Review

Association of risk factors with type 2 diabetes: A systematic review

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Abstract

Diabetes is the leading cause of severe health complications and one of the top 10 causes of death worldwide. To date, diabetes has no cure, and therefore, it is necessary to take precautionary measures to avoid its occurrence. The main aim of this systematic review is to identify the majority of the risk factors for the incidence/prevalence of type 2 diabetes mellitus on one hand, and to give a critical analysis of the cohort/cross-sectional studies which examine the impact of the association of risk factors on diabetes. Consequently, we provide insights on risk factors whose interactions are major players in developing diabetes. We conclude with recommendations to allied health professionals, individuals and government institutions to support better diagnosis and prognosis of the disease.

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1. Introduction

Diabetes Mellitus (DM) commonly referred to as diabetes, is a chronic disease that affects how the body turns food into energy [1]. It is one of the top 10 causes of death worldwide causing 4 million deaths in 2017 [2,3]. According to a report by the International Diabetes Federation (IDF) [3], the total number of adults (20–79 years) with diabetes in 2045 will be 629 million from 425 million in 2017 (48% increase). In 2017, diabetes caused at least 727 billion USD in health expenditure, which is 12% of the total spending on adults [3]. According to the National Diabetes Statistics Report [4], 30.3 million (9.4% of the US population) people have diabetes, and 84.1 million (29.06% of the population) have prediabetes. 1 in 2 people (212 million) with diabetes was undiagnosed in 2017 according to IDF [5]. Diabetes if left untreated can cause serious medical issues, such as cardiovascular disease, stroke, chronic kidney disease, foot ulcers, damage to the eyes, and prolonged kidney ailment. To date, there is no permanent cure for diabetes and the patients have to rely on healthy lifestyle and timely medication [6].

There are three main types of diabetes: type 1, type 2, and gestational diabetes (diabetes while pregnant) [1]. Type 1 diabetes mostly occurs in children and adolescents. 1,106,500 children were suffering from type 1 diabetes in 2017 [3]. The symptoms of type 1 diabetes include abnormal thirst and dry mouth, frequent urination, fatigue, constant hunger, sudden weight loss, bed-wetting, and blurred vision. Type 2 diabetes is mostly seen in adults, but it is increasing in children and adolescents due to the rising level of obesity, physical inactivity and unhealthy diet [5]. 372 million adults were at the risk of developing type 2 diabetes in 2019 [3]. In 2017, more than 21 million live births were affected by diabetes during pregnancy [3]. In this paper, we focus on type 2 diabetes due to the alarming numbers.

Type 2 Diabetes is thought to prevail in an individual from an interaction between several lifestyle, medical condition, hereditary, psychosocial and demographic risk factors such as high-level serum uric acid, sleep quality/quantity, smoking, depression, cardiovascular disease, dyslipidemia, hypertension, aging, ethnicity, family history of diabetes, physical inactivity, and obesity [6]. In this paper, we present a systematic review of the literature on the association of these risk factors with the incidence/prevalence of type 2 diabetes. We give insights on the contribution of independent risk factors in the development of type 2 diabetes along with possible solutions towards a preventive approach.

2. Methods

We conduct a systematic literature search using CINAHL, IEEE Xplore, Embase, MEDLINE, PubMed Central, ScienceDirect, Scopus, Springer, and Web of Science databases. Our search criteria does not include a time bound. Its main objective is to retrieve all the studies which examine the association between individual risk factors and the incidence/prevalence of type 2 diabetes. Table A1 shows the search string used for each risk factor. The relevant studies have to meet the following inclusion criteria: 1) published in the English language, 2) prospective cohort or cross-sectional study, 3) type 2 diabetes as a specified risk, 4) one of its risk factors, 5) findings in terms of Odds Ratio (OR), Risk Ratio/Relative Risk (RR), or Hazard Ratio (HR), and the corresponding 95% Confidence Intervals (CIs) for the association between the risk factor and type 2 diabetes. To assess the quality of the studies, we use the National Institutes of Health (NIH) quality assessment tool [7]. The tool consists of 14 questions to evaluate the validity and bias risk of a study. We answered each question by either yes, no, cannot be determined, not applicable, or not reported. The tool then classifies each study as high quality (Good), moderate quality (Fair) and low quality (Poor).

