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Adverse employment histories and allostatic load: associations over the working life

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ABSTRACT

Background Most studies on the health impact of occupational stress use single-point measures of stress at work. This study analyses the associations of properties of entire employment trajectories over an extended time period with a composite score of allostatic load (AL).

Methods Data come from the French CONSTANCES cohort, with information on adverse employment histories between ages 25 and 45 and a composite score of AL (based on 10 biomarkers, range 0–10) among people aged 45 or older (47 680 women and 45 035 men). Data were collected by questionnaires (including retrospective employment histories) or by health examinations (including blood-based biomarkers). We distinguish six career characteristics: number of temporary jobs, number of job changes, number of unemployment periods, years out of work, mode occupational position and lack of job promotion.

Results For both men and women, results of negative binomial regressions indicate that adverse employment histories are related to higher levels of AL, particularly histories that are characterised by a continued disadvantaged occupational position, repeated periods of unemployment or years out of work. Findings are adjusted for partnership, age and education, and respondents with a health-related career interruption or early retirement are excluded.

Conclusions Our study highlights physiological responses as a mechanism through which chronic stress during working life is linked to poor health and calls for intervention efforts among more disadvantaged groups at early stages of labour market participation.

that are most likely to activate bodily stress reaction, such as jobs characterised by high demands and limited opportunities of exercising control and autonomy (the demand control model³), or jobs where workers receive limited rewards and recognition for invested efforts (the effort-reward imbalance model⁴). Several studies have reported associations of work stress (as measured by the two work stress models) with AL, either assessed by single indicators or composite AL scores.^{5–7}

However, these work stress models focus on a typical work environment and assume a long-lasting full-time employment characterises a person's main or continuous job. They neither include information on the chronicity of exposure nor on the cumulative and repeated experience of stress in different jobs, thus disregarding intraindividual changes of working and employment conditions over time.⁸ In fact, as an example, a recent study highlights that the accumulation of work-related stress is linked to a higher level of AL.⁹ Therefore, these theoretical notions need to be extended by shifting the analytical perspective from stable to dynamic work arrangements, considering entire trajectories and their properties over an extended time period. This shift is further justified by profound changes of working life due to economic globalisation and technological transformation, resulting in a growing proportion of employment relations that are characterised by flexibility, instability and insecurity.¹⁰ Extending research along these lines corresponds to a life course perspective,¹¹ specifically, the idea of considering employment histories that cover an extended time frame.⁸

With the increasing availability of retrospective information from occupational cohort studies collecting data on exposure duration, timing and its sequential character over time (including job changes and periods of unemployment), this analytical shift can now be applied.^{12–15} In this context, a typology of health-adverse employment histories has been proposed with a distinction between precarious careers (eg, temporary contracts and frequent job changes), discontinuous careers (eg, unemployment interruptions) and disadvantaged working careers (eg, cumulative disadvantaged occupational positions or downward mobility).¹⁶ As in the case of the work stress models mentioned previously, these types of employment histories involve—although to a different extent—recurrent threats to, or loss of important psychosocial needs of working persons, such as job security and continuity,¹⁷ control and autonomy,^{3 18} and fairness and

INTRODUCTION

The concept of allostatic load (AL) has been used to understand the potential biological pathways between exposure to recurrent or long-lasting stressors and the development of stress-associated disorders.¹ AL refers to the cumulative burden of adaptive physiological responses to stressors or environmental threats that result in a dysregulation of bodily response patterns and functional impairment of different organ systems (including cardiovascular, metabolic and immune systems). Multiple epidemiological studies have documented its relevance when studying social determinants of health, where the concept of AL helped to understand health consequences of adverse psychosocial conditions.² Adverse psychosocial conditions at work define one such condition and are usually measured according to theoretical models of work stress. These models help to identify conditions at work



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reward.^{4 19} It is therefore likely that working under these circumstances promotes the initiation and progression of disease later on.²⁰

Along these lines, this paper analyses associations between properties of entire employment trajectories between ages 25 and 45, and a composite score of AL. In doing so, we extend current knowledge in two ways: first, building on previous evidence on relationships between psychosocial stress at work and AL, we examine whether this association holds true when assessing entire working careers and their properties over an extended time period rather than static working conditions. Second, with an emphasis on AL, this study elucidates pathways from a chronically adverse work environment to a stress-associated disease development.

