

Metabolic syndrome increases the risk for premature employment exit: A longitudinal study among 60 427 middle-aged and older workers from the Lifelines Cohort Study and Biobank

by Katharina Runge, MSc,^{1,2} Sander KR van Zon, PhD,² Kène Henkens, PhD,^{1,2,3} Ute Bültmann, PhD²

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Objectives This study aimed to examine whether (i) metabolic syndrome (MetS) increases the risk for premature employment exit and (ii) a dose–response relationship exists between an increasing number of MetS components and premature employment exit among middle-aged and older workers.

Methods A sample of N=60 427 Dutch workers (40–64 years old) from the Lifelines Cohort Study and Biobank were examined using data from five measurement waves during a total median follow-up time of 4.2 years. MetS components were based on physical measures, blood markers, and medication use. Premature employment exit types (ie, unemployment, work disability, and early retirement) were determined using questionnaires. MetS and number of MetS components were examined as risk factors for premature employment exit using competing risk regression analysis.

Results MetS significantly increased the risk for work disability [adjusted sub distribution hazard ratio (SHR) 1.78, 95% confidence interval (CI) 1.54–2.05] and unemployment (adjusted SHR 1.16, 95% CI 1.06–1.26). A clear dose–response relationship was found for an increasing number of MetS components and work disability. No associations were found between MetS (components) and early retirement after adjusting for sociodemographic factors.

Conclusions MetS was identified as a modifiable early-stage cardio-metabolic risk factor especially for work disability and, to a lesser extent, for unemployment. Further, a clear dose–response relationship was found between an increasing number of MetS components and work disability. MetS interventions and prevention might help to prolong working lives. More awareness is needed among employers and occupational health professionals about the premature employment exit risk faced by middle-aged and older workers with MetS.

Key terms cardio-metabolic risk factor; early retirement; unemployment; work disability.

Many Western countries currently face a combination of increasing life expectancy, decreasing fertility rates, and at the same time a large number of older workers from the baby boomer generation transitioning into retirement (1). At the societal level, it is important to maintain older workers in employment longer to counteract labor market shortages. This need is reflected in extending working life policies aimed at increasing statutory retirement ages, making early retirement less attractive, and promoting working beyond pension age (2). At the individual level, it is critical to ensure that healthy and meaning-

ful working years are added to the working career (3). To date, however, many workers still exit employment before reaching the state pension age, eg, through unemployment, work disability, or early retirement (4). Premature employment exit, especially when involuntary, is associated with adverse mental and physical health outcomes (5–8). For longer working lives in good health, it is relevant to identify early risk factors for premature employment exit throughout the working career.

Cardiovascular disease (CVD) and diabetes are known risk factors for premature employment exit

¹ Netherlands Interdisciplinary Demographic Institute, The Hague, The Netherlands.

² Department of Health Sciences, Community and Occupational Medicine, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands.

³ Faculty of Social and Behavioral Sciences, University of Amsterdam, Amsterdam, The Netherlands.

Correspondence to: Katharina Runge, Department of Health Sciences, Community and Occupational Medicine, University of Groningen, University Medical Center Groningen, Hanzplein 1, 9700 RB Groningen, The Netherlands. [E-mail: k.runge@umcg.nl]

through unemployment, work disability, and early retirement (9). For instance, in a Finnish cohort study, CVD and diabetes were associated with a 3- and 2-fold increased risk for work disability during seven years of follow-up, respectively (10). It is unclear whether an early-stage modifiable cardio-metabolic risk factor like the metabolic syndrome (MetS) already increases the risk for premature employment exit. For a MetS classification, at least three out of the following five risk factor components need to be present: abdominal obesity, hypertension, raised triglycerides, reduced high-density lipoprotein (HDL) cholesterol, and raised blood glucose (11). MetS has been declared an emerging global epidemic that is associated with the worldwide increase of obesity and diabetes (12). MetS prevalence rates in Europe and the United States are estimated to range from 13.2% up to 39.0% depending on the study population and the applied MetS definition criteria (13). The development of MetS differs by socioeconomic factors and is closely linked to modifiable health behaviors, such as smoking, physical inactivity, alcohol consumption, and an unhealthy diet (14, 15). Further, a MetS classification is associated with a 5-fold increased risk for developing type two diabetes mellitus (T2DM) and a 2-fold increased risk for developing CVD over the next 5–10 years (11).

A recent study among Swedish workers aged 15–64 years found that workers with MetS are at 1.4-fold increased risk for work disability after adjustment for sociodemographic, work, and health-related factors (16). MetS might lead to premature employment exit due to its adverse health impact. For instance, hypertension and obesity have been linked to health complaints such as headaches and chronic pain, respectively (17, 18). Further, Burton et al (19) found that classifying for an increasing number of MetS components is associated with an increasing prevalence of sickness absence days. Compared to workers without MetS who reported ≥ 3 absence days in the previous year (26.5%), the reported percentage of ≥ 3 absence days among workers who classified for three, four or all five MetS components was 34.2%, 35.7%, and 39.9%, respectively (19). Lastly, a literature review showed the negative impact of MetS on multiple cognitive domains such as memory, processing, or overall intellectual functioning (20). Consequently, MetS might increase the risk for premature employment exit due to its detrimental impact on cognitive aspects, which are crucial for work ability and productivity.

