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Can self-rated health be useful to primary care physicians as a diagnostic indicator of metabolic dysregulations amongst patients with type 2 diabetes? A population-based study.

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Article

1 **Title**
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4 metabolic dysregulations amongst patients with type 2 diabetes? A population-based study
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6 **Running title**: Self-rated health, metabolic dysfunction, and type 2 diabetes
7

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44 **ABSTRACT**
45

46 **Background**
47 Although most of the management of type 2 diabetes (T2DM) occurs in primary care, and
48 physicians are tasked with using a 'whole person' approach, there is currently a lack of
49 research on psychosocial diagnostic indicators for detecting metabolic abnormalities in
50 T2DM patients. This study examined relations between SRH and metabolic abnormalities in
51 patients with type 2 diabetes, adjusting for metabolic comorbidity.
52

53 **Method**
54 A total of 583 adults with type 2 diabetes were identified from the 2019 HSE (Health Survey
55 for England). Data on metabolic syndrome (MetS) was extracted, including lipids (high
56 density lipoprotein cholesterol (HDL-C)), glycated haemoglobin (HbA1c), blood pressure
57 (systolic/diastolic), and anthropometric measures (BMI, waist/hip ratio). Bootstrapped
58 hierarchical regression and structural equation modelling (SEM) were used to analyse the
59 data.
60

61 **Results**
62 Adjusting for metabolic covariates attenuated significant associations between SRH and
63 metabolic abnormalities (HDL-C, HbA1c), regardless of MetS status. Analysis by gender
64 uncovered covariate-adjusted associations between SRH and both HDL-C (in men) and
65 HbA1c (in women) (p's = 0.01), albeit these associations were no longer significant when
66 evaluated against a Bonferroni-adjusted alpha value ($p > 0.004$). Sensitivity analysis
67 indicated most findings were unaffected by the type of algorithm used to manage missing
68 data. SEM revealed no indirect associations between SRH, metabolic abnormalities, and
69 lifestyle factors.
70

71 **Conclusions**
72 While poor SRH can help primary care physicians identify T2DM patients with metabolic
73 dysfunction, it may not offer added diagnostic usefulness over clinical biomarkers.
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75

76 **Key words**
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78 Diabetes; Metabolic syndrome; Self-perception; Cardiometabolic Risk Factors
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88 **1. BACKGROUND**
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90 **1.1 Primary care**
91
92 Most of the management of type 2 diabetes (T2DM) occurs in primary care (1). Primary care
93 physicians are expected to adopt a 'whole-person' (holistic) approach, including bio-psycho-
94 social evaluations, when working with patients to detect and manage metabolic abnormalities
95 that increase the risk of cardiovascular disease, and other cardiometabolic complications (2),
96 such as insulin resistance, elevated fasting glucose ($\geq$ 100mg/dL), waist circumference (>0.9
97 (men) or > 0.85 (women)), triglycerides ($\geq$ 150 mg/dL (1.7 mmol/L), blood pressure (systolic
98 $\geq$ 130 and/or diastolic $\geq$ 85 mm Hg), and reduced HDL-C (< 40 mg/dL (1.0 mmol/L) in
99 males; < 50 mg/dL (1.3 mmol/L) in females) (see Fig 1) (3). The presence of insulin
100 resistance or elevated fasting glucose, and any two of the aforementioned criteria, is
101 considered diagnostic of metabolic syndrome (MetS) (2).
102   While MetS is especially problematic in people with T2DM (4), metabolic irregularities
103 often do not produce overt symptoms (besides visible abdominal adiposity in some patients)
104 (5). This can be problematic in primary care settings, where the focus is on identifying and
105 reducing metabolic abnormalities (1). Clinicians need to conduct a thorough physical
106 examination to diagnose the condition (6). Despite the growing emphasis on a
107 biopsychosocial approach in the management of T2DM in primary care settings (7), there has
108 been limited research on psychological diagnostic indicators that primary care physicians can
109 use to detect metabolic dysregulations in asymptomatic T2DM patients.
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111   ………………………………………………..
112 **[Fig 1** Diagnostic criteria for metabolic syndrome based on WHO
113 (1999) guidelines (Source: Saklayen, 2018)]
114   ………………………………………………..
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116 **1.2 Self-rated health**
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118 Self-rated health (SRH) is an increasingly important construct in epidemiological and
119 biomedical research (8-10). It refers to a person's assessment of their health status and is
120 thought to be a more accurate health indicator than biomedical risk factors (11). For example,
121 SRH may depict undiagnosed illness at preclinical or prodromal stages (i.e., before major
122 symptoms appear) (8). It is a simple and easy to administer measure and hence can be a
123 useful risk indicator in clinical settings (e.g., during doctor-patient consultations). Decades of
124 research suggests SRH is a reliable predictor of mortality, over and beyond physical health
125 indicators, with its predictive power increasing over time (9). Research also suggests SRH
126 independently predicts morbidity, including cardio cerebral vascular diseases, after adjusting
127 for biomedical and sociodemographic covariates (12-15).
128   Recently, there has been growing interest in the relationship between SRH and metabolic
129 health (16-18), notably the specific metabolic abnormalities used to define MetS, such as
130 insulin resistance, hyperlipidaemia (high cholesterol), blood pressure, and anthropometric

131   factors (19-21). An association between SRH and metabolic function may be underpinned by
132   several mechanisms. First, a person may simply perceive *symptoms* of metabolic dysfunction
133   (e.g., weight gain), and consequently infer that they are in a poor state of health (8). This
134   scenario assumes that illness symptoms are perceptible (i.e., the person is not asymptomatic)
135   (22, 23). Second, an individual may evaluate their health status based on *biomarker*
136   information depicting metabolic functioning, such as clinical test results, or data from
137   medical tests performed at home (e.g., blood pressure monitoring) (10). Third, SRH may
138   reflect the presence of various *risk factors* for metabolic dysfunction, including family
139   history, behavioural risk factors, and/or or signs of declining health, such as functional
140   impairment (8).
141
142   **1.3 Ambiguity in the literature**
143
144   Historically, previous research demonstrating associations between SRH and MetS have
145   rarely controlled for the specific clinical biomarkers that define MetS (21). SRH has been
146   linked to various metabolic abnormalities including high density lipoprotein cholesterol
147   (HDL-C) (24, 25), triglycerides (20), and blood pressure (26-28). While some studies have
148   adjusted for anthropometric markers, notably BMI (20), we found no study controlling for
149   other metabolic dysfunctions in MetS (e.g., HDL-C, triglycerides, blood glucose,
150   systolic/diastolic blood pressure). Thus, it remains unclear how associations between SRH
151   and metabolic abnormalities is affected by related metabolic factors.
152   This problem is well illustrated in a large-scale investigation using data from three
153   European populations (approximately 15,000 individuals). The study found that SRH was
154   associated with at least 57 (out of 150) biomarkers, including biochemical factors that define
155   MetS, such as HDL-C (mmol/L), triglycerides (mg/dl) glycaeted haemoglobin (HbA1c, %),
156   and insulin (mU/ml) (10). Although these associations were independent of disease and
157   physical functioning (e.g., number of diseases), there was no adjustment for metabolic
158   covariates. This methodological constraint was also manifest in another large-scale
159   population-based study using data from 18,000 adults (13). Although SRH was found to be
160   associated with metabolic anomalies such as haemoglobin, triglycerides, LDL-C (low-density
161   lipoprotein cholesterol), and fasting plasma glucose, the study did not adjust for covariance
162   between these metabolic biomarkers.
163   The ambiguity in the SRH literature is problematic since biomedical research indicates
164   significant multimorbidity in metabolic biomarkers (29-31). For example, consider a scenario
165   in which poor SRH depicts a specific aspect of hyperlipidemia, such as HDL-C deficiency
166   (32). SRH may simply be capturing comorbid cardiometabolic abnormalities that primary
167   care physicians can easily observe, and/or detect using available clinical options (e.g.,
168   obesity, HbA1c) (10). In this scenario, SRH does not provide primary care practitioners with
169   any unique insights in detecting and managing cardiometabolic complications in T2DM
170   patients. Consequently, in order to show that SRH offers unique diagnostic utility for
171   detecting metabolic dysfunction in T2DM patients, over and beyond comorbid biomarkers
172   (10), it is necessary to adjust for cardiometabolic covariates.
173
174

1.4 Asymptomatic patients

Although research has implicated SRH in cardiometabolic health amongst patients with T2DM (33, 34), evidence is limited, and it remains unclear how SRH contributes to metabolic abnormalities in this clinical population. Not every T2DM patient meets the criteria for MetS (2). Contrary to the prevailing pathophysiological perspective that metabolic dysfunction applies to all T2DM cases, a cross-sectional analysis of 414 T2DM cases (including body weight and fat mass, systolic/diastolic blood pressure, and glucose tolerance) found that 15% displayed no components of MetS, other than hyperglycaemia (35). Although these cases showed insulin resistance, other metabolic levels (e.g., triglycerides, HDL-C, and blood pressure) matched concentrations in healthy controls. Certain forms of metabolic dysregulation do not generate any symptoms (e.g., high cholesterol), meaning clinicians need to conduct thorough physical examinations and blood testing to diagnose the condition (6). Thus, a significant relationship between SRH and metabolic abnormalities, independent of other metabolic biomarkers, will be clinically relevant to T2DM patients, since poor SRH may help identify asymptomatic patients with subclinical metabolic dysfunctions, before the development of overt clinical MetS (8). SRH is an easily measured metric (11), and hence may be especially useful in clinical settings by providing doctors with an extra diagnostic tool to identify high risk T2DM patients requiring additional clinical evaluation, to detect metabolic anomalies.

1.5 Research objectives

Professionals in primary care settings face a growing plethora of available clinical options for detecting and managing metabolic abnormalities in T2DM (1). However, despite the emphasis on a holistic approach in primary care (7), there has been limited research on useful psychological diagnostic indicators for detecting metabolic dysregulations in T2DM patients. While it is possible SRH may be a useful diagnostic indicator for detecting asymptomatic metabolic dysfunction in T2DM patients, currently there has been little or no research testing this premise. Although past studies have demonstrated significant associations between SRH and metabolic anomalies (16, 18-21), independent of disease and physical functioning (10), these relationships may be confounded by comorbid metabolic biomarkers (29, 30). Thus, it is necessary to demonstrate extent to which SRH depicts metabolic abnormalities in T2DM patients, while accounting for cardiometabolic covariates (1).

