
Low	406 (27.8)		132 (9.0)	
Covariates				
Patient Characteristics				
Age group		0,03		0,24
[18-35]	172 (28.8)	(7.1 - 2)	48 (8.0)	(2.8 - 2)
[36-50]	306 (35.1)		87 (10.0)	
[51-65]	169 (30.6)		60 (10.9)	
Sex		<0,01		<0,01
H	266 (28.3)	(10.5 - 1)	140 (14.9)	(53.7 - 1)
F	382 (35.2)		56 (5.2)	
Occupational grade		0.32		<0.01
Blue collar	79 (28.9)	(2.3 - 2)	53 (19.4)	(37.8 - 2)
Pink collar	386 (32.6)		86 (7.3)	
White collar	152 (29.6)		50 (9.7)	
Educational level		0.13		<0.01
< High school degree	266 (34.1)	(2.3 - 1)	98 (12.6)	(11.7 - 1)
≥ High school degree	381 (30.8)		97 (7.8)	
Family status		0.01		<0.01
Lives alone	471 (30.5)	(6.3 - 1)	63 (13.1)	(7.9 - 1)
Lives with a partner or parents	177 (36.8)		133 (8.6)	
Household income (in €)		0.03		0.30
[0-3.000]	184 (37.5)	(4.8 - 1)	53 (10.8)	(1.1- 1)
3.000 +	353 (31.7)		100 (9.0)	
Number of worker in the company		0.03		<0.01
1 to 5	108 (29.9)	(9.1 - 3)	51 (14.1)	(16.5 - 3)
6 to 25	183 (37.3)		53 (10.8)	
26 to 250	138 (32.9)		43 (10.2)	
250 +	203 (29.5)		45 (6.6)	
Past psychiatric problems		<0.01		<0.01
Yes	108 (57.1)	(57.1 - 1)	30 (15.9)	(16.5 - 1)
No	516 (29.8)		150 (8.6)	
Past somatic problems		0.82		0.84
Yes	185 (33.1)	(0.05 - 1)	53 (9.5)	(0.04- 1)
No	445 (32.4)		136 (9.9)	

p: Chi-square test
df: degree of freedom

Table 2: *(continued)*

	MDD and GAD (n=648)		Alcohol (n=196)	
	N (%)	p (χ2-df)	N (%)	p (χ2-df)
Purpose of consultation with GP				
Somatic		<0.01		0.04
Yes	335 (25.2)	(81.5 - 1)	115 (8.6)	(4.4 - 1)
No	313 (45.0)		81 (11.6)	
Psychological		<0.01		<0.01
Yes	312 (73.4)	(422.3 - 1)	61 (14.4)	(12.8 - 1)
No	336 (21.0)		135 (8.4)	
Chronic disease management		<0.01		<0.01
Yes	75 (24)	(10.5 - 1)	46 (14.7)	(10.0 - 1)
No	573 (33.4)		150 (8.8)	
Past unemployment		0.57		<0.01
Yes	202 (33.0)	(0.33 - 1)	80 (13.1)	(11.0 - 1)
No	446 (31.5)		116 (8.2)	
Job insecurity		<0.01		<0.01
Yes	229 (43.9)	(47.0 - 1)	70 (13.4)	(12.0 - 1)
No	400 (27.5)		118 (11.1)	
GPs Characteristics				
GP's gender		<0.01		<0.01
Male	375 (27.5)	(37.8 - 1)	152 (11.1)	(9.9 - 1)
Female	273 (41.2)		44 (6.6)	
GP's age		0.13		0.14
[18-39]	72 (37.1)	(5.7 - 3)	18 (9.3)	(5.5 - 3)
[40-49]	190 (30.4)		49 (7.8)	
[50-59]	254 (30.5)		95 (11.4)	
60 +	132 (35.2)		34 (9.1)	
Size of practice population		<0.01		0.06
0-500	79 (37.4)	(14.7 - 3)	18 (8.5)	(7.4 - 3)
5000 - 1000	295 (29.7)		82 (8.3)	
1000- 1500	136 (31.4)		47 (10.9)	
1500+	104 (41.1)		34 (13.4)	
Comfort with mental health problems		0.21		0.48
High	500 (31.3)	(1.6 - 1)	155 (9.7)	(0.5 - 1)
Low	118 (34.9)		28 (8.3)	
High opportunity to work with mental health specialists		<0.01		0.05
High	345 (36.7)	(18.2 - 1)	103 (9.9)	(3.7 - 1)
Low	286 (27.6)		86 (9.1)	
Contextual characteristics				
Social deprivation		0.32		0.87
High	167 (30.2)	(1.0 - 1)	52 (9.4)	(0.03 - 1)
Low	481 (32.6)		144 (9.8)	
Material deprivation		<0.01		0.74
High	306 (36.0)	(10.4 - 1)	85 (10)	(0.1 - 1)
Low	342 (29.1)		111 (9.4)	
Density of psychiatrist		0.02		0.97
High	522 (33.3)	(5.1 - 1)	45 (9.8)	(0.01 - 1)
Low	126 (27.5)		151 (9.6)	
Density of psychologist		0.05		0.10
High	515 (33.1)	(4.0 - 1)	36 (7.6)	(2.7 - 1)
Low	133 (28.1)		160 (10.3)	
Density of GP		0.06		0.88
High	505 (33.1)	(3.6 - 1)	50 (10.0)	(0.02 - 1)
Low	143 (28.4)		146 (9.6)	

p: Chi-square test
df: degree of freedom

Multivariable analysis (Table 3)

All occupational factors were associated with our two study outcomes in unadjusted analysis. In adjusted analyses, patients reporting high levels of work intensity (RR=1.16 [1.06 - 1.27]; p<0.01) (absolute risk = 52.8%) and emotional demands (RR=1.24 [1.13 - 1.35]; p<0.01) (absolute risk = 54.9%) had a higher risk of MDD/GAD whereas patients with high social relations at work had lower risk to have MDD/GAD (RR=0.78 [0.70 – 0.87]; p<0.01) (absolute risk = 15.0%).

Regarding alcohol abuse, social relations at work were associated with higher risk (RR=1.25 [1.0 - 1.53]; p=0.03) (absolute risk = 7.6%) and higher autonomy was protective (RR=0.82 [0.67 – 0.99]; p=0.05) (absolute risk = 8.9%) (Table 3).

Result for the adjustment variables are presented as a supplementary file (appendix 3).

Table 3: major depressive disorders **(**MDD), generalized anxiety disorders (GAD) and alcohol abuse work-related factors, Héraclès study, France, 2014. Multilevel Poisson regression models

	MDD/GAD (n=1782)						Alcohol (n=1776)					
	Unadjusted			Adjusted			Unadjusted			Adjusted		
	RR[1]	CI 95%	P	RR[2]	CI 95%	P	RR[1]	CI 95%	P	RR[3]	CI 95%	P
Work intensity	**1.46**	**[1.35 - 1.57]**	**<0.01**	**1.16**	**[1.06 - 1.27]**	**<0.01**	**1.31**	**[1.14 - 1.50]**	**<0.01**	1.16	[0.97 - 1.38]	0.10
Emotional demands	**1.53**	**[1.43 - 1.64]**	**<0.01**	**1.24**	**[1.13 - 1.35]**	**<0.01**	**1.40**	**[1.23 - 1.59]**	**<0.01**	1.16	[0.97 - 1.38]	0.10
Autonomy	**0.68**	**[0.63 - 0.73]**	**<0.01**	0.94	[0.85 - 1.04]	0.26	**0.72**	**[0.63 - 0.83]**	**<0.01**	**0.82**	**[0.67 - 0.99]**	**0.05**
Conflict of values	**1.45**	**[1.35 - 1.56]**	**<0.01**	1.06	[0.96 - 1.17]	0.26	**1.30**	**[1.14 - 1.49]**	**<0.01**	1.16	[0.96 - 1.40]	0.13
Social relationships at work	**0.61**	**[0.56 - 0.66]**	**<0.01**	**0.78**	**[0.70 - 0.87]**	**<0.01**	**0.83**	**[0.72 - 0.96]**	**0.01**	**1.25**	**[1.01 - 1.53]**	**0.03**
Insecurity	**1.13**	**[1.05 - 1.22]**	**<0.01**	1.03	[0.95 - 1.11]	0.49	**1.14**	**[1.00 - 1.30]**	**0.05**	0.95	[0.82 - 1.11]	0.52

RR : relative risk
[1] No adjustment: each occupational factor are studied one at the time
[2] Adjusted on : each occupational factors, age, sex, occupational grade, past psychiatric problems, alcohol abuse, material deprivation and GP's gender
[3] Adjusted on : each occupational factors, age, sex, occupational grade, family status, number of person in the company, past psychiatric problems, job instability, education level, past unemployment, GAD and MDD
For MDD/GAD model explained variance was 0.21 and 0.11 for Alcohol model

4 DISCUSSION

4.1 Main results

In our study conducted among a large sample of persons consulting a GP, we found that several work characteristics are associated with mental health. Unfavourable social relations at work are associated with a higher risk of MDD/GAD, but a lower risk of alcohol abuse. High work intensity and high emotional demands at work are associated with a higher risk of MDD/GAD. Finally, low autonomy at work is significantly associated with a higher risk of alcohol abuse.