METHODS

Data source

Our study uses latest data from the French CONSTANCES project,²¹ a population-based cohort study that relies on a random sample of people aged 18–69 years that are insured by the French General Health Insurance Fund (85% of the French population). This covers all salaried workers, professionally active or retired and their family, as well as self-employed and agricultural workers that are insured through a family member. The baseline data collection takes place in 22 national health screening centres and started in 2012 until early 2020, with currently more than 217 000 participants. Data in this study were collected by self-administered questionnaires (including retrospective information on employment histories) and as part of a clinical health examination at baseline (including biomarkers of AL and blood samples). For this study, baseline data are available for 186 501 participants (aged 18–73 years at baseline) with baseline assessment between 2012 and 2019.

Study population

Our study relies on a subsample of 96 193 men and women aged 45 or older who worked at least once between age 25 and 45 (and thus had employment histories with potential change or stability). Then, to address potential reversed causality (with ill health causing specific employment histories), we exclude people with a health-related career interruption prior to age 45 (3.4% of the initial sample, 3235 participants), and respondents who retired prior to age 45 (probably due to health-reasons) are not included either (additional 243 participants). This results in a final study sample of 92 715 participants (47 680 women and 45 035 men). Details on sample selection are summarised as flowchart in the supplementary material (online supplemental figure 1).

Measures

Adverse employment histories

CONSTANCES provides retrospective information on each job respondents had (including contract type, occupational position, begin and end) and on potential career interruptions that lasted 6 months or longer (eg, health and unemployment). Combining these data allow us to rearrange the data into a state sequence format, where the data contain a variable that describes the occupational situation for each age between 25 and 45 (covering 21 years). On this basis, we ascertained the following six career characteristics—all referring to employment histories between age 25 and 45: (1) number of jobs with temporary contract (per 10 years in paid work) and (2) number of job changes (per 10 years in paid work) as available indicators of

‘precarious careers’, (3) number of unemployment interruptions and (4) years out of work as available indicators of ‘involuntary interruptions’, and (5) the mode occupational position between age 25 and 45 and (6) lack of job promotion as indicators of ‘cumulative disadvantages’. The mode occupational position is based on the longest held job (or the most recent in case of two-mode jobs) and measured with seven categories according to the European Socio-Economic Classification scheme.²² Self-employed and agricultural workers were grouped into one class, as well as higher-grade blue collar workers and higher-grade white collars (because of small numbers resulting from the sample strategy). Lack of promotion was measured in terms of ‘no promotion’ or ‘failed promotion’ (ie, upward and downward mobility processes). Unemployment interruptions measure the number of interruptions due to unemployment. Years out of work counts the number of years without paid work (three categories). Finally, since number of temporary jobs and number of job changes may depend on years in paid work, we calculated the respective numbers per 10 years in paid work (eg, number of temporary jobs/years with paid work×10) that we regrouped into three categories. Table 1 shows details for each variable (including information on missing values).

Allostatic load

AL is measured with an index based on 10 biomarkers from the baseline clinical examination. These biomarkers cover four systems involved in AL²³: the cardiovascular and pulmonary systems (systolic blood pressure, diastolic blood pressure and lung function); the anthropometric system (waist to hip ratio); the metabolic system (fasting glycoses, ratio of total cholesterol (TC) to high-density lipoprotein (HDL) cholesterol (TC:HDL), triglycerides (TGs), low-density lipoproteins and creatinine clearance rate (CCR); and the immune and inflammatory system (white blood cell (WBC) counts). Lung function is based on the ratio of forced expiratory volume in 1 s to forced vital capacity (FEV₁:FVC), measured with a standard handheld Vitalograph spirometer using the highest of three measurements. For calculating the CCR, we used the Cockcroft and Gault formula.²⁴ The six blood-based biomarkers were considered valid if participants had been fasting for at least 8 hours. To create the index, we followed the common procedure,² and created a count-based summary measure of AL that ranges from 0 to 10, based on sex-specific high-risk quartiles for each biomarker (each coded 0 for ‘not at risk’ and 1 for ‘at risk’). Lowest quartiles were used for CCR and FEV₁:FVC (where low values indicated high AL) and the highest quartiles in all remaining cases (where high values indicated high AL). To contribute to the overall AL-index, participants had to have information for at least one biomarker of each one of the four systems covered, and in case participants still had missing values for single biomarkers, they were considered not at risk (‘0’). Hence, only respondents who had no information for one or more dimensions were excluded from the analysis (3418 participants, less than 4% of the final sample). This strategy makes maximum use of available data and guarantees that people still contribute in case information is available for the four systems while adopting a conservative approach of handling missing values. Details on each biomarker, with summary measures, number of observations and sex-specific cut-off points, are presented in table 2, and the online supplemental material includes information on its application (online supplemental table 1).