The current study examined two specific questions:

a) Does SRH *independently* predict metabolic abnormalities in T2DM patients? Consistent with previous research on SRH in relation to biomarkers (10), and MetS (20), we expected independent associations between SRH and metabolic variables after adjusting for metabolic covariates (Hypothesis 1).

b) Does SRH *independently* predict metabolic abnormalities differentially in T2DM patients who do and those who do not meet MetS diagnostic criteria? Based on

219   research linking SRH to biomarkers, independent of disease diagnosis (10), we
220   hypothesised independent associations between SRH and metabolic factors after
221   adjusting for metabolic covariance, irrespective of MetS status (Hypothesis 2) (8, 36,
222   37).
223
224

225   **2.**   <u>**MATERIALS & METHODS**</u>
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227 **2.1 Ethics Statements**
228

229 The study was conducted according to the guidelines of the Declaration of Helsinki and
230 approved by the Institutional Review Board (or Ethics Committee) of Liverpool John Moores
231 University, covering research with archived data from the Health Survey for England (HSE)
232 (approval number 16/NSP/035, 14 June 2016).
233

234 **2.2 Data availability**
235

236 The Health Survey for England (HSE) is managed by the National Centre for Social Research
237 (NatCen) and the Department of Epidemiology and Public Health at University College
238 London. HSE data cannot be shared publicly for legal and ethical reasons, third party rights,
239 and institutional or national regulations or laws. The UK Data Service provides restricted
240 access to HSE data, to protect confidential or proprietary information. Individuals and
241 organisations seeking access need to be registered with the UK Data Service, albeit access is
242 limited to applicants from UK HE/FE institutions, central and local government, NHS,
243 research companies and charities for not-for-profit education and research purposes. Users
244 not in the above categories can submit access requests to surveys.queries@nhs.net and will be
245 subject to approval. For more information, please contact the UK Data Service website.
246 https://rb.gy/vhi5uf.
247

248 **2.3 Design**
249

250 Fig 2 shows participant recruitment and eligibility data. We extracted data from the 2019
251 Health Survey for England (HSE), which monitors health-related trends in adults (aged > 16)
252 and children (aged 0 to 15) living in England, United Kingdom (38). The HSE is conducted
253 by the National Centre for Social Research (NatCen) and the Department of Epidemiology
254 and Public Health at University College London. HSE data cannot be shared publicly for
255 legal and ethical reasons, due to third party rights, institutional or national regulations or
256 laws, and the nature of data gathered. Access to HSE data is provided by the UK Data
257 Service under restrictions to protect confidential or proprietary information. The survey
258 assesses various biomedical parameters, including metabolic risk factors (e.g., height, weight,
259 blood pressure, lipid profiles), lifestyle (e.g., smoking and alcohol use) and SRH. In general,
260 survey protocol involves an interview and/or completion of a questionnaire followed by a
261 visit from a nurse who collects biomedical data including saliva samples. Details of 2019

262 HSE methodology and scope, including the questionnaire, have been published elsewhere
263 (39).
264 …………………………………………..
265 [**Fig 2** Flow Diagram]
266 …………………………………………
267 **2.4 Sample**
268
269 A total of 8,205 adults and 2,095 children (total = 10,300) participated in the 2019 survey. Of
270 these, 4,947 adults and 1,169 children were visited by a nurse. Participants were recruited
271 using stratified probability sampling, to ensure the sample is representative of the household
272 population in England. Only participants diagnosed with T2DM by a doctor or nurse were
273 eligible to participate in the present study. We identified 584 individuals with T2DM, of
274 whom 353 (60.4%) met the diagnostic criteria for MetS.
275
276 **2.5 Self-rated health**
277
278 SRH data was assessed via the question "How is your health in general? Would you say it
279 was ..." (respondents selected one of five responses options: "Very good" (coded 1), "Good"
280 (coded 2), "Fair" (coded 3) "Bad" (coded 4), and "Very bad" (coded 5)). These response
281 options differ from categories used in some other research, which for example include an
282 "excellent" option (10)). For linear regression SRH was collapsed into a simple dichotomous
283 (dummy) variable due to the very small number of MetS cases in the "Very good" (n = 27)
284 and "Very bad" (n = 27) categories. For this new variable "fair"/"bad"/"very bad" responses
285 were coded 0, while "good"/"very good" responses were coded 1. For the purposes of
286 conducting structural equation modelling (SEM) with maximum likelihood estimation (which
287 requires continuous data), SRH was treated as continuous variable with the five original
288 categories (recoded from 0 ("Very good") through to 4 ("Very bad")). Thus, a higher value
289 indicated poorer SRH.
290
291 **2.6 Metabolic variables**
292
293 Metabolic data was based on blood samples taken during the nurse visit (38). All measures
294 were treated as both continuous variables (for regression analysis) and dichotomised
295 variables, based on MetS diagnostic criteria, in order to identify MetS cases (2). Serum HDL-
296 C was measured in mmol/L, with 0.9 mmol/L (35 mg/dl) for men used as the critical
297 threshold ($\geq$ 0.9 mmol/L (coded 0) vs. < 0.9 mmol/L (coded 1)). Anthropometric markers
298 consisted of waist/hip ratio data, with 0.85 (women) used as the critical threshold (> 0.85
299 (coded 1) vs. < 0.85 (coded 0)) and BMI scores, dichotomised based on the cut-off for
300 obesity (> 30 kg/m^2 (coded 1) vs. < 30 kg/m^2 (coded 0)). Diagnosis with hypertension by a
301 health professional was a simple dichotomy ('Yes' (coded 1) vs. 'No' (coded 0)). We also
302 extracted systolic and diastolic blood pressure data, viewed as separate biomarkers due to
303 differential effects on health outcomes (40). Both variables were dichotomised: systolic ($\leq$
304 120 mm Hg (coded 0) vs. > 120 mm Hg (coded 1)); diastolic ($\leq$ 80 mm Hg (coded 0) vs. > 80
305 mm Hg (coded 1)). Finally, we extracted glycaeted haemoglobin (HbA1c (mmol/mol)) data,

in place of fasting glucose. Inclusion of HbA1c here reflects the new clinical definition for MetS proposed by the IDF (International Diabetes Federation), (41). HbA1c scores were dichotomised at the 48 mmol/mol clinical threshold for diabetes; < 48 mmol/mol (coded 0) or = > 48 mmol/mol (coded 1) (42).

WHO criteria were used to identify MetS cases (5). This entails insulin resistance or glucose > 6.1 mmol/L (110 mg/dl), 2 hour glucose > 7.8 mmol (140 mg/dl), and any two of four additional diagnostic requirements: (a) serum HDL-C (cholesterol) < 0.9 mmol/L (35 mg/dl) for men, and < 1.0 mmol/L (40 mg/dl) for women, (b) triglycerides > 1.7 mmol/L (150 mg/dl), (c) a waist/hip ratio > 0.9 for men, or > 0.85 for women, or a BMI value > 30 kg/m2, and (d) blood pressure > 140/90 mmHg. Since data on insulin resistance and impaired glucose tolerance was unavailable (39), we assumed poor insulin sensitivity from T2DM status (43). Furthermore, BMI (> 30 kg/m^2) rather than waist/hip ratio was used as the primary anthropometric measure since the former criterion is not gender-specific (44). We also applied the HDL-C threshold for men (< 0.9 mmol/L (35 mg/dl)) as this is more conservative. Additionally, diagnosis with hypertension was used in place of systolic/diastolic blood pressure readings, due to the greater proportion of missing data for the latter. Overall, MetS caseness was based on the presence of T2DM and any two of the following: serum HDL-C< 0.9 mmol/L (35 mg/dl); BMI (kg/m^2) > 30; diagnosis with hypertension by a health professional. A total of 352 MetS cases (60.3 %) were identified using these criteria (MetS cases = 1, non-cases = 0).

2.7 Other covariates

We assessed two lifestyle factors: cigarette smoking and alcohol consumption. Both behaviours are heavily implicated in MetS and increased cardiovascular risk (45, 46). For example, a population-based study of 64,046 adults (aged 18 to 80) found MetS prevalence varied as a function of both smoking and alcohol consumption. Current alcohol and cigarette use predicted higher cholesterol (triglycerides) levels, and alcohol intake was linked to truncal obesity and increased blood pressure, with the latter effect more pronounced in heavy smokers (47). We extracted two lifestyle items from the HSE data, each treated as a single-item measure: one assessed number of cigarette smoked per day (respondents provided a numerical figure), while the other assessed the frequency of alcohol consumption in the past twelve months: respondents selected one of eight categories ("Almost every day" (coded 1), "Five or six days a week" (coded 2), "Three or four days a week" (coded 3), "Once or twice a week" (coded 4), "Once or twice a month" (coded 5), "Once every couple of months" (coded 6), "Once or twice a year" (coded 7), and "Not at all in the last 12 months" (coded 8)). Both lifestyle measures were treated as quantitative variables, with a higher score denoting higher levels of cigarette use or alcohol consumption.

We extracted data for four demographic factors: age, gender, socio-economic status, educational level, and ethnicity. Age was calibrated in twenty-two bands: ages 1 to 16 were classified into six 1- or 2-year age bands (e.g., 2-4, 13-15), while ages over 16 were grouped into 3- or 4-year age bands (e.g., 16-19, 30-34, 75-70). Gender was a dichotomy: male (coded 1), female (coded 0). Socio-economic classification contained eight bands using the UK Registrar General's scale: (code = 0) 'higher managerial and professional', (code = 1) 'lower

350   managerial and professional', (code = 2) 'intermediate occupations', (code = 3) 'small
351   employers & own account workers', (code = 4) 'lower supervisory and technical', (code = 5)
352   'semi-routine occupations', (code = 6) 'routine occupations', and (code = 7) 'never worked &
353   long-term unemployed'. Level of educational level was dichotomised: 'below degree or
354   none' (coded 0) and 'degree or equivalent' (coded 1). Finally, ethnicity was also a simple
355   dichotomy: 'White' (coded 0) and 'non-White' (coded 1).

356

357   **2.8 Data analysis**

358

359   We performed chi-square and independent samples t-tests to evaluate group differences in
360   metabolic function based on MetS status. Bootstrapped hierarchical multiple regression was
361   used to test each hypothesis. In each regression analysis we predicted an individual metabolic
362   variable (e.g., HDL-C), with all other metabolic factors treated as covariates. We constructed
363   three models for each regression analysis: Model 1 (metabolic variable = Intercept + Age +
364   Gender + Social Class + Ethnicity + Lifestyle factors), Model 2 (metabolic variable =
365   Intercept + Age + Gender + Social Class + Ethnicity + Lifestyle factors + SRH), Model 3
366   (metabolic variable = Intercept + Age + Gender + Social Class + Ethnicity + Lifestyle factors
367   + SRH + other metabolic factors). Thus, metabolic covariates were included in the equation
368   after first evaluating the predictive utility of SRH. We initially adopted a lower alpha level (p
369   ≤ 0.01), to reduce type 1 errors, but interpreted significant regression results using a more
370   conservative Bonferroni-adjusted alpha value ($p < 0.004$), to further reduce the risk of false
371   positives (48). Power analysis for multiple regression using G*Power 3.1.7 (49) indicated a
372   minimum total sample size of N = 234, to detect a medium effect ($f^2 = 0.15$), at a 0.01 alpha
373   level, and 95% power ($1 - \beta$ err prob) (50).

374

375

376   3. <u>**RESULTS**</u>

377

378   **3.1 Descriptive statistics**

379

380   We employed listwise deletion to manage missing data (51), which ranged from 0% for
381   demographics (age, gender, ethnicity) to > 20% for BMI, and > 40% for diastolic/systolic
382   blood pressure (40.1% each), and waist/hip ratio (40.6%), to as high as 60% for education
383   level (61%), HbA1c (60.3%), and HDL-C (60.1%) (see Figure 2). Despite the limitations of
384   listwise deletion, this approach was preferred to inputting (replacing) missing data using
385   estimated parameters (e.g., expectation maximisation). The latter methods require
386   assumptions of multivariate normality, which is problematic with categorical variables (e.g.,
387   SRH, MetS) (52). Regardless, we performed sensitivity analysis to compare the effects of
388   listwise deletion versus expectation maximisation on regression results.
389   Of 584 patients diagnosed with T2DM, 353 patients (60.3%) met the criteria for MetS. It
390   should be noted that occurrence of MetS in diabetes patients varies, and may be influenced by
391   various factors including MetS diagnostic criteria: thus not every diabetes patient is
392   diagnosed with MetS (53). The percentage of patients meeting each individual diagnostic
393   criterion are as follows: HDL-C < = 0.9 mmol/L (35 mg/dl) (n = 391 (67%)), waist/hip ratio

394　= > 0.85cm (n = 316 (54.1%)); BMI > 30 kg/m2 (n = 229 (39.2%)); diagnosed with

395　hypertension by a doctor or nurse; (n = 370 (63.4%)): systolic blood pressure > 140 mmHg (n

396　= 82 (14%)) and diastolic blood pressure > 90 mmHg (n = 14 (2.4%)). Just over a quarter of

397　patients had a HbA1c > 48 mmol/mol (n = 167 (28.6%)). The percentage of participants per

398　SRH category were 'very good' (9.8%), 'good' (32.9%), 'fair' (34.8%), 'bad' (16.1%), and

399　'very bad' (6.5%). Thus, just over 40% of patients reported 'good'/'very good' health.