4.2 Comparison with literature

We confirm, for the first time in primary care, the association between common mental disorders and work social support. This is consistent with data from a cross sectional study conducted in Japan (using the K10 questionnaire to assess depression): higher risk of depressive symptoms for workers with low social support at work (OR=3.8)[50]. It is also coherent with data from a meta-analysis of 17 other studies investigating depressive disorders.[51] Low social support at work is also associated with anxiety disorders as already observed in the population based study by Wang *et al*: employees with poor social support from superior or co-workers had higher risk of having anxiety disorders for both gender.[52] However, the causal direction of this association cannot be determined due to the cross sectional design of our study. It is possible that low social support increases the risk of having depression or anxiety as it has been shown in different longitudinal studies.[53] Moreover, it is well known that social relations and support (outside or inside work) affect psychological health,[54] but it is also possible that individual with no depression or anxiety disorders have better social support.[54] Finally, the association between GAD/MDD and social support could also be related to negative views of social support when depressed or anxious.[55] For alcohol abuse an inverse association is observed: higher risk associated with high social relationship at work and this result is consistent with results of a cross sectional study conducted among Canadian workers.[24] It raises question about festive alcohol

consumption with colleagues in or outside the company.[56] We perform a subgroup analysis by occupational group to explore this result and we found that white collar were the most exposed group to alcohol abuse with high social relationship at work (RR=1.89 [1.21 – 2.9]). Others studies have approached this subject by pointing out afterwork with colleagues.[57]

Work intensity, or high psychological demand in terms of high working time and intensity is associated with depressive symptoms in the meta-analysis by Theorell *et al* (10 studies).[51] The meta-analysis of longitudinal studies by Netterstrom *et al* highlights the adverse effect of high psychological demand on the occurrence of depressive disorders.[53] However, this association could also ensue that persons with depressive disorders have distorted views of psychological demands.[55]

High emotional demands at work have already been observed for depressive disorders among women in a population-based nested case-control study of 14,166 psychiatric patients in Denmark (IRR=1.39)[25] or for GAD in the French prospective study SIP (using the same diagnostic tool MINI) (RR=1.66 among workers with high emotional demand[21]). The designs of those two studies argue for the negative effect of high emotional demand on depression and anxiety, but in our cross sectional study the causal attribution is not possible thus it is also possible that people with depression and/or anxiety have a different view towards those demands.[55]

Autonomy appears related to alcohol abuse, as reported in an English prospective study: low decision latitude, which is a part of the autonomy axis in our study, is associated to higher risk of alcohol dependence within women.[58]

We do not confirm the association found earlier between CMD and high job insecurity or conflict of value.[20 21 23]

Based on stress models, our study shows that work intensity and emotional demand are stress factors for GAD/MDD and that social relations at work have a positive effect. For alcohol, autonomy is a stress factor and social relations at work seems to be induced by another mechanism described above.

4.3 Strengths and limitations of the study

Several limitations of our study should be acknowledged.

First, our study was conducted in the Nord - Pas-de-Calais region, i.e. one of the poorest in France with a total of four millions inhabitants. This region during the first half of the 20th century was highly industrialized and has suffered since the 1950s from industrial decline and mines, textile and steel industries gradually closing. Despite the growth of services and some specialized industries (car, rail and glass), levels of education, unemployment (15%), poverty and health indicators (e.g. life expectancy) are unfavourable. The Nord - Pas-de-Calais region has a low density of GPs (11% fewer than in France) and other medical specialities (24% fewer).[59] Moreover, the study was conducted after the 2008 recession, which has been associated with an increase in the prevalence of common mental health disorders worldwide.[60 61] This could lead to a high level of mental disorders. The prevalence of MDD, GAD and alcohol abuse within patient consulting a GP is respectively 19.1%, 25.8% and 9.7%. This is consistent in the superior limits with studies in primary care ranging prevalence from 6% to 25% for depression, 3% to 25% for anxiety and 2% to 11% for alcohol abuse.[10 12 27-30] Results should be replicated in others areas.

Second, a possible weakness is the selective participation of GPs. GPs who have participated in the study could be especially interested in common mental disorders. This interest may be related to the personal interest of the GP, but it could also be related to the GP patient rate of common mental disorders. Therefore, it may cause a larger selection of patient with psychological disorders. However, response rate are similar to previous studies[28 62] and GPs were selected to be representative of the Nord - Pas-de-Calais GPs in term of geographical localization, thereby limiting possible bias. In general practice, GPs' response rate is known to be low[63], and in order to favour an optimal response rate, we tested the questionnaire to make it parsimonious, GPs were paid for their participation, and GPs who were asked to participate were individually called. Participating GP had similar age, practice and years of practice than all GPs in the region. Patient selection should also be considered. However, a random procedure to define patients included in the study limits this bias. Indeed, GPs were asked to include patient following an inclusion schedule that was provided at the start of the study. This allowed us to include patient in different time slots of the week. Moreover a non-respondent form had to be filled by the GPs but we suppose that the filling rate was low because only 41 GPs filled this form and declare that 495 patient were not included. Characteristics of patients

included and those not included did not differ in term of age and sex. However it is important to note that compared to studies in work environment settings, it is possible that patients included in this primary care setting have a different level of health than other employees who do not consult their GPs.

The measurement of psychosocial work factors was based on an unpublished work of experts in this field who based their work on international literature, measurement of reliability in our sample was rather low for some axis (α=0.34 for ethical conflict). The use of a validated questionnaire could have allowed for a better comparison with the existing literature and better psychometric quality.

We were able to take into account many covariates (characterizing individuals, GPs and patients' context), but nevertheless we missed some other important variables. Indeed, it would have been informative to control for individual characteristics such as prior history of mental health problems, social support outside of work or life events that are known to be associated with CMD, thus they could have an effect on the relationship between CMD and work related factors.

Despite these limitations, the results of this work are of interest because they study occupational factors related to CMD (MDD/GAD and alcohol abuse) among working adults in primary care with a standardized diagnostic tool (MINI) in a large sample (n=2,027).[35] The primary care sample used allows the inclusion of a representative panel of workers in the labour force including independent workers, workers in small companies or workers who don't have an occupational physician which is not the case in most of studies in occupational setting. Indeed, an international study including 49 countries shows that the average occupational health services coverage of workers was 24.8% with a larger gap among workers in small-scale enterprises, the self-employed, agriculture, and the informal sector.[64] Moreover the exploratory character of our study confirm the increased risk of anxiety/depression for work intensity, social support and emotional demands and the link between autonomy and alcohol abuse in a primary care setting. This study also shows a negative effect of social support at work for alcohol abuse.[7 21 25 58] However we have to be cautious about these results and further studies in other areas have to be done in order to confirm our findings.

4.4 Conclusion

Our study is one of the first to investigate simultaneously well-known factors related to job strain and effort-reward imbalance models and new occupational factors described in recent literature. To the best of our knowledge, it is the first conducted among working individuals in primary care. Results emphasise the importance of social support at work and different occupational factors that are associated with MDD, GAD and alcohol abuse. These results could be a starting point for the GPs to apprehend these factors with the patient and to communicate with the occupational physician in order to prevent the onset of CMD.

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CONTRIBUTORS

Study concept and design: MR, NY, MM, AL, TB, LP. Data analysis and collection: MR, LFC, MM, LP. Drafting of the manuscript: MR. Critical revision of the manuscript: NY, MM, AL. All authors have approved the final manuscript.

COMPETING INTERESTS

All authors declare that they do not have any competing interests and declare independence from the funders.

