Metabolic syndrome and the increased risk of medically-certified long-term sickness absence : a prospective analysis among Japanese workers

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Metabolic syndrome and the increased risk of medically-certified long-term sickness absence: a prospective analysis among Japanese workers

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Abstract

Background: Metabolic syndrome (MetS) has been associated with various chronic diseases which may lead to long-term sickness absence (LTSA), but there is lacking information on the direct association between MetS and LTSA. The present study aimed to investigate the all-cause and cause-specific associations between MetS and the risk of medically-certified LTSA among Japanese workers.

Method: We recruited 67,403 workers (57,276 men and 10,127 women), aged 20-59 years, of 13 companies in Japan, during their health check-ups in 2011 (11 companies) and 2014 (2 companies), and followed them up for LTSA events (≥ 30 consecutive days) until March 31, 2020. MetS was defined according to the Joint Interim Statement. A Cox proportional hazards regression model was used to estimate hazard ratio (HR) and its 95% confidence interval (CI) for LTSA associated with MetS and its components.

Results: During 408,324 person-years of follow-up, 2,915 workers experienced LTSA. The adjusted HR for all-cause LTSA was 1.54 (95% CI, 1.41-1.68) among those with vs without MetS. In cause-specific analysis, HRs associated with MetS significantly increased for LTSA due to overall physical disorders (1.76), cardiovascular diseases (3.16), diseases of the musculoskeletal system and connective tissue (2.01), cancers (1.24), obesity-related cancers (1.35), mental, behavioral and neurodevelopmental disorders (1.28), reaction to severe stress and adjustment disorders (1.46) and external causes (1.46). The number of MetS components were also significantly associated with increased LTSA risk.

Conclusion: MetS was associated with an increase in the risk of LTSA due to various diseases among Japanese workers.

Metabolic syndrome (MetS)

- **A clustering of cardiometabolic risk factors** *(Alberty 2009)*
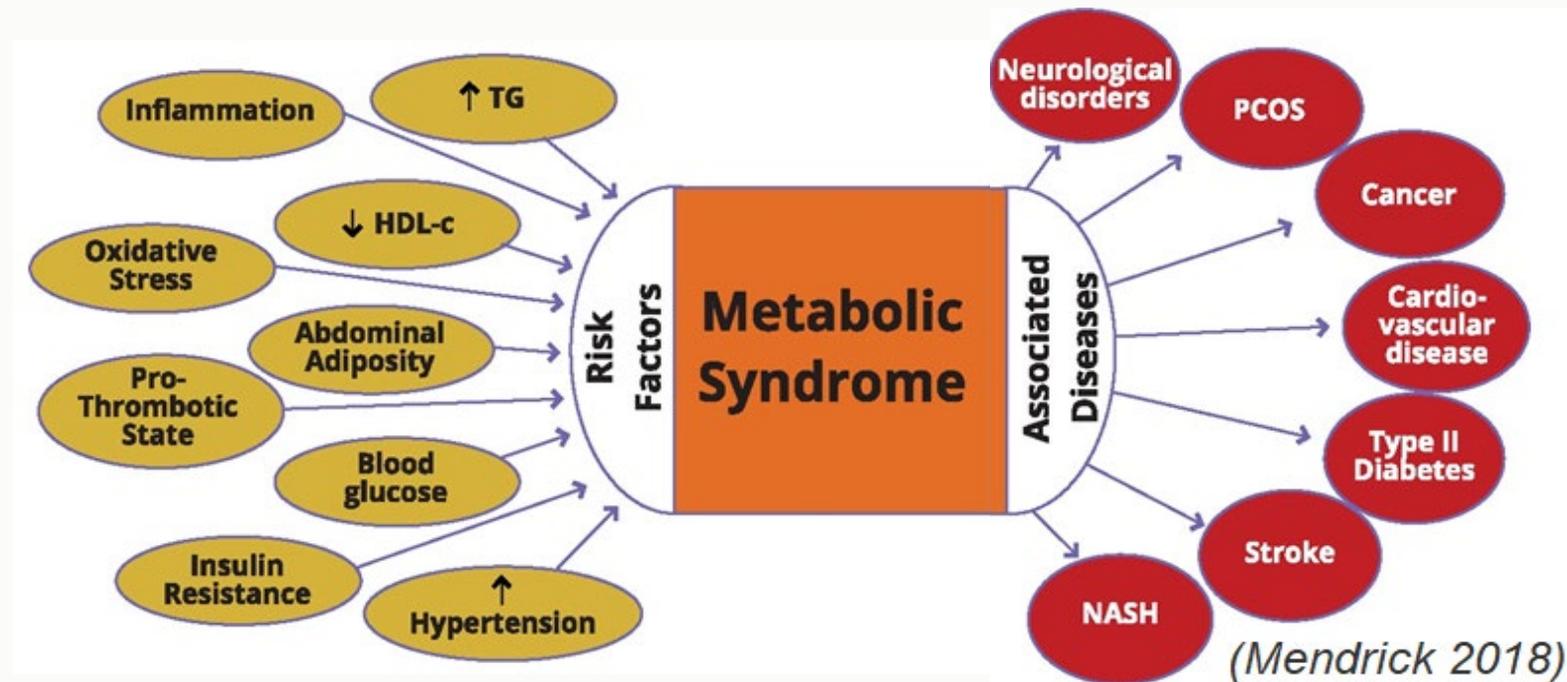
(Mendrick 2018)