400　　　Table 1 shows means, SDs, and frequencies for the overall sample and by MetS status

401　(cases versus non-cases). All participants were aged ≥ 16 years, with most participants

402　(56.8%) aged ≥ 65 years. The youngest age band was 16 to 19 years, the oldest was 90+

403　years, while the median age band was 65 to 69 years. The sample was predominantly male

404　(54.1%), 486 (83.2%) identified as Caucasian, 105 (47.1%) had a university education at

405　degree level or equivalent, and 184 (33%) came from the top three socio-economic groups

406　(higher/lower managerial, professional, intermediate occupations).

407　　　Respondents smoked an average of 2.28 cigarettes a day, and consumed alcohol 5.6 times

408　in the past 12 months. The sample met WHO thresholds for obesity (BMI (kg/m2) > 0.30 (M

409　= 31.22)), high central adiposity (waist/hip ratio (cm) > 0.9 (men) (M = 1.00), > 0.85

410　(women) (M = 0.91)), and poor glycaemic control (HbA1c > 48 mmol/mol) (M = 57.50).

411　HDL-C levels were normal (i.e., above minimum thresholds of < 0.9 mmol/L in men (M =

412　1.19) and < 1.0 mmol/L in women (M = 1.31)). Systolic/diastolic blood pressure values were

413　also below the critical thresholds of >140/90 mmHg (M = 129/69.72).

414　　　MetS cases were significantly less likely to report 'very good'/'good' SRH ($\chi2$ (1, N =

415　583) = 13.344, $p < 0.001$). There were no group differences in demographic factors or

416　systolic/diastolic blood pressure (all p's > 0.01), albeit a slightly higher proportion of MetS

417　cases (59.1%) were aged 65 years or older, compared with non-cases (53.2%). MetS cases

418　were significantly more likely than non-cases to be HDL-C deficient (HDL-C < = 0.9

419　mmol/L (35 mg/dl)) ($\chi2$ (1, N = 583) = 92.768, $p < 0.001$), and generally overweight (BMI >

420　30 kg/m2), ($\chi2$ (1, N = 583) =159.041, $p < 0.001$), but less likely to be centrally obese

421　(waist/hip ratio = > 0.85cm), ($\chi2$ (1, N = 583) =12.960, $p < 0.001$). MetS cases were also

422　more likely to be hypertensive ($\chi2$ (1, N = 583) = 231.923, $p < 0.001$), but show better

423　glycaemic control (HbA1c > 48 mmol/mol), ($\chi2$ (1, N = 583) = 45.034, $p < 0.001$).

424　　　Independent samples t-tests comparing MetS cases and non-cases showed the former

425　group had significantly higher BMI (kg/m2), exceeding the threshold for obesity (M = 33.41

426　versus 27.54), $t(459.82)$ = -12.74, $p < 0.001$, greater waist/hip ratio (M = 0.98 versus 0.94),

427　$t(343.70)$ = -4.22, $p < 0.001$, and lower serum HDL-C (M = 1.18 versus 1.30), $t(183.65)$ =

428　2.69, p < 0.01. There were no group differences in blood pressure, HbA1c, or lifestyle factors

429　(all p's > 0.01).

430　　　　　…………………………………………..

431　　　　　　　**[Insert Table 1 about here]**

432　　　　　Sample characteristics by metabolic syndrome status

433　　　　　…………………………………………………

434　　　　　…………………………………………..

435　　　　　　　**[Insert Table 2 about here]**

436　　　Final regression models predicting metabolic factors from self-rated health and

437　　　　　　metabolic covariates in the whole sample

438 ………………………………………………

439

440 **3.2 Hypothesis 1: Does SRH predict metabolic abnormalities in T2DM patients?**

441

442 Table 2 shows results of bootstrapped hierarchical multiple regression predicting metabolic

443 abnormalities. SRH significantly predicted HDL-C (mmol/L) (Model 2) (β = -0.17, p =

444 0.015), increasing the explained variance, ΔR^2 = 0.029, F (1, 176) = 6.035, p = 0.015.

445 However, adjusting for metabolic factors (Model 3) negated this association, accounting for

446 an additional 6.7% of the variance in HDL-C (ΔR^2 = 0.067, F (5, 171) = 2.976, p = 0.013).

447 SRH failed to predict systolic blood pressure (mmHg) (Model 2). Adding metabolic

448 covariates (Model 3) significantly improved the model (ΔR^2 = 0.254, F (5, 171) = 13.269, p <

449 0.001), primarily due to diastolic covariance (β = 0.53, p < 0.001). Similarly, SRH failed to

450 predict diastolic blood pressure (mmHg), whereas adding metabolic factors significantly

451 improved model fit (ΔR^2 = 0.271, F (5, 171) = 15.660, p < 0.001), mainly due to systolic

452 effects (β = 0.47, p < 0.001) and HbA1c (mmol/mol) (β = 0.18, p = 0.003).

453 The association between SRH and HbA1c (mmol/mol) was significant (β = -0.20, p =

454 0.008) prior to adjusting for metabolic covariates (Model 2) (ΔR^2 = 0.082, F (1, 176) = 7.241,

455 p = 0.008). Adding metabolic variables (Model 3) significantly improved the model (ΔR^2 =

456 0.084, F (5, 171) = 3.454, p = 0.005), negating the SRH–HbA1c relationship (p = 0.04).

457 Finally, SRH failed to predict anthropometric criteria (BMI, (kg/m^2), waist/hip ratio (cm))

458 (Model 2). Including metabolic factors explained additional variance for both BMI (ΔR^2 =

459 0.090, F (5, 171) = 3.835, p = 0.003) and waist/hip ratio (ΔR^2 = 0.069 F (5, 171) = 4.027, p =

460 0.002).

461 …………………………………………..

462 **[Insert Table 3 about here]**

463 Final regression models predicting metabolic factors from self-rated health and

464 metabolic covariates in T2DM patients with MetS

465 …………………………………………..

466

467 **3.3 Hypothesis 2: Does SRH predict metabolic abnormalities in T2DM patients by MetS**

468 **status?**

469 Table 3 shows the results for T2DM patients who met MetS diagnostic criteria. Crucially,

470 SRH failed to predict any metabolic variable (Model 2) prior to adjusting for metabolic

471 covariates (Model 3) (all p's > 0.01).

472 BMI was predicted by both age (β = -0.44, p = 0.001) and gender (β = -0.42, p = 0.009).

473 Gender also predicted waist/hip ratio (p < 0.001), while age predicted diastolic blood pressure

474 (p = 0.001). Adding metabolic predictors (Model 3) significantly improved the predicted

475 variance for systolic blood pressure (ΔR^2 = 0.286, F (5, 63) = 5.517, p < 0.001) and diastolic

476 blood pressure (ΔR^2 = 0.229, F (5, 63) = 5.395, p < 0.001).

477 Table 4 shows coefficients for patients who did *not* meet MetS criteria (i.e., T2DM-only

478 patients). Again, SRH failed to predict any metabolic factor (Model 2), prior to accounting

479 for metabolic covariates (all p's > 0.01). Adjusting for metabolic variables (Model 3)

480 explained significant additional variance for both systolic (ΔR^2 = 0.211, F (5, 96) = 7.069, p <

481 0.001) and diastolic (ΔR^2 = 0.286, F (5, 96) = 9.236, p < 0.001) blood pressure.

482 …………………………………………..
483 [Insert **Table 4** about here]
484 Final regression models predicting metabolic factors from self-rated health and
485 metabolic covariates in T2DM patients without MetS
486 …………………………………………

487

488 **3.4 Exploratory analysis by age and gender**

489

490 Research suggests gender differences in cardiometabolic risk (54, 55). Given the strong
491 associations between gender and anthropometric markers observed here (see above), we
492 decided to rerun regression analysis stratified by gender. The results are shown in Table 5.
493   SRH significantly predicted HDL-C (mmol/L) in male patients (Model 2) (β = 0.25, p =
494 0.01), accounting for a significant 6.1% increase in the explained variance, after accounting
495 for demographic and lifestyle factors, ΔR^2 = 0.061, F (1, 93) = 6.712, p = 0.011. Adjusting
496 for metabolic factors (Model 3) did not negate the association between SRH and HDL-C (β =
497 0.25, p = 0.01) in males and failed to improve the model (ΔR^2 = 0.095, F (5, 88) = 2.253, p =
498 0.056). SRH also predicted HbA1c (mmol/mol) in female patients (Model 2) (β = -0.31, p =
499 0.007), explaining 8.4% variance (ΔR^2 = 0.084, F (1, 77) = 7.696, p = 0.007). Adjusting for
500 metabolic abnormalities (Model 3) significantly improved the model, predicting another 15%
501 of the variance (ΔR^2 = 0.156, F (5, 72) = 3.287, p = 0.01), but did not nullify the
502 SRH–HbA1c association (β = -0.27, p = 0.01). SRH failed to predict the other metabolic
503 variables, irrespective of metabolic adjustment (all p's > 0.01).
504   Regardless, the associations of SRH with HDL-C (in men) and HbA1c (in women) were
505 not significant based on the Bonferroni adjusted alpha level (both p's > 0.004).
506   Given that age is implicated in metabolic health (56), and was significantly associated
507 with various metabolic covariates, notably systolic/diastolic blood pressure (see Table 2), we
508 repeated the analysis, to see whether SRH significantly predicts metabolic variables across
509 older ($\geq$ age 65) and younger (< age 65) respondents, based on a median split. SRH was not
510 reliably associated with any metabolic outcome, irrespective of age group (all p's > 0.004).

