



# BMJ Open Prevalence of metabolic syndrome and metabolic dysfunction-associated fatty liver disease in Malaysia 2023: study protocol for a community-based nationwide cross-sectional survey

Kim Sui Wan ,<sup>1</sup> Halizah Mat Rifin ,<sup>1</sup> Muhammad Fadhli Mohd Yusoff,<sup>1</sup> Kishwen Kanna Yoga Ratnam,<sup>1</sup> Wah Kheong Chan,<sup>2</sup> Masni Mohamad,<sup>3</sup> Nurain Mohd Noor,<sup>3</sup> Feisul Mustapha,<sup>4,5</sup> Noor Ani Ahmad<sup>1</sup>

**To cite:** Wan KS, Mat Rifin H, Mohd Yusoff MF, *et al*. Prevalence of metabolic syndrome and metabolic dysfunction-associated fatty liver disease in Malaysia 2023: study protocol for a community-based nationwide cross-sectional survey. *BMJ Open* 2023;**13**:e074432. doi:10.1136/bmjopen-2023-074432

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2023-074432>).

Received 07 April 2023  
Accepted 28 September 2023



© Author(s) (or their employer(s)) 2023. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

## Correspondence to

Dr Kim Sui Wan;  
kimsui@moh.gov.my

## ABSTRACT

**Introduction** Metabolic syndrome (MetS) is a cluster of cardio-metabolic dysfunctions characterised by increased fasting plasma glucose, waist circumference, blood pressure, triglycerides and reduction in high-density lipoprotein cholesterol. Meanwhile, metabolic dysfunction-associated fatty liver disease (MAFLD) is the new term for fatty liver associated with MetS. People with MetS or MAFLD have higher risks for adverse cardiovascular outcomes and mortalities. However, large-scale data on MetS and MAFLD prevalence in Malaysia is mainly unknown. This study aims to determine the prevalence of MetS and MAFLD among the general adult population in Malaysia.

**Methods and analysis** This is a community-based nationwide cross-sectional study in Malaysia. The data collection period is from July 2023 until September 2023, with a planned sample size of 1296 participants. We use a two-stage proportionate stratified random sampling method to ensure national representativeness. The definition of MetS follows the Harmonised Joint Interim Statement in 2009. A diagnosis of MAFLD is made if a participant has fatty liver, defined as having a Fatty Liver Index  $\geq 60$  and has type 2 diabetes, a body mass index  $\geq 23$  kg/m<sup>2</sup>, or  $\geq 2$  metabolic risk abnormalities. Complex sample analysis will be conducted, and the disease prevalence will be reported with 95% CIs, unweighted counts and estimated populations.

**Ethics and dissemination** The protocol has been approved by the Medical Research and Ethics Committee of the Ministry of Health Malaysia (NMRR ID-22-02845-GUT). The findings will be disseminated through a formal report, policy brief, scientific publications, conference presentations, social media, print media and stakeholder engagement activities.

## INTRODUCTION

Metabolic syndrome (MetS) is a cluster of cardio-metabolic dysfunctions characterised by the increase in fasting plasma glucose, waist circumference, blood pressure (BP),

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Nationally representative data collection at the population-based level by a research institute with proven track records.
- ⇒ A single service provider with accredited laboratory standards to prevent information bias.
- ⇒ Concurrent field data collection with another study optimises human resources, materials and budget.
- ⇒ A multidisciplinary team of researchers, public health practitioners, clinicians and policymakers to ensure various study aspects are meticulously managed.
- ⇒ Does not account for factors associated with the study outcomes during the sample size calculation, which may limit the study's power to investigate the associated factors.

triglycerides (TG) and reduction in high-density lipoprotein cholesterol (HDL-C).<sup>1</sup> A meta-analysis estimated that people with MetS have a twofold higher risk for adverse cardiovascular outcomes and a 1.5-fold risk for all-cause mortality.<sup>2</sup> Many large-scale clinical trials also reported that MetS is highly predictive of new-onset type 2 diabetes, and those with MetS have up to 5.8 times the risk of developing diabetes.<sup>3</sup>

In recognising MetS's growing prevalence and threat to the world, many diagnostic criteria for MetS have been established in recent decades. The prominent ones include the first definition by the WHO in 1998,<sup>4</sup> followed by the US National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) in 2001,<sup>5</sup> and the International Diabetes Federation (IDF) in 2005.<sup>6</sup> In 2009, the Joint Interim Statement (JIS) was introduced to harmonise the differences



between various diagnostic definitions and is being widely adopted by studies worldwide.<sup>1</sup>

The global prevalence of MetS is estimated to be about one-quarter of the world population or over a billion global citizens.<sup>7</sup> There is a significant geographical variation in MetS prevalence. A systematic review reported that a wide range of 12–49% of the Asia-Pacific population had MetS.<sup>8</sup> Due to its association with increased morbidity and mortality, MetS is considered a disorder with a high socioeconomic impact on global health.<sup>9</sup> According to a nationwide Malaysian survey in 2008, the overall prevalence of MetS was 32.1%, 34.3%, 37.1% and 42.5%, based on the WHO, ATP III, IDF and JIS definitions, respectively.<sup>10</sup> However, recent large-scale data on MetS prevalence in Malaysia is unavailable. A review of MetS research in the country showed that many local studies were restricted to specific populations, and a few had relatively small sample sizes.<sup>11</sup> Thus, there is a need to know the latest nationwide prevalence of MetS in Malaysia.

Non-alcoholic fatty liver disease (NAFLD) is increasingly recognised as the liver disease component of MetS.<sup>12</sup> NAFLD is defined as the presence of  $\geq 5\%$  of hepatic steatosis in the absence of other liver disease aetiologies, such as chronic viral hepatitis and significant alcohol consumption.<sup>13</sup> With the ongoing obesity and MetS epidemic, NAFLD has become the most common cause of chronic liver disease globally.<sup>13–15</sup> A meta-analysis estimated the global prevalence of NAFLD at 25.2% and postulated that the clinical and economic burden of NAFLD is enormous.<sup>13</sup>

While NAFLD has been the conventional disease name for several decades, the term has been subjected to criticism largely because its diagnosis is made by excluding other conditions and the name does not reflect its underlying metabolic cause.<sup>16</sup> A new term, metabolic dysfunction-associated fatty liver disease (MAFLD), was introduced in 2020 as a more appropriate term for fatty liver associated with MetS.<sup>17</sup> MAFLD is diagnosed in an adult with fatty liver detected by either imaging techniques, blood biomarkers/scores or liver histology, AND the person is either overweight/obese, has type 2 diabetes or has at least two metabolic risk abnormalities.<sup>17</sup>