- **MetS may be LTSA risk factor**
  - ➤ MetS increased risk of various chronic diseases *(Mendrick 2018)*
  - ➤ MetS increased 31% sickness absence risk (≥ 3 days) *(Burton 2008)*
  - ➤ MetS increased dental care days and cost *(Nishikawa 2020)*

Background

Research gap & questions

➢ **No studies have examined the MetS-LTSA relationship**

➢ **Are there associations between:**

- MetS and all-cause LTSA?

- MetS and cause-specific LTSA?

- MetS components and LTSA?

Objectives

➢ **Primary objective:** to examine the all-cause and cause-specific associations between MetS and LTSA risk among Japanese workers.

➢ **Secondary objectives:** to examine relationship between:

- The number of MetS components and LTSA risk.

- Individual MetS components and LTSA risk.

Data collection

Method

- **Study setting: J-ECOH study**
  - Japan Epidemiology Collaboration on Occupational Health Study
  - Investigating health determinants in Japanese workers
- **Baseline data:** used 2011 survey
  - Measures: height, weight, waist circumference, blood pressure
  - Blood lipid: triglycerides, high-density lipoprotein cholesterol
  - Medical history: medications, cancer, CVDs, & psychiatric disorders
  - Other information: age, sex, smoking
- **Follow-up data**
  - Cohort registry: April 2012 → March 2020
  - First LTSA: date & causes
  - Others: health check, retirement, death

Eligible participants at baseline surveys (n = 103,743)

→ 8,421 excluded (≥ 60 or < 20 years old)
→ 21,566 excluded (missing MetS)
→ 2,846 excluded (missing smoking status)
→ 1 excluded (missing body weight)

Participants included in cohort registry (n = 70,909)

→ 3,298 excluded (lost follow-up)
→ 208 excluded (missing LTSA)