511

512 …………………………………………..
513 [Insert **Table 5** about here]
514 Final regression models predicting HDL-C and HbA1c from self-rated health and
515 metabolic covariates in males and females
516 …………………………………………

517

518 **3.5 Sensitivity analysis**

519

520 We reanalysed the data with expectation maximisation applied to missing values, to compare
521 the effects of different methods for resolving incomplete data (list wise deletion versus EM).
522 As observed in previous analysis, SRH failed to predict HDL-C (mmol/L), waist/hip ratio
523 (cm), and systolic/diastolic blood pressure (mmHg) after adjusting for metabolic covariates
524 (all p's > 0.01). However, contrary to expectations, SRH significantly predicted BMI (kg/m2)
525 after metabolic adjustment (Model 3) (β = -0.12, p = 0.002). Furthermore, the previously

526 significant SRH – HbA1c association was no longer reliable (β = -0.06, *p* = 0.10). Collapsing
527 the data by MetS status (cases versus non-cases) did not change the results: SRH failed to
528 predict any metabolic variable after adjusting for metabolic covariates (Model 3) (all *p*'s >
529 0.004). Overall, sensitivity analysis indicated most findings were unaffected by the
530 management of missing data using expectation maximisation algorithms.
531
3.6 Structural equation modelling
533
534 We used SEM to explore direct and indirect associations between SRH and metabolic
535 abnormities. We were curious to see whether relations between SRH and metabolic factors
536 are indirect, mediated by lifestyle factors (e.g., SRH negates health-protective behaviours,
537 which in turn precipitate metabolic dysfunction) (8). Model fit was based on standard criteria:
538 chi-square χ2 (CMIN) (*p* > 0.05), χ2 (CMIN)/df < 5.00, root mean square error of
539 approximation (RMSEA) < 0.07, comparative fit index (CFI) ≥ 0.95, Tucker and Lewis Index
540 (TLI) ≥ 0.95, and normed fit index (NFI) ≥ 0.95 (57). Metabolic factors were allowed to affect
541 SRH, that in turn was allowed to predict lifestyle factors, which then affected metabolic
542 variables (representing a vicious cycle in which lifestyle was a mediating factor). SEM
543 analysis using IBM SPSS AMOS™ (version 26), with specification search, generated 192
544 candidate models, none of which provided a satisfactory fit. The 'best' model (BIC (Bayesian
545 Information Criterion) = 0, χ2 (CMIN)/df < 5.00) suggested a cyclical relationship between
546 HDL-C, SRH, and alcohol intake. However, this model did not satisfy most other fit criteria:
547 CMIN (*p* < 0.05), RMSEA (> 0.07), CFI (< 0.95), and TLI (< 0.95)) and was therefore
548 discarded.
549
550
4. **DISCUSSION**
552
553 There is currently a lack of research on psychosocial tools that primary care physicians can
554 use for detecting metabolic abnormalities in people diagnosed with T2DM. Overall, we found
555 little evidence SRH reliably predicts metabolic dysfunction in T2DM patients, after
556 accounting for metabolic covariates. This finding contradicts previous population-based study
557 suggesting SRH independently predicts metabolic variables, irrespective of health status (10).
558 Although that investigation controlled for physical illness (e.g., number of diseases), there
559 was no adjustment metabolic covariates. We argued this was problematic given metabolic
560 comorbidity (29-31), which may partly explain reported associations between SRH and
561 biomarkers. Our findings suggest the contribution of SRH to HDL-C and HbA1c when
562 stratified by gender is notable but negligible in the context of clinical biomarkers. SRH may
563 simply be a psychological manifestation of metabolic comorbidity (30, 31). For example,
564 given widespread awareness of HbA1c and its relevance in glycaemic control (58), a poor
565 HbA1c test result (or symptoms suggesting hyperglycaemia) is likely to be viewed as a sign
566 of poor health by most T2DM patients (59). Poor SRH may also reflect feedback from other
567 cardiometabolic tests highlighting metabolic dysfunction (60).
568   Future research needs to explore the role of gender in the relationship between SRH and
569 metabolic health. Evidence suggests women are less likely to achieve HbA1c targets, which

570 may their affect health judgements. Women with diabetes are also more prone to blood sugar
571 changes overnight (nocturnal hypoglycaemia) (61), which perhaps may contribute to health
572 evaluations. Thus, there is a need to better understand women's greater sensitivity to HbA1c,
573 and whether SRH might be a useful indicator of poor glycaemic control in certain female
574 T2DM patients, irrespective of related metabolic abnormalities. This diagnostic utility
575 becomes especially relevant if HbA1c is used to define MetS (41). It is also necessary to
576 determine whether men and women use similar frames of reference when making judgements
577 about their health (62). For example, evidence suggests cholesterol management is worse in
578 women (63), including those with T2DM, and women with T2DM less frequently achieve
579 cholesterol targets compared with men (64). This suggests male and female T2DM patients
580 may have very different perceptions of health based on varied cardiometabolic profiles (65).

581   Despite a slight tendency for MetS cases to be older, age played no role in the association
582 between SRH and metabolic health. This is a curious finding given that age and metabolic
583 health are inextricably connected (56). Interestingly, previous studies with young people have
584 found SRH reliably predicts both mortality (14) and morbidity (15), despite their better health
585 status. However, it should be noted that some of this research examined disease conditions
586 characterised by overt symptoms or pain, such as infections, allergy and injuries (15), which
587 people are likely to perceive as indications of poor health. By contrast, the *asymptomatic*
588 nature of some cardiometabolic dysfunctions, such as hypertension (22) and obesity (23),
589 means people's SRH may not adequately capture underlying metabolic abnormalities,
590 regardless of their age.

591   Interestingly, the relationship between SRH and metabolic factors was unaffected by
592 MetS status. The concept of MetS as a distinct illness may have limited *psychological*
593 relevance in T2DM. There is considerable ambiguity even amongst health professionals
594 regarding what defines MetS, and different criteria have been proposed (2, 5). Awareness of
595 MetS is low, amongst both health care providers (66) and people at high risk (67). Thus,
596 diagnostic metabolic dysfunctions may not be experienced by T2DM patients as a sign of
597 poor health. Furthermore, it is notable the regression models (R^2 values) were particularly
598 weak in predicting outcomes amongst patients who did *not* meet MetS criteria. Demographic
599 factors, notably age and gender, seemed particularly relevant in this group. Unfortunately, the
600 biological mechanisms underpinning gender differences, aging, and longevity, are
601 complicated and poorly understood (68, 69), and more research is needed to better understand
602 the interrelationships between demographic factors, SRH, and metabolic dysregulation in
603 T2DM patients.

604

605 **4.1 Implications for primary care**

606

607 Although management of type 2 diabetes (T2DM) typically occurs in primary care settings
608 (1), and physicians are tasked with using a 'whole person' approach (7), there has been a
609 paucity of evidence-based psychosocial diagnostic tools for detecting metabolic dysfunction
610 in T2DM patients. Our data suggests T2DM patients incorporate HDL-C and HbA1c
611 anomalies into their subjective health assessments. While this suggests SRH can be used to
612 screen for HDL-C deficiency in male patients, and elevated HbA1c concentrations in female
613 patients, before they have developed overt clinical metabolic dysfunction (8), the added

614   diagnostic value over clinical data is marginal at best. This raises an important question:
615   should T2DM patients be asked to rate their own health during routine medical assessments
616   or consultations with their primary care physician, pending further research? As this was a
617   single-cohort study with sex-stratified analyses, more research is needed to further explore
618   the gender-specific themes. For example, it remains unclear from the current data whether
619   female patients with poor SRH need to be prioritised for further blood tests, to measure
620   HbA1c levels, or male patients with bleak SRH should be recommended for HDL-C testing.
621   Future studies should focus on the association between SRH and lipid profiles (10). Unlike
622   high blood sugar, which generates overt symptoms such as increased thirst, fatigue, or
623   frequent urination, patients with high cholesterol don't typically show any symptoms, and
624   hence can be sent for further clinical assessment if they disclose poor SRH (6).
625
626   **4.2 Limitations**
627
628   This study did not assess triglycerides (> 1.7 mmol/L (150 mg/dl), which is an important
629   diagnostic criterion for MetS (2). Also, the analysis of HbA1c in place of fasting glucose is
630   debatable (5), albeit this reflects new MetS diagnostic criteria proposed by the IDF (41). The
631   assumption insulin resistance defines T2DM is problematic. Although poor insulin sensitivity
632   is characteristic of T2DM, it may not apply to nonobese patients (circa 10-15% of T2DM
633   patients) (43). Overall, it remains unclear how direct measures of insulin resistance, fasting
634   glucose, and triglycerides would have impacted the current findings. Given the paucity of
635   independent associations between SRH and metabolic factors in the current data, it is unlikely
636   adjusting for these additional biomarkers will dramatically alter the results. Nevertheless,
637   complex mediator effects are possible, and future research needs to further explore viable
638   indirect pathways, using SEM. Sensitivity analysis showed that most findings were
639   unaffected by the type of algorithm used to manage missing data. One notable exception was
640   a previously non-significant association between SRH and BMI (kg/m^2), which became
641   significant after applying the expectation maximisation method. While this algorithm may
642   generate biased estimates and models (52), it is nevertheless essential that future research
643   authenticate the current findings by comparing different methods of handling incomplete
644   data. Another issue is that the Bonferroni adjustment may have increased the risk of a false
645   negatives (48). Finally, as this was a single-cohort study the findings require replication in
646   another cohort using the same research design.
647
648   **4.3 Conclusions**
649
650   While primary care professionals have a growing plethora of clinical options for detecting
651   metabolic abnormalities in T2DM, there has been limited research on useful psychological
652   tools for detecting metabolic dysfunction in this clinical population, despite the emphasis on a
653   holistic approach in primary care. This is the first study to assess the link between SRH and
654   metabolic dysfunction in T2DM patients, while accounting for metabolic comorbidity.
655   Overall, our findings suggest that while SRH may help primary care physicians identify
656   T2DM patients with HDL-C and HbA1c abnormalities, the added diagnostic utility over
657   clinical biomarkers is negligible.

658
659 ## LIST OF ABBREVIATIONS
660
661 • EM – Expectation maximisation
662 • BMI – Body mass index
663 • HDL-C – High density lipoprotein (cholesterol)
664 • HSE – Health survey for England
665 • IDF – International diabetes federation
666 • LDL – Low density lipoprotein
667 • MetS – Metabolic syndrome
668 • NatCen – National centre for social research
669 • SEM – Structural equation modelling
670 • SRH – Self-rated health
671 • T2DM – Type 2 diabetes
672 • HE/FE – Higher education/Further education
673
674 ## DECLARATIONS
675
676 • **Ethics approval and consent to participate**
677
678 This study was performed in line with the ethical standards as laid down in the 1964
679 Declaration of Helsinki and its later amendments. Ethics approval was granted by the
680 Liverpool John Moores University Research Ethics Committee (UREC reference:
681 16/NSP/035). Written informed consent was obtained from all subjects prior to participation.
682 Parents provided written or verbal consent on behalf of their children (aged under 16), while
683 the children gave verbal consent for the interview, nurse visit and measurements.
684
685 • **Consent for publication**
686
687 Not applicable
688
689 • **Availability of data and materials**
690
691 The Health Survey for England (HSE) is managed by the National Centre for Social Research
692 (NatCen) and the Department of Epidemiology and Public Health at University College
693 London. HSE data cannot be shared publicly for legal and ethical reasons, third party rights,
694 and institutional or national regulations or laws. The UK Data Service provides restricted
695 access to HSE data, to protect confidential or proprietary information. Individuals and
696 organisations seeking access need to be registered with the UK Data Service, albeit access is
697 limited to applicants from UK HE/FE institutions, central and local government, NHS,
698 research companies and charities for not-for-profit education and research purposes. Users
699 not in the above categories can submit access requests to surveys.queries@nhs.net and will be

700 subject to approval. For more information, please contact the UK Data Service website.
701 https://rb.gy/vhi5uf.
702
703 • **Competing interests**
704
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711 • **Authors' contributions**
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713 KU conceived the study, extracted, and analysed the data, and wrote the manuscript. SA
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719

720 **REFERENCES**
721
722 1.   Seidu S, Cos X, Brunton S, Harris SB, Jansson SPO, Mata-Cases M, et al. 2022
723 update to the position statement by Primary Care Diabetes Europe: a disease state approach to
724 the pharmacological management of type 2 diabetes in primary care. Prim Care Diabetes.
725 2022;16(2):223-44.
726 2.   Saklayen MG. The Global Epidemic of the Metabolic Syndrome. Curr Hypertens
727 Rep. 2018;20(2):12.
728 3.   Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al.
729 Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes
730 Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood
731 Institute; American Heart Association; World Heart Federation; International Atherosclerosis
732 Society; and International Association for the Study of Obesity. Circulation.
733 2009;120(16):1640-5.
734 4.   Regufe VMG, Pinto C, Perez P. Metabolic syndrome in type 2 diabetic patients: a
735 review of current evidence. Porto Biomed J. 2020;5(6):e101.
736 5.   Rochlani Y, Pothineni NV, Kovelamudi S, Mehta JL. Metabolic syndrome:
737 pathophysiology, management, and modulation by natural compounds. Ther Adv Cardiovasc
738 Dis. 2017;11(8):215-25.
739 6.   Swarup S, Goyal A, Grigorova Y, Zeltser R. Metabolic Syndrome. Treasure Island
740 (FL): StatPearls Publishing LLC; 2022.
741 7.   Juanamasta IG, Aungsuroch Y, Gunawan J, Suniyadewi NW, Nopita Wati NM.
742 Holistic Care Management of Diabetes Mellitus: An Integrative Review. Int J Prev Med.
743 2021;12:69.