To the best of our knowledge, MetS – as an early-stage (ie, pre-disease) cardio-metabolic health measure that might increase the risk for unemployment or early retirement – has not been examined yet. Moreover, little is known about a possible dose–response relationship between an increasing number of MetS components and the risk for premature employment exit. If MetS and an

increasing number of its components are identified as early-stage risk factors for premature employment exit, this knowledge would be of relevance for workers with MetS, employers, and occupational health professionals and may add important insight into which modifiable factors can be addressed to prolong working lives.

The aims of this study are to examine whether (i) MetS increases the risk for premature employment exit through unemployment, work disability, and early retirement and (ii) a dose–response relationship exists between an increasing number of MetS components and the risk for premature employment exit among middle-aged and older workers.

Methods

Study design and sample

The present longitudinal study was embedded within the large-scale Lifelines Cohort Study and Biobank (21, 22). Lifelines is a multi-disciplinary prospective population-based cohort study examining the health and health behaviors of 167 729 persons living in the north of The Netherlands (baseline age: 0–93 years). The Lifelines population is broadly representative of the population of the north of The Netherlands on sociodemographic characteristics, lifestyle factors, chronic disease prevalence, and general health (23). Lifelines employs a broad range of investigative procedures in assessing the biomedical, socio-demographic, behavioral, physical, and psychological factors, which contribute to the health and disease of the general population. Eligible participants and their family members were recruited through general practitioners and online self-registration. The ongoing data collection started in 2007 with a comprehensive baseline assessment (T0) at a Lifelines research center, including filling out extensive questionnaires, collecting biological samples, and a physical examination (21, 22). On average, every 1.5 years, follow-up questionnaires are completed (T1, T2, and T4). Approximately five years after T0, participants re-visited a Lifelines research center for the second comprehensive assessment (T3) (21, 22). Approximately 71% of participants took part in both comprehensive assessments, T0 and T3. The response rates for the follow-up questionnaires T1, T2, and T4 were 84%, 68%, and 58%, respectively (22). The current study includes information from the first five measurement waves (T0–T4) with a total median follow-up time of 4.2 [standard deviation (SD) 1.9] years.

The inclusion criteria for the present study were as follows: middle-aged and older workers at T0 (ie, 40–64 years old and working ≥ 12 hours per week following the

Dutch definition of employment at the time of the data collection) (24) who have information on ≥ 1 follow-up employment status measure after T0. At T0, the Lifelines adult study population (aged 18–93 years) consisted of N=152 728 participants. From this study population, we excluded a total of N=92 301 participants because they did not meet the age criterion (42.6%, N=65 106), worked <12 hours per week at T0 (13.2%, N=20 159), were lost to follow-up after T0 (3.4%, N=5258), or did not have any follow-up measure of employment status after T0 (0.4%, N=679). Additionally, participants in the category educational level ‘other’ (0.7%, N=1023) were excluded as this category is potentially more diverse than the other categories. Lastly, we excluded participants in the International Standard Classification of Occupations (ISCO) 08 category ‘armed forces’ (0.05%, N=76) as there is no task specified for this category (25, 26). The final study sample includes N=60 427 participants.

Measures

Premature employment exit. Employment status was self-reported at each assessment wave by the question ‘Which situation applies to you?’ including the following answer options: paid work (including the number of hours per week), unemployment (registered with the job center), work disability, homemaker, student, retirement, early retirement, or other. Participants could choose several answer options and paid work was given priority in the coding over the other response options. Based on the first self-reported employment status change after T0, the following premature employment exit groups were defined: unemployment (ie, being eligible for work but out of employment while actively searching for work), work disability (ie, having a long-lasting illness leading to an inability to execute or obtain employment), and early retirement (ie, retiring before reaching the state pension age) (27–29). Participants who self-reported to be continuously in employment during the four follow-up waves (T1–T4) built the working control group. Participants who reached the state pension age of 65 years at the time of the data collection or became economically inactive (ie, reported employment status homemaker, student, or other) were censored. Participants with missing values on employment status during follow-up were included if at least one follow-up employment status after T0 is known.

Metabolic syndrome. MetS was assessed at T0 using the joint interim criteria (11). For a MetS classification, ≥ 3 out of the following components need to be present: abdominal obesity [waist circumference (WC) ≥ 88 cm in females, WC ≥ 102 cm in males], hypertension (systolic ≥ 130 and/or diastolic ≥ 85 mm Hg) or hypertension treatment [anatomical therapeutic chemical (ATC)

code C02, C03, C07, C08, or C09], raised triglycerides (≥ 1.7 mmol/L) or medication to treat lipid abnormalities (ATC code C10A or C10B), reduced HDL-cholesterol (<1.0 mmol/L in males, <1.3 mmol/L in females) or medication to treat lipid abnormalities (ATC code C10A or C10B), raised blood glucose (fasting ≥ 5.6 mmol/L, non-fasting ≥ 11 mmol/L) or medication for T2DM (ATC codes A10A or A10B) (11, 30). MetS components were measured by trained research staff using standardized protocols and calibrated measuring instruments (21). WC was measured in the middle between the front end of the lower ribs and the iliac crest in an upright position. Triglycerides, HDL-cholesterol, and glucose were assessed using blood samples. Systolic and diastolic blood pressure was based on the mean value of the final three out of ten measurements from an automatic blood pressure monitor (31).