The new term MAFLD is diagnosed based on a set of positive criteria, does not require the exclusion of other causes of chronic liver disease and clearly attributes the disease to its underlying aetiology.<sup>17</sup> Unlike NAFLD, there is no need to rule out competing liver disease aetiologies, such as chronic viral hepatitis, use of medications that induce steatosis, other chronic liver diseases (eg, autoimmune hepatitis, haemochromatosis) and significant alcohol consumption.<sup>13</sup> MAFLD is now widely adopted worldwide, with several meta-analyses being published; the scopes include and not limited to cardiovascular disease, mortality, COVID-19, colorectal neoplasm and adverse maternal and fetal outcomes.<sup>18–26</sup> The Malaysian Society of Gastroenterology and Hepatology endorsed the redefinition of fatty liver disease

in 2021<sup>27</sup> and published the consensus statement on MAFLD in 2022.<sup>14</sup>

MAFLD has been shown to have better clinical utility than NAFLD.<sup>14 28–30</sup> For example, a recent analysis reported that MAFLD was associated with an increased risk of all-cause mortality, and NAFLD demonstrated no association with all-cause mortality after adjusting for metabolic risk factors.<sup>29</sup> Another study found that MAFLD criteria may identify more individuals with metabolically complicated fatty liver and increased risk for incident cardiovascular events.<sup>30</sup> Besides that, meta-analyses have concluded that MAFLD was associated with more severe COVID-19 and adverse maternal and fetal outcomes.<sup>24 25</sup> In addition, the severity of MAFLD was independently related to colorectal neoplasms, and severe MAFLD was more likely to cause left colon tumours.<sup>23</sup>

A recent meta-analysis estimated the global MAFLD prevalence at 38.77% (95% CI: 32.94% to 44.95%).<sup>21</sup> Among overweight and obese adults, another meta-analysis reported the global MAFLD prevalence at 50.7% (95% CI: 46.9% to 54.4%).<sup>26</sup> There is a wide variation in MAFLD prevalence between geographical regions, with  $< 36\%$ , 36–55% and  $> 55\%$  prevalence estimated in North America, Asia and Europe, respectively.<sup>21</sup> However, information on the newly defined MAFLD is scarce in Malaysia and poses a knowledge gap.<sup>14</sup> Nationwide data is essential to catalyse the planning and implementation of early intervention strategies to prevent and treat MetS and MAFLD in Malaysia. Therefore, this study aims to determine the prevalence of MetS and MAFLD among adults aged 18 years and above in Malaysia.

## METHODS AND ANALYSIS

### Study design, location and target population

Malaysia is a middle-income country, and this population-based cross-sectional study will involve all 13 states and 3 federal territories in the country in 2023. The target population is adults aged 18 years and above in Malaysia. They are residents from non-institutional living quarters (LQ) at the community level. The inclusion criteria are: (1) adults aged 18 years and above and (2) stay in non-institutionalised LQ for at least 2 weeks before data collection. It is essential only to collect data from eligible households in this population-based study. The exclusion criteria are: (1) institutionalised people, such as those staying in hotels and hospitals, which are not the usual LQ in a community to prevent selection bias<sup>31</sup>; (2) women during pregnancy and 12 weeks postpartum period due to physiological changes to prevent information bias<sup>32</sup>; and (3) people who do not give consent to participate in this study.<sup>33</sup>

### Sample size determination

The sample size is calculated using a single proportion formula for the estimation of prevalence.<sup>34 35</sup>

$$n_{SRS} \geq \frac{Z_{\alpha/2}^2 P(1-P)}{e^2}$$

**Table 1** Sample size calculation using difference prevalence of MetS and NAFLD

Outcome	Prevalence	Margin of error	Design effect	n	Non-response	Final population sample
MetS: WHO criteria <sup>10</sup>	0.321	0.05	2.00	670	0.40	1116
MetS: NCEP ATP III criteria <sup>10</sup>	0.343	0.05	2.00	693	0.40	1154
MetS: IDF criteria <sup>10</sup>	0.371	0.05	2.00	717	0.40	1195
MetS: Harmonised JIS criteria <sup>10</sup>	0.425	0.05	2.00	751	0.40	<b>1252</b>
NAFLD <sup>36</sup>	0.227	0.05	2.00	539	0.40	899
NAFLD <sup>37</sup>	0.374	0.05	2.00	720	0.40	1199

IDF, International Diabetes Federation; NCEP ATP III, US National Cholesterol Education Program Adult Treatment Panel III; JIS, Joint Interim Statement; MetS, metabolic syndrome ; NAFLD, non-alcoholic fatty liver disease.

Where,

- $n_{SRS}$  is the sample size based on simple random sampling.
- $Z_{\alpha/2}^2$  is the critical value of the normal distribution; for a 95% confidence level and 5% margin of error, the value is 1.96.
- Expected prevalence ( $P$ ). The prevalence of MetS using different definitions is between 32.1% and 42.5%.<sup>10</sup> Meanwhile, the prevalence of NAFLD based on previous local studies was 22.7% and 37.4%.<sup>36 37</sup>
- 5% margin of error,  $e$ .

A few adjustments are made to ensure optimum sample size:

- Finite population correction was adjusted for the total number of the target population ( $N$ ),<sup>34</sup> which is based on the estimated Malaysian population in 2021 by the Department of Statistics Malaysia.<sup>38</sup>

$$n \geq \frac{n_{SRS}}{1 + \frac{n_{SRS}}{N}}$$

- Adjusted for the design effect (deff) whereby  $n(\text{complex}) = n \times \text{deff}$ . A design effect of 2.00 is used, similar to the Malaysian National Health and Morbidity Survey (NHMS).<sup>39</sup>

- Adjusted the  $n(\text{complex})$  by considering the non-response rate whereby,  $n(\text{adj}) = n(\text{complex}) \times (1 + \text{non-response rate})$ . A non-response rate of 40% is used, higher than the Malaysian NHMS due to the need for venipuncture.<sup>39</sup>

**Table 1** summarises the sample size estimation using different prevalences of MetS and NAFLD. The largest sample size of 1252 is determined from the prevalence of MetS using the Harmonised criteria. Online supplemental table 1 details the sample size calculation.