744 8.   Idler EL, Benyamini Y. Self-rated health and mortality: a review of twenty-seven
745 community studies. J Health Soc Behav. 1997;38(1):21-37.
746 9.   Schnittker J, Bacak V. The increasing predictive validity of self-rated health. PLoS
747 One. 2014;9(1):e84933.
748 10.   Kananen L, Enroth L, Raitanen J, Jylhava J, Burkle A, Moreno-Villanueva M, et al.
749 Self-rated health in individuals with and without disease is associated with multiple
750 biomarkers representing multiple biological domains. Sci Rep. 2021;11(1):6139.
751 11.   Bombak AE. Self-rated health and public health: a critical perspective. Front Public
752 Health. 2013;1:15.
753 12.   Latham K, Peek CW. Self-rated health and morbidity onset among late midlife U.S.
754 adults. J Gerontol B Psychol Sci Soc Sci. 2013;68(1):107-16.
755 13.   Wu S, Wang R, Zhao Y, Ma X, Wu M, Yan X, et al. The relationship between self-
756 rated health and objective health status: a population-based study. BMC Public Health.
757 2013;13:320.
758 14.   Vie TL, Hufthammer KO, Meland E, Breidablik HJ. Self-rated health (SRH) in young
759 people and causes of death and mortality in young adulthood. A prospective registry-based
760 Norwegian HUNT-study. SSM Popul Health. 2019;7:100364.
761 15.   Hetlevik O, Meland E, Hufthammer KO, Breidablik HJ, Jahanlu D, Vie TL. Self-rated
762 health in adolescence as a predictor of 'multi-illness' in early adulthood: A prospective
763 registry-based Norwegian HUNT study. SSM Popul Health. 2020;11:100604.
764 16.   Liu Y, Ozodiegwu ID, Nickel JC, Wang K, Iwasaki LR. Self-reported health and
765 behavioral factors are associated with metabolic syndrome in Americans aged 40 and over.
766 Prev Med Rep. 2017;7:193-7.
767 17.   Lee BG, Lee JY, Kim SA, Son DM, Ham OK. [Factors associated with Self-Rated
768 Health in Metabolic Syndrome and Relationship between Sleep Duration and Metabolic
769 Syndrome Risk Factors]. J Korean Acad Nurs. 2015;45(3):420-8.
770 18.   Botoseneanu A, Ambrosius WT, Beavers DP, de Rekeneire N, Anton S, Church T, et
771 al. Prevalence of metabolic syndrome and its association with physical capacity, disability,
772 and self-rated health in Lifestyle Interventions and Independence for Elders Study
773 participants. J Am Geriatr Soc. 2015;63(2):222-32.
774 19.   Okosun IS, Airhihenbuwa C, Henry TL. Allostatic load, metabolic syndrome and self-
775 rated health in overweight/obese Non-Hispanic White, non-Hispanic Black and Mexican
776 American adults. Diabetes Metab Syndr. 2021;15(4):102154.
777 20.   Kim MH, Chang Y, Jung HS, Shin H, Ryu S. Impact of Self-Rated Health on
778 Progression to a Metabolically Unhealthy Phenotype in Metabolically Healthy Obese and
779 Non-Obese Individuals. J Clin Med. 2019;8(1).
780 21.   Kim MJ, Kim IW. Self-rated health may be a predictor for metabolic syndrome and
781 high hs-CRP prevalences in healthy adults in South Korea: Based on the 2015 Korea National
782 Health and Nutrition Examination Survey. Nutr Res. 2022;102:71-83.
783 22.   Gauer R. Severe Asymptomatic Hypertension: Evaluation and Treatment. Am Fam
784 Physician. 2017;95(8):492-500.
785 23.   Robinson E. Overweight but unseen: a review of the underestimation of weight status
786 and a visual normalization theory. Obes Rev. 2017;18(10):1200-9.

787 24.   Shirom A, Toker S, Melamed S, Shapira I. The relationships between self-rated health
788 and serum lipids across time. Int J Behav Med. 2012;19(1):73-81.
789 25.   Tomten SE, Hostmark AT. Self-rated health showed a consistent association with
790 serum HDL-cholesterol in the cross-sectional Oslo Health Study. Int J Med Sci.
791 2007;4(5):278-87.
792 26.   Uchino BN. Self-Rated Health and Age-Related Differences in Ambulatory Blood
793 Pressure: The Mediating Role of Behavioral and Affective Factors. Psychosom Med.
794 2020;82(4):402-8.
795 27.   Shin HY, Shin MH, Rhee JA. Gender differences in the association between self-rated
796 health and hypertension in a Korean adult population. BMC Public Health. 2012;12:135.
797 28.   Shankar A, Wang JJ, Rochtchina E, Mitchell P. Association between self-rated health
798 and incident severe hypertension among men: a population-based cohort study. Singapore
799 Med J. 2008;49(11):860-7.
800 29.   Kim YJ, Hwang HR. Clustering Effects of Metabolic Factors and the Risk of
801 Metabolic Syndrome. J Obes Metab Syndr. 2018;27(3):166-74.
802 30.   Parapid B, Ostojic MC, Lalic NM, Micic D, Damjanovic S, Bubanja D, et al. Risk
803 factors clustering within the metabolic syndrome: a pattern or by chance? Hellenic J Cardiol.
804 2014;55(2):92-100.
805 31.   Melka MG, Abrahamowicz M, Leonard GT, Perron M, Richer L, Veillette S, et al.
806 Clustering of the metabolic syndrome components in adolescence: role of visceral fat. PLoS
807 One. 2013;8(12):e82368.
808 32.   Hill MF, Bordoni B. Hyperlipidemia. StatPearls. Treasure Island (FL) ineligible
809 companies. Disclosure: Bruno Bordoni declares no relevant financial relationships with
810 ineligible companies.2024.
811 33.   Umeh K. Self-rated health and multimorbidity in patients with type 2 diabetes. J
812 Health Psychol. 2021:13591053211001419.
813 34.   Noh JW, Chang Y, Park M, Kwon YD, Ryu S. Self-rated health and the risk of
814 incident type 2 diabetes mellitus: A cohort study. Sci Rep. 2019;9(1):3697.
815 35.   Rottenkolber M, Gar C, Then C, Wanger L, Sacco V, Banning F, et al. A
816 Pathophysiology of Type 2 Diabetes Unrelated to Metabolic Syndrome. J Clin Endocrinol
817 Metab. 2021;106(5):1460-71.
818 36.   Hsieh HH, Chang CM, Liu LW, Huang HC. The Relative Contribution of Dietary
819 Habits, Leisure-Time Exercise, Exercise Attitude, and Body Mass Index to Self-Rated Health
820 among College Students in Taiwan. Int J Environ Res Public Health. 2018;15(5).
821 37.   Zarini GG, Vaccaro JA, Canossa Terris MA, Exebio JC, Tokayer L, Antwi J, et al.
822 Lifestyle behaviors and self-rated health: the living for health program. J Environ Public
823 Health. 2014;2014:315042.
824 38.   Mindell J, Biddulph JP, Hirani V, Stamatakis E, Craig R, Nunn S, et al. Cohort
825 profile: the health survey for England. Int J Epidemiol. 2012;41(6):1585-93.
826 39.   NHS Digital. Health Survey for England 2019 [NS] - NHS Digital 2022 [cited 2022
827 30 June]. Available from: https://digital.nhs.uk/data-and-
828 information/publications/statistical/health-survey-for-england/2019.

829   40.   Taylor BC, Wilt TJ, Welch HG. Impact of Diastolic and Systolic Blood Pressure on
830   Mortality: Implications for the Definition of "Normal". Journal of General Internal Medicine.
831   2011;26(7):685-90.
832   41.   Cavero-Redondo I, Martinez-Vizcaino V, Alvarez-Bueno C, Agudo-Conde C,
833   Lugones-Sanchez C, Garcia-Ortiz L. Metabolic Syndrome Including Glycated Hemoglobin
834   A1c in Adults: Is It Time to Change? J Clin Med. 2019;8(12).
835   42.   Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of
836   HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. Biomark Insights. 2016;11:95-
837   104.
838   43.   Gerich JE. Insulin resistance is not necessarily an essential component of type 2
839   diabetes. J Clin Endocrinol Metab. 2000;85(6):2113-5.
840   44.   Nuttall FQ. Body Mass Index: Obesity, BMI, and Health: A Critical Review. Nutr
841   Today. 2015;50(3):117-28.
842   45.   Sun K, Liu J, Ning G. Active smoking and risk of metabolic syndrome: a meta-
843   analysis of prospective studies. PLoS One. 2012;7(10):e47791.
844   46.   Sun K, Ren M, Liu D, Wang C, Yang C, Yan L. Alcohol consumption and risk of
845   metabolic syndrome: a meta-analysis of prospective studies. Clin Nutr. 2014;33(4):596-602.
846   47.   Slagter SN, van Vliet-Ostaptchouk JV, Vonk JM, Boezen HM, Dullaart RP, Kobold
847   AC, et al. Combined effects of smoking and alcohol on metabolic syndrome: the LifeLines
848   cohort study. PLoS One. 2014;9(4):e96406.
849   48.   VanderWeele TJ, Mathur MB. Some Desirable Properties of the Bonferroni
850   Correction: Is the Bonferroni Correction Really So Bad? Am J Epidemiol. 2019;188(3):617-
851   8.
852   49.   Faul F, Erdfelder E, Buchner A, Lang AG. Statistical power analyses using G*Power
853   3.1: Tests for correlation and regression analyses. Behav Res Methods. 2009;41(4):1149-60.
854   50.   Gelman A, Hill J. Sample size and power calculations. Data analysis using regression
855   and multilevel/hierarchical models (analytical methods for social research). . Cambridge:
856   Cambridge University Press; 2006.
857   51.   Rubin LH, Witkiewitz K, Andre JS, Reilly S. Methods for Handling Missing Data in
858   the Behavioral Neurosciences: Don't Throw the Baby Rat out with the Bath Water. J
859   Undergrad Neurosci Educ. 2007;5(2):A71-7.
860   52.   Stavseth MR, Clausen T, Roislien J. How handling missing data may impact
861   conclusions: A comparison of six different imputation methods for categorical questionnaire
862   data. SAGE Open Med. 2019;7:2050312118822912.
863   53.   James M, Varghese TP, Sharma R, Chand S. Association Between Metabolic
864   Syndrome and Diabetes Mellitus According to International Diabetic Federation and National
865   Cholesterol Education Program Adult Treatment Panel III Criteria: a Cross-sectional Study. J
866   Diabetes Metab Disord. 2020;19(1):437-43.
867   54.   Yoon J, Kim J, Son H. Gender Differences of Health Behaviors in the Risk of
868   Metabolic Syndrome for Middle-Aged Adults: A National Cross-Sectional Study in South
869   Korea. Int J Env Res Pub He. 2021;18(7).
870   55.   Meloni A, Cadeddu C, Cugusi L, Donataccio MP, Deidda M, Sciomer S, et al. Gender
871   Differences and Cardiometabolic Risk: The Importance of the Risk Factors. Int J Mol Sci.
872   2023;24(2).