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DATA SHARING STATEMENT

No additional data are available

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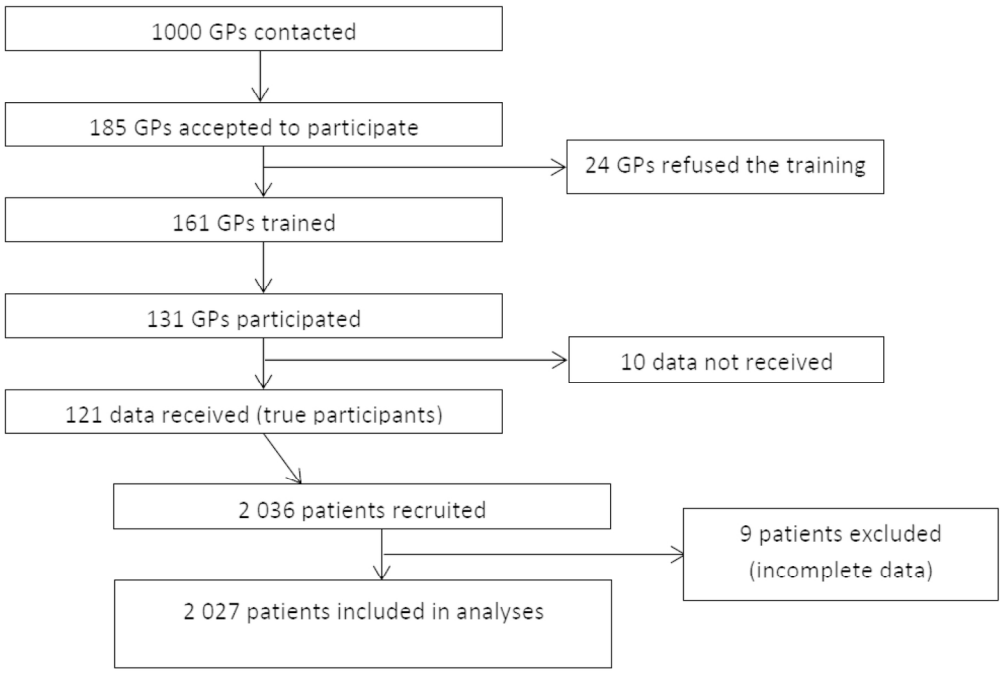
Legends:

Figure 1: Flow chart of participation in the Héraclès study, France, 2014



Flow chart of participation in the Heracles study, France, 2014

154x104mm (300 x 300 DPI)

Appendix 1: Work's factor questionnaire

1) **Work intensity**

- I receive contradictory orders or indication ("Yes"/"No")
- I am asked excessive amounts of work ("Always"/"Often"/"Sometimes"/"Never")
- I have too much to think about at work ("Always"/"Often"/"Sometimes"/"Never")
- I have difficulties in balancing work and family life ("Always"/"Often"/"Sometimes"/"Never")
- I have the time needed to do my work ("Always"/"Often"/"Sometimes"/"Never")

2) **Emotional demands**

- I work in contact with customers/beneficiaries ("Yes"/"No")
- I am in contact with people in distress ("Yes"/"No")
- I have conflicts with customers/beneficiaries ("Always"/"Often"/"Sometimes"/"Never")
- I have to hide my emotions and pretend to be in a good mood ("Always"/"Often"/"Sometimes"/"Never")
- I sometimes experience fear during my work ("Always"/"Often"/"Sometimes"/"Never")
- During my work, I am exposed to physical, verbal, psychological aggressions ("Always"/"Often"/"Sometimes"/"Never")

3) **Autonomy**

- I have very little freedom to decide how I do my job ("Always"/"Often"/"Sometimes"/"Never")
- I can fully employ my skills ("Always"/"Often"/"Sometimes"/"Never")

4) **Conflict of values**

- I have the possibility to make a work of quality ("Always"/"Often"/"Sometimes"/"Never")
- In my work, I have to do disapproved things ("Always"/"Often"/"Sometimes"/"Never")

5) **Social relationships at work**

- My work is fully recognized ("Always"/"Often"/"Sometimes"/"Never")
- I have support from colleagues ("Always"/"Often"/"Sometimes"/"Never")
- I have support from superior ("Always"/"Often"/"Sometimes"/"Never")

6) **Insecurity of work**

- I feel able to do my current job until retirement ("Yes"/"No")
- I work with fear of losing my job ("Always"/"Often"/"Sometimes"/"Never")

Appendix 2: Correlation matrix of work characteristics, Héraclès study, France. 2014, Pearson correlation coefficient

	Work intensity	Emotional demands	Autonomy	Conflict of values	Social relationships at work	Insecurity
Work intensity		0.70	-0.72	0.70	-0.81	0.08
Emotional demands	0.70		-0.86	0.78	-0.84	0.23
Autonomy	-0.72	-0.86		-0.91	0.87	-0.42
Conflict of values	0.70	0.78	-0.91		-0.91	0.17
Social relationships at work	-0.81	-0.84	0.87	-0.91		-0.33
Insecurity	0.08	0.23	-0.42	0.17	-0.33	

Appendix 3: major depressive disorders **(**MDD), generalized anxiety disorders (GAD) and alcohol abuse related factors adjusted on work related factors, Héraclès study, France, 2014. Multilevel regression models

	MDD GAD (n=1782)			Alcohol (n=1776)		
	RR[1]	CI 95%	P	RR[1]	CI 95%	P
Age group			0.38			0.34
[18 - 35]	1	-		1	-	
[36 - 50]	1.13	[0.93 - 1.39]		1.29	[0.86 - 1.92]	
[51 - 65]	1.03	[0.82 - 1.29]		1.37	[0.87 - 2.16]	
Sexe			0.34			<0.01
Male	1	-		1	-	
Female	1.09	[0.91 - 1.31]		0.37	[0.25 - 0.53]	
Past unemployment						0.13
No				1	-	
Yes				1.30	[0.93 - 1.83]	
Occupational grade			0.71			0.09
Blue collar	1	-		1	-	
Pink collar	1.12	[0.86 - 1.46]		0.61	[0.39 - 0.98]	
White collar	1.11	[0.82 - 1.5]		0.80	[0.46 - 1.4]	
Family status						0.11
Lives alone				1	-	
Lives with partner or parents				1.34	[0.94 - 1.9]	
Educational level						0.51
< High school degree				1	-	
≥ High school degree				1.14	[0.77 - 1.7]	
Job instability						0.21
No				1	-	
Yes				1.31	[0.86 - 1.98]	
Number of workers in the company						0.02
1 to 10				1	-	
11 to 49				0.70	[0.45 - 1.09]	
50 to 250				0.83	[0.52 - 1.3]	
250 +				0.49	[0.31 - 0.78]	
Past psychiaric problems			<0.01			0.02
No	1	-		1	-	
Yes	1.58	[1.27 - 1.96]		1.65	[1.07 - 2.55]	
Major depressive disorders						0.01
No				1	-	
Yes				1.66	[1.12 - 2.44]	
Generalized anxiety disorders						0.25
No				1	-	
Yes				1.24	[0.86 - 1.8]	
Alcohol			0.01			
No	1	-				
Yes	1.38	[1.09 - 1.75]				
Material deprivation			0.04			
No	1	-				
Yes	1.19	[1.01 - 1.4]				
GPs Gender			0.02			
Male	1	-				
Female	1.22	[1.03 - 1.44]				

RR : relative risk

[1] Adjusted on: Work intensity, Emotional demands, Autonomy, Conflict of values, Social relationships at work, Insecurity

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **page 1 and 2**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found - **page 1 and 2**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **page 4 and 5**
Objectives	3	State specific objectives, including any prespecified hypotheses - **page 4 and 5**
Methods		
Study design	4	Present key elements of study design early in the paper - **page 6**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection - **page 6**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants - **page 6**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable – **page 6 to 8**
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 - **page 6 to 8**
Bias	9	Describe any efforts to address potential sources of bias – **page 6**
Study size	10	Explain how the study size was arrived at – **page 6**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why – **page 8 and 9**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **page 8 and 9**
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
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 – **page 10 and figure 1**
		(b) Give reasons for non-participation at each stage – **figure 1**
		(c) Consider use of a flow diagram – **figure 1**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders – **page 10 to 12**
		(b) Indicate number of participants with missing data for each variable of interest
Outcome data	15*	Report numbers of outcome events or summary measures – **page 13**
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 – **page 13 to 17**
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a

		meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives – **page 18**
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 – **page 19 and 20**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence – **page 18 and 19**
Generalisability	21	Discuss the generalisability (external validity) of the study results – **page 20 and 21**
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 – **page 21**

*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 www.strobe-statement.org.

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Which work-related characteristics are most strongly associated with common mental disorders?: A cross-sectional study

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Which work-related characteristics are most strongly associated with common mental disorders? : A cross-sectional study

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ABSTRACT

OBJECTIVES: Studies exploring work-related risk factors of common mental disorders (CMD) such as major depressive disorder (MDD), generalized anxiety disorder (GAD) or alcohol abuse, have generally focused on a limited set of work characteristics. For the first time in a primary care setting, we examine simultaneously multiple work-related risk factors in relation to CMDs.

METHOD: We use data from a study of working individuals recruited among 2,027 patients of 121 general practitioners (GPs) representative of the Nord - Pas-de-Calais region in the North of France (April-August 2014). CMDs (MDD; GAD; alcohol abuse) were assessed using the MINI (Mini International Neuropsychiatric Interview). Six worked-related factors were examined (work intensity, emotional demands, autonomy, social relations at work, conflict in values, and job insecurity). Several covariates were considered (patient, GP and contextual characteristics). To study the association between workplace risk factors and CMDs, we used multilevel Poisson regression models adjusted for covariates.