Additional variables

Alongside sex and age, we also included a variable measuring at which screening centre the data were collected, partnership

Table 1 Sample description: observations (number) and percentage (col %) or mean and SD, by sex (n=92 715)

	Categories or range	Women		Men	
		Number	Col % or mean (SD)	Number	Col % or mean (SD)
Age (years)	45–73	47 680	57.20 (7.26)	45 035	57.63 (7.35)
Partnership*	Living with partner	33 476	71.5	36 151	81.8
	Living as single	13 368	28.5	8045	18.2
Education†	Low	5692	12.1	4856	11.0
	Medium	16 980	36.2	18 410	41.7
	High	24 188	51.6	20 864	47.3
Current work situation	In paid work	26 877	56.4	24 706	54.9
	Not in paid work	20 803	43.6	20 329	45.1
Temporary jobs (per 10 years in paid work)	No temporary job	39 569	83.0	39 544	87.8
	One or less temporary job	5900	12.4	4690	10.4
	More than one temporary job	2211	4.6	801	1.8
Job changes (per 10 years in paid work)	No change	17 303	36.3	13 694	30.4
	Two or less changes	23 522	49.3	26 481	58.8
	More than two changes	6855	14.4	4860	10.8
Number of unemployed periods	No unemployment period	40 857	85.7	40 533	90.0
	One unemployment period	5439	11.4	3623	8.0
	2+ unemployment periods	1384	2.9	879	2.0
Years out of work	No years out of work	23 530	49.3	30 768	68.3
	1–5 years out of work	12 104	25.4	10 327	22.9
	6+ years out of work	12 046	25.3	3940	8.7
Mode occupational position	Large employers, higher managers and professionals	3823	8.0	7168	15.9
	Lower managers and professionals	16 920	35.5	9381	20.8
	Intermediate employee	11 646	24.4	7184	16.0
	Small employers and self-employed	744	1.6	1114	2.5
	Lower-grade white collar workers	4207	8.8	1190	2.6
	Skilled workers	757	1.6	5406	12.0
	Semiskilled or unskilled workers	1815	3.8	3111	6.9
	Main position unknown	7768	16.3	10 481	23.3
Lack of promotion	Promotion	7334	15.4	9119	20.2
	No promotion	39 243	82.3	34 361	76.3
	Failed promotion	1103	2.3	1555	3.5
AL index‡	0–10	45 858	2.35 (1.75)	43 439	2.38 (1.71)

*1675 participants had missing values for partnership (1.8%).
†1725 participants had missing values for education (1.9%).
‡Based on measurement approach, 3418 participants had missing values for AL index (3.7%).
AL, allostatic load.

situation (regardless of marital status), labour market status (in paid work or not) and participants' educational level. The latter is measured according to the International Standard Classification

of Educational Degrees (ISCED) 2011 that we regroup into 'low' (preprimary, primary or lower secondary education, ISCED 0–2), 'medium' (upper secondary or post-secondary education,

Table 2 Distribution of the allostatic load biomarkers

Biological system	Biomarker	Unit	Mean	SD	Number	Cut-off Men	Cut-off Women
Cardiovascular and pulmonary system	Systolic blood pressure	mm Hg	132.37	17.20	90 234	>146	>138
	Diastolic blood pressure	mm Hg	78.54	9.86	90 234	>87	>82
	FEV ₁ /FVC		0.79	0.07	66 891	<0.75	<0.76
Anthropometric system	Waist to hip ratio	waist (cm)/hip (cm)	0.88	0.09	91 853	>0.99	>0.87
Metabolic system	Fasting glucose	mmol/L	5.52	0.94	89 223	>5.99	>5.56
	Total cholesterol to HDL ratio		4.01	1.48	87 732	>4.92	>4.11
	Triglyceride	mmol/L	1.21	0.74	89 041	>1.59	>1.27
	Low-density lipoprotein	mmol/L	3.66	0.93	87 624	>4.20	>4.27
	Creatinine clearance rate	Creatinine (μmol/L)	93.02	24.02	89 284	<83.87	<71.08
Immune and inflammatory system	White blood cell counts	Counts (cell 10 ⁹ /L)	6.06	1.66	90 738	>6.90	>6.80

FEV₁/FVC, ratio of forced expiratory volume in 1 s to forced vital capacity; HDL, high-density lipoprotein.