873   56.   Palmer AK, Jensen MD. Metabolic changes in aging humans: current evidence and
874   therapeutic strategies. J Clin Invest. 2022;132(16).
875   57.   Hooper D, Coughlan J, Mullen MR. Structural equation modelling: guidelines for
876   determining model fit. The Electronic Journal of Business Research Methods. 2008;6(1):53-
877   60.
878   58.   Memon R, Levitt D, Salgado Nunez Del Prado SR, Munir K, Lamos E. Knowledge of
879   Hemoglobin A1c and Glycemic Control in an Urban Population. Cureus. 2021;13(3):e13995.
880   59.   Gopalan A, Kellom K, McDonough K, Schapira MM. Exploring how patients
881   understand and assess their diabetes control. BMC Endocr Disord. 2018;18(1):79.
882   60.   Nielsen AB, Gannik D, Siersma V, Olivarius Nde F. The relationship between HbA1c
883   level, symptoms and self-rated health in type 2 diabetic patients. Scand J Prim Health Care.
884   2011;29(3):157-64.
885   61.   Kautzky-Willer A, Kosi L, Lin J, Mihaljevic R. Gender-based differences in
886   glycaemic control and hypoglycaemia prevalence in patients with type 2 diabetes: results
887   from patient-level pooled data of six randomized controlled trials. Diabetes Obes Metab.
888   2015;17(6):533-40.
889   62.   Zajacova A, Huzurbazar S, Todd M. Gender and the structure of self-rated health
890   across the adult life span. Soc Sci Med. 2017;187:58-66.
891   63.   Goldstein KM, Stechuchak KM, Zullig LL, Oddone EZ, Olsen MK, McCant FA, et
892   al. Impact of Gender on Satisfaction and Confidence in Cholesterol Control Among Veterans
893   at Risk for Cardiovascular Disease. J Womens Health (Larchmt). 2017;26(7):806-14.
894   64.   Russo G, Pintaudi B, Giorda C, Lucisano G, Nicolucci A, Cristofaro MR, et al. Age-
895   and Gender-Related Differences in LDL-Cholesterol Management in Outpatients with Type 2
896   Diabetes Mellitus. Int J Endocrinol. 2015;2015:957105.
897   65.   Roeters van Lennep JE, Tokgozoglu LS, Badimon L, Dumanski SM, Gulati M, Hess
898   CN, et al. Women, lipids, and atherosclerotic cardiovascular disease: a call to action from the
899   European Atherosclerosis Society. Eur Heart J. 2023;44(39):4157-73.
900   66.   Havakuk O, Perl ML, Praisler O, Barkagan M, Sadeh B, Margolis G, et al. The
901   awareness to metabolic syndrome among hospital health providers. Diabetes Metab Syndr.
902   2017;11(3):193-7.
903   67.   Wang Q, Chair SY, Wong EM, Taylor-Piliae RE, Qiu XCH, Li XM. Metabolic
904   Syndrome Knowledge among Adults with Cardiometabolic Risk Factors: A Cross-Sectional
905   Study. Int J Environ Res Public Health. 2019;16(1).
906   68.   Ostan R, Monti D, Gueresi P, Bussolotto M, Franceschi C, Baggio G. Gender, aging
907   and longevity in humans: an update of an intriguing/neglected scenario paving the way to a
908   gender-specific medicine. Clin Sci (Lond). 2016;130(19):1711-25.
909   69.   Abad-Diez JM, Calderon-Larranaga A, Poncel-Falco A, Poblador-Plou B, Calderon-
910   Meza JM, Sicras-Mainar A, et al. Age and gender differences in the prevalence and patterns
911   of multimorbidity in the older population. BMC Geriatr. 2014;14:75.
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917 **Table 1 – Sample characteristics by metabolic syndrome status.**

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	Whole sample	Metabolic syndrome		P
		Non-cases	Cases	
Age, n (%) ≥ 65 years	332 (56.8%)	123 (53.2%)	208 (59.1%)	P > 0.01
Gender, n (%) male	316 (54.1%)	123 (53.2%)	193 (54.8%)	P > 0.01
Socio-economic class, n (%) managerial, professional, intermediate	184 (32.9%), missing 25 (4.3%)	77 (35.6%)	107 (31.4%)	P > 0.01
Ethnicity, n (%) White	486 (83.2%)	183 (79.2%)	302 (85.8%)	P > 0.01
Education, n (%) university/college degree or equivalent	105 (18%), missing 361 (61.8%)	48 (48%)	57 (46.3%)	P > 0.01
Cigarette smoking (number of cigarettes smoked a day)	2.28 (7.10)	2.25 (6.59)	2.31 (7.44)	P > 0.01
Alcohol consumption frequency in past year, n (%) not at all/non-drinker	183 (31.3%), missing 1 (0.2%)	72 (31.3%)	111 (31.5%)	P > 0.01
Self-rated health, n (%) 'fair'/ 'bad'/ 'very bad' health	335 (57.4%)	111 (48.1%)	223 (63.4%)	P < 0.01*
HDL-C (mmol/L), n (%) ≤ 0.9	391 (67%)	101 (43.7%)	289 (82.1%)	P < 0.01*
HDL-C (mmol/L)	1.25 (0.33)	1.30 (0.32)	1.18 (0.33)	P < 0.01*
Waist/hip ratio (cm), n (%) ≥ 0.85	316 (54.1%)	146 (63.2%)	169 (48%)	P < 0.01*
Waist/hip ratio (cm)	0.96 (0.08)	0.94 (0.07)	0.98 (0.08)	P < 0.01*
BMI, n (%) ≥ 30kg/m^2	229 (39.2%)	18 (7.8%)	211 (59.9%)	P < 0.01*
BMI kg/m^2	31.22 (6.11)	27.54 (3.63)	33.41 (6.25)	P < 0.01*
Systolic blood pressure, n (%) > 140 mmHg	82 (14%)	38 (16.5%)	43 (12.2%)	P > 0.01
Systolic blood pressure, mmHg	129 (16.18)	128.49 (15.96)	129.34 (16.37)	P > 0.01
Diastolic blood pressure, n (%) > 90 mmHg	14 (2.4%)	6 (2.6%)	8 (2.3%)	P > 0.01
Diastolic blood pressure, mmHg	69.72 (10.53)	69.46 (10.23)	69.99 (10.84)	P > 0.01
Hypertension (diagnosed)	370 (63.4%)	60 (26%)	310 (88.1%)	P < 0.01*
HbA1c, n (%) > 48 mmol/mol	167 (28.6%)	102 (44.2%)	65 (18.5%)	P < 0.01*

HbA1c, mmol/mol	57.5 (16.56)	56.17 (15.05)	59.61 (18.60)	$P > 0.01$

All values are means (SDs), unless percentage (%) stated. P values relate to comparisons between metabolic syndrome cases versus non-cases, are based on Chi-square or independent samples t-tests (* indicates significant).

942 **Table 2 Final regression models predicting metabolic factors from self-rated health and metabolic covariates in the whole sample**
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	Outcome variables					
	Serum HDL cholesterol (mmol/L)	BMI (kg/m^2)	Waist/hip ratio (cm)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Glycated haemoglobin - HbA1c (mmol/mol)
Predictors (Model 3)	*B* 95%CI [LL, UL], *beta*	*B* 95%CI [LL, UL], *beta*	*B* 95%CI [LL, UL], *beta*	*B* 95%CI [LL, UL], *beta*	*B* 95%CI [LL, UL], *beta*	*B* 95%CI [LL, UL], *beta*
Demographics, lifestyle factors						
Age (three-year bands for 0-15, five-year bands for ages 16+)	0.01 [-0.00, 0.03], 0.11	-0.36 [-0.70, -0.02], -0.17[a]	0.00 [0.00, 0.01], 0.20[b]	2.66 [1.77, 3.55], 0.45[c]	-1.67 [-2.22, -1.13], -0.41[c]	-0.52 [-1.69, 0.64], -0.07
Gender (male = 1, female = 0)	-0.08 [-0.20, 0.02], -0.13	-3.31 [-5.08, -1.54], -0.31[c]	0.09 [0.07, 0.11], 0.55[c]	3.84 [-1.33, 9.02], 0.11	-1.99 [-5.18, 1.19], -0.09	0.55 [-5.70, 6.80], 0.01
Socio-economic class (eight categories, coded 0 to 7: 0 = higher managerial/professional, 7 = never worked or unemployed)	-0.00 [-0.03, 0.03], -0.01	-0.00 [-0.54, 0.53], -0.00	0.00 [-0.00, 0.01], 0.05	0.73 [-0.78, 2.25], 0.06	-0.18 [-1.12, 0.75], -0.02	-0.21 [-2.04, 1.62], -0.01

Ethnicity (White = 1, non-white = 0)	-0.02 [-0.16, 0.12], -0.02	3.64 [1.43, 5.86], 0.24[c]	-0.00 [-0.03, 0.02], -0.03	-1.64 [-8.10, 4.82, -0.03	-3.54 [-7.48, 0.39], -0.11	4.76 [-2.97, 12.49], 0.09
Lifestyle factor: Smoking (number of cigarettes smoked per day)	-0.00 [-0.01, 0.00], -0.11	-0.02 [-0.11, 0.06], -0.03	0.00 [-0.00, 0.00], -0.03	0.09 [-0.16, 0.36], 0.04	-0.00 [-0.16, 0.16], 0.00	-0.01 [-0.33, 0.30], -0.00
Lifestyle factor: Alcohol consumption (frequency drunk in past 12 months)	-0.03 [-0.05, -0.01], -0.22[b]	0.24 [-0.10, 0.58], 0.10	-0.00 [-0.00, 0.00], -0.01	-0.23 [-1.21, 0.74], -0.03	0.01 [-0.59, 0.61], 0.00	-0.61 [-1.78, 0.55], -0.08
Self-rated health (very good/good = 1, fair/bad very bad = 0)	0.08 [-0.01, 0.17], 0.12	-0.39 [-1.92, 1.12], -0.03	-0.01 [-0.03, 0.00], -0.07	-2.22 [-6.53, 2.08], -0.06	0.81 [-1.84, 3.46], 0.03	-5.38 [-10.51, 0.25], -0.15[a]
Anthropometric Markers						
BMI (kg/m²)	-0.00 [-0.01, 0.00], -0.07	_	0.00 [0.00, 0.00], 0.22[c]	0.12 [-0.30, 0.55], 0.03	0.14 [-0.12, 0.40], 0.07	-0.02 [-0.54, 0.48], -0.00
Waist/hip ratio (cm)	-0.53 [-1.24, 0.17], -0.12	20.18 [9.13, 31.22], 0.31[c]	_	-1.81 [-34.28, 30.65], -0.00	6.39 [-13.54, 26.34], 0.04	18.05 [-20.84, 56.95], 0.08
Biomarkers						
Serum HDL cholesterol (mmol/L)	-	-1.24 [-3.65, 1.17], -0.07	-0.02 [-0.05, 0.00], -0.09	4.19 [-2.62, 11.01], 0.08	2.18 [-2.01, 6.38], 0.06	10.10 [-18.19, -2.02], -0.19[a]
Systolic blood pressure (mmHg)	0.00 [-0.00, 0.00], 0.10	0.01 [-0.03, 0.06], 0.04	0.00 [-0.00, 0.00], -0.00	_	0.31 [0.23, 0.39], 0.47[c]	-0.07 [-0.25, 0.10], -0.06