The calculated sample size constitutes less than 1% of Malaysia's 23.5 million general adult population, which is small relative to the general population. We acknowledge that a higher sample size will increase the study power and improve the precision of the national prevalence estimate.<sup>34 35</sup> Nevertheless, it should be noted that the sample size has been meticulously calculated using the established single proportion formula to estimate

prevalence.<sup>34 35</sup> In addition, finite population correction is adjusted to account for the total number of the target population. We further adjust the design effect to reflect the two-stage stratified random sampling to ensure samples from all states and federal territories in Malaysia are included in this study. Furthermore, increasing the sample size will increase the cost of this study, delay the completion of data collection and additional samples beyond the calculated number may raise ethical issues.<sup>35</sup>

Nevertheless, factors associated with the study outcomes are not accounted for in the sample size estimation. Thus, the study power may not be adequate to investigate the factors associated with MetS and MAFLD, and this is a limitation of this protocol.

### Sampling frame

The Department of Statistics Malaysia divides the geographical areas in Malaysia into enumeration blocks (EB) for census operations.<sup>40</sup> Each EB contains 80–120 LQ with an estimated 500–600 people.<sup>39 40</sup> There are over 75 000 EB in Malaysia.<sup>39 40</sup>

We use a two-stage proportionate stratified random sampling method to ensure national representativeness. The primary sampling unit is the EB, and the secondary sampling unit is the LQ selected within the selected EB. The allocation of samples to all states and federal territories in Malaysia is done proportionally to the population size. Twelve LQ are randomly selected from each randomly chosen EB.<sup>39</sup> We estimated that there are 2.4 adults aged  $\geq 18$  years per household based on the population pyramid and average household size.<sup>38 40</sup> Thus, for a minimum sample size of 1252, the minimum number of EB is 43.5 (1252 divided by 12 divided by 2.4).

A total of 45 EB with 540 LQ will be randomly selected by the Department of Statistics. All eligible household members with an estimated 1296 people will be included, above the largest calculated required sample size of 1252.

## Study definitions

### Metabolic syndrome

The definition of MetS follows the Harmonised JIS (2009) criterion as it identifies more Malaysian adults with MetS compared with the NCEP-ATP III and IDF criteria.<sup>41</sup> Therefore, the JIS definition is recommended as the preferred diagnostic criterion and is adopted in this study.<sup>41</sup> Three relatively recent Malaysian studies have determined the prevalence of MetS using the JIS criterion alone.<sup>42–44</sup> Based on the JIS criterion, a person has MetS if they have at least three out of five risk factors, namely<sup>1</sup>:

- Waist circumference  $\geq 90$  cm for men and  $\geq 80$  cm for women.
- Systolic BP  $\geq 130$  and/or diastolic BP  $\geq 85$  mm Hg or on treatment for hypertension.
- Fasting plasma glucose  $\geq 5.6$  mmol/L or previously diagnosed diabetes
- TG  $\geq 1.7$  mmol/L or on treatment for TG.
- HDL-C  $< 1.0$  mmol/L for men or  $< 1.3$  mmol/L for women or on treatment for HDL-C.

### Metabolic dysfunction-associated fatty liver disease

The definition of MAFLD is adopted from the Malaysian consensus statement,<sup>14</sup> which is based on the original definition proposed by Eslam *et al.*<sup>17</sup> For this study, MAFLD is diagnosed if the person fulfils both criteria (a) and (b).

Fatty liver is defined as having a Fatty Liver Index (FLI)  $\geq 60$ .<sup>45</sup> The algorithm is based on body mass index (BMI), waist circumference, TG and gamma-glutamyl-transferase (GGT).<sup>45</sup>

$$FLI = \frac{e^{0.953 \times \log_e(\text{triglycerides}) + 0.139 \times \text{BMI} + 0.718 \times \log_e(\text{GGT}) + 0.053 \times \text{waist circumference} - 15.745}}{1 + e^{0.953 \times \log_e(\text{triglycerides}) + 0.139 \times \text{BMI} + 0.718 \times \log_e(\text{GGT}) + 0.053 \times \text{waist circumference} - 15.745}} \times 100$$

### AND

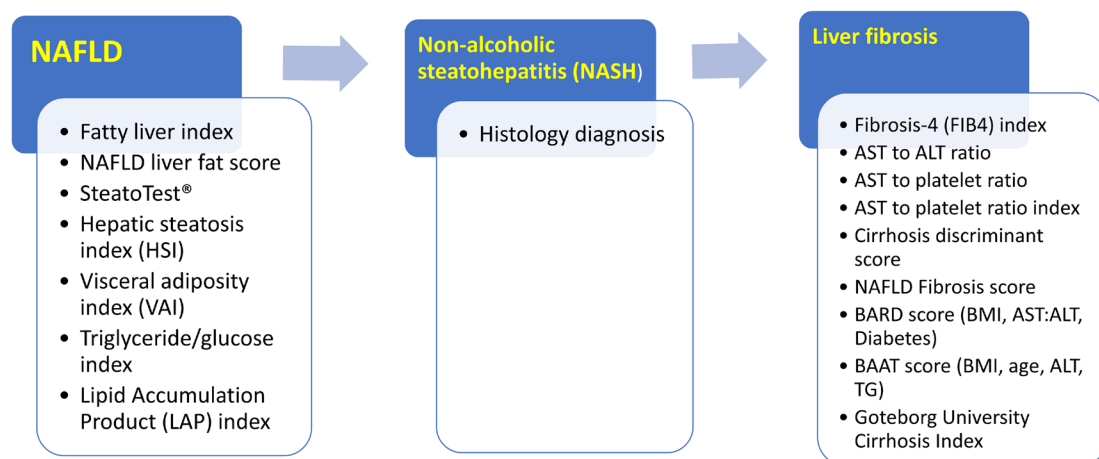
- Has type 2 diabetes **OR**
- Overweight or obese, defined as BMI  $\geq 23$  kg/m<sup>2</sup> **OR**
- Presence of  $\geq 2$  metabolic risk abnormalities:
  - ▶ Waist circumference  $\geq 90$  cm for men and  $\geq 80$  cm for women.

- ▶ Systolic BP  $\geq 130$  and/or diastolic BP  $\geq 85$  mm Hg or on treatment for hypertension.
- ▶ TG  $\geq 1.7$  mmol/L or on treatment for TG.
- ▶ HDL-C  $< 1.0$  mmol/L for men or  $< 1.3$  mmol/L for women or on treatment for HDL-C.
- ▶ Pre-diabetes, defined as fasting glucose levels 5.6–6.9 mmol/L or glycosylated haemoglobin A1c 5.7–6.4%.