Sociodemographic factors. Age, sex, partner status, educational level, weekly working hours, and occupational group were self-reported at T0. *Partner status* was categorized as married/partnered and not married/partnered. *Educational level* was categorized as low (no education; primary education; lower or preparatory secondary vocational education; junior general secondary education), medium (secondary vocational education or work-based learning; senior general secondary education, pre-university secondary education), or high (higher vocational education; university education) (32). *Weekly working hours* were measured on a scale of 12–40 hours per week. *Occupational group* was coded according to the ISCO-08 by Statistics Netherlands (25, 33). Based on the major ISCO-08 categories, four overarching occupational groups were compiled: high skilled white-collar (ie, managers, professionals, technicians and associate professionals), low skilled white-collar (ie, clerical support workers, services and sales workers), high skilled blue-collar (ie, skilled agricultural forestry and fishery workers, craft and related trades workers), and low skilled blue-collar workers (ie, plant and machine operators and assemblers, elementary occupations) (34).

Multiple imputation. Multiple imputation was carried out to handle missing data on occupational group (N=1617), weekly working hours (N=577), MetS components (highest missing N=503), educational level (N=44), and partner status (N=26). Imputations were predicted by follow-up time, age, gender, and follow-up employment status. In total, ten datasets were imputed (35).

Statistical analyses

First, baseline MetS, (number of) MetS components, and sociodemographic characteristics were examined

by premature employment exit type and for the working control group. Second, the effect of MetS on premature employment exit was investigated using Fine & Gray's proportional sub distribution hazards survival analysis (36). This analysis is suitable to examine competing exit routes from employment (32, 37). By controlling for competing employment exit types, the analysis acknowledges that one employment exit type 'prevents' the occurrence of other employment exit types. Sub distribution hazard ratios (SHR) and corresponding 95% confidence intervals (CI) were presented for MetS and sociodemographic factors. An individual time-to-event variable, reflecting the follow-up time in months until premature employment exit, censoring, or staying in employment, is by default included in the analysis to take the different follow-up times of participants into account. In model 1, the crude association between MetS and premature employment exit types was examined. In model 2, the association between MetS and premature employment exit types was adjusted for sociodemographic factors. This analysis was repeated for the number of classified MetS components (ranging 0–5) to examine whether a dose–response relationship exists between an increasing number of MetS components and premature employment exit types. The MetS classification cut-off value of three MetS components was used as the reference category. Data preparation, multiple imputation of missing values, and descriptive analyses were performed using SPSS Statistics version 28 (IBM Corp, Armonk, NY, USA). Competing risk regression analyses were performed using StataMP 13.1 (StataCorp, College Station, TX, USA).

Sensitivity analyses

To examine the robustness of the results, the main analyses were repeated including all working participants (N=64 796). In other words, participants who work ≥ 1 but < 12 hours per week at T0 were included (N=4369), following the international definition of employment (27). Additionally, the individual MetS components were investigated as risk factors for premature employment exit.

Results

Sample characteristics

At baseline, the mean age of the study sample was 48.3 (SD 5.8) years, 53.8% of the participants were female (N=32 497), and 17.6% of the participants had MetS (N=10 605) (table 1 and supplementary material www.sjweh.fi/article/4113, table S1). During the median

follow-up time of 4.2 (SD 1.9) years, 5.6% (N=3403) participants transitioned from employment to unemployment [mean time to event: 2.9 (SD 1.8) years], 1.6% (N=942) to work disability (mean time to event: 2.9 (SD 1.9) years), and 2.1% (N=1297) to early retirement (mean time to event: 3.1 (SD 1.8) years). A total of 3.9% (N=2354) participants were censored because they reached the age of 65 years and 1.2% (N=752) participants were censored because they became economically inactive (N=524 homemakers, N=36 students, and N=192 employment status 'other'). Participants who transitioned from employment to early retirement during follow-up, were on average ten years older at baseline [59.2 (SD 2.7) years] than participants who transitioned to unemployment [48.9 (SD 5.8) years] or work disability [49.8 (SD 5.9) years]. Compared to the study sample, participants who were lost to follow-up (N=5258) or did not have any follow-up measure of employment status after T0 (N=679) had a slightly higher MetS prevalence at baseline, and were more likely to be lower educated and blue-collar workers (supplementary table S1). Compared to the total T0 adult Lifelines population (22), participants in this study sample are slightly older, and somewhat more likely to be male and lower educated.

Baseline MetS status and the risk of premature employment exit during follow-up

Baseline MetS prevalence differed by 4.2-year follow-up employment states (table 1). The highest baseline MetS prevalence was present among participants who became work disabled (29.5%), followed by early retirement (27.6%), unemployment (20.6%), and lastly the working control group (16.5%).