Diastolic blood pressure (mmHg)	0.00 [-0.00, 0.00], 0.08	0.04 [-0.04, 0.13], 0.09	0.00 [-0.00, 0.00], 0.04	0.82 [0.60, 1.03], 0.53[c]	–	0.43 [0.14, 0.72], 0.26[b]
Glycated haemoglobin - HbA1c (mmol/mol)	-0.00 [-0.00, -0.00], -0.17[a]	-0.00 [-0.04, 0.04], -0.00	0.00 [0.00, 0.00], 0.05	-0.05 [-0.17, 0.07], -0.05	0.11 [0.03, 0.18], 0.18[b]	–
R^2 (adjusted R^2)	0.23 (0.18)	0.19 (0.14)	0.41 (0.37)	0.34 (0.29)	0.40 (0.36)	0.40 (0.16)
F	$F_{(12, 171)} = 4.35$, $p < 0.001$	$F_{(12, 171)} = 3.51$, $p < 0.001$	$F_{(12, 171)} = 9.94$, $p < 0.001$	$F_{(12, 171)} = 7.47$, $p < 0.001$	$F_{(12, 171)} = 9.86$, $p < 0.001$	$F_{(12, 171)} = 2.84$, $p \leqq 0.001$

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945 *Note*. Model 1 (+ demographics, lifestyle factors), Model 2 (+ SRH), Model 3 (+ cardiometabolic covariates). Coefficients shown are from final
946 step (Model 3).
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948 [a]($p < 0.05$), [b]($p \leq 0.01$), [c]($p \leq 0.001$)
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963 **Table 3 Final regression models predicting metabolic factors from self-rated health and metabolic covariates in T2DM patients with**
964 **MetS**
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	Outcome variables					
	Serum HDL cholesterol (mmol/L)	BMI (kg/m^2)	Waist/hip ratio (cm)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Glycated haemoglobin - HbA1c (mmol/mol)
Predictors (Model 3)	B 95%CI [LL, UL], *beta*	B 95%CI [LL, UL], *beta*	B 95%CI [LL, UL], *beta*	B 95%CI [LL, UL], *beta*	B 95%CI [LL, UL], *beta*	B 95%CI [LL, UL], *beta*
Demographics, Lifestyle factors						
Age (three-year bands for 0-15, five-year bands for ages 16+)	0.00 [-0.04, 0.04], 0.00	-0.75 [-1.21, -0.30], -0.44[c]	0.00 [-0.00, 0.01], 0.17	2.01 [0.17, 3.84], 0.29[a]	-1.78 [-2.77, -0.80], -0.41[c]	-1.59 [-3.88, 0.68], -0.20
Gender (male = 1, female = 0)	-0.09 [-0.34, 0.14], -0.14	-3.59 [-6.26, 0.92], -0.42[b]	0.12 [0.09, 0.16], 0.74c	3.53 [-7.38, 14.44], 0.10	0.66 [-5.58, 6.91], 0.03	-5.18 [-18.48, 8.11], -0.13
Socio-economic class (eight categories, coded 0 to 7: 0 = higher managerial/professional, 7 = never worked or unemployed)	0.01 [-0.05, 0.07], 0.03	-0.21 [-0.93, 0.50], -0.06	0.00 [-0.00, 0.02], 0.12	-1.32 [-4.10, 1.45], -0.10	-0.21 [-1.81, 1.38], -0.02	-1.16 [-4.57, 2.23], -0.07

Lifestyle factor: Smoking (number of cigarettes smoked per day)	-0.00 [-0.01, 0.00], -0.08	-0.05 [-0.16, 0.06], -0.10	0.00 [-0.00, 0.00], -0.02	-0.14 [-0.58, 0.30], -0.06	0.02 [-0.23, 0.27], 0.01	-0.29 [-0.83, 0.24], -0.12
Lifestyle factor: Alcohol consumption (frequency drunk in past 12 months)	-0.03 [-0.07, 0.00], 0.23	0.23 [-0.20, 0.67], 0.13	-0.00 [-0.00, 0.00, -0.03	0.78 [-0.93, 2.50], 0.10	0.00 [-0.98, 0.98], 0.00	-1.12 [-3.22, 0.96], -0.13
Self-rated health (very good/good = 1, fair/bad very bad = 0)	0.09 [-0.07, 0.25], 0.13	-0.19 [-2.10, 1.71], -0.02	-0.01 [-0.04, 0.01], -0.07	1.51 [-5.88, 8.91], 0.04	-0.33 [-4.56, 3.89], -0.01	-6.26 [-15.16, 2.63], -0.16
Anthropometric Markers						
BMI (kg/m^2)	-0.00 [-0.02, 0.01], -0.05	_	0.00 [0.00, 0.00], 0.19[a]	0.16 [-0.81, 1.13], 0.04	0.25 [-0.30, 0.80], 0.10	-0.91 [-2.08, 0.25], -0.19
Waist/hip ratio (cm)	-0.49 [-1.83, 0.84], -0.12	15.41 [0.22, 30.59], 0.31[a]	_	16.21 [-44.50, 76.93], 0.08	-16.83 [-51.30, 17.63], -0.13	28.95 [-44.93, 102.84], 0.12
Biomarkers						
Serum HDL cholesterol (mmol/L)	_	-0.61 [-3.54, 2.31], -0.05	-0.01 [-0.06, 0.03], -0.07	6.82 [-4.43, 18.08], 0.14	1.11 [-5.37, 7.61], 0.03	-12.94 [-26.45, 0.56], -0.23
Systolic blood pressure (mmHg)	0.00 [-0.00, 0.00], 0.16	0.01 [-0.05, 0.07], 0.04	0.00 [-0.00, 0.00], 0.05	_	0.29 [0.16, 0.41], 0.45[c]	-0.16 [-0.47, 0.13], -0.14
Diastolic blood pressure (mmHg)	0.00 [-0.00, 0.01], 0.05	0.05 [-0.06, 0.16], 0.13	-0.00 [-0.00, 0.00], -0.11	0.88 [0.50, 1.26], 0.56[c]	_	0.43 [-0.09, 0.96], 0.23

Glycated haemoglobin - HbA1c (mmol/mol)	-0.00 [-0.00, 0.00], -0.23	-0.04 [-0.09, 0.01], -0.18	0.00 [-0.00, 0.00], 0.07	-0.11 [-0.31, 0.09], -0.12	0.09 [-0.02, 0.21], 0.17	_
R^2 (adjusted R^2) F	0.24 (0.11) $F_{(11, 63)} =$ 1.85, $p > 0.05$	0.29 (0.17) $F_{(11, 63)} =$ 2.44, $p < 0.05$	0.56 (0.49) $F_{(11, 63)} =$ 7.59, $p < 0.001$	0.34 (0.23) $F_{(11, 63)} =$ 3.03, $p < 0.01$	0.46 (0.37) $F_{(11, 63)} =$ 4.99, $p < 0.001$	0.26 (0.13) $F_{(11, 63)} = 2.01$, $p < 0.05$

Note. Model 1 (+ demographics, lifestyle factors), Model 2 (+ SRH), Model 3 (+ cardiometabolic covariates). Coefficients shown are from final step (Model 3). Ethnicity was excluded due to low frequencies for non-whites [check this]

[a]($p < 0.05$), [b]($p \leq 0.01$), [c]($p \leq 0.001$)

989 **Table 4 Final regression models predicting metabolic factors from self-rated health and metabolic covariates in T2DM patients without**
990 **MetS**
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	Outcome variables					
	Serum HDL cholesterol (mmol/L)	BMI (kg/m^2)	Waist/hip ratio (cm)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Glycated haemoglobin - HbA1c (mmol/mol)
Predictors (Model 3)	B 95%CI [LL, UL], *beta*	B 95%CI [LL, UL], *beta*	B 95%CI [LL, UL], *beta*	B 95%CI [LL, UL], *beta*	B 95%CI [LL, UL], *beta*	B 95%CI [LL, UL], *beta*
Demographics, Lifestyle factors						
Age (three-year bands for 0-15, five-year bands for ages 16+)	0.02 [-0.00, 0.05], 0.19	0.02 [-0.36, 0.40], 0.01	0.00 [0.00, 0.01], 0.30[b]	2.72 [1.60, 3.83], 0.45[c]	-1.51 [-2.28, -0.73], -0.38[c]	-0.62 [-2.09, 0.83], -0.10
Gender (male = 1, female = 0)	-0.09 [-0.23, 0.04], -0.14	-2.34 [-4.15, -0.53], -0.28[a]	0.06 [0.03, 0.09], 0.43[c]	1.97 [-4.04, 7.99], 0.06	-2.92 [-6.90, 1.06], -0.13	2.74 [-4.35, 9.84], 0.08
Socio-economic class (eight categories, coded 0 to 7: 0 = higher managerial/professional, 7 = never worked or unemployed)	-0.01 [-0.05, 0.03], -0.05	0.39 [-0.19, 0.98], 0.13	0.00 [-0.00, 0.01], 0.04	1.92 [0.03, 3.81], 0.16[a]	-0.38 [-1.66, 0.90], -0.04	0.28 [-1.98, 2.56], 0.02

Ethnicity (White = 1, non-white = 0)	0.00 [-0.16, 0.17], 0.00	1.77 [-0.51, 4.06], 0.17	-0.00 [-0.04, 0.03], -0.03	1.26 [-6.21, 8.75], 0.03	-5.45 [-10.32, -0.57], -0.20[a]	7.67 [-1.02, 16.37], 0.19
Lifestyle factor: Smoking (number of cigarettes smoked per day)	-0.00 [-0.01, 0.00], -0.15	-0.00 [-0.11, 0.10], -0.01	0.00 [-0.00, 0.00], -0.04	0.17 [-0.17, 0.51], 0.08	-0.04 [-0.27, 0.19], -0.03	0.25 [-0.15, 0.66], 0.12
Lifestyle factor: Alcohol consumption (frequency drunk in past 12 months)	-0.03 [-0.05, -0.00], -0.22[a]	0.13 [-0.24, 0.51], 0.07	0.00 [-0.00, 0.00], 0.00	-0.51 [-1.73, 0.71], -0.07	0.01 [-0.80, 0.83], 0.00	0.44 [-0.99, 1.89], 0.06
Self-rated health (very good/good = 1, fair/bad very bad = 0)	0.06 [-0.06, 0.18], 0.09	-0.27 [-1.98, 1.43], -0.03	-0.01 [-0.03, 0.01], -0.06	-4.52 [-9.95, 0.91], -0.13	2.16 [-1.49, 5.81], 0.10	-3.35 [-9.83, 3.11], -0.10
Anthropometric Markers						
BMI (kg/m^2)	-0.00 [-0.01, 0.01], -0.04	_	0.00 [-0.00, 0.00], 0.13	-0.17 [-0.82, 0.48], -0.04	0.02 [-0.41, 0.46], 0.00	0.15 [-0.61, 0.93], 0.04
Waist/hip ratio (cm)	-0.57 [-1.50, 0.36], -0.13	9.33 [-3.12, 21.79], 0.17	_	-9.32 [-49.94, 31.29], -0.04	19.17 [-7.69, 46.04], 0.13	15.81 [-32.07, 63.70], 0.07
Biomarkers						
Serum HDL cholesterol (mmol/L)	_	-0.69 [-3.40, 2.01], -0.05	-0.02 [-0.07, 0.01], -0.11	1.50 [-7.23, 10.23], 0.03	2.97 [-2.82, 8.78], 0.09	-5.57 [-15.82, 4.67], -0.11
Systolic blood pressure (mmHg)	0.00 [-0.00, 0.00], 0.04	-0.01 [-0.07, 0.04], -0.06	0.00 [-0.00, 0.00], -0.05	_	0.32 [0.21, 0.44], 0.50[c]	0.01 [-0.22, 0.25], 0.01