It is important to note that serum biomarkers of fatty liver can replace imaging methods, but this would only be appropriate for large epidemiological studies.<sup>17</sup> The European guidelines noted that biomarkers are acceptable alternatives for diagnosing fatty liver when imaging tools are not available or feasible, such as in large epidemiological surveys.<sup>46</sup> In the original article on MAFLD, FLI is specified as the appropriate blood biomarker of steatosis.<sup>17</sup>

FLI is a simple and accurate predictor of hepatic steatosis in the general population.<sup>45</sup> An FLI of  $< 30$  rules out, and an FLI of  $\geq 60$  rules in fatty liver.<sup>45</sup> A recent meta-analysis was conducted to assess FLI's performance in identifying NAFLD in population studies. It was concluded that FLI showed an adequate performance in stratifying the risk of NAFLD and supported its use as a tool in large population studies.<sup>47</sup> In a recently published meta-analysis to determine the global prevalence of MAFLD, FLI was the only serum biomarker used (besides ultrasound, biopsy and MRI).<sup>21</sup>

It is essential to note that there are many biomarkers for NAFLD and liver fibrosis, as shown in [figure 1](#), which follow the natural pathophysiology of disease progression.<sup>48–50</sup> However, FLI and NAFLD liver fat scores are the stated biomarkers for steatosis by several clinical guidelines in a systematic review.<sup>51</sup> NAFLD liver fat score consists of MetS, type 2 diabetes, fasting serum insulin, aspartate aminotransferase (AST) and AST-to-alanine aminotransferase ratio.<sup>52</sup> Although NAFLD liver fat score is reliable and easy to use, the need for fasting serum insulin limits its real-life application due to availability and costs.<sup>53</sup> Thus, FLI is used as the biomarker of steatosis in this study.



**Figure 1** Various biomarkers for NAFLD and liver fibrosis.<sup>48–50</sup> ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; NAFLD, non-alcoholic fatty liver disease; TG, triglycerides.

Due to logistical and financial challenges, we cannot do liver scans in this community-based study. Even though imaging-based tests are not required to diagnose steatosis, transient elastography (eg, FibroScan, FibroTouch) can provide additional clinical information, such as the degree of MAFLD or the severity of liver fibrosis.<sup>54</sup>

Two metabolic risk factors for MAFLD, namely Homeostasis Model Assessment of Insulin Resistance score of  $\geq 2.5$  and a plasma high-sensitivity C reactive protein level  $> 2\text{ mg/L}$ , are not included in the study definition. This is due to the high costs of these tests, safety concerns arising from the need for a higher blood volume drawn in respondents' LQ and possibly a lower study response rate in this population-based survey.

At the time when this study protocol was conceived and approved, MAFLD was the new term used to replace NAFLD.<sup>17 27</sup> However, MAFLD terminology has also raised some concerns, such as the continued use of the stigmatising term 'fatty', the mixing of underlying causes, restricting patients to those with two metabolic risk factors and the potential negative consequences on therapeutic development.<sup>16 55</sup> This led to a recent Delphi consensus statement with steatotic liver disease (SLD) chosen as the overarching name to cover different causes of steatosis.<sup>55</sup> The subclassification includes metabolic dysfunction-associated steatotic liver disease (MASLD), alcohol-associated liver disease (ALD), an overlap of MASLD and ALD (known as MetALD), specific aetiology SLD and cryptogenic SLD.<sup>55</sup> Specifically, MASLD was the term chosen to replace NAFLD, and its definition required only one out of five metabolic risk factors.<sup>55</sup> Meanwhile, MetALD was defined as people with MASLD who consume higher amounts of alcohol per week.<sup>55</sup>

At the time of preparation of this revised manuscript, MAFLD is still the term endorsed by the Malaysian Society of Gastroenterology and Hepatology and the Asian Pacific Association for the Study of the Liver, among others.<sup>14 27</sup> On the contrary, the new MASLD and MetALD definitions will add strength to this study as additional analyses can be conducted later on to determine the various definitions of MAFLD, MASLD and MetALD. However, we do not explicitly state this as a new study objective as we intend to describe the protocol as it is when accepted by the ethics committee and research grant body.

### Data collection

A defining feature of this study is the collection of nationally representative data at the population-based level by the Institute of Public Health, a research institute under the National Institutes for Health with proven track records for field implementation.<sup>56</sup> The data collection is from July 2023 until September 2023, concurrently with the NHMS non-communicable disease (NCD) 2023. The 3-month enrolment period is typical and sufficient even for more extensive population-based prevalence studies in Malaysia, such as the NHMS.<sup>57</sup> All 45 EB in this study are randomly selected across the country, and the data collection teams constantly move from one place to another

in the field. After data collection is completed in one block, they will move on to another one. In other words, they are not stationed at the same place throughout the data collection period. This requires meticulous logistic planning such as shifting rented lodgings every few days, coordinating paramedics' assistance from nearby public healthcare facilities and working overtime on weekends, early morning and late at night when respondents are home. The financial costs for vehicle and accommodation rentals and staff allowances are substantial. Thus, a 3-month enrolment period is optimal, and extending it is not logistically and financially feasible for this national-level population-based study.

The data collection takes place together with the NHMS, a rolling annual population-based survey conducted by the Institute of Public Health.<sup>56</sup> Relevant authorities have approved the NHMS NCD 2023 survey with the required funding secured. Concurrent field data collection allows sharing of common resources such as workforces, vehicles, lodgings, instrument calibration fees and training workshops. Expenses are only incurred once instead of twice if the data collection for the two studies is carried out separately. It is estimated that half of the initial budget for this study is saved by running the data collection together. Hence, the arrangement leads to financial savings and is highly efficient. Besides that, information collected in these two surveys complements one another and allows further data analysis later. Secondary data analysis of the data set linked with the NHMS NCD 2023 will help answer new research objectives cost-efficiently.