RESULTS: Among study participants, 389 (19.1%) met criteria for MDD, 522 (25.8%) for GAD and 196 (9.7%) for alcohol abuse. In multivariable analyses adjusted for covariates, MDD/GAD was significantly associated with work intensity (RR=1.16 [1.06 - 1.27]) (absolute risk = 52.8%), emotional demands (RR=1.24 [1.13 - 1.35]) (absolute risk = 54.9%) and social relations at work (RR=0.78 [0.70 – 0.87]) (absolute risk = 15.0%); alcohol abuse was associated with social relations at work (RR=1.25 [1.01 - 1.53]) (absolute risk = 7.6%) and autonomy (OR=0.82 [0.67 – 0.99]) (absolute risk = 8.9%).

CONCLUSIONS: Several workplace factors are associated with CMDs among working individuals seen by a GP. These findings confirm the role of organizational characteristics of work as a correlate of psychological difficulties above and beyond other sources of risk.

Key terms: mental health; primary care; workplace factors

STRENGTHS AND LIMITATIONS OF THE STUDY

- Cross-sectional study design
- Study of occupational factors in relation to common mental disorders among working adults in primary care evaluated with a standardized diagnostic tool in a large sample
- The inclusion of participants living in the Nord Pas de Calais region – one of the poorest in France – and the selective participation of general practitioners (GPs) who took part in the study, may have led to an overrepresentation of patients with psychological disorders.

1 INTRODUCTION

Individuals who are part of the labour force are generally in better health than the unemployed,[1] however work can also have negative effects on somatic and psychosocial health.[2] A study conducted among general practitioners (GP) trained in occupational medicine found that mental health issues are frequently attributed to work.[3] They are responsible for most of sickness absence and long-term work incapacity.[4] In France, data from the national health insurance shows that 20% of sickness absences are caused by mental disorders, and this proportion is even higher for long term sickness absences (on average 111 days).[5] The most frequent mental health difficulties among working individuals include mood, anxiety and substance use disorders (particularly alcohol-related problems), which can be grouped as "Common Mental Disorders" (CMDs).[6] A systematic review of the literature in European countries shows that there is great diversity in the ascertainment of mental disorders and thus the prevalence estimates vary between countries. The authors suggest that the study of a larger range of diagnoses and the standardization of methods can help the comparability across countries.[7]

The association between work and CMDs is bidirectional: work has been shown to be a risk factor of poor mental health[8], but the presence of a CMD can also influence job performance and well-being.[9 10] Other risk factors of CMDs include individuals' sociodemographic characteristics including being divorced or widowed, having a low educational level, older age, female gender,[11-13], certain genetic factors[14] and a history of chronic somatic or psychiatric disorders.[15] Environmental factors (e.g. social and material deprivation, etc.) were described and show that low socio-economic status was associated with higher rates of depression.[11 12]

Psychosocial factors related to the work environment are of particular interest because they may be more easily prevented than those which result from life events and are often unavoidable. Three main theoretical models have been proposed to explain relations between work characteristics and mental health. First, Karasek and Theorell[16] argued that psychological demands, decision latitude and social support are especially important. Second, Siegrist[17] proposed that what matters most is the subjectively ascertained effort-reward balance. A third model, developed by

Elovainio, put an emphasis on the role of organizational justice including interpersonal comparison, that is to say comparison of the response of the company in the same situation for different employees.[18]

Several studies evaluate the impact of work on mental health using these theoretical models.[8 19 20] Overall, the risk of mental disorders is higher when individuals experience high job demands, low job control, high effort-reward imbalance or low organizational justice. As work organization is evolving, other psychosocial factors described as "emergent" have appeared in recent studies (e.g. job insecurity, conflicts in values)[21-24]: Workers experiencing high job insecurity or role conflicts also seem to have a higher levels of CMDs.[21 22] A recent systematic meta-review identified three overlapping categories of work-related risk factors that may contribute to the development of common mental health problems: imbalanced job design, occupational uncertainty and a lack of values and respect in the workplace.[8] This review did not precisely describe different CMDs (MDD was the most frequent outcome, GAD and alcohol abuse being less explored[8 25 26]). Additionally, most studies were based on self-reported questionnaires and not validated diagnostic interviews.

Work-related risk factors are also influenced by changes in society and work environments (globalization, demographic change, job specialization, communication load, new forms of work organization, industry 4.0[27], etc). A French study assessed changes in psychosocial work factors between 2006 and 2011 and reported that some worsened (decision latitude, social support, reward, role conflict and work life imbalance) over that period. These changes have been shown to vary with age, occupation, sector activity and type of contract.[28]

The objective of this study is to assess the association between GAD, MDD and alcohol abuse in a primary care setting, testing different psychosocial work-related risk factors. Combining emergent and classical factors is important in order to identify which are most strongly related to workers' mental health, as outlined in the meta-review conducted by Harvey *et al*.[8] Since GPs usually are the first contact point for employees in the health care process, the evaluation of primary care patients is of paramount importance.[29 30] In primary care, the prevalence of CMDs is high, ranging from 3%[22] to 25% for anxiety disorders,[13 29-32] 6%[13] to 25% for depression[11 29-32] and 2%[30] to 11% for alcohol abuse.[29 30] Two studies conducted in the United Kingdom show that a third of

patients seeing a GP for work-related reasons have a mental health issue.[3 33] Yet GPs often have difficulties managing their patients' work-related mental health problems, as they often lack negotiation strategies regarding sick leave, communication skills and cooperation with occupational physicians.[34] GPs encounter a variety of workers with systematic, unsystematic or non-existing occupational health services at their workplace. A better understanding of work-related factors associated with individuals' mental health is important to help GPs consider specific actions.

2 METHODS

2.1 Design and Study population

Heracles is a cross-sectional exploratory study conducted between April and August 2014 among working individuals consulting a primary care physician in the Nord - Pas-de-Calais region in the North of France.

2.1.1 Patient and Public Involvement

The number of subjects needed and the set-up of the study have previously been described[35]. Briefly, with an estimated prevalence of 20%, to have a precision of 10%, we aimed to include 2,000 patients via their GP. Participating GPs gave an oral consent to participate and were asked to randomly include a maximum of 24 patients who met the following criteria: being a) actively employed and b) aged 18 to 65 years, regardless of the reason of their medical appointment. GPs were asked to include the first two patients who met study inclusion criteria in each randomly selected time slot which had previously been defined with the GP. Approximately ¼ of the GPs in the region, selected to be representative of those practicing in 15 areas of Nord – Pas-de-Calais region, were contacted to participate in the study. Participating GPs gave written information to their patients regarding the study and asked them to sign an informed consent.

This study was conducted by the Sentinelles network,[36] part of the INSERM-Paris Sorbonne University research unit UMR-S 1136. This research group has a standing authorization from the French independent administrative authority protecting privacy and personal data to conduct research among GPs and their patients (CNIL n°471 393).

2.2 Data collection

Participating GPs received a 15 minute phone training regarding the study protocol and questionnaire. After their regular appointment, GPs interviewed participating patients for the purposes of the study. Study questionnaires included information on:

2.2.1 Measurement of common mental disorders

CMDs were measured using a standardised diagnostic interview: the Mini International Neuropsychiatric Interview (MINI) that was used as a screening tool. The MINI is, a structured clinical interview that enables the diagnosis of mental disorders based on the Diagnosis and Statistical Manual of Mental Disorders, fourth edition (DSM-IV).[37] Specifically, three different diagnoses were ascertained: Major Depressive Disorder (MDD) (in the preceding 2 weeks), Generalised Anxiety Disorder (GAD) (in the preceding 6 months), and alcohol abuse (in the preceding 12 months).

The sensibility of the MINI varied between 83 to 94% (MDD: 94%; GAD: 88%; Alcohol: 83%), the specificity between 72 to 97% (MDD: 79%; GAD: 72%; Alcohol: 97%) and the Kappa concordance coefficient between 0.36 to 0.82 (MDD: 0.73; GAD: 0.36; Alcohol: 0.82). The inter-rater and test-retest reliability measured by Kappa coefficient were good, respectively 0.88 to 1 and 0.76 to 0.93.[38]

2.2.2 Work characteristics

Work characteristics were self-reported by the patient to their GP. We used a national French questionnaire proposed by experts in the field based on the international scientific literature and after auditioning Robert Karasek and Johannes Siegrist.[23] It combines a) questions measuring psychological demands – work control – social support developed in Karasek's model[16] (two questions about decision latitude, four questions about psychological demands and two questions about social support) ; b) questions measuring effort/reward balance based on Siegrist's model[17] (three questions about rewards and one question about overinvestment); c) questions about organizational justice from Moorman's questionnaire;[39] d) questions from the Copenhagen Psychosocial Questionnaire[40] and from the General Nordic Questionnaire for Psychological and Social Factors at Work[41] or from WOrking Conditions and Control Questionnaire (WOCCQ)[42]. Overall, the questionnaire included twenty work-related items exploring six different areas (Appendix 1): 1) five related to work intensity and duration (contradictory orders, excessive amount of work, too much to think about at work, difficulties in balancing work and family life, time needed for work), 2) six concerning emotional demands (contacts with customers/beneficiaries, contact with people in

distress, conflicts with customers/beneficiaries, the need to hide emotions, fear, exposure to aggressions), 3) two regarding autonomy (limited decision making possibility, full use of skills), 4) three on the quality of social work relations (full-recognition of the work performed, support from colleagues, support from superiors), 5) two concerning conflicts in values (possibility to perform quality work, doing disapproved things), 6) two about job insecurity (ability to work until retirement, fear of job loss). For four of these items (contacts with the public at work, contacts with people in distress, contradictory orders, ability to work until retirement) the response was either "yes" or "no", and for other factors the responses were "always"/"often"/"sometimes"/"never" numbered from 1 to 4. The reliability of questions pertaining to work characteristics was assessed by computing an omega coefficient[43]. This coefficient varied between 0.35 to 0.79. The reliability was higher for social relations at work (ω =0.72), emotional demands (ω =0.75) and work intensity (ω =0.79) than for autonomy (ω =0.66), job insecurity (ω =0.50), or conflicts in values (ω=0.35).