Diastolic blood pressure (mmHg)	0.00 [-0.00, 0.01], 0.11	0.00 [-0.08, 0.09], 0.01	0.00 [0.00, 0.00], 0.15	0.73 [0.47, 1.00], 0.48[c]	–	0.40 [0.05, 0.75], 0.27[a]
Glycated haemoglobin - HbA1c (mmol/mol)	-0.00 [-0.00, 0.00], -0.10	0.01 [-0.04, 0.06], 0.04	0.00 [-0.00, 0.00], 0.06	0.01 [-0.15, 0.18], 0.01	0.13 [0.01, 0.24], 0.19[a]	–
R^2 (adjusted R^2)	0.21 (0.12)	0.12 (0.01)	0.33 (0.25)	0.42 (0.35)	0.40 (0.33)	0.17 (0.06)
F	$F_{(12, 96)} = 2.24$, $p < 0.05$	$F_{(12, 96)} = 1.14$, $p > 0.05$	$F_{(12, 96)} = 3.99$, $p < 0.001$	$F_{(12, 96)} = 5.93$, $p < 0.001$	$F_{(12, 96)} = 5.47$, $p < 0.001$	$F_{(12, 96)} = 1.66$, $p > 0.05$

Note. Model 1 (+ demographics, lifestyle factors), Model 2 (+ SRH), Model 3 (+ cardiometabolic covariates). Coefficients shown are from final step (Model 3).

[a]($p < 0.05$), [b]($p \leq 0.01$), [c]($p \leq 0.001$)

1013 **Table 5 Final regression models predicting HDL-C and HbA1c from self-rated health and metabolic covariates in males and females**
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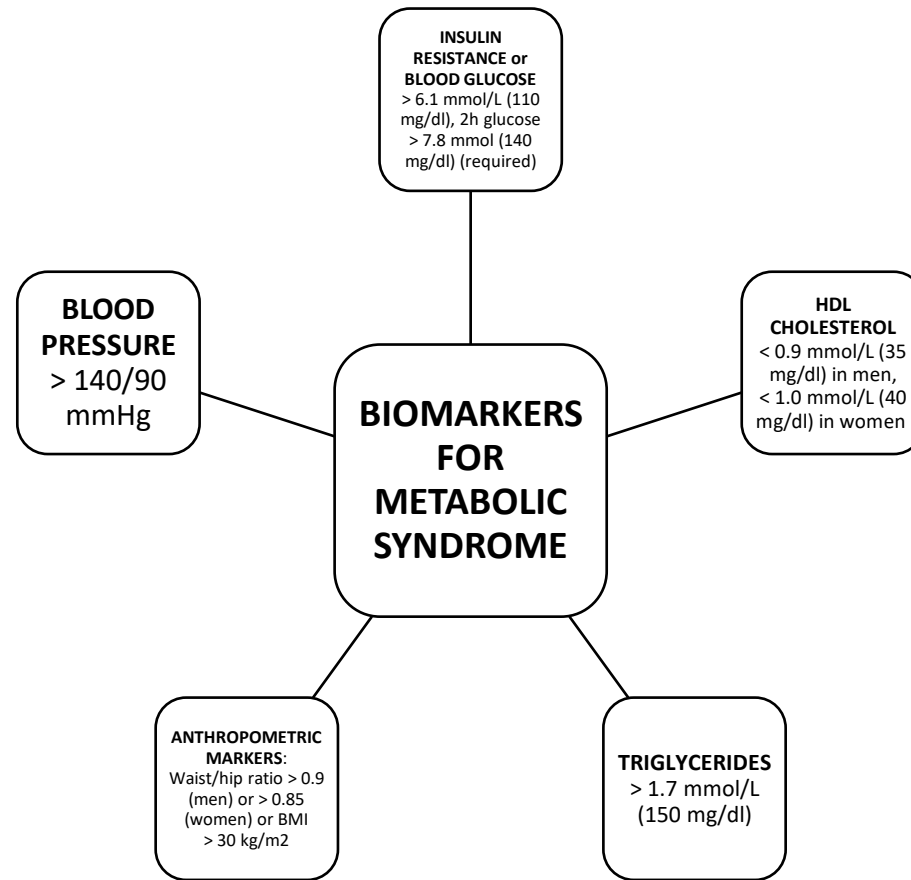|	Outcome variables			
	Serum HDL cholesterol (mmol/L)		Glycated haemoglobin - HbA1c (mmol/mol)	
	Female	Male	Female	Male
Predictors (Model 3)	B 95%CI [LL, UL], *beta*	B 95%CI [LL, UL], *beta*	B 95%CI [LL, UL], *beta*	B 95%CI [LL, UL], *beta*
Demographics, lifestyle				
Age (three-year bands for 0-15, five-year bands for ages 16+)	0.03 [0.00, 0.06], 0.29[a]	-0.01 [-0.05, 0.01], -0.13	0.07 [-1.46, 1.62], 0.01	-2.22 [-4.06, -0.37], -0.29[b]
Socio-economic class (eight categories, coded 0 to 7: 0 = higher managerial/professional, 7 = never worked or unemployed)	0.00 [-0.04, 0.05], 0.01	-0.02 [-0.06, 0.02], -0.08	-0.72 [-3.35, 1.90], -0.05	-0.47 [-3.04, 2.08], -0.03
Ethnicity (White = 1, non-white = 0)	-0.27 [-0.52, -0.03], -0.27[a]	0.11 [-0.07, 0.29], 0.12	2.87 [-10.02, 15.76], 0.05	3.63 [-6.70, 13.98], 0.07
Lifestyle factor: Smoking (number of	-0.00 [-0.01, 0.00], -0.10	-0.00 [-0.01, 0.00], -0.12	0.07 [-0.36, 0.50], 0.03	-0.01 [-0.47, 0.44], -0.00

cigarettes smoked per day)				
Lifestyle factor: Alcohol consumption (frequency drunk in past 12 months)	-0.03 [-0.06, -0.00], -0.23[a]	-0.03 [-0.05, 0.00], -0.20[a]	0.54 [-1.17, 2.27], 0.07	-1.89 [-3.51, -0.26], -0.24[a]
Self-rated health (very good/good = 1, fair/bad very bad = 0)	0.02 [-0.12, 0.17], 0.04	0.16 [0.03, 0.29], 0.25[b]	-9.30 [-16.68, -1.93], -0.27[b]	0.68 [-6.59, 7.97], 0.01
Cardiometabolic factors				
BMI (kg/m^2)	0.00 [-0.01, 0.01], 0.02	-0.01 [-0.03, 0.00], -0.22	0.43 [-0.28, 1.15], 0.13	-0.93 [-1.81, -0.05], -0.26[a]
Waist/hip ratio (cm)	-1.12 [-2.14, -0.09], -0.23[a]	0.19 [-0.99, 1.39], 0.04	17.25 [-36.56, 71.07], 0.07	45.01 [-20.80, 110.83], 0.16
Serum HDL cholesterol (mmol/L)	_	_	-9.61 [-21.37, 2.13], -0.18	-14.09 [-25.52, -2.66], -0.25[b]
Systolic blood pressure (mmHg)	0.00 [-0.00, 0.00], 0.17	0.00 [-0.00, 0.00], 0.11	-0.01 [-0.26, 0.24], -0.01	-0.06 [-0.32, 0.20], -0.05
Diastolic blood pressure (mmHg)	0.00 [-0.00, 0.01], 0.06	0.00 [-0.00, 0.01], 0.05	0.45 [0.08, 0.83], 0.31[b]	0.28 [-0.18, 0.75], 0.15
Glycated haemoglobin - HbA1c (mmol/mol)	-0.00 [-0.00, 0.00], -0.18	-0.00 [-0.00, -0.00], -0.24[b]	_	_
R^2 (adjusted R^2)	0.32 (0.21)	0.25 (0.16)	0.31 (0.21)	0.21 (0.11)
F	$F(11, 72) = 3.10$, $p < 0.01$	$F(11, 88) = 2.73$, $p < 0.01$	$F(11, 72) = 3.04$, $p < 0.01$	$F(11, 88) = 2.21$, $p < 0.05$

1016 *Note*. Model 1 (+ demographics, lifestyle factors), Model 2 (+ SRH), Model 3 (+ cardiometabolic covariates). Coefficients shown are from final
1017 step (Model 3).
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1019 [a]($p < 0.05$), [b]($p \leq 0.01$), [c]($p \leq 0.001$)
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1036   **Figure 2** Diagnostic criteria for metabolic syndrome based on WHO (1999) guidelines (Source: Saklayen, 2018)
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Figure 2 Flow Diagram

Health Survey for England sample size (SPSS data file)

(n=10,300)

Ineligible
(n = 9,715 (94.3%))
Major reasons for ineligibility
Has Type 1 diabetes (56 (0.5%))
Not been told whether they have Type 1 or
Type 2 diabetes (18 (0.2%))
Not sure which type of diabetes (38 (0.4%))
Missing data or N/A (9603 (93.2%))

Eligible
Has Type 2 diabetes
(n = 584 (5.7%))

Exclusion
None. We included three (0.5%) patients
Type 2 diabetes patients not told by a
doctor they had diabetes.

Metabolic data
BMI (n=463)
Diastolic BP (n=350)
Systolic BP (n=350)
Waist/hip ratio (n=347)
HDL-C (n=233)
HbA1c (n=232)
Self-rated health
(n=584)

Missing
BMI (n=121 (20.7%))
Diastolic BP (n=234 (40.1%))
Systolic BP (n=234 (40.1%))
Waist/hip ratio (n=237 (40.6%))
HDL-C (n=351 (60.1%))
HbA1c (n=352 (60.3%))
Self-rated health (n=0 (0%))

Eligible
Assessed on criteria for
metabolic syndrome
(n = 583 (0.2% of
sample with Type 2
diabetes))

Exclusion
Missing data for one case (0.2% of sample
with Type 2 diabetes).

Metabolic syndrome
Just over 60% of patients met the criteria for metabolic syndrome
(n = 352 (60.3%)), based on presence of Type 2 diabetes, and any
two of HDC-C < 0.9, BMI > 30, or having hypertension. The
remainder (n = 231 (39.6%)) did not meet the criteria.