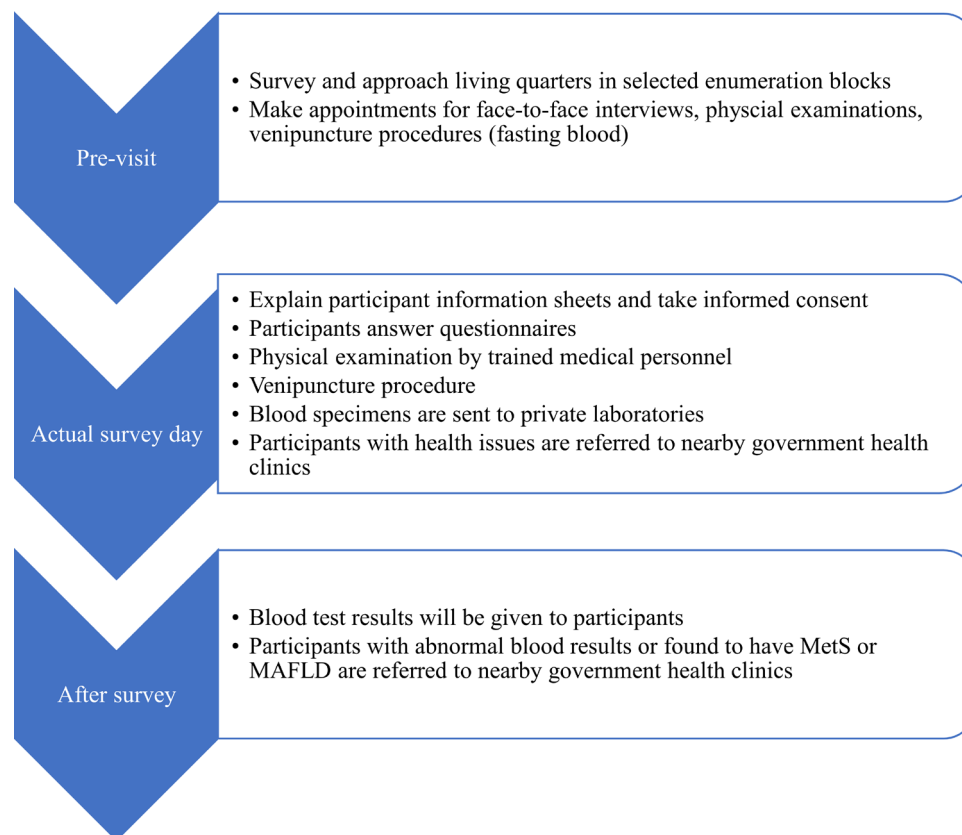
Each data collection team comprises four members, including one team leader, one research assistant, one driver cum research assistant and one trained medical personnel as a phlebotomist. The teams will visit all LQ to make appointments for data collection. Data collection consists of three components: (1) face-to-face interviews using structured questionnaires, (2) physical examinations and (3) blood specimen collection. Three visits at different times of the day during weekdays and weekends will be attempted before the selected LQ is classified as non-response. **Figure 2** shows the data collection process.

#### Face-to-face interviews using structured questionnaires

The interviewers will be trained before actual data collection. The questionnaire consists of socioeconomic (age, ethnicity, sex, marital status, educational level, occupation and household income) and medical information (previous diagnosis and treatment status for diabetes, hypertension and hypercholesterolaemia.) The questionnaire is adapted from the WHO STEPwise approach to NCD risk factor surveillance questionnaire<sup>58</sup> and is available in Bahasa Malaysia and English.

#### Physical examination

BMI is the weight in kilograms divided by squared standing height in metres. Calibrated digital weighing scale, Tanita Personal Scale HD 319 (manufactured by Tanita Corporation, Tokyo, Japan), SECA Stadiometer



**Figure 2** Flow chart of the data collection process. MAFLD, metabolic dysfunction-associated fatty liver disease; MetS, metabolic syndrome.

213 (manufactured by SECA GmbH & Co. KG, Hamburg, Germany) and SECA 201 measuring tape (manufactured by SECA GmbH & Co. KG, Hamburg, Germany) will be used to measure body weight, height and waist circumference, respectively. These measuring devices have been validated for community surveys and used in the previous NHMS.<sup>39 59 60</sup> Waist circumference is measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest.<sup>58</sup> Respondents need to stand with their feet together with arms relaxed at the sides. The tape is then held horizontally and wrapped around the waist. Measurement is taken (to the nearest 0.1 cm) at the end of a normal exhalation.<sup>58</sup>

BP is measured using a digital sphygmomanometer (Omron Japan Model HEM-907), which has been validated.<sup>61</sup> Per the WHO STEPwise manual, measurement is made after the respondent has 15 min of rest in a seated position with uncrossed legs.<sup>58</sup> The left arm is measured thrice, with 3 min intervals between measurements.<sup>58</sup> The mean of the second and third readings will be used for analysis purposes.<sup>58</sup> Medical personnel will be trained to follow standardised procedures before data collection to minimise variability in the anthropometric measurements between recorders at various study sites.

#### Collection of blood samples

Respondents will be asked to fast for at least 8 hours before blood-taking procedures. The phlebotomist will explain the risks of blood taking and ask if respondents have

bleeding/clotting problems or are on blood-thinning medications before the procedure. Around 7.5 mL of venous blood will be drawn following aseptic principles to ensure cleanliness and prevent cross-infection. The collected blood samples will be stored in a portable freezer at 4°C–8°C and sent to private laboratories on the same day for analysis. The tests include fasting blood sugar, lipid profile, liver function test and glycosylated haemoglobin A1c. The laboratories are under a single company, able to cater to all states and federal territories in Malaysia, and accredited under the *Skim Akreditasi Makmal Malaysia*, a national unified laboratory accreditation scheme under the Department of Standards Malaysia (Standards Malaysia).<sup>62</sup> Laboratories certified under the scheme meet the requirements of MS ISO/IEC 17025 general requirements for the competence of testing and calibration laboratories, published by the International Organisation for Standardisation (ISO).<sup>62</sup> A single service provider with accredited laboratory standards for testing competence and calibration prevents information bias. Standardised training of all interviewers and medical personnel before the data collection phase commences will minimise measurement errors.

#### Data analysis

IBM SPSS Statistics (V.23 or higher) will be used for statistical analysis. Depending on the data distribution, we will present continuous variables using mean±SD or median (IQR). Continuous variables such as age and household

income will be categorised appropriately. Categorical variables such as ethnicity and marital status will be presented as frequency counts with percentages. Complex sample analysis procedures will be conducted, and the prevalence of MetS and MAFLD will be reported with 95% CIs, unweighted counts and estimated populations.

### Gantt chart

Online supplemental table 2 shows the Gantt chart of this study. At the time of this writing, our progress is aligned with the planned schedule.