3. Results

Fig. 1 shows the result of our systematic approach that is used to screen the relevant studies. Irrelevant studies that do not meet the inclusion criteria mentioned in the previous section were excluded after screening titles, abstracts and full texts. At last, 106 papers are considered for this review. These papers are divided into ten categories based on the risk factor under study (Fig. 1). Our review reveals that there is no study that examines the association of age or physical inactivity as an independent risk factor with type 2 diabetes. Table A2 shows the quality assessment results for the studies included in this paper. For smoking, cardiovascular disease and hypertension risk factors, the majority of the studies are of high quality. For serum uric acid, sleep quantity/quality, depression, dyslipidemia, ethnicity, family history of diabetes and obesity, the majority of the studies are of moderate quality.

3.1. Serum uric acid

Serum uric acid, a common component of urine generated by the metabolic breakdown of purines, have been associated with insulin resistance and type 2 diabetes [8]. High serum uric acid level in an individual leads to: 1) nitric-oxide mediated vasoconstriction (contraction of blood vessels) leading to impaired glucose uptake in the muscles [9], 2) increase in oxidative stress [10] and 3) increase in inflammation leading to a decrease in adiponectin [11,12]. Consequently, the blood glucose level increases leading to dysfunctional and eventually dead beta-cells [13]. As a result, the individual develops type 2 diabetes. Table 1 shows the characteristics and findings of the work in the literature studying the association between high serum uric acid level and type 2 diabetes.

Perry et al. [14] found that an individual having a uric acid level of more than 411 μmol/l is at 1.5 times more risk of developing type 2 diabetes compared to an individual having uric acid level less than 302 μmol/l. Niskanen et al. [15] also confirmed that change in uric acid levels is associated with a 2 times increase in the risk of incidence type 2 diabetes. Dehghan et al. [16] in their study showed that individuals having uric acid level >370 μmol/l are at high risk of incidence type 2 diabetes (HR 1.68, 95% CI 1.22–2.30) compared to those having uric acid level ≤267 μmol/l.
The association between high serum uric acid level and diabetes is independent of other risk factors such as obesity, age, family history of diabetes, hypertension, and dyslipidemia, and type 2 diabetes [20]. Chou et al. show that uric acid has a significant association with type 2 diabetes in old and obese individuals [21]. Another study by Meisinger et al. [22] shows that high-level uric acid is associated with incidence of type 2 diabetes in women only with HR 2.5 per 1 mmol/L increase. Carnethon et al. [23] found that the risk of incidence type 2 diabetes increases (OR 1.3, (1.2–1.4)) with every 1.4 mg/dl increase in uric acid level. However, this is in combination with an increase in waist/hip ratio, smoking and obesity. Chien et al. [24] stated that individuals with a uric acid level of 0.486 mmol/L and having metabolic syndrome have a 3.3 times more risk of incidence type 2 diabetes compared to those with a uric acid level of 0.211 mmol/L and not having metabolic syndrome. Nan et al. [25] examined the impact of ethnicity and gender on the association between uric acid and incidence of type 2 diabetes. The authors found that the high serum uric acid is an independent risk factor for type 2 diabetes in Mauritian Indian men compared to Creole men, and there is a no-to-weak association in women of both ethnicity. Similarly, Choi et al. [26] studied the association between uric acid and type 2 diabetes in men having cardiovascular risk profile. The authors concluded that men with cardiovascular profile having high uric acid level are twice likely to develop type 2 diabetes. The authors also stated that this association between uric acid and diabetes is independent of other risk factors such as obesity, age, family history of diabetes, hypertension, and metabolic syndrome. Kramer et al. [27] analyzed the impact of age and impaired fasting glucose (IFG) on the association and found that high uric acid level can independently predict incidence of type 2 diabetes (OR 1.65, 95% CI 1.25–2.18) in older adults having IFG. Lv et al. [28] found that high serum uric acid level is associated to type 2 diabetes in middle-aged or older people (RR 1.56, 95% CI 1.39–1.76).