In the crude analysis, MetS increased the risk for all premature employment exits types: work disability (SHR 2.01, 95% CI 1.74–2.31), unemployment (SHR 1.24, 95% CI 1.14–1.34), and early retirement (SHR 1.82, 95% CI 1.61–2.06) (table 2, model 1). After adjusting for sociodemographic factors, the associations between MetS and work disability (adjusted SHR 1.78, 95% CI 1.54–2.05) and unemployment (adjusted SHR 1.16, 95% CI 1.06–1.26) were attenuated but remained statistically significant, while the associations for early retirement were not significant anymore (table 2, Model 2).

Increasing number of baseline MetS components and the risk of premature employment exit during follow-up

The number of baseline MetS components classifications differed by 4.2-year follow-up employment states. Classifying for the MetS cut-off value, ie, three components, was most common among participants who became early retirees during follow-up (14.3%). Classifying for four (11.1%) and five MetS components (5.3%) was

Table 1. Baseline (T0) characteristics of the working control group and by premature employment exit type during 4.2 years follow-up. [SD=standard deviation; MetS=metabolic syndrome; HDL=high-density lipoprotein]

Baseline	Working control group (N=51 679)		Premature employment exit type during 4.2 years follow-up					
			Unemployment (N=3403)		Work disability (N=942)		Early retirement (N=1297)	
	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)
Health status								
MetS	16.5		20.6		29.5		27.6	
MetS components								
Abdominal obesity	35.4		40.4		49.9		40.1	
Hypertension	43.5		47.4		54.4		59.1	
Raised triglycerides	20.3		22.5		30.7		28.9	
Reduced HDL-Cholesterol	16.0		19.3		28.0		22.7	
Raised blood glucose	12.9		16.6		20.3		23.3	
Number of MetS components								
0	32.7		28.0		20.3		21.7	
1	31.3		30.2		27.5		28.1	
2	19.5		21.2		22.7		22.6	
3	9.9		11.4		13.1		14.3	
4	4.8		6.6		11.1		8.6	
5	1.8		2.6		5.3		4.8	
Sociodemographic factors								
Age (years)		47.4 (4.9)		48.9 (5.8)		49.8 (5.9)		59.2 (2.7)
Sex								
Female	53.7		57.2		56.8		47.6	
Male	46.3		42.8		43.2		52.4	
Partner status								
Married / partnered	90.4		84.5		84.6		93.1	
Not married / partnered	9.6		15.5		15.4		6.9	
Occupational group								
High skilled white-collar	50.6		41.4		34.8		60.1	
Low skilled white-collar	30.4		38.7		33.2		27.0	
High skilled blue-collar	10.8		9.9		16.1		7.6	
Low skilled blue-collar	8.1		9.9		15.8		5.2	
Educational level								
High	31.8		23.6		18.7		38.2	
Medium	41.7		39.1		35.9		27.1	
Low	26.5		37.3		45.4		34.7	
Weekly working hours		31.7 (8.6)		30.7 (8.8)		28.2 (9.7)		29.6 (8.8)

Table 2. The association between metabolic syndrome (MetS) and premature employment exit: competing risk regression analysis. [SHR=sub distribution hazard ratio; CI=confidence interval; HSWC=high skilled white-collar; LSWC=low skilled white-collar; HSBC=high skilled blue-collar; LSBC=low skilled blue-collar; Ref=reference group]. **BOLD indicates statistically significant (P<0.05).**

Baseline	Premature employment exit type during 4.2 years follow-up					
	Unemployment		Work disability		Early retirement	
	Model 1 ^a	Model 2 ^b	Model 1 ^a	Model 2 ^b	Model 1 ^a	Model 2 ^b
	SHR (95% CI)	SHR (95% CI)	SHR (95% CI)	SHR (95% CI)	SHR (95% CI)	SHR (95% CI)
MetS	1.24 (1.14–1.34)	1.16 (1.06–1.26)	2.01 (1.74–2.31)	1.78 (1.54–2.05)	1.82 (1.61–2.06)	1.11 (0.97–1.26)
Age (years)		1.01 (1.00–1.01)		1.02 (1.01–1.03)		1.37 (1.36–1.38)
Male sex		0.94 (0.86–1.04)		1.32 (1.07–1.62)		0.99 (0.86–1.14)
Not married / partnered		1.59 (1.44–1.75)		1.70 (1.42–2.03)		0.54 (0.43–0.68)
Occupation						
HSWC		Ref.				
LSWC		1.30 (1.19–1.42)		1.07 (0.89–1.28)		0.75 (0.64–0.87)
HSBC		0.95 (0.83–1.09)		1.94 (1.56–2.42)		0.61 (0.48–0.76)
LSBC		1.13 (0.99–1.30)		1.67 (1.33–2.10)		0.47 (0.35–0.62)
Education						
High		Ref.				
Medium		1.21 (1.10–1.34)		1.19 (0.97–1.45)		0.83 (0.72–0.97)
Low		1.60 (1.43–1.79)		1.69 (1.36–2.10)		0.87 (0.74–1.02)
Working hours		1.00 (0.99–1.00)		0.95 (0.94–0.96)		0.99 (0.98–0.99)

^a Model 1 = crude.^b Model 2 = model 1 adjusted for age, sex, occupational group, education, and working hours.