### Patient and public involvement

Patients and the public are not involved in the design of this research. However, the public will be involved in the conduct, reporting and dissemination plans. Before and during the data collection phase, promotional activities about this survey will be carried out through social media (eg, posts on the official Facebook page), radio talk and news coverage (eg, launching by top Ministry of Health personnel). Visits to local leaders (eg, village heads and community leaders) will be made before data collection to gain their support to disseminate information about this survey to their communities. Banners will be put up at strategic points in the EB, and pamphlets will be distributed to the public to raise awareness and knowledge about MetS, MAFLD and the survey. The study report, press release and findings in the form of infographics or research highlights will be disseminated to the public through press media, websites and official social media accounts.

### ETHICS AND DISSEMINATION

The researchers adhere to the principles of the Declaration of Helsinki, the Medical Research and Ethics Committee's guidelines and the Malaysian Good Clinical Practice Guidelines. The Medical Research and Ethics Committee of the Ministry of Health Malaysia has granted ethical approval to conduct this study (NMRR ID-22-02845-GUT).

Detailed participant information sheets will be available to all respondents. Verbal and written consent will be obtained from respondents on a voluntary participation basis before initiating the study. All information obtained will be treated as strictly confidential and stored according to the Ministry of Health data storage regulations. Each respondent will be assigned unique anonymous identifiers and kept following the local Data Protection Act. Respondents found to have MetS or MAFLD will be referred to the nearest government health clinics. All personal identifying information will be deleted before data analysis to maintain the anonymity of the survey.

One consistent problem with clinical and health services research is the failure to translate research into practice and policy.<sup>63</sup> Our multidisciplinary team of researchers, public health practitioners, clinicians and policymakers from the Ministry of Health and academia

will help in stakeholder mapping and setting the agenda for policymaking.<sup>63</sup> Our result dissemination plan has explicit target outputs to be fulfilled: one full report, one policy brief, at least two publications in peer-reviewed journals and two presentations at relevant conferences. The dissemination plan covers various target audiences, including policymakers, public health practitioners, clinicians and researchers. Importantly, we will create infographics, research highlights and press release to target the general population through different channels in this information age to increase awareness and knowledge. De-identified granular data will also be shared with the main stakeholders to translate knowledge and inform policymaking.

### Author affiliations

<sup>1</sup>Institute for Public Health, National Institutes of Health, Ministry of Health Malaysia, Shah Alam, Selangor, Malaysia

<sup>2</sup>Gastroenterology and Hepatology Unit, Department of Medicine, Faculty of Medicine, Universiti Malaya, Kuala Lumpur, Malaysia

<sup>3</sup>Department of Medicine, Putrajaya Hospital, Ministry of Health Malaysia, Putrajaya, Malaysia

<sup>4</sup>Disease Control Division, Ministry of Health Malaysia, Putrajaya, Malaysia

<sup>5</sup>Perak State Health Department, Ministry of Health Malaysia, Perak, Malaysia

**Acknowledgements** We thank the Director General of Health Malaysia for permission to publish this paper. We appreciate the support of the Deputy Director General of Health (Research and Technical Support) in conducting this study. We also thank all our colleagues at the National Institutes of Health, specifically the Institute for Public Health, who gave constructive feedback on this project.

**Contributors** KSW contributed to the conceptualisation, funding acquisition, methodology, project administration, visualisation, original draft writing and final manuscript review and editing. HMR contributed to the conceptualisation, funding acquisition, methodology, project administration and review and editing of the final manuscript. MFM and NAA contributed to the conceptualisation, funding acquisition, methodology, supervision and review and editing of the final manuscript. KKYR, WKC, MM, NMN and FIM contributed to the conceptualisation, methodology and review and editing of the final manuscript. All authors contributed to the article and approved the submitted version.

**Funding** This work was supported by the Ministry of Health Malaysia, grant number 91000050.

**Competing interests** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**Patient and public involvement** Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

**Patient consent for publication** Not applicable.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Supplemental material** This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

## ORCID iDs

Kim Sui Wan <http://orcid.org/0000-0002-0859-1648>Halizah Mat Rifin <http://orcid.org/0000-0002-5067-5677>