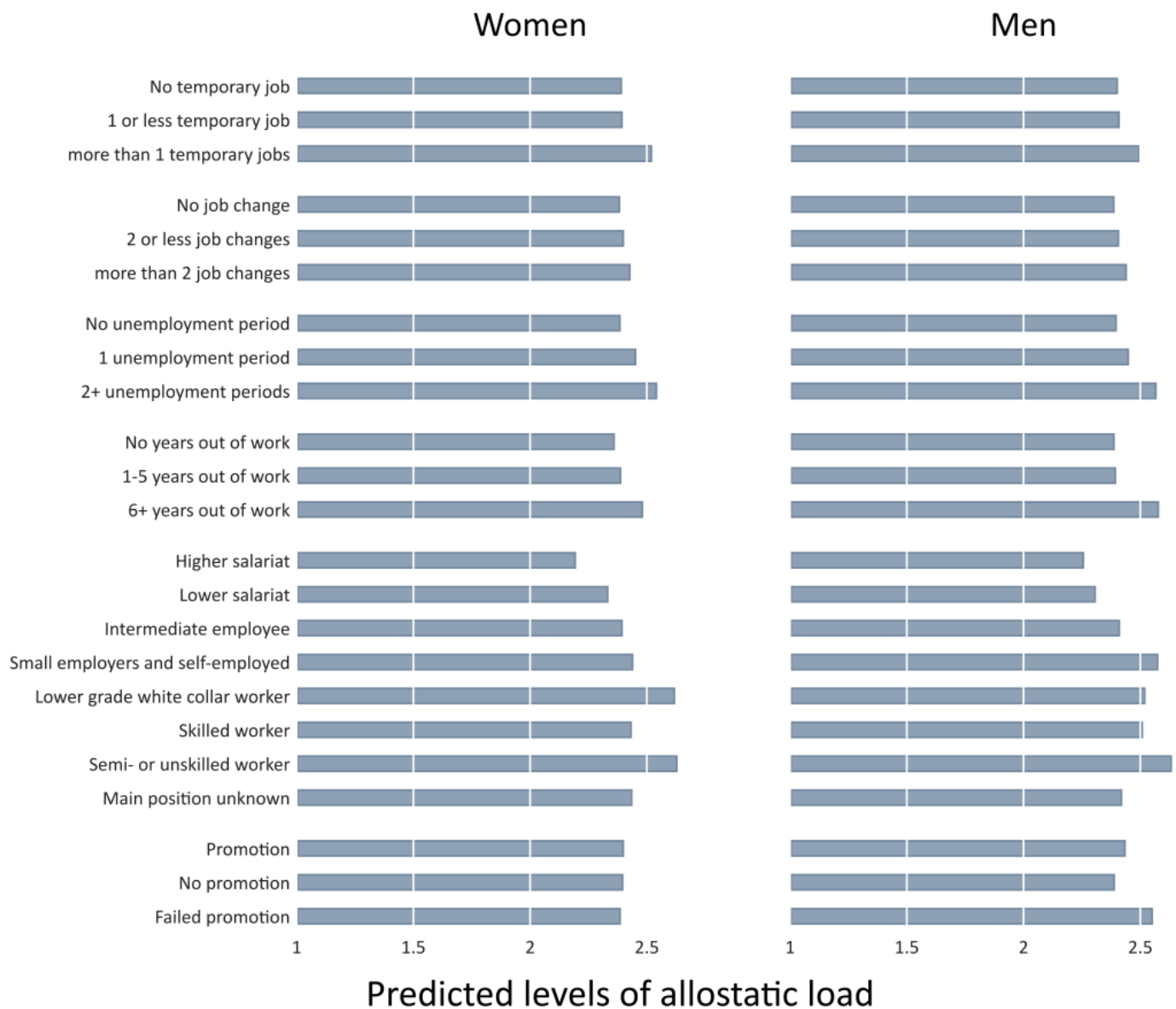


Figure 1 Predicted levels of allostatic load by adverse employment histories, estimated from coefficients of model 1 in tables 3 and 4. Number of temporary jobs and number of job changes are numbers per 10 years in paid work.

ISCED 3–4) and ‘high’ (first and second stage of tertiary education, ISCED 5 or higher).