2.2.3 Covariates

Patient's characteristics

We considered already previously risk-factors of CMD.[11]

- Past somatic problems;
- Previous mental health problems/disorders;
- Sociodemographic (age, gender, family status, family income, level of education);
- Occupational grade[44]: blue collar (farmer/manual worker), pink collar (technician/associate professional/clerk/service worker) or white collar (manager/professional);[45]
- Company size;
- Job instability assessed based on the type of contract (temporary vs. permanent)

Health care characteristics[46]

- Reason for medical appointment (somatic, psychological, chronic disease management);

- GP's sociodemographic characteristics (age, gender);
- Practice characteristics (size; comfort with psychological distress issues; opportunity to collaborate with mental health specialists).

Contextual characteristics (by the 15 proximity area of the region)

Contextual characteristics shown to be associated with CMDs in primary care[11 12]:

- Density of psychiatrists, psychologists and GPs;
- Social deprivation (loneliness, single parenthood, widowhood/divorce) and material deprivation (unemployment, income, level of not graduated);[47 48]
- Geographical area: 15 proximity areas defined by the regional health agency of the Nord – Pas-de-Calais region.

2.3 Statistical Analyses

Some of the covariates were recoded to use fewer categories. For family status, participants living alone or living with parents were grouped into one category. For family income, participants were grouped in two categories: [0-3,000] euros (which corresponds to approximately two times the minimum wage in France) and >3,000 euros. For educational level, we created two categories: less than a high school degree (no degree, degree below high school) or a degree higher or equivalent to a high school degree. For age, our continuous variable was studied in three categories based on the distribution 18-35; 36-50; 51-65.

Associations between sociodemographic characteristics and GAD, MDD and alcohol abuse were studied using the Chi-square test. Covariates associated with the outcomes with $p<0.2$ were included in the multivariate analysis.

Work-related factors were regrouped according to 6 previously suggested dimensions transformed each into a Z-score to be comparable to each other.[23] A correlation matrix of different work characteristics was computed and presented in a supplementary file (Appendix 2). Each dimension was dichotomized based on the third quartile or studied as continuous variable in the multivariable models. At first, statistical analyses were conducted separately for each outcome, but factors

associated with MDD and GAD were very similar, therefore to gain statistical power we merged these two disorders into one outcome. To study the association between occupational factors and GAD/MDD and alcohol we used multilevel Poisson regression models using a robust error variance procedure (sandwich estimation)[49] with patient as level one and geographical area as level two. Given the high prevalence of these problems, Poisson regression was preferred to logistic regression to avoid the overestimation of risk ratios.[50] GAD/MDD or alcohol abuse were the dependent variables and the six dimensions of work-related factors were the exposure variables. Statistical models were adjusted for each exposure variable and for other covariates that were associated with GAD/MDD (previous mental health problems/disorders, alcohol abuse, material deprivation and GP's gender) or alcohol abuse (family status, company size, previous mental health problems/disorders, job instability, education level, past unemployment, GAD and MDD) ($p<0.05$) in a multivariable Poisson regression model excluding occupational factors. Age, gender and occupational grade were included directly in the adjustment variable. Absolute risks among persons who were exposed were computed for each of the studied work dimensions.

All analyses were performed using GNU R software version 3.1.1. (lme4 package).[51 52]

3 RESULTS

3.1 Participation and description of the population

Of the 1,000 GPs contacted by mail, 185 accepted to participate (response rate= 18.5%) and 121 completed the study (Figure 1). Participating GPs were more likely to be male (sex ratio=1.82), and to be 50 years or older; they were disseminated throughout the Nord - Pas-de-Calais region (Table 1). Participating GPs were representative of those practicing in the region in terms of geography, age, type and years of practice.

Participating GPs recruited 2,027 patients among which 389 (19.1%) had MDD, 522 (25.8%) GAD and 196 (9.7%) alcohol abuse. Participating patients were mostly female (53.6%), aged 42.3 years (sd 10.6) on average, mainly living with a partner (76.2%), working in pink collar occupations (60.1%). 61.3% had graduated from high school and 30.2% had been unemployed in the past. Among study participants, 21.0% came to see their GP for psychological reasons (Table 1). Characteristics of participants with MDD, GAD or alcohol abuse are presented in Table 2.

The study response rate was 80%: 41 GPs filled a non-respondent form for 495 patients who refused to participate. Non-respondents did not differ from participants in term of age (p= 0.47) and gender (p=0.23). Compared with working age patients consulting a GP in the study region, study participants were older (p<0.01) but had a similar gender distribution (p=0.08).

Table 1: Description of the study population, Héraclès study, France, 2014

	N	%
Work Characteristics		
Work intensity		
High	437	21.6
Low	1,588	78.3
Emotional demands		
High	476	23.5
Low	1,549	76.4
Autonomy		
High	598	29.5
Low	1,427	70.4
Conflict in values		
High	685	33.8
Low	1,340	66.1
Social relations at work		
High	688	33.9
Low	1,337	66.0
Job Insecurity		
High	565	27.9
Low	1,460	72.0
Covariates		
Patient Characteristics		
Gender		
Male	939	46.4
Female	1,086	53.6
Age group		
[18-35]	597	29.5
[36-50]	872	43.1
[51-65]	552	27.3
Occupational grade		
Blue collar	273	13.9
Pink collar	1,185	60.1
White collar	513	26.0
Educational level		
< High school degree	780	38.7
≥ High school degree	1,238	61.3
Family status		
Lives alone	481	23.8
Lives with a partner or parents	1,543	76.2
Household income (in €)		
[0-3.000]	491	30.6
3.000 +	1,112	69.4
Company size		
1 to 10	361	18.4
11 to 50	490	25.0
51 to 250	420	21.5
250 +	687	35.1
Previous mental health problems/disorders		
Yes	189	9.8
No	1,735	90.2
Past somatic problems		
Yes	559	28.9
No	1,373	71.1

Table 1: *(continued)*

	N	%
Purpose of consultation with GP		
Somatic		
Yes	1,331	65.7
No	696	34.3
Psychological		
Yes	425	21.0
No	1,602	79.0
Chronic disease management		
Yes	313	15.4
No	1,714	84.6
Past unemployment		
Yes	613	30.2
No	1,414	69.8
Job instability		
Yes	522	33.0
No	1,061	67.0
GPs characteristics		
GP's gender		
Male	1,364	67.3
Female	663	32.7
GP's age		
[18-39]	194	9.6
[40-49]	626	30.9
[50-59]	832	41.0
60 +	375	18.5
Size of practice population		
0-500	211	11.2
5000 - 1000	993	52.5
1000- 1500	433	22.9
1500+	253	13.4
Comfort with Mental health problems		
High	1,600	82.6
Low	338	17.4
High opportunity to work with mental health specialists		
High	1,036	52.4
Low	941	47.6
Contextual characteristics		
Social deprivation		
High	552	27.2
Low	1,475	72.8
Material deprivation		
High	850	41.9
Low	1,177	58.1
Density of psychiatrist		
High	1,569	77.4
Low	458	22.6
Density of psychologist		
High	1,554	76.7
Low	473	23.3
Density of GP		
High	1,525	75.2
Low	502	24.8
Geographical area		
Métropole Flandre intérieure	1,035	51.1
Hainault - Cambrésis	333	16.4
Artois - Douaisis	337	16.6
Littoral	322	15.9

3.2 MDD, GAD and alcohol abuse and related work factors

Bivariate analysis (Table 2)

In bivariate analyses, female gender was significantly associated with GAD/MDD and male gender with alcohol abuse. Family status, company size, previous mental health problems/disorders, consultation for psychiatric, somatic or chronic diseases and job insecurity were also significantly associated with the two outcomes. Occupational grade, education level and past unemployment were significantly associated ($p<0.01$) only with alcohol abuse, with elevated rates in blue collar workers, patients who experienced unemployment and individuals with an education level lower than a high school degree. Age and household income were only associated with MDD/GAD.

Regarding GP characteristics, GP gender and opportunity to work with mental health specialist was associated with the two outcomes. Size of practice population was associated only with MDD/GAD.