Table 3. The association between number of metabolic syndrome (MetS) components and premature employment exit: competing risk regression analysis. [SHR=sub distribution hazard ratio; CI=confidence interval; HSWC=high skilled white-collar; LSWC=low skilled white-collar; HSBC=high skilled blue-collar; LSBC=low skilled blue-collar; Ref=reference group]. **BOLD indicates statistically significant (P<0.05).**

Baseline	Premature employment exit type during 4.2 years follow-up					
	Unemployment		Work disability		Early retirement	
	Model 1 ^a	Model 2 ^b	Model 1 ^a	Model 2 ^b	Model 1 ^a	Model 2 ^b
	SHR (95% CI)	SHR (95% CI)	SHR (95% CI)	SHR (95% CI)	SHR (95% CI)	SHR (95% CI)
MetS components						
0	0.78 (0.69–0.88)	0.84 (0.74–0.95)	0.49 (0.39–0.62)	0.55 (0.44–0.70)	0.48 (0.40–0.58)	0.90 (0.74–1.10)
1	0.87 (0.78–0.98)	0.91 (0.81–1.02)	0.69 (0.56–0.86)	0.74 (0.60–0.91)	0.65 (0.54–0.77)	0.89 (0.74–1.07)
2	0.96 (0.85–1.09)	0.97 (0.85–1.09)	0.89 (0.71–1.11)	0.91 (0.73–1.13)	0.82 (0.68–0.98)	0.97 (0.80–1.18)
3	Ref.					
4	1.15 (0.98–1.36)	1.13 (0.96–1.33)	1.70 (1.31–2.20)	1.62 (1.25–2.10)	1.19 (0.94–1.50)	1.01 (0.79–1.30)
5	1.14 (0.90–1.43)	1.05 (0.83–1.33)	2.06 (1.48–2.86)	1.81 (1.29–2.52)	1.71 (1.28–2.28)	1.06 (0.78–1.44)
Age (years)		1.01 (1.00–1.01)		1.02 (1.01–1.03)		1.37 (1.36–1.38)
Male sex		0.94 (0.85–1.03)		1.29 (1.05–1.58)		0.99 (0.86–1.14)
Not married / partnered		1.59 (1.44–1.74)		1.67 (1.40–2.00)		0.54 (0.43–0.68)
Occupation						
HSWC		Ref.				
LSWC		1.30 (1.19–1.42)		1.07 (0.89–1.28)		0.75 (0.64–0.87)
HSBC		0.95 (0.83–1.09)		1.96 (1.57–2.44)		0.61 (0.48–0.77)
LSBC		1.13 (0.98–1.30)		1.64 (1.31–2.06)		0.47 (0.35–0.62)
Education						
High		Ref.				
Medium		1.20 (1.09–1.33)		1.15 (0.94–1.41)		0.83 (0.71–0.97)
Low		1.58 (1.42–1.76)		1.61 (1.30–2.00)		0.87 (0.74–1.02)
Working hours		1.00 (0.99–1.00)		0.95 (0.94–0.96)		0.99 (0.98–0.99)

^a Model 1 = crude.^b Model 2 = model 1 adjusted for age, sex, occupational group, education, and working hours.

most common among participants who became work disabled during follow-up. Regarding the specific MetS components, the lowest baseline prevalence rates were present among the working control group, ranging from 12.9% for raised blood glucose to 43.5% for hypertension (table 1). Hypertension and abdominal obesity were most prevalent among workers who prematurely exited employment during follow-up through early retirement (59.1%) and work disability (49.9%), respectively.

A dose–response relationship was found for an increasing number of MetS components and the risk for work disability (table 3). After adjustment for sociodemographic factors, the relationships remained statistically significant and the highest risk for work disability was present among participants who classified for all five MetS components (adjusted SHR 1.81, 95% CI 1.29–2.52). No associations were found between an increasing number of MetS components and unemployment or early retirement after adjusting for sociodemographic factors.

Sensitivity analyses

The main study findings were similar when all working participants, ie, also participants who worked ≥ 1 but < 12 hours per week at baseline (N=4369), were included in the analysis (supplementary tables S2 and S3). Further, all MetS components except raised blood glucose were identified as risk factors for work disability, while only

raised blood glucose was identified as a risk factor for unemployment (supplementary table S4, Model 2).

Discussion

In this 4.2 year follow-up study among 60 427 middle-aged and older Dutch workers, MetS increased the risk for premature employment exit especially through work disability and to a lesser extent through unemployment. Specifically, middle-aged and older workers with MetS at baseline were 1.8-times more likely to become work disabled during follow-up. Further, a clear dose–response relationship was found for an increasing number of MetS components and the risk for work disability. In other words, workers who classified for four or all five MetS components had a higher risk to become work disabled during follow-up than workers who classified for three MetS components. Further, workers with MetS at baseline were 1.2-times more likely to become unemployed during follow-up. No dose–response relationship was found between an increasing number of MetS components and unemployment. Neither MetS nor an increasing number of MetS components was associated with early retirement in this study. The total study sample MetS prevalence was 17.6% which is comparable to MetS prevalence rates found in other European countries (13).