In summary, the association between high-level serum uric acid remains obscure. It is debatable whether serum uric acid is an independent risk factor for type 2 diabetes or it only emphasizes the association between other independent risk factors and type 2 diabetes. Some studies reported a positive association between high serum uric acid level and incidence of type 2 diabetes [14–16,19,24], whereas others [25,29] reported no association. On the contrary, some studies reported an inverse association between uric acid and diabetes [30–32]. Furthermore, some studies argue that there is a reverse association, i.e., diabetes leads to high uric acid levels [33,34].

### 3.2. Sleep quantity/quality

The quality and quantity of sleep are affected by several cultural, social, behavioral, psychological, and environmental factors. The working professionals often experience fatigue, tiredness and daytime napping due to irregular working hours and shifts. Evidence shows that the current average sleep of an individual, i.e., 6.8 h/night, is 1.5 h less than that a century ago [45]. The cause of sleep loss is multi-factorial. For instance 45% of adults report that they sleep fewer hours to get more work done, 43% reported that they watch television or use the Internet, and 22% reported to be suffering from insomnia. The unusual, disturbed and reduced sleep is associated with glucose intolerance [46].

An individual suffering from sleep disorder, known as obstructive sleep apnea (OSA), experiences: 1) deficiency in the amount of oxygen reaching the tissues by total/partial collapse of upper airways while sleeping (hypoxia) and 2) inflammation. Frequent Hypoxia triggers an increase in sympathetic activity [47]. Increased sympathetic activity and inflammation lead to insulin resistance condition [48,49] and eventually to type 2 diabetes. Table 2 shows the characteristics and findings of the work in the literature studying the association between sleep quantity/quality and type 2 diabetes.
### Table 1
Characteristics and findings of the studies examining the association between high level serum uric acid and type 2 diabetes.