Most of the contextual variables studied were not associated with our study outcomes, except for material deprivation and the density of psychiatrists and psychologists which were significantly associated with MDD/GAD. To the contrary, work characteristics were almost all significantly associated with the two study outcomes, except job insecurity and autonomy which were not associated with alcohol abuse (Table 2).

Table 2: Association between common mental disorders (major depressive disorders (MDD), generalised anxiety disorders (GAD) and Alcohol abuse) and covariates, Héraclès study, France, 2014 (Chi-square test)

	MDD and GAD (n=648)		Alcohol (n=196)	
	N (%)	p (χ2-df)	N (%)	p (χ2-df)
Work Characteristics				
Work intensity		<0.01		0.01
High	232 (52.8)	(111.1 - 1)	58 (13.3)	(7.5 - 1)
Low	416 (26.2)		138 (8.7)	
Emotional demands		<0.01		<0.01
High	262 (54.9)	(149.8 - 1)	73 (15.3)	(21.8 - 1)
Low	386 (24.9)		123 (7.9)	
Autonomy		<0.01		0.48
High	158 (26.4)	(11.6 - 1)	53 (8.9)	(0.6 - 1)
Low	490 (34.3)		143 (10.0)	
Conflict in values		<0.01		<0.01
High	335 (48.8)	(134.4 - 1)	90 (13.1)	(13.5 - 1)
Low	313 (23.3)		106 (7.9)	
Social relations at work		<0,01		0,03
High	103 (15.0)	(137.2 - 1)	52 (7.6)	(4.9 - 1)
Low	545 (40.7)		144 (10.8)	
Job insecurity		<0,01		0,14
High	242 (42.8)	(41.8 - 1)	64 (11.3)	(2.2 - 1)
Low	406 (27.8)		132 (9.0)	
Covariates				
Patient Characteristics				
Age group		0,03		0,24
[18-35]	172 (28.8)	(7.1 - 2)	48 (8.0)	(2.8 - 2)
[36-50]	306 (35.1)		87 (10.0)	
[51-65]	169 (30.6)		60 (10.9)	
Gender		<0,01		<0,01
Male	266 (28.3)	(10.5 - 1)	140 (14.9)	(53.7 - 1)
Female	382 (35.2)		56 (5.2)	
Occupational grade		0.32		<0.01
Blue collar	79 (28.9)	(2.3 - 2)	53 (19.4)	(37.8 - 2)
Pink collar	386 (32.6)		86 (7.3)	
White collar	152 (29.6)		50 (9.7)	
Educational level		0.13		<0.01
< High school degree	266 (34.1)	(2.3 - 1)	98 (12.6)	(11.7 - 1)
≥ High school degree	381 (30.8)		97 (7.8)	
Family status		0.01		<0.01
Lives alone	471 (30.5)	(6.3 - 1)	63 (13.1)	(7.9 - 1)
Lives with a partner or parents	177 (36.8)		133 (8.6)	
Household income (in €)		0.03		0.30
[0-3.000]	184 (37.5)	(4.8 - 1)	53 (10.8)	(1.1- 1)
3.000 +	353 (31.7)		100 (9.0)	
Company size		0.03		<0.01
1 to 5	108 (29.9)	(9.1 - 3)	51 (14.1)	(16.5 - 3)
6 to 25	183 (37.3)		53 (10.8)	
26 to 250	138 (32.9)		43 (10.2)	
250 +	203 (29.5)		45 (6.6)	
Previous mental health problems/disorders		<0.01		<0.01
Yes	108 (57.1)	(57.1 - 1)	30 (15.9)	(16.5 - 1)
No	516 (29.8)		150 (8.6)	
Past somatic problems		0.82		0.84
Yes	185 (33.1)	(0.05 - 1)	53 (9.5)	(0.04- 1)
No	445 (32.4)		136 (9.9)	

p: Chi-square test
df: degree of freedom

Table 2: *(continued)*

	MDD and GAD (n=648)		Alcohol (n=196)	
	N (%)	p (χ2-df)	N (%)	p (χ2-df)
Purpose of consultation with GP				
Somatic		<0,01		0,04
Yes	335 (25,2)	(81.5 - 1)	115 (8,6)	(4.4 - 1)
No	313 (45)		81 (11,6)	
Psychological		<0,01		<0,01
Yes	312 (73,4)	(422.3 - 1)	61 (14,4)	(12.8 - 1)
No	336 (21)		135 (8,4)	
Chronic disease management		<0,01		<0,01
Yes	75 (24)	(10.5 - 1)	46 (14,7)	(10.0 - 1)
No	573 (33,4)		150 (8,8)	
Past unemployment		0,57		<0,01
Yes	202 (33)	(0.33 - 1)	80 (13,1)	(11.0 - 1)
No	446 (31,5)		116 (8,2)	
Job instability		<0,01		<0,01
Yes	229 (43,9)	(47.0 - 1)	70 (13,4)	(12.0 - 1)
No	400 (27,5)		118 (11,1)	
GPs Characteristics				
GP's gender		<0,01		<0,01
Male	375 (27,5)	(37.8 - 1)	152 (11,1)	(9.9 - 1)
Female	273 (41,2)		44 (6,6)	
GP's age		0,13		0,14
[18-39]	72 (37,1)	(5.7 - 3)	18 (9,3)	(5.5 - 3)
[40-49]	190 (30,4)		49 (7,8)	
[50-59]	254 (30,5)		95 (11,4)	
60 +	132 (35,2)		34 (9,1)	
Size of practice population		<0,01		0,06
0-500	79 (37,4)	(14.7 - 3)	18 (8,5)	(7.4 - 3)
5000 - 1000	295 (29,7)		82 (8,3)	
1000- 1500	136 (31,4)		47 (10,9)	
1500+	104 (41,1)		34 (13,4)	
Comfort with mental health problems		0,21		0,48
High	500 (31,3)	(1.6 - 1)	155 (9,7)	(0.5 - 1)
Low	118 (34,9)		28 (8,3)	
High opportunity to work with mental health specialists		<0,01		0,05
High	345 (36,7)	(18.2 - 1)	103 (9,9)	(3.7 - 1)
Low	286 (27,6)		86 (9,1)	
Contextual characteristics				
Social deprivation		0,32		0,87
High	167 (30,2)	(1.0 - 1)	52 (9,4)	(0.03 - 1)
Low	481 (32,6)		144 (9,8)	
Material deprivation		<0,01		0,74
High	306 (36)	(10.4 - 1)	85 (10)	(0.1 - 1)
Low	342 (29,1)		111 (9,4)	
Density of psychiatrist		0,02		0,97
High	522 (33,3)	(5.1 - 1)	45 (9,8)	(0.01 - 1)
Low	126 (27,5)		151 (9,6)	
Density of psychologist		0,05		0,10
High	515 (33,1)	(4.0 - 1)	36 (7,6)	(2.7 - 1)
Low	133 (28,1)		160 (10,3)	
Density of GP		0,06		0,88
High	505 (33,1)	(3.6 - 1)	50 (10)	(0.02 - 1)
Low	143 (28,4)		146 (9,6)	

p: Chi-square test
df: degree of freedom

Multivariable analysis (Table 3)

All occupational factors were associated with our two study outcomes in unadjusted analyses. In adjusted analyses, patients reporting high levels of work intensity (RR=1.16 [1.06 - 1.27]; p<0.01) (absolute risk = 52.8%) and emotional demands (RR=1.24 [1.13 - 1.35]; p<0.01) (absolute risk = 54.9%) had a higher risk of MDD/GAD, whereas patients with high social relations at work had a lower risk to have MDD/GAD (RR=0.78 [0.70 – 0.87]; p<0.01) (absolute risk = 15.0%).

Regarding alcohol abuse, social relations at work were associated with a higher risk (RR=1.25 [1.0 - 1.53]; p=0.03) (absolute risk = 7.6%) and higher autonomy was protective (RR=0.82 [0.67 – 0.99]; p=0.05) (absolute risk = 8.9%) (Table 3). A sensitivity analyses by occupational group showed a higher risk of alcohol abuse for white collar workers in case of high social relations at work (RR=1.89 [1.21 – 2.9]).

Associations between covariates and the study outcomes are presented in supplementary material (Appendix 3).