The finding that MetS increased the risk for work disability corresponds with the result of a recent population-based prospective cohort study among Swedish employees (16). The present study is the first to show that MetS also increases the risk for unemployment. Taken together, these findings suggest that not only chronic diseases like CVD and T2DM are risk factors for premature employment exit (9), but that MetS as a modifiable early-stage cardio-metabolic risk factor is already an important indicator for future work participation. It is worth mentioning that the overall unemployment rate was slightly higher in the catchment area of the current study (ie, Groningen, Friesland, and Drenthe) during the time of data collection compared to the rest of The Netherlands (38). Consequently, the chance to become unemployed might have been somewhat higher for the study participants compared to workers in other regions of The Netherlands. The finding that neither MetS nor an increasing number of MetS components was associated with early retirement suggests that early retirement seems to be less dependent on cardio-metabolic risk factors than work disability or unemployment. For early retirement, other factors such as the voluntariness of premature employment exit or age might play a more important role. First, early retirement can generally be considered a more voluntary choice to stop working, compared to work disability and unemployment where workers might be involuntarily forced to exit employment due to ill-health (5). Second, participants who transitioned into early retirement were on average ten years older at baseline compared to the total study sample and MetS prevalence increases with age (39).

The current study findings may inform policy and practice. More awareness is needed among employers and occupational health professionals about the premature employment exit risk faced by middle-aged and older workers with MetS. Further, MetS and MetS components might be included as modifiable risk factors in interventions to prevent work disability and unemployment. As this is one of the first studies investigating MetS as an early-stage risk factor for premature employment exit types, more research is needed. It might be of particular interest to gain more insight into which MetS component clusters act as main drivers for premature employment exit and to elaborate on the specific pathways and mechanisms between MetS and premature employment exit through work disability and unemployment. Possible linking mechanisms might be the adverse effect of MetS on work productivity, cognitive functioning, and increased absence days (19, 40).

Study strengths are the longitudinal design with a clear temporal order of measurements, which minimizes the risk of reverse causation. Further, MetS components were measured by trained research staff and included information on medication use, which reduces the risk

of information bias. Lastly, although more comparative research is needed from other geographical areas, the Lifelines population is broadly representative of the population of the north of The Netherlands, which facilitates the generalizability of results (23). A study limitation concerns the possibility of misclassification of premature employment exit types as employment states were self-reported. However, previous research suggests high agreement between self-reported and register-based employment history data (41). Another limitation is the limited follow-up time of 4.2 years and that employment states have only been assessed every 1.5 years. Consequently, it cannot be ruled out that participants experienced transitions between premature employment exit types or temporarily left employment between two assessment points. Further, participants may leave or re-enter employment, which is more likely to be captured with a longer follow-up period. Moreover, the limited follow-up time in combination with the baseline mean age of 48.3 years makes the premature employment exit types unemployment and work disability more likely to occur than early retirement in the current study. The use of longer follow-up data and linkages with register data on employment status in future studies would allow to investigate long-term effects of MetS on work participation and more detailed employment trajectories. Lastly, a slight underestimation of MetS prevalence and some selection bias may have occurred as participants who were lost to follow-up or did not have any follow-up measure of employment status were slightly unhealthier and more likely to be lower educated than study sample participants.

In conclusion, MetS was identified as a modifiable early-stage cardio-metabolic risk factor for premature employment exit especially through work disability and to a lesser extent through unemployment. Further, a clear dose-response relationship was found for an increasing number of MetS components and the risk for work disability. MetS prevention and MetS interventions might help to prolong working lives. More awareness is needed among employers and occupational health professionals about the premature employment exit risk faced by middle-aged and older workers with MetS.

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The authors declare no conflicts of interest.

Ethics and data availability

The Lifelines Cohort Study is conducted according to the principles of the Declaration of Helsinki and in accordance with the research code of the University Medical Center Groningen (UMCG). The medical ethical committee of UMCG, The Netherlands approved the Lifelines study (ethics number: 2007/152). Participants gave informed consent to participate in the study before taking part.

Data are available on reasonable request. Data may be obtained from a third party and are not publicly available. Researchers can apply for the data and biomaterial through a proposal that is submitted to the Lifelines research office (research@lifelines.nl).