Analytical strategy

All analyses are conducted for men and women separately, and we started with a sample description and pairwise correlations of all components of AL index. We then estimated a series of mixed regression models (multilevel models with individuals nested in screening centres) to study associations between the career characteristics and the AL index. Specifically, as the AL index was overdispersed (variance greater than the mean), we applied mixed effects negative binomial models for count data (number of AL risk indicators).²⁵ Because the number of missing data was small (see table 1 for details), we conducted complete case analyses. The Results section presents estimated coefficients together with CIs (95%) and p values. Furthermore, since coefficients are difficult to interpret, we also show average marginal effects (AMEs) and summarise predicted levels of AL (average adjusted predictions) in figure 1. More specifically, we applied the ‘margins’ procedure in Stata,²⁶ where the average adjusted

predictions of levels of AL are calculated for each category of the career characteristics (based on our regression models). AMEs then represent the difference in adjusted predictions to the reference group. We report estimates of two models. Model 1 is calculated for each career characteristic separately and is adjusted for potential confounders age (linear and squared because of non-linear association), education and partnership (both included as categorical variable). Model 2 includes all career characteristics simultaneously (with same adjustments). As such, model 1 allows evaluation of the total effect of each characteristic on AL, and model 2 helps to explore which of the career characteristics may still have a direct effect after conditioning for the remaining characteristics, that is, the partial effect after removing contributions through other career characteristics.²⁷ We also report results of linear multilevel regression models for each AL biomarker (with same adjustments as in model 1, presented in online supplemental tables 4 and 5). In these models, outcomes were log-transformed in case of skewness (ie, WBC counts, blood sugar levels, ratio of total to HDL cholesterol, TGs and lung function) and standardised to enable comparisons.

Table 3 Association between career characteristics and AL index for women (n=44 786): negative binomial regression coefficients (β), CIs, p values and AMEs

		Model 1				Model 2			
		β	CI (95%)	P value	AME	β	CI (95%)	P value	AME
Temporary jobs (per 10 years in paid work)	No temporary job (ref.)	–				–			
	One or less temporary job	0.001	(–0.020 to 0.022)	0.916	0.027	–0.001	(–0.023 to 0.020)	0.913	–0.003
	More than one temporary job	0.052	(0.021 to 0.084)	0.001	0.129	0.025	(–0.009 to 0.059)	0.147	0.061
Job changes (per 10 years in paid work)	No change (ref.)	–				–			
	Two or less changes	0.007	(–0.007 to 0.021)	0.341	0.017	0.000	(–0.015 to 0.016)	0.976	0.001
	More than two changes	0.019	(–0.002 to 0.040)	0.084	0.045	–0.021	(–0.046 to 0.005)	0.116	–0.049
Number of unemployment periods	No unemployment period (ref.)	–				–			
	One unemployment period	0.028	(0.007 to 0.048)	0.009	0.067	0.016	(–0.007 to 0.038)	0.179	0.037
	2+ unemployment periods	0.063	(0.024 to 0.103)	<0.001	0.157	0.044	(0.003 to 0.085)	0.036	0.108
Years out of work	No years out of work (ref.)	–				–			
	1–5 years out of work	0.012	(–0.004 to 0.028)	0.153	0.028	0.003	(–0.015 to 0.020)	0.758	0.007
	6+ years out of work	0.050	(0.034 to 0.066)	<0.001	0.121	0.032	(0.014 to 0.051)	0.001	0.077
Mode occupational position	Large employers to higher managers and professionals (ref.)	–				–			
	Lower managers and professionals	0.061	(0.034 to 0.089)	<0.001	0.139	0.062	(0.034 to 0.090)	<0.001	0.141
	Intermediate employee	0.087	(0.057 to 0.117)	<0.001	0.200	0.083	(0.052 to 0.113)	<0.001	0.190
	Small employers and self-employed	0.106	(0.049 to 0.163)	<0.001	0.245	0.100	(0.044 to 0.157)	0.001	0.233
	Lower grade white collar workers	0.177	(0.141 to 0.212)	<0.001	0.425	0.165	(0.129 to 0.201)	<0.001	0.396
	Skilled workers	0.103	(0.046 to 0.161)	<0.001	0.239	0.098	(0.040 to 0.156)	0.001	0.227
	Semiskilled or unskilled workers	0.181	(0.138 to 0.224)	<0.001	0.435	0.172	(0.129 to 0.215)	<0.001	0.413
	Main position unknown	0.104	(0.074 to 0.135)	<0.001	0.241	0.101	(0.070 to 0.132)	<0.001	0.234
Lack of promotion	Promotion (ref.)	–				–			
	No promotion	–0.001	(–0.020 to 0.017)	0.888	–0.003	–0.003	(–0.023 to 0.016)	0.739	–0.008
	Failed promotion	–0.006	(–0.053 to 0.042)	0.815	–0.014	–0.017	(–0.066 to 0.031)	0.478	–0.042

Note: All models are based on multilevel models (individuals nested in health examination centre, adjusted for age, age square, partnership situation and education) (complete case analyses). Model 1 is calculated for each career characteristic separately (separate models). Model 2 includes all career characteristics simultaneously (simultaneous model). Respondents who retired or had a health-related career interruption prior to age 45 are excluded from the analyses. AL, allostatic load; AME, average marginal effect; ref., reference.