Analytic sample (n = 67,403) (57,276 men, 10,127 women)
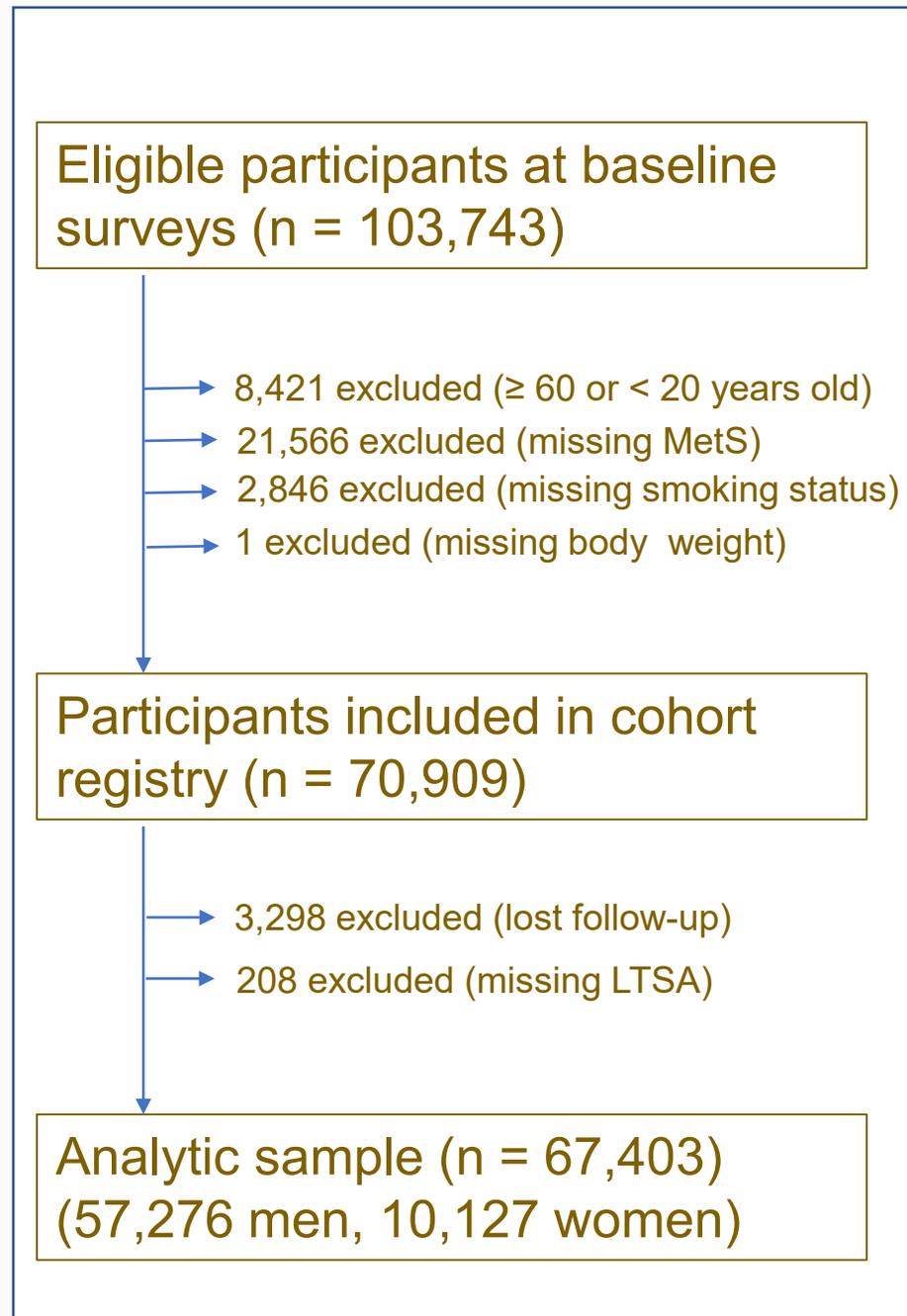
Exposures & outcomes

- **Exposures**

  ➢ MetS: ≥ 3 of the following:

  ① Central obesity: WC in men ≥ 90 cm, WC in women ≥ 80 cm

  ② High FPG: FPG ≥ 100 mg/dL, or using antidiabetic medication

  ③ High BP: BP ≥ 130/85 mmHg, or using antihypertensive medication

  ④ High TG: TG ≥ 150 mg/dL, or lipid lowering medication

  ⑤ Reduced HDL-C: HDL-C in men ≤ 40, ≤ 50 in women mg/dL

  (JIS: Joint interim statement; Alberty 2009)

  ➢ MetS components: central obesity, high FPG, high BP, high TG, low HDL-C

- **Outcomes**

  ➢ Primary: all-cause LTSA (≥ 30 days) which was medically certified.