References

- Wheaton F, Crimmins EM. The Demography of Aging and Retirement. *The Oxford handbook of retirement*. 2012:22-41. <https://doi.org/10.1093/oxfordhb/9780199746521.013.0019>.
- Henkens K, van Dalen HP. The Employer's Perspective on Retirement. *The Oxford handbook of retirement*. 2012:215-227. <https://doi.org/10.1093/oxfordhb/9780199746521.013.0085>.
- Staudinger UM, Finkelstein R, Calvo E, Sivaramakrishnan K. A global view on the effects of work on health in later life. *Gerontologist* 2016 Apr;56 Suppl 2:S281-92. <https://doi.org/10.1093/geront/gnw032>.
- Robroek SJ, Schuring M, Croezen S, Stattin M, Burdorf A. Poor health, unhealthy behaviors, and unfavorable work characteristics influence pathways of exit from paid employment among older workers in Europe: a four year follow-up study. *Scand J Work Environ Health* 2013 Mar;39(2):125-33. <https://doi.org/10.5271/sjweh.3319>.
- Schaap R, de Wind A, Coenen P, Proper K, Boot C. The effects of exit from work on health across different socioeconomic groups: A systematic literature review. *Soc Sci Med* 2018 Feb;198:36-45. <https://doi.org/10.1016/j.socscimed.2017.12.015>.
- van der Heide I, van Rijn RM, Robroek SJ, Burdorf A, Proper KI. Is retirement good for your health? A systematic review of longitudinal studies. *BMC Public Health* 2013 Dec;13(1):1180. <https://doi.org/10.1186/1471-2458-13-1180>.
- Roelfs DJ, Shor E, Davidson KW, Schwartz JE. Losing life and livelihood: a systematic review and meta-analysis of unemployment and all-cause mortality. *Soc Sci Med* 2011 Mar;72(6):840-54. <https://doi.org/10.1016/j.socscimed.2011.01.005>.
- Runge K, van Zon SK, Bültmann U, Henkens K. Transitioning out of work and metabolic syndrome incidence: a longitudinal study among 13 303 older workers from the Lifelines Cohort Study and Biobank. *J Epidemiol Community Health* 2022 Jun;76(9):779-85. <https://doi.org/10.1136/jech-2021-218569>.
- Kouwenhoven-Pasmooij TA, Burdorf A, Roos-Hesselink JW, Hunink MG, Robroek SJ. Cardiovascular disease, diabetes and early exit from paid employment in Europe; the impact of work-related factors. *Int J Cardiol* 2016 Jul;215:332-7. <https://doi.org/10.1016/j.ijcard.2016.04.090>.
- Ervasti J, Kivimäki M, Pentti J, Salo P, Oksanen T, Vahtera J et al. Health- and work-related predictors of work disability among employees with a cardiometabolic disease--A cohort study. *J Psychosom Res* 2016 Mar;82:41-7. <https://doi.org/10.1016/j.jpsychores.2016.01.010>.
- Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA et al.; International Diabetes Federation Task Force on Epidemiology and Prevention; Hational Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; International Association for the Study of Obesity. Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; national heart, lung, and blood institute; American heart association; world heart federation; international atherosclerosis society; and international association for the study of obesity. *Circulation* 2009 Oct;120(16):1640-5. <https://doi.org/10.1161/CIRCULATIONAHA.109.192644>.
- Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. *Lancet* 2005 Apr;365(9468):1415-28. [https://doi.org/10.1016/S0140-6736\(05\)66378-7](https://doi.org/10.1016/S0140-6736(05)66378-7).
- O'Neill S, O'Driscoll L. Metabolic syndrome: a closer look at the growing epidemic and its associated pathologies. *Obes Rev* 2015 Jan;16(1):1-12. <https://doi.org/10.1111/obr.12229>.
- Pérez-Martínez P, Mikhailidis DP, Athyros VG, Bullo M, Couture P, Covas MI et al. Lifestyle recommendations for the prevention and management of metabolic syndrome: an international panel recommendation. *Nutr Rev* 2017 May;75(5):307-26. <https://doi.org/10.1093/nutrit/nux014>.
- Hoveling LA, Liefbroer AC, Bültmann U, Smidt N. Understanding socioeconomic differences in incident metabolic syndrome among adults: what is the mediating role of health behaviours? *Prev Med* 2021 Jul;148:106537. <https://doi.org/10.1016/j.ypmed.2021.106537>.
- Lidén E, Karlsson B, Torén K, Andersson E. Metabolic syndrome - a risk factor for all-cause disability pension: a prospective study based on the Swedish WOLF cohort. *Scand J Work Environ Health* 2020 Jul;46(4):402-9. <https://doi.org/10.5271/sjweh.3881>.