## REFERENCES

- Alberti K, Eckel RH, Grundy SM, *et al.* Harmonizing the metabolic syndrome: a joint interim statement of the International diabetes federation task force on epidemiology and prevention; National heart, lung, and blood Institute; American heart Association; world heart federation; International atherosclerosis society; and International Association for the study of obesity. *Circulation* 2009;120:1640–5.
- Mottillo S, Filion KB, Genest J, *et al.* The metabolic syndrome and cardiovascular risk: a systematic review and meta-analysis. *J Am Coll Cardiol* 2010;56:1113–32.
- Shin J-A, Lee J-H, Lim S-Y, *et al.* Metabolic syndrome as a predictor of type 2 diabetes, and its clinical interpretations and usefulness. *J Diabetes Investig* 2013;4:334–43.
- Alberti K, Zimmet PZ, WHO Consultation. Definition, diagnosis and classification of diabetes mellitus and its complications. part 1: diagnosis and classification of diabetes mellitus. provisional report of a WHO consultation. *Diabet Med* 1998;15:539–53.
- National cholesterol education program. expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). Third report of the National cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III) final report. *Circulation* 2002;106:3143–421.
- Alberti K, Zimmet P, Shaw J, *et al.* The metabolic syndrome—a new worldwide definition. *Lancet* 2005;366:1059–62.
- Saklayen MG. The global epidemic of the metabolic syndrome. *Curr Hypertens Rep* 2018;20:12:12..
- Ranasinghe P, Mathangasinghe Y, Jayawardena R, *et al.* Prevalence and trends of metabolic syndrome among adults in the Asia-Pacific region: a systematic review. *BMC Public Health* 2017;17:101.
- Misra A, Khurana L. Obesity and the metabolic syndrome in developing countries. *J Clin Endocrinol Metab* 2008;93:S9–30.
- Mohamud WNW, Ismail A-S, Sharifuddin A, *et al.* Prevalence of metabolic syndrome and its risk factors in adult Malaysians: results of a nationwide survey. *Diabetes Res Clin Pract* 2011;91:239–45.
- Lim KG, Cheah WK. A review of metabolic syndrome research in Malaysia. *Med J Malaysia* 2016;71:20–8.
- Chalasanani N, Younossi Z, Lavine JE, *et al.* The diagnosis and management of Non-Alcoholic fatty liver disease: practice guideline by the American Association for the study of liver diseases: American college of Gastroenterology, and the American Gastroenterological Association. *Hepatology* 2012;55:2005–23.
- Younossi ZM, Koenig AB, Abdelatif D, *et al.* Global epidemiology of Nonalcoholic fatty liver disease—meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology* 2016;64:73–84.
- Chan W-K, Tan S-S, Chan S-P, *et al.* Malaysian society of Gastroenterology and Hepatology consensus statement on metabolic dysfunction-associated fatty liver disease. *J Gastroenterol Hepatol* 2022;37:795–811.
- Wree A, Broderick L, Canbay A, *et al.* From NAFLD to NASH to cirrhosis—new insights into disease mechanisms. *Nat Rev Gastroenterol Hepatol* 2013;10:627–36.
- Yilmaz Y. The heated debate over NAFLD renaming: an ongoing saga. *Hepatology Forum* 2023.
- Eslam M, Newsome PN, Sarin SK, *et al.* A new definition for metabolic dysfunction-associated fatty liver disease: an international expert consensus statement. *J Hepatol* 2020;73:202–9.
- Lim GEH, Tang A, Ng CH, *et al.* An observational data meta-analysis on the differences in prevalence and risk factors between MAFLD vs NAFLD. *Clin Gastroenterol Hepatol* 2023;21:619–29.
- Quek J, Ng CH, Tang ASP, *et al.* Metabolic associated fatty liver disease increases the risk of systemic complications and mortality. A meta-analysis and systematic review of 12 620 736 individuals. *Endocr Pract* 2022;28:667–72.
- Ayada I, van Kleef LA, Alferink LJM, *et al.* Systematically comparing epidemiological and clinical features of MAFLD and NAFLD by meta-analysis: focusing on the non-overlap groups. *Liver Int* 2022;42:277–87.
- Chan KE, Koh TJL, Tang ASP, *et al.* Global prevalence and clinical characteristics of metabolic associated fatty liver disease. A meta-analysis and systematic review of 10,739,607 individuals. *J Clin Endocrinol Metab* 2022;107:2691–700.
- Wen W, Li H, Wang C, *et al.* Metabolic dysfunction-associated fatty liver disease and cardiovascular disease: a meta-analysis. *Front Endocrinol (Lausanne)* 2022;13.
- Zeng Y, Cao R, Tao Z, *et al.* Association between the severity of metabolic dysfunction-associated fatty liver disease and the risk of colorectal neoplasm: a systematic review and meta-analysis. *Lipids Health Dis* 2022;21:52.
- Hegyi PJ, Váncsa S, Ocskay K, *et al.* Metabolic associated fatty liver disease is associated with an increased risk of severe COVID-19: a systematic review with meta-analysis. *Front Med (Lausanne)* 2021;8.
- Dyah AA, Rahadina R. Metabolic associated fatty liver disease and adverse maternal and fetal outcomes: a systematic review and meta-analysis. *Clin Exp Hepatol* 2021;7:305–11.
- Liu J, Ayada I, Zhang X, *et al.* Estimating global prevalence of metabolic dysfunction-associated fatty liver disease in overweight or obese adults. *Clin Gastroenterol Hepatol* 2022;20:e573–82.
- Tan SS, Lee YY, Ali RAR, *et al.* Endorsing the redefinition of fatty liver disease. *Lancet Gastroenterol Hepatol* 2021;6:163.
- Zheng KI, Sun D-Q, Jin Y, *et al.* Clinical utility of the MAFLD definition. *J Hepatol* 2021;74:989–91.
- Kim D, Konyon P, Sandhu KK, *et al.* Metabolic dysfunction-associated fatty liver disease is associated with increased all-cause mortality in the United States. *J Hepatol* 2021;75:1284–91.
- Lee H, Lee Y-H, Kim SU, *et al.* Metabolic dysfunction-associated fatty liver disease and incident cardiovascular disease risk: a nationwide cohort study. *Clin Gastroenterol Hepatol* 2021;19:2138–47.
- Department of Statistics Malaysia. Living quarters 2023. 2023. Available: <https://dev.dosm.gov.my/assets/documents/living.pdf> [Accessed 18 Sep 2023].
- ACOG committee opinion No.736: optimizing postpartum care. *Obstet Gynecol* 2018;131:e140–50.
- Ministry of Health Malaysia. *Malaysian Guideline for Good Clinical Practice. 4th edition.* 2018. Available: [https://www.crc.gov.my/wp-content/uploads/2018/03/Malaysian\\_gcp\\_4th\\_Edition28Final\\_29.pdf](https://www.crc.gov.my/wp-content/uploads/2018/03/Malaysian_gcp_4th_Edition28Final_29.pdf)
- Israel GD. Determining sample size: University of Florida cooperative extension service. EDIS Institute of food and Agriculture sciences; 1992.
- Serdar CC, Cihan M, Yücel D, *et al.* Sample size, power and effect size revisited: simplified and practical approaches in pre-clinical, clinical and laboratory studies. *Biochem Med (Zagreb)* 2021;31.
- Goh S-C, Ho E-M, Goh K-L. Prevalence and risk factors of non-alcoholic fatty liver disease in a Multiracial suburban Asian population in Malaysia. *Hepatol Int* 2013;7:548–54.
- Khammas ASA, Hassan HA, Salih SQM, *et al.* Prevalence and risk factors of sonographically detected non alcoholic fatty liver disease in a screening centre in Klang valley, Malaysia: an observational cross-sectional study. *Porto Biomed J* 2019;4:e31.
- Department of Statistics Malaysia. Current population estimates. Malaysia Putrajaya; 2021.
- Institute for Public Health. National health and morbidity survey (NHMS) 2019: vol 1: Ncds - non-communicable diseases: risk factors and other health problems; 2020.
- Department of Statistics Malaysia. Key findings population and housing census of Malaysia, 2020 version 2.0. Malaysia Putrajaya; 2022.
- Ramli AS, Daher AM, Nor-Ashikin MNK, *et al.* JIS definition identified more Malaysian adults with metabolic syndrome compared to the NCEP-ATP III and IDF criteria. *Biomed Res Int* 2013;2013.
- Ching YK, Chin YS, Appukutty M, *et al.* Prevalence of metabolic syndrome and its associated factors among vegetarians in Malaysia. *Int J Environ Res Public Health* 2018;15:2031.
- Iqbal SP, Ramadas A, Fatt QK, *et al.* Relationship of Sociodemographic and lifestyle factors and diet habits with metabolic syndrome (Mets) among three ethnic groups of the Malaysian population. *PLoS One* 2020;15.
- Manaf MRA, Nawi AM, Tauhid NM, *et al.* Prevalence of metabolic syndrome and its associated risk factors among staffs in a Malaysian public University. *Sci Rep* 2021;11:8132.
- Bedogni G, Bellentani S, Miglioli L, *et al.* The fatty liver index: a simple and accurate predictor of hepatic steatosis in the general population. *BMC Gastroenterol* 2006;6:33.
- European Association for the study of the liver, European Association for the study of diabetes. EASL-EASD-EASO clinical practice guidelines for the management of non-alcoholic fatty liver disease. *Obes Facts* 2016;9:65–90.
- Castellana M, Donghia R, Guerra V, *et al.* Performance of fatty liver index in identifying non-alcoholic fatty liver disease in population studies. a meta-analysis. *J Clin Med* 2021;10:1877.