  ➢ Secondary: cause-specific LTSA:

  ① Physical disorders & sub-groups (CVDs, musculoskeletal diseases, & cancer)

  ② Mental disorders & sub-groups (depressive episode, and RSSAD [reaction to severe stress & adjustment disorders])

  ③ External causes

Statistical analyses

Method

- **Person-time**
  - ➢ Starting date: April 1, 2012
  - ➢ Endpoint date: first LTSA, last health check, retirement, death, or end of follow-up [March 31, 2020], whichever occurred first

- **Cox regression models:** HR (95% CI) for LTSA relative to MetS
  - ➢ Model 1: age and sex
  - ➢ Model 2: age, sex, smoking, & baseline pre-existing conditions

- **Main associations**
  - ➢ MetS and all-cause LTSA
  - ➢ MetS and cause-specific LTSA

- **Additional associations**
  - ➢ MetS components with all-cause LTSA

Main results

Results

Baseline characteristics

- Age: 44.6 [8.8]
- Men: 85%
- Obesity: < 5%
- Nonsmokers: ~ 33%
- MetS: 17.2%

Characteristics	All participants	MetS status	
		Yes	No
N	67,403	11,630	55,773
Age, mean [SD]	44.6 [8.8]	48.2 [7.4]	43.9 [8.9]
Sex (men)	57,276 (85.0)	10,743 (92.4)	46,533 (83.4)
Body mass index (kg/m^2)			
< 18.5	3,059 (4.5)	25 (0.2)	3,034 (5.4)
18.5 - 24.9	45,265 (67.2)	3,043 (26.2)	42,222 (75.7)
25.0 - 29.9	15,965 (23.7)	6,359 (54.7)	9,606 (17.3)
≥ 30.0	3,114 (4.6)	2,203 (18.9)	911 (1.6)
Smoking status			
Never-smoker	27,336 (40.6)	3,587 (30.8)	23,749 (42.6)
Former smoker	17,669 (26.2)	3,514 (30.3)	14,155 (25.4)
Current smoker	22,398 (33.2)	4,529 (38.9)	17,869 (32.0)
Pre-existing conditions [a]	2,247 (3.3)	616 (5.3)	1,631 (2.9)
MetS components			
High BP [b]	22,788 (33.8)	9,270 (79.7)	13,518 (24.2)
High FPG [c]	23,017 (34.1)	9,001 (77.4)	14,016 (25.1)
High TG [d]	18,953 (28.1)	9,208 (79.2)	9,745 (17.5)
Central obesity [e]	15,893 (23.6)	8,477 (72.9)	7,416 (13.3)
Low HDL-C [f]	5,377 (8.0)	3,279 (28.2)	2,098 (3.8)
Number of MetS components			
0	22,519 (33.4)	-	22,519 (40.4)
1	19,715 (29.3)	-	19,715 (35.3)
2	13,539 (20.1)	-	13,539 (24.3)
3	7,842 (11.6)	7,842 (67.4)	-
4	3,231 (4.8)	3,231 (27.8)	-
5	557 (0.83)	557 (4.8)	-

Follow-up results

- Follow-up time: 408,324 PY

- LTSA: 2915 (2,433 men, 482 women)

- Incidence rate per 1,000 PY:

  - Overall: 7.1 (95% CI, 6.9-7.4)

  - Men: 7.0 (95% CI, 6.7-7.2)

  - Women: 8.2 (95% CI, 7.5-9.1)

- Common causes:

  - Depressive episodes

  - Cancers

  - Diseases of circulatory system

Medically-certified causes	ICD-10	N
Physical disorders		**1,481**
Cancers	C00-D49	501
Diseases of the circulatory system	I00-I99	288
Diseases of the musculoskeletal system and connective tissue	M00-M99	272
Diseases of the nervous system	G00-G99	98
Diseases of the digestive system	K00-K93	88
Others		234
Mental, behavioral and neurodevelopmental disorders		**1,132**
Depressive episode	F32	689
Reaction to severe stress and adjustment disorders	F43	200
Others		243
External causes	S00-T99	**285**
Not available		**17**
Total		**2915**

Results

MetS and all-cause LTSA

- **MetS significantly increased LTSA risk**

HR for LTSA, comparing MetS vs without MetS:

- Model 1: **1.62; 95% CI 1.49-1.77**
- Model 2: **1.54; 95% CI 1.41-1.68**

MetS and cause-specific LTSA

Results

- **MetS significantly increased the risk of LTSA due to:**

  ➤ Physical disorders: HR 1.76; 95% CI 1.56-1.98

      - CVDs: **HR 3.16; 95% CI 2.35-4.25**

      - Musculoskeletal diseases: HR 2.01; 95% CI 1.54-2.63

      - Overall cancer: HR 1.24; 95% CI 1.00-1.53

         ✓ *Obesity-related cancer:*   HR 1.35; 95% CI 1.00-1.81

  ➤ Mental disorders: HR 1.28; 95% CI 1.10-1.49

      - Reaction to severe stress and adjustment disorders:

                                        HR 1.46; 95% CI 1.02-2.09

  ➤ External causes: HR 1.46; 95% CI 1.10-1.93

MetS-LTSA findings

Results

- **Consistent with studies on similar topic**
  - ➢ MetS and sickness absence *(Burton 2008)*
  - ➢ Central obesity and sickness absence *(Burton 2008; Korpela 2013)*
  - ➢ Epidemiological data linking MetS to CVD, cancers *(mendrick 2018)*, musculoskeletal diseases *(Zhou 2013)*

- **Contribute to**
  - ➢ Extends previous observations by showing all-cause and cause-specific MetS-LTSA association
  - ➢ Highlight the importance of integrating psychological assessment and intervention in the prevention of LTSA for those with MetS.

LTSA events		HR (95% CI)	
Causes	N	Model 1	Model 2
All-causes			
MetS (-)	2189	1.00 (ref)	1.00 (ref)
MetS (+)	726	**1.62 (1.49, 1.77)**	**1.54 (1.41, 1.68)**
Physical disorders			
MetS (-)	1053	1.00 (ref)	1.00 (ref)
MetS (+)	428	**1.83 (1.62, 2.05)**	**1.76 (1.56, 1.98)**
Cardiovascular diseases			
MetS (-)	101	1.00 (ref)	1.00 (ref)
MetS (+)	88	**3.40 (2.53, 4.57)**	**3.16 (2.35, 4.25)**
Musculoskeletal diseases			
MetS (-)	186	1.00 (ref)	1.00 (ref)
MetS (+)	86	**2.09 (1.60, 2.72)**	**2.01 (1.54, 2.63)**
Cancers			
MetS (-)	386	1.00 (ref)	1.00 (ref)
MetS (+)	115	**1.27 (1.03, 1.57)**	**1.24 (1.00, 1.53)**
Obesity-related cancers			
MetS (-)	186	1.00 (ref)	1.00 (ref)
MetS (+)	61	**1.37 (1.02, 1.84)**	**1.35 (1.00, 1.81)**
Other cancers			
MetS (-)	200	1.00 (ref)	1.00 (ref)
MetS (+)	54	1.18 (0.87, 1.60)	1.14 (0.83, 1.55)
Mental disorders			
MetS (-)	907	1.00 (ref)	1.00 (ref)
MetS (+)	225	**1.38 (1.19, 1.61)**	**1.28 (1.10, 1.49)**
Depressive episode			
MetS (-)	565	1.00 (ref)	1.00 (ref)
MetS (+)	124	1.18 (0.96, 1.44)	1.08 (0.88, 1.32)
Reaction to severe stress and adjustment disorders			
MetS (-)	160	1.00 (ref)	1.00 (ref)
MetS (+)	40	**1.53 (1.07, 2.19)**	**1.46 (1.02, 2.09)**
External causes			
MetS (-)	216	1.00 (ref)	1.00 (ref)
MetS (+)	69	**1.50 (1.13, 1.99)**	**1.46 (1.10, 1.93)**

MetS components & LTSA

Results

- **Individual components increased LTSA risk**

  ➢ High fasting plasma glucose

  ➢ Central obesity

  ➢ High triglycerides

  ➢ High blood pressure

- **Number of components increased LTSA risk**

  ➢ Dose-response relationship

  ➢ Highlight the importance of studying MetS as a whole instead of individual components