17. Arca KN, Halker Singh RB. The hypertensive headache: a review. *Curr Pain Headache Rep* 2019 Mar;23(5):30. <https://doi.org/10.1007/s11916-019-0767-z>.
18. Chin SH, Huang WL, Akter S, Binks M. Obesity and pain: a systematic review. *Int J Obes* 2020 May;44(5):969–79. <https://doi.org/10.1038/s41366-019-0505-y>.
19. Burton WN, Chen CY, Schultz AB, Edington DW. The prevalence of metabolic syndrome in an employed population and the impact on health and productivity. *J Occup Environ Med* 2008 Oct;50(10):1139–48. <https://doi.org/10.1097/JOM.0b013e318188b8eb>.
20. Yates KF, Sweat V, Yau PL, Turchiano MM, Convit A. Impact of metabolic syndrome on cognition and brain: A selected review of the literature. *Arterioscler Thromb Vasc Biol* 2012 Sep;32(9):2060–7. <https://doi.org/10.1161/ATVBAHA.112.252759>.
21. Scholtens S, Smidt N, Swertz MA, Bakker SJ, Dotinga A, Vonk JM et al. Cohort Profile: LifeLines, a three-generation cohort study and biobank. *Int J Epidemiol* 2015 Aug;44(4):1172–80. <https://doi.org/10.1093/ije/dyu229>.
22. Sijtsma A, Rienks J, van der Harst P, Navis G, Rosmalen JG, Dotinga A. Cohort Profile Update: Lifelines, a three-generation cohort study and biobank. *Int J Epidemiol* 2022 Oct;51(5):e295–302. <https://doi.org/10.1093/ije/dyab257>.
23. Klijs B, Scholtens S, Mandemakers JJ, Snieder H, Stolk RP, Smidt N. Representativeness of the LifeLines cohort study. *PLoS One* 2015 Sep;10(9):e0137203. <https://doi.org/10.1371/journal.pone.0137203>.
24. Janssen B, Dirven H. Sociaaleconomische trends. Werkloosheid: twee afbakeningen (English translation: Socioeconomic trends. Unemployment: two demarcations). Statistics Netherlands, Den Haag. 2015.
25. International Labour Office. International Standard Classification of Occupations 2008 (ISCO-08): structure, group definitions and correspondence tables. International Labour Office; 2012.
26. Mihaylov E, Tijdens KG. Measuring the Routine and Non-Routine Task Content of 427 Four-Digit ISCO-08 Occupations. Tinbergen Institute Discussion Paper 2019;035/V. <https://doi.org/10.2139/ssrn.3389681>
27. International Labour Office (ILO). Resolution I: resolution concerning statistics of work, employment and labour underutilization 2013. Available from: https://www.ilo.org/wcmsp5/groups/public/---dgreports/---stat/documents/normativeinstrument/wcms_230304.pdf. [Accessed May 2022].
28. Organisation for Economic Co-operation and Development. *Sickness, disability and work: breaking the barriers* (vol. 3): Denmark, Finland, Ireland and the Netherlands. OECD Publishing, 2008. <https://doi.org/10.1787/9789264049826-en>
29. Rijksoverheid. AOW-leeftijd stijgt minder snel (English translation: State pension age is rising less rapidly). Available from: <https://www.rijksoverheid.nl/onderwerpen/pensioen/toekomst-pensioenstelsel/aow-leeftijd-stijgt-minder-snel> [Accessed May 2022].
30. WHO collaborating centre for drug statistics methodology. ATC/DDD index, 2021. Available from: http://www.whooc.no/atc_ddd_index/ [Accessed Dec 2021].
31. Physical State - Blood Pressure. Lifelines Wiki; 2021. Available from: http://wiki.lifelines.nl/doku.php?id=blood_pressure. [Accessed Sep 2022].
32. Ots P, van Zon SK, Schram JL, Burdorf A, Robroek SJ, Oude Hengel KM et al. The influence of unhealthy behaviours on early exit from paid employment among workers with a chronic disease: A prospective study using the Lifelines cohort. *Prev Med* 2020 Oct;139:106228. <https://doi.org/10.1016/j.ypmed.2020.106228>.
33. van Zon SK, Amick Iii BC, de Jong T, Brouwer S, Bültmann U. Occupational distribution of metabolic syndrome prevalence and incidence differs by sex and is not explained by age and health behavior: results from 75 000 Dutch workers from 40 occupational groups. *BMJ Open Diabetes Res Care* 2020 Jul;8(1):e001436. <https://doi.org/10.1136/bmjdr-2020-001436>.
34. Brønnum-Hansen H, Foverskov E, Andersen I. Occupational inequality in health expectancy in Denmark. *Scand J Public Health* 2020 May;48(3):338–45. <https://doi.org/10.1177/1403494819882138>.
35. White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Stat Med* 2011 Feb;30(4):377–99. <https://doi.org/10.1002/sim.4067>.
36. Fine JP, Gray RJ. A proportional hazards model for the sub distribution of a competing risk. *J Am Stat Assoc* 1999;94(446):496–509. <https://doi.org/10.1080/01621459.1999.10474144>
37. Reeuwijk KG, van Klaveren D, van Rijn RM, Burdorf A, Robroek SJ. The influence of poor health on competing exit routes from paid employment among older workers in 11 European countries. *Scand J Work Environ Health* 2017 Jan;43(1):24–33. <https://doi.org/10.5271/sjweh.3601>.
38. Arbeidsdeelname; regionale indeling 2014, 2003-2014 (English translation: Work participation, regional division 2014, 2003-2014). Statistics Netherlands, StatLine, 2015. Available from: <https://opendata.cbs.nl/#/CBS/nl/dataset/82208NED/table?dl=92E8A>. [Accessed July 2023].
39. Saklayen MG. The global epidemic of the metabolic syndrome. *Curr Hypertens Rep* 2018 Feb;20(2):12. <https://doi.org/10.1007/s11906-018-0812-z>.
40. Taylor VH, MacQueen GM. Cognitive dysfunction associated with metabolic syndrome. *Obes Rev* 2007 Sep;8(5):409–18. <https://doi.org/10.1111/j.1467-789X.2007.00401.x>.
41. Wahrendorf M, Marr A, Antoni M, Pesch B, Jöckel KH, Lunau T et al. Agreement of self-reported and administrative data on employment histories in a German cohort study: a sequence analysis. *Eur J Popul* 2018 Mar;35(2):329–46. <https://doi.org/10.1007/s10680-018-9476-2>.

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