- 48 Hernandez Roman J, Siddiqui MS. The role of noninvasive biomarkers in diagnosis and risk stratification in nonalcoholic fatty liver disease. *Endocrinol Diabetes Metab* 2020;3:e00127.
- 49 Fedchuk L, Nascimbeni F, Pais R, *et al*. Performance and limitations of steatosis biomarkers in patients with nonalcoholic fatty liver disease. *Aliment Pharmacol Ther* 2014;40:1209–22.
- 50 Shah AG, Lydecker A, Murray K, *et al*. Use of the Fib4 index for non-invasive evaluation of fibrosis in Nonalcoholic fatty liver disease. *Clin Gastroenterol Hepatol* 2009;7:1104–12.
- 51 Leoni S, Tovoli F, Napoli L, *et al*. Current guidelines for the management of non-alcoholic fatty liver disease: a systematic review with comparative analysis. *World J Gastroenterol* 2018;24:3361–73.
- 52 Kotronen A, Peltonen M, Hakkarainen A, *et al*. Prediction of non-alcoholic fatty liver disease and liver fat using metabolic and genetic factors. *Gastroenterology* 2009;137:865–72.
- 53 Jeong S, Kim K, Chang J, *et al*. Development of a simple nonalcoholic fatty liver disease scoring system indicative of metabolic risks and insulin resistance. *Ann Transl Med* 2020;8:1414.
- 54 Ng YZ, Lai LL, Wong SW, *et al*. Attenuation parameter and liver stiffness measurement using fibrotouch vs Fibroscan in patients with chronic liver disease. *PLoS One* 2021;16:e0250300.
- 55 Rinella ME, Lazarus JV, Ratziu V, *et al*. A multi-society Delphi consensus statement on new fatty liver disease nomenclature. *Hepatology* 2023.
- 56 Institute for Public Health. Welcome to Institute for public health centre for Epidemiological survey research. 2022. Available: <https://iku.gov.my> [Accessed 22 Jan 2023].
- 57 Institute for Public Health. Welcome to NHMS national health & morbidity survey. 2023. Available: <https://iku.gov.my/nhms> [Accessed 22 Jan 2023].
- 58 World Health Organization, Noncommunicable D, Mental Health C. *Who Steps Surveillance Manual: the Who Stepwise Approach to Chronic Disease Risk Factor Surveillance / Noncommunicable Diseases and Mental Health*, World Health Organization. Geneva: World Health Organization, 2005.
- 59 Baharudin A, Ahmad MH, Naidu BM, *et al*. Reliability, technical error of measurement and validity of height measurement using portable stadiometer. *Pertanika J Sci & Technol* 2017;25:675–86.
- 60 Geeta A, Jamaiyah H, Safiza MN, *et al*. Reliability, technical error of measurements and validity of instruments for nutritional status assessment of adults in Malaysia. *Singapore Med J* 2009;50:1013–8.
- 61 El Assaad MA, Topouchian JA, Darné BM, *et al*. Validation of the Omron HEM-907 device for blood pressure measurement. *Blood Press Monit* 2002;7:237–41. 10.1097/00126097-200208000-00006 Available: <https://doi.org/10.1097/00126097-200208000-00006>
- 62 Ministry of International Trade and Industry (MITI). Testing & calibration laboratories (SAMM). 2022. Available: <https://www.jsm.gov.my/accreditation/get-accredited/fields-programmes> [Accessed 29 Nov 2022].
- 63 Grimshaw JM, Eccles MP, Lavis JN, *et al*. Knowledge translation of research findings. *Implement Sci* 2012;7:50.

**Supplementary Table 1: Sample size calculation using difference prevalence of MetS and NAFLD**

<i>Outcome</i>	<i>Target population</i>	<i>Population projection in 2021</i>	<i>Prevalence, p</i>	<i>Margin of error, e</i>	<i>Design effect (Deff)</i>	<i>n</i>	<i>Non-response</i>	<i>Final population sample (n adjusted)</i>	<i>Expected standard error</i>	<i>Relative standard error, RSE (%)</i>
MetS: WHO criteria (18)	18 and above	23,478,780	0.321	0.05	2.00	670	0.40	1,116	0.036	11.24
MetS: NCEP ATP III criteria (18)	18 and above	23,478,780	0.343	0.05	2.00	693	0.40	1,154	0.036	10.52
MetS: IDF criteria (18)	18 and above	23,478,780	0.371	0.05	2.00	717	0.40	1,195	0.036	9.72
MetS: Harmonised JIS criteria (18)	18 and above	23,478,780	0.425	0.05	2.00	751	0.40	<b>1,252</b>	0.036	8.49
NAFLD (39)	18 and above	23,478,780	0.227	0.05	2.00	539	0.40	899	0.036	15.89
NAFLD (40)	18 and above	23,478,780	0.374	0.05	2.00	720	0.40	1,199	0.036	9.65

Abbreviations: IDF: International Diabetes Federation; MAFLD: JIS: Joint Interim Statement; NAFLD: non-alcoholic fatty liver disease; NCEP ATP III: United States National Cholesterol Education Program Adult Treatment Panel III; WHO: World Health Organization

**Supplementary Table 2: Gantt chart of the study**

Activities	2022												2023												2024					
	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	
Literature review	█	█	█	█	█	█	█	█	█	█															█					
Meeting with stakeholders				█	█	█	█	█		█	█						█	█								█	█	█	█	
Proposal development				█	█	█	█			█	█																			
Approval of study protocols by the ethics committee											█	█	█																	
Logistic preparations												█	█	█	█															
Training of data collectors																█	█													
Data collection																			█	█	█									
Data management & analysis																					█	█	█	█						
Report writing																									█	█				
Dissemination of research findings																											█	█	█	
Printing of full reports																												█	█	