Table 3: Work-related factors and major depressive disorder (MDD), generalized anxiety disorders (GAD) and alcohol abuse, Héraclès study, France, 2014. Multilevel Poisson regression models

	MDD/GAD (n=1782)						Alcohol (n=1776)					
	Unadjusted			Adjusted			Unadjusted			Adjusted		
	RR[1]	CI 95%	P	RR[2]	CI 95%	P	RR[1]	CI 95%	P	RR[3]	CI 95%	P
Work intensity	**1.46**	**[1.35 - 1.57]**	**<0.01**	**1.16**	**[1.06 - 1.27]**	**<0.01**	**1.31**	**[1.14 - 1.50]**	**<0.01**	1.16	[0.97 - 1.38]	0.10
Emotional demands	**1.53**	**[1.43 - 1.64]**	**<0.01**	**1.24**	**[1.13 - 1.35]**	**<0.01**	**1.40**	**[1.23 - 1.59]**	**<0.01**	1.16	[0.97 - 1.38]	0.10
Autonomy	**0.68**	**[0.63 - 0.73]**	**<0.01**	0.94	[0.85 - 1.04]	0.26	**0.72**	**[0.63 - 0.83]**	**<0.01**	**0.82**	**[0.67 - 0.99]**	**0.05**
Conflict in values	**1.45**	**[1.35 - 1.56]**	**<0.01**	1.06	[0.96 - 1.17]	0.26	**1.30**	**[1.14 - 1.49]**	**<0.01**	1.16	[0.96 - 1.40]	0.13
Social relations at work	**0.61**	**[0.56 - 0.66]**	**<0.01**	**0.78**	**[0.70 - 0.87]**	**<0.01**	**0.83**	**[0.72 - 0.96]**	**0.01**	**1.25**	**[1.01 - 1.53]**	**0.03**
Job insecurity	**1.13**	**[1.05 - 1.22]**	**<0.01**	1.03	[0.95 - 1.11]	0.49	**1.14**	**[1.00 - 1.30]**	**0.05**	0.95	[0.82 - 1.11]	0.52

RR: relative risk
[1] No adjustment: each occupational factor are studied one at the time
[2] Adjusted on: each occupational factors, age, gender, occupational grade, previous mental health problems/disorders, alcohol abuse, material deprivation and GP's gender
[3] Adjusted on: each occupational factors, age, gender, occupational grade, family status, company size, previous mental health problems/disorders, job instability, education level, past unemployment, GAD and MDD
For MDD/GAD model explained variance was 0.21 and 0.11 for Alcohol model

4 DISCUSSION

4.1 Main results

In our study conducted among a large sample of persons consulting a GP, we found that several work characteristics are associated with mental health. Unfavourable social relations at work are associated with a higher risk of MDD/GAD, but a lower risk of alcohol abuse. High work intensity and high emotional demands at work are associated with a higher risk of MDD/GAD. Finally, low autonomy at work is associated with a higher risk of alcohol abuse.

4.2 Comparison with literature

We confirm, for the first time in primary care, the association between common mental disorders and social relations at work which was reported in other studies. A cross sectional study conducted in Japan (using the K10 questionnaire to assess depression) reported a higher risk of depressive symptoms among workers who receive low social support at work (OR=3.8)[53]. A meta-analysis of 17 studies investigating depressive disorders[54] found that low social support at work is also associated with anxiety disorders, as had already been observed in a study conducted by Wang *et al*.[55] However, the causal direction of this association cannot be determined due to the cross-sectional design of our study. It is possible that low social relations at work increases the risk of depression or anxiety, as has been shown in different longitudinal studies.[56] Moreover, social relations and support (outside or at work) affect psychological health,[57] but it is also possible that individuals who are not depressed or experiencing anxiety disorders receive better social support.[57] Finally, the association between GAD/MDD and social relations at work could also be related to negative visions of social relations among persons who are depressed or anxious.[58] For alcohol abuse, an inverse association with social relations was observed: higher risk associated with high social relations at work, which is consistent with results of a cross sectional study conducted among Canadian workers.[25] It raises the possibility of festive alcohol consumption with colleagues in or outside work.[59] We performed

sensitivity analyses by occupational group to explore this result and found that white collar workers were most likely to report alcohol abuse in case of high social relations at work (RR=1.89 [1.21 – 2.9]). Other studies have approached this subject by pointing out afterwork with colleagues.[60]

Work intensity, or high work time and intensity, is associated with depressive symptoms in the meta-analysis conducted by Theorell *et al* (10 studies).[54] The meta-analysis of longitudinal studies by Netterstrom *et al* highlights the adverse effects of high psychological demands on the occurrence of depressive disorders.[56] However, this association could also be due to distorted views of psychological demands among persons with depressive disorders.[58]

High emotional demands at work have previously been shown to predict depressive disorders among women in a population-based nested case-control study of 14,166 psychiatric patients conducted in Denmark (IRR=1.39)[26] or for GAD in a French prospective study (using the same diagnostic tool MINI) (RR=1.66 among workers with high emotional demand[22]). In our cross sectional study, the causal attribution is not possible, thus it is also possible that people with depression and/or anxiety have a different view towards those demands.[58]

Work autonomy appears related to alcohol abuse, as reported in an English prospective study: low decision latitude, which is a part of the autonomy axis in our study, is associated to higher risk of alcohol dependence within women.[61]

We did not confirm the association found earlier between CMD and high job insecurity or conflict in value.[21 22 24]

Overall, our study shows that work intensity and emotional demands are associated with GAD/MDD and social relations at work have a positive effect. For alcohol abuse, autonomy and social relations at work are negative risk factors.

4.3 Strengths and limitations of the study

Several limitations of our study should be acknowledged. First, our study was conducted in the Nord - Pas-de-Calais region, i.e. one of the poorest in France with a total of four millions inhabitants. During the first half of the 20th century, this region was highly industrialized and since the 1950s it has suffered from industrial decline as mines, as well as the textile and steel industries gradually closed.

Despite the growth of services and some specialized industries (car, rail and glass), levels of education, unemployment (15%), poverty and health indicators (e.g. life expectancy) are unfavourable. The Nord - Pas-de-Calais region has a low density of GPs (-11% than in France overall) and other medical specialities (-24%).[62] Moreover, the study was conducted after the 2008 recession, which has been associated with an increase in the prevalence of common mental health disorders worldwide.[63 64] This could lead to a high level of mental disorders. The prevalence of MDD, GAD and alcohol abuse among patients consulting a GP is respectively 19.1%, 25.8% and 9.7%. This is consistent with studies in primary care where the prevalence of CMDs ranges from 6% to 25% for depression, 3% to 25% for anxiety and 2% to 11% for alcohol abuse.[11 13 29-32] Results should be replicated in others areas. Second, a possible weakness is GPs' selective participation. GPs who participated in the study could be especially interested in common mental disorders. This interest may be related to the personal interest of the GP, but it could also be related to the GP's patients' rate of common mental disorders. Therefore, it may cause a larger selection of patients with psychological disorders. However, the study response rate is similar to previous studies among GPs[30 65] and physicians who participated were representative of the region, thereby limiting possible bias. In general practice, GPs' response rate is generally low[66], and in order to favour an optimal response rate, we tested the questionnaire to make it parsimonious, GPs were paid for their participation, and GPs who were asked to participate were individually called. A random procedure to select patients included in the study limited bias. Indeed, GPs were asked to include patients following an inclusion schedule that was provided at the start of the study. This allowed us to include patients in different time slots of the week. Moreover a non-respondent form had to be filled by participating GPs but we suppose that the filling rate was low because only 41 GPs filled this form and declare that 495 patient were not included. Characteristics of patients included and those not included did not differ in term of age and gender. However it is important to note that compared to studies in work environment settings, it is possible that patients included in this primary care setting have a different level of health than other employees who do not consult their GP. The measurement of psychosocial work factors in our study was based on an unpublished expert report based on the international literature, and measurement of reliability in our sample was rather low for some axis (ω=0.35 for conflict in values,

0.50 for job insecurity and 0.66 for autonomy). These dimensions are only composed of 2 items, this can explain partly the rather low reliability. However, the use of a validated questionnaire could have allowed for a better comparison with the existing literature and better psychometric quality.

We were able to take into account many covariates (characterizing individuals, GPs and patients' context), but some relevant variables were not included, such as participants' prior history of mental health problems, social support outside of work, or life events.

Despite these limitations, the results of this study are of interest because it identifies occupational factors related to CMD (MDD/GAD and alcohol abuse) among working adults in primary care with a standardized diagnostic tool (MINI) in a large sample (n=2,027).[37] The primary care sample used allows the inclusion of a panel of workers in the labour force including independent workers, workers in small companies or workers who don't have an occupational physician which is not the case in most of studies in occupational setting. Indeed, an international study including 49 countries shows that the average occupational health services coverage of workers was 24.8% with a larger gap among workers in small-scale enterprises, the self-employed, agriculture, and the informal sector.[67] Moreover, the present study confirms the increased risk of anxiety and depression associated with work intensity, social relations at work and emotional demands as well as the association between reduced autonomy and alcohol abuse in a primary care setting. Furthermore, we could demonstrate a negative association between social relations at work and alcohol abuse.[8 22 26 61]

4.4 Conclusion

Our study is one of the first to investigate simultaneously well-known occupational risk factors such as job strain and effort-reward imbalance and new occupational factors described in recent literature. Our results emphasise the importance of social relations at work and different occupational factors that are associated with MDD, GAD and alcohol abuse. These results could be a starting point for the GPs to apprehend these factors with their patients and to communicate with occupational physicians in order to prevent the onset of CMD.