As part of sensitivity analyses, models were recalculated with adjustments of reported health conditions at the time of the AL measurement (body mass index (BMI) (linear) and activity limitations (Global Activity Limitation Instrument). All calculations and graphs are produced with Stata V.16.1.

RESULTS

Table 1 shows that the sample consists of slightly less men than women (45 035 men vs 47 680 women), with an average age of 57 years for both sexes and the majority in paid work. When comparing employment histories between men and women, we see that men had spent more years in paid work, had fewer temporary jobs and worked in more advantaged occupational positions. Based on our definition of the AL index, we see that scores were similar between sexes, with less than 4% of missing values and a mean score of 2.35 for women and 2.37 for men (representing the average times of having a high-risk group profile across all biomarkers). For less than 2% of observations, information on partnership or education was missing. Correlations between all biomarkers of AL (presented in online supplemental table 2) were generally low in all cases, with highest values between two measures of the metabolic system (ratio of total to HDL cholesterol and TGs).

Results of our main research question are presented in table 3 for women and in table 4 for men, with four findings worth noting. First, we see that men and women who mainly worked in a disadvantaged occupational position have a higher AL score with p values providing strong evidence against the null

hypothesis. For example, the AMEs of model 1 (representing the difference in predicted AL scores) indicate that women who mainly worked as semiskilled or unskilled workers have a 0.43 higher score compared with managers and professionals (for men 0.38 higher). Likewise, women and men who had two or more unemployment periods have higher scores compared with those without unemployment period (0.16 higher for women and 0.17 higher for men), as well as those who were out of the labour market for 6 or more years (women: 0.12, men: 0.19 higher than continuously working). Second, focussing on men, we also see that men who reported failed promotion had slightly higher AL scores (0.12 higher scores), and, focussing on women, we found that a higher number of temporary jobs (per 10 years in paid work) was related to higher scores (0.13 higher scores). Third, we found no clear associations for men and women who had frequent job changes. Fourth, when comparing results between model 1 and model 2, findings remain consistent (with the only exception of unemployment in case of men), thus suggesting that the reported associations are probably independently related to AL, even after conditioning for the remaining career characteristics.

Findings also remain consistent in sensitivity analyses that additionally adjusted for BMI and activity limitations (online supplemental table 3). In addition, when estimating the associations between career characteristics and each AL biomarker separately (online supplemental tables 4 and 5 and figure 2), we found that associations were similar for most of the biomarkers except of CCR, where associations were not in the expected direction.

Table 4 Association between career characteristics and AL index for men (n=42 386): negative binomial regression coefficients (β), confidence intervals, p values and AMEs

		Model 1				Model 2			
		β	CI (95%)	P value	AME	β	CI (95%)	P value	AME
Temporary jobs (per 10 years in paid work)	No temporary job (ref.)	–				–			
	One or less temporary job	0.003	(–0.020 to 0.026)	0.785	0.008	0.000	(–0.023 to 0.023)	0.972	0.001
	More than one temporary job	0.038	(–0.014 to 0.090)	0.149	–0.094	–0.009	(–0.064 to 0.046)	0.758	–0.021
Job changes (per 10 years in paid work)	No change (ref.)	–				–			
	Two or less changes	0.008	(–0.006 to 0.023)	0.272	0.020	–0.006	(–0.022 to 0.011)	0.500	–0.013
	More than two changes	0.022	(–0.003 to 0.046)	0.080	0.053	–0.030	(–0.059 to –0.001)	0.039	–0.073
Number of unemployment periods	No unemployment period (ref.)	–				–			
	One unemployment period	0.022	(–0.003 to 0.046)	0.083	0.053	0.008	(–0.020 to 0.037)	0.554	0.020
	2+ unemployment periods	0.069	(0.021 to 0.117)	0.005	0.171	0.031	(–0.020 to 0.083)	0.228	0.077
Years out of work	No years out of work (ref.)	–				–			
	1–5 years out of work	0.003	(–0.014 to 0.019)	0.763	0.006	0.001	(–0.019 to 0.020)	0.948	0.002
	6+ years out of work	0.077	(0.052 to 0.101)	<0.001	0.190	0.071	(0.043 to 0.098)	<0.001	0.175
Mode occupational position	Large employers to higher managers and professionals (ref.)	–				–			
	Lower managers and professionals	0.022	(–0.001 to 0.045)	0.060	0.050	0.023	(–0.001 to 0.046)	0.056	0.052
	Intermediate employee	0.066	(0.040 to 0.091)	<0.001	0.154	0.066	(0.040 to 0.091)	<0.001	0.154
	Small employers and self-employed	0.132	(0.088 to 0.176)	<0.001	0.318	0.122	(0.078 to 0.166)	<0.001	0.293
	Lower-grade white collar workers	0.110	(0.065 to 0.156)	<0.001	0.263	0.101	(0.055 to 0.146)	<0.001	0.239
	Skilled workers	0.106	(0.077 to 0.134)	<0.001	0.252	0.106	(0.078 to 0.135)	<0.001	0.253
	Semiskilled or unskilled workers	0.154	(0.121 to 0.187)	<0.001	0.376	0.152	(0.119 to 0.185)	<0.001	0.370
	Main position unknown	0.070	(0.047 to 0.093)	<0.001	0.163	0.076	(0.053 to 0.100)	<0.001	0.179
Lack of promotion	Promotion (ref.)	–				–			
	No promotion	–0.019	(–0.036 to –0.003)	0.023	–0.046	–0.034	(–0.052 to –0.016)	<0.001	–0.082
	Failed promotion	0.047	(0.009 to 0.084)	0.016	0.116	0.033	(–0.005 to 0.072)	0.092	0.083