LTSA causes	LTSA events	HR (95% CI)	
		Model 1	Model 2
High FPG			
MetS (-)	1714	1.00 (ref)	1.00 (ref)
MetS (+)	1201	1.49 (1.37, 1.62)	1.38 (1.27, 1.50)
Central obesity			
MetS (-)	2011	1.00 (ref)	1.00 (ref)
MetS (+)	904	1.42 (1.31, 1.53)	1.22 (1.12, 1.33)
High TG			
MetS (-)	1889	1.00 (ref)	1.00 (ref)
MetS (+)	1026	1.40 (1.29, 1.51)	1.18 (1.09, 1.29)
High BP			
MetS (-)	1742	1.00 (ref)	1.00 (ref)
MetS (+)	1173	1.28 (1.19, 1.39)	1.14 (1.05, 1.24)
Reduced HDL-C			
MetS (-)	2630	1.00 (ref)	1.00 (ref)
MetS (+)	285	1.25 (1.11, 1.42)	1.01 (0.89, 1.15)

$P_{trend} < 0.001$

Hazard ratio (95%CI)

Number of components	0	1	2	3	4	5
HR	1.00 (ref.)	1.22	1.48	1.81	2.04	2.14
Person-years	138,860	120,763	80,629	45,876	18,890	3,306
LTSA events	736	795	658	468	216	42
LTSA rate	5.3	6.6	8.2	10.2	11.4	12.7
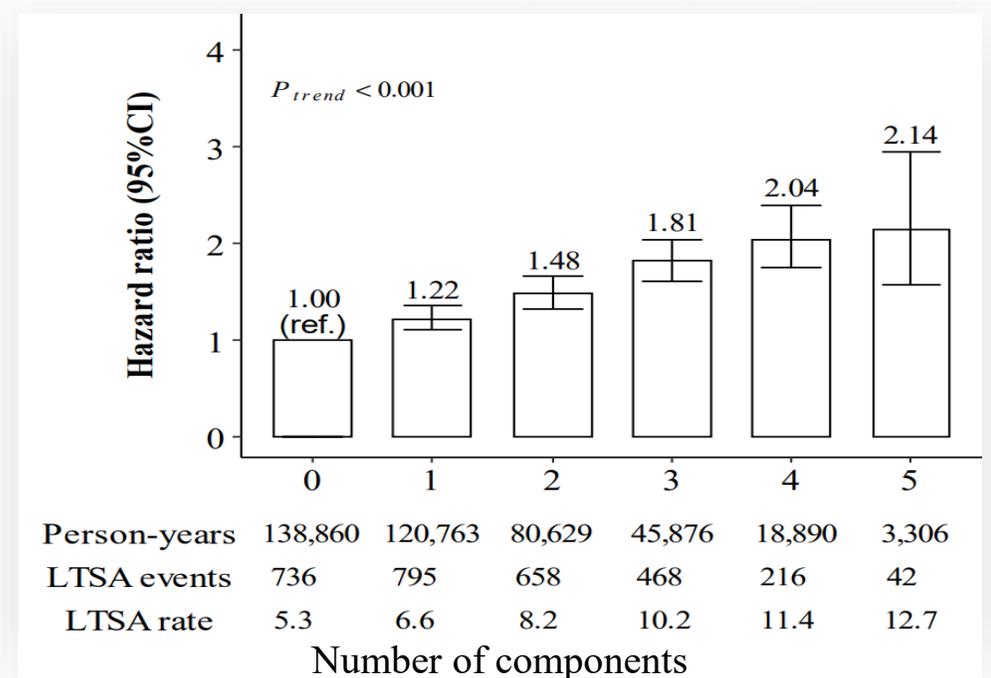
Conclusion

➢ **MetS was associated with higher risk of LTSA due to various causes, especially LTSA due to CVDs.**

➢ **High FPG, high TG, central obesity and high BP were each associated with LTSA.**

➢ **There was a dose-response association between the number of MetS components and the LTSA risk.**

Thank you for your attention!