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CONTRIBUTORS

Study concept and design: MR, NY, MM, AL, TB, LP. Data analysis and collection: MR, LFC, MM, LP. Drafting of the manuscript: MR. Critical revision of the manuscript: NY, MM, AL. All authors have approved the final manuscript.

COMPETING INTERESTS

All authors declare that they do not have any competing interests and declare independence from the funders.

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DATA SHARING STATEMENT

No additional data are available

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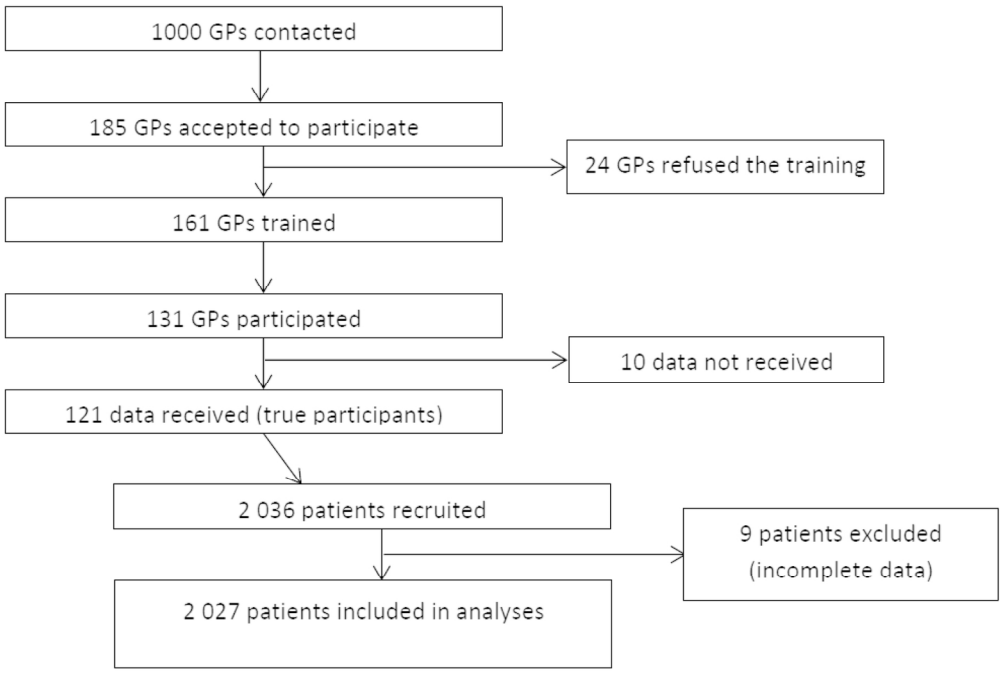
Legends:

Figure 1: Flow chart of participation in the Héraclès study, France, 2014



Flow chart of participation in the Heracles study, France, 2014

154x104mm (300 x 300 DPI)

Appendix 1: Work's factor questionnaire

1) **Work intensity**
   - I receive contradictory orders or indication ("Yes"/"No")
   - I am asked excessive amounts of work ("Always"/"Often"/"Sometimes"/"Never")
   - I have too much to think about at work ("Always"/"Often"/"Sometimes"/"Never")
   - I have difficulties in balancing work and family life ("Always"/"Often"/"Sometimes"/"Never")
   - I have the time needed to do my work ("Always"/"Often"/"Sometimes"/"Never")

2) **Emotional demands**
   - I work in contact with customers/beneficiaries ("Yes"/"No")
   - I am in contact with people in distress ("Yes"/"No")
   - I have conflicts with customers/beneficiaries ("Always"/"Often"/"Sometimes"/"Never")
   - I have to hide my emotions and pretend to be in a good mood ("Always"/"Often"/"Sometimes"/"Never")
   - I sometimes experience fear during my work ("Always"/"Often"/"Sometimes"/"Never")
   - During my work, I am exposed to physical, verbal, psychological aggressions ("Always"/"Often"/"Sometimes"/"Never")

3) **Autonomy**
   - I have very little freedom to decide how I do my job ("Always"/"Often"/"Sometimes"/"Never")
   - I can fully employ my skills ("Always"/"Often"/"Sometimes"/"Never")

4) **Conflict in values**
   - I have the possibility to make a work of quality ("Always"/"Often"/"Sometimes"/"Never")
   - In my work, I have to do disapproved things ("Always"/"Often"/"Sometimes"/"Never")

5) **Social relations at work**
   - My work is fully recognized ("Always"/"Often"/"Sometimes"/"Never")
   - I have support from colleagues ("Always"/"Often"/"Sometimes"/"Never")
   - I have support from superior ("Always"/"Often"/"Sometimes"/"Never")

6) **Insecurity of work**
   - I feel able to do my current job until retirement ("Yes"/"No")
   - I work with fear of losing my job ("Always"/"Often"/"Sometimes"/"Never")

Appendix 2: Correlation matrix of work characteristics, Héraclès study, France. 2014, Pearson correlation coefficient

	Work intensity	Emotional demands	Autonomy	Conflict in values	Social relations at work	Insecurity
Work intensity		0.70	-0.72	0.70	-0.81	0.08
Emotional demands	0.70		-0.86	0.78	-0.84	0.23
Autonomy	-0.72	-0.86		-0.91	0.87	-0.42
Conflict in values	0.70	0.78	-0.91		-0.91	0.17
Social relations at work	-0.81	-0.84	0.87	-0.91		-0.33
Insecurity	0.08	0.23	-0.42	0.17	-0.33	

Appendix 3: major depressive disorders **(**MDD), generalized anxiety disorders (GAD) and alcohol abuse related factors adjusted on work related factors, Héraclès study, France, 2014. Multilevel regression models

	MDD GAD (n=1782)			Alcohol (n=1776)		
	RR[1]	CI 95%	P	RR[1]	CI 95%	P
Age group			0.38			0.34
[18 - 35]	1	-		1	-	
[36 - 50]	1.13	[0.93 - 1.39]		1.29	[0.86 - 1.92]	
[51 - 65]	1.03	[0.82 - 1.29]		1.37	[0.87 - 2.16]	
Gender			0.34			<0.01
Male	1	-		1	-	
Female	1.09	[0.91 - 1.31]		0.37	[0.25 - 0.53]	
Past unemployment						0.13
No				1	-	
Yes				1.30	[0.93 - 1.83]	
Occupational grade			0.71			0.09
Blue collar	1	-		1	-	
Pink collar	1.12	[0.86 - 1.46]		0.61	[0.39 - 0.98]	
White collar	1.11	[0.82 - 1.5]		0.80	[0.46 - 1.4]	
Family status						0.11
Lives alone				1	-	
Lives with partner or parents				1.34	[0.94 - 1.9]	
Educational level						0.51
< High school degree				1	-	
≥ High school degree				1.14	[0.77 - 1.7]	
Job instability						0.21
No				1	-	
Yes				1.31	[0.86 - 1.98]	
Company size						0.02
1 to 10				1	-	
11 to 49				0.70	[0.45 - 1.09]	
50 to 250				0.83	[0.52 - 1.3]	
250 +				0.49	[0.31 - 0.78]	
Past psychiaric problems			<0.01			0.02
No	1	-		1	-	
Yes	1.58	[1.27 - 1.96]		1.65	[1.07 - 2.55]	
Major depressive disorders						0.01
No				1	-	
Yes				1.66	[1.12 - 2.44]	
Generalized anxiety disorders						0.25
No				1	-	
Yes				1.24	[0.86 - 1.8]	
Alcohol			0.01			
No	1	-				
Yes	1.38	[1.09 - 1.75]				
Material deprivation			0.04			
No	1	-				
Yes	1.19	[1.01 - 1.4]				
GPs Gender			0.02			
Male	1	-				
Female	1.22	[1.03 - 1.44]				

RR : relative risk

[1] Adjusted on: Work intensity, Emotional demands, Autonomy, Conflict in values, Social relations at work, Insecurity

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **page 1 and 2**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found - **page 1 and 2**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **page 4 - 6**
Objectives	3	State specific objectives, including any prespecified hypotheses - **page 4 - 6**
Methods		
Study design	4	Present key elements of study design early in the paper - **page 7**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection - **page 7**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants - **page 7**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable – **page 8 to 10**
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 - **page 8 to 10**
Bias	9	Describe any efforts to address potential sources of bias – **page 6**
Study size	10	Explain how the study size was arrived at – **page 6**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why – **page 10 and 11**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **page 10 and 11**
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
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 – **page 12 and figure 1**
		(b) Give reasons for non-participation at each stage – **figure 1**
		(c) Consider use of a flow diagram – **figure 1**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders – **page 12 to 14**
		(b) Indicate number of participants with missing data for each variable of interest
Outcome data	15*	Report numbers of outcome events or summary measures – **page 15**
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 – **page 15 to 19**
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a

		meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives – **page 20**
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 – **page 21 to 23**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence – **page 21 to 23**
Generalisability	21	Discuss the generalisability (external validity) of the study results – **page 20 and 21**
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 – **page 24**

*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 www.strobe-statement.org.