Note: All models are based on multilevel models (individuals nested in health examination centre, adjusted for age, age square, partnership situation and education) (complete case analyses). Model 1 is calculated for each career characteristic separately (separate models). Model 2 includes all career characteristics simultaneously (simultaneous model). Respondents who retired or had a health-related career interruption prior to age 45 are excluded from the analyses. AL, allostatic load; AME, average marginal effect; ref., reference.

To summarise the main findings, [figure 1](#) presents the predicted levels of AL for each category of the career characteristics (as based on model 1 from the regression models), showing again that levels of AL are particularly high for men and women with a continuous disadvantaged occupational position, with repeated periods of unemployment and with years out of work.

DISCUSSION

This study provides some evidence that adverse employment histories over an extended time period (between age 25 and 45) are related to higher levels of AL beyond age 45, particularly histories that are characterised by a continued disadvantaged occupational position and discontinuous careers that are characterised by repeated periods of unemployment or years out of work. This adds to current knowledge by extending concepts of occupational stress and suggesting that cumulative disadvantage and disruptive elements of employment histories are linked to chronic stress reactions and related physiological processes that lead to a state of AL. Also, by conducting separate analyses for men and women—a distinction that has often been neglected in previous studies²⁸—we find that associations were similar for men and women. In addition, findings remained stable after adjusting for partnership history, age and education, as well as after excluding respondents with a health-related career interruption or early retirement, as well as when all career characteristics were included simultaneously into a model (supporting an association with AL that is independent of the remaining characteristics). However, we also found that some of the studied

career characteristics were not clearly related to AL, including the number of temporary jobs for men and the number job changes for both sexes.

Overall, the observed associations for disadvantaged and discontinuous careers are in line with studies that investigated repeated exposure to job insecurity or stress at work in conjunction with health.^{9 29 30} Findings also correspond to studies on health consequences of continuously disadvantaged socioeconomic positions.^{31 32} Yet, by specifying adverse characteristics of employment histories over an extended time period of the life course (between 25 and 45), this study adds to existing research. Specifically, we confirm the importance of extending the rather static concepts of stressful work that received main attention in recent research on this topic and of studying the burden of work-related disease in a life course perspective.^{8 20} Our study also illustrates the usefulness of a theory-driven approach that specifies adverse characteristics of employment histories based on the notion of recurrent threats to important psychosocial needs of working persons (ie, job security,¹⁷ control^{3 18} and reward^{4 19}). The notion of ‘employment strain’ represents a similar approach towards assessing chronic adversity at work (with a focus on threats to control and autonomy at work³³). Its association with health, though, still needs more empirical research.

The observed differences in associations of the career characteristics under study with AL deserve further methodological as well as conceptual discussion. With regard to measurement, our way of assessing frequency of job changes as an indicator of precarious employment possibly failed to distinguish between

involuntary and voluntary (and potentially health-beneficial) changes. Likewise, the nature of temporary jobs may be different for men and women, and future analyses may incorporate information on employment status (eg, self-employed or not), or more information on reasons for not working may be important as well (eg, information on interruptions due to home or family work or because of education). Similarly, in the case of failed promotion, the used categories may also be refined and include information on the class of origin and of destination. At the conceptual level, our finding that AL was associated rather consistently with indicators of career discontinuity (ie, periods of unemployment or years out of work) raises the question whether career discontinuity elicits a particularly high intensity and perseverance of stressful experience due to its disruptive nature. This, in fact, corresponds to earlier research on health impacts of negative life events, suggesting that the extent to which a disruptive event threatens a person's routines of everyday life matters most for stress.^{34 35}

Furthermore, our composite score of AL differs to some extent from previous studies, although a standard measure of AL has not yet been established.³⁶ Given the restrictions of available data, it includes quite a comprehensive set of indicators representing subclinical (or secondary) aspects, but it contains only a reduced representation of autonomic nervous system, cardiovascular and immune (or primary) parameters. Nevertheless, the fact that associations of employment characteristics with single AL indicators by and large follow the patterns observed for the composite score supports the usefulness of our measure. It also suggests that adverse employment histories are linked to poorer biomarker levels across the four systems involved in AL (see online supplemental tables 4 and 5). The only exception was observed in case of CCR—a finding that is not in line with research supporting socioeconomic inequalities in kidney function,³⁷ but that nevertheless corresponds to a previous study that also used CONSTANCES data.⁷ This finding needs additional exploration. In addition, although we followed the most common approach by using high-risk quartiles for each AL biomarker,² we may have adopted alternative methods of calculating the AL index, for example, based on clinical cut-points for some of the biomarkers. This, however, may result in greater weight to some components than others, while the relative importance of different AL biomarkers in the stress response remains an open question.

The study has several limitations. First, the core measures of our study, career characteristics between ages 25 and 45 years, were collected retrospectively. We thus need to consider a potential recall bias, with a tendency to reduce complexity or to under-report unfavourable events.³⁸ Compared with prospective data collection though, our retrospective data make sure that information (referring to different time points) are comparable throughout time, and they do not produce missing data due to panel attrition. There is also increasing support that retrospective data, in particular when asking about sociodemographic conditions and employment histories,^{39 40} provide reliable and valid information. Second, although information on employment histories refers to previous life stages, far-reaching conclusions on a causal association are not possible for at least two reasons. First, we again need to consider potential selection into adverse employment histories, where people with poor health are more likely to have adverse careers. We addressed this issue by excluding people with poor health before and during the observation period, but we still cannot fully exclude this selection. Second, while we included a number of potential confounders into the analyses (ie, age, partnership and education), we cannot

rule out that other aspects (eg, conditions of material deprivation in early life) act as potential confounders, as well as potential confounding through unobserved factors remains an issue in our observational study. Another limitation relates to the generalisation of results. While our sample represents a large fraction of the French labour market, people who were self-employed are under-represented because of the sample strategy. Since this group of workers is likely to have less continuous and more insecure careers (eg, due to the expansion of independent contracting⁴¹ and the gig economy⁴²), the strength of associations observed in our study may be underestimated.

In conclusion, our study builds on and extends existing research on the impact of psychosocial stress at work on health by analysing adverse employment histories and their properties over an extended time period and their associations with biomarkers of AL. This underlines the importance of physiological responses as a key mechanism through which chronic stress at work is linked to poor health and disease development. Our findings point to a potentially beneficial role of promoting healthy working and employment conditions, particularly among more disadvantaged groups of the labour market in early stages of labour market participation.

What is already known on this subject

⇒ Previous studies have linked single-point measures of psychosocial stress at work to allostatic load (AL), but current changes in working life necessitate the extensions of concepts of occupational stress by investigating properties of entire employment histories in relation to biomarkers of physiological systems.

What this study adds

⇒ This study adds to current knowledge by suggesting that cumulative disadvantage and discontinuous careers over the course of an extended time period are linked to chronic stress reactions and related physiological processes that lead to a state of AL for both men and women.

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Contributors All authors (MW, TC, MG, MZ, HH and JS) have contributed as follows: MG and MZ designed the study, including quality assurance and control, and helped supervise the field activities and provided the data. MW, TC and JS developed the study's analytical strategy and the conceptual frame of the study. HH helped to conduct the literature review and assisted in the data analyses. MW had the main responsibility for data management and analyses, and drafted the first version of the manuscript. All authors critically reviewed the first draft of the manuscript and approved its submission.

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à la Santé and Commission Nationale Informatique et Liberté), and participants signed an informed consent.

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Data availability statement Data may be obtained from a third party and are not publicly available. Access to raw data requires the submission of a research project, that is examined by the CONSTANCES international scientific Committee and authorised by the Institutional Steering Committee. The code of data management and data analyses are available upon request from the corresponding author.

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