| Work Year | Study Design | Sample Size (SM/W) | Age (Years) | Ethnicity | Follow-up Duration (Years) | Adjusted variables | Findings |
|-----------|--------------|--------------------|-------------|-----------|---------------------------|------------------|----------|
| 1995      | RS           | PCS                | 7577 (2.56%)| Britain   | 12.8                      | Age, BMI, history of heart disease, physical activity, alcohol intake, smoking status, high blood pressure, HDL cholesterol, and heart rate | Uric acid (μ mol/l)) | OR | 1.0 | 1.5 (0.9-2.5) |
| 1998      | RS           | PCS                | 481 (17.6%) | Chinese   | 3                         | Age, sex, BMI, WHR, history of hypertension, HDL cholesterol, fasting insulin, and triglycerides | Uric acid (μ mol/l)) | OR | 1.0 | 2.581 (1.083-6.149) |
| 2002      | MONICA [35]  | PCS                | 6166 (3.45%)| Germany   | Mean 7.6                  | Age and BMI       | Uric acid (μ mol/l)) increase by | OR | 2.05 (1.49-1.29) |
| 2003      | ARIC [36]    | PCS                | 8574 (9.90%)| Blacks and Whites (USA) | 11               | Age, sex, education, baseline insulin concentration, BMI and blood pressure | Uric acid (μ mol/l)) increase by | OR | 1.3 (1.2-1.4) |
| 2005      | RS           | PCS                | 60          | USA       | 1                         | Age, sex, BMI, baseline insulin concentration, and glomerular filtration rate | Uric acid (μ mol/l)) | OR | 5.47 (1.6-17.7) |
| 2006      | FDPS [37]    | –                  | 475 (21.68%)| Finland   | 3.2                       | Age, sex, and baseline fasting | Uric acid (μ mol/l)) | OR | 1.11 (0.82-1.49) |
| 2008      | CSCCS [38]   | PCS                | 2960 (20.37%)| Chinese   | Median 9                  | Age, sex, BMI, alcohol intake, exercise, marital status, educational level, occupation and family history of diabetes | Uric acid (μ mol/l)) | OR | 1.29 (0.96-11.73) |
| 2008      | Rotterdam [39]| PCS                | 4536 (10.18%)| Netherlands | 10.1                   | Age, sex, BMI, waist circumference, systolic and diastolic blood pressure, and HDL cholesterol | Uric acid (μ mol/l)) | OR | 1.63 (1.20-2.23) |
| 2008      | RS           | PCS                | 4259 (16.81%)| Indians and Creoles | 5                       | Ethnicity, serum creatinine, alcohol consumption, family history of diabetes and fasting serum insulin | Uric acid (μ mol/l)) | OR | 1.19 (1.07-1.34) |
| 2008      | MRFIT [40–42]| PCS                | 11351 (10.70%)| Blacks and Whites (USA) | 6                      | Smoking status, BMI, hypertension, physical activity, alcohol consumption, total energy intake, cereal fibre, intake of polyunsaturated, mono saturated and saturated fat, coffee intake, high fasting blood glucose, and low HDL cholesterol | Uric acid (μ mol/l)) | OR | 1.05 (0.95-1.16) |
| 2009      | RS           | PCS                | 556 (9.89%) | Brazil    | 13                        | Age, sex, BMI, diuretic use, and glomerular filtration rate | Uric acid (μ mol/l)) increase by | OR | 1.88 (1.52-2.32) |
| 2011      | NHANES III [43,44] | CSS             | 14144       | USA       | –                         | Age, sex, race, educational level, smoking, alcohol consumption, BMI, hypertension, and serum total cholesterol | Uric acid (μ mol/l)) | OR | 0.54 (0.36-0.80) |

RS-Random Sample, MONICA-Multinational MONItoring of trends and determinants in CArdiovascular disease, ARIC-Atherosclerosis Risk in Communities, FDPS-Finnish Diabetes Prevention Study, CSCCS-Chin Shan Community Cardiovascular study, MRFIT-Multiple Risk Factor Intervention Trial, NHANES-National Health and Nutrition Examination Survey, QFS-Quebec Family Study, M-Men, W-Women, PCS-Prospective Cohort Study, C3S-Cross-Sectional Study.
### Table 2
Characteristics and findings of the studies examining the association between sleep quantity/quality and type 2 diabetes.

| Work Year | Study Design | Sample Size (N=DM) | %M/W | Age (Years) | Ethnicity | Follow-up Duration (Years) | Adjusted Variables | Findings |
|-----------|--------------|--------------------|------|-------------|-----------|-----------------------------|-------------------|---------|
| [79] 2003 | NHS [80] PCS | 70026 (2.81%) | 0/100 | 40–65 | United States | 10 | Working hours, hypercholesterolemia, hypertension, smoking, snoring, exercise, alcohol, depression, postmenopausal hormone use, BMI, and family history of diabetes | Sleep (Hours) | ≤5 1.18 (0.96–1.44) 6 1.10 (0.97–1.25) 7 1.02 (0.91–1.16) 8 1.0 9 1.29 (1.05–1.59) |
| [56] 2004 | RS [81] PCS | 2265 (1.67%) | 100/0 | – | Japanese | 8 | Age, education, occupation, shift work, BMI, leisure time, physical activity, smoking, alcohol consumption and family history of diabetes | Sleep DIS (low frequency) | 1.0 2.98 (1.36–6.53) |
| [57] 2004 | MPP [82] PCS | 6599 (4.3%) | 100/0 | Mean 42.6 | Swedish and Caucasians | 15.2 | Age, lifestyle, family history of diabetes, social class, physical activity, BMI, smoking, and alcohol intake | Sleep DIS No | 1.0 1.52 (1.05–2.20) |
| [59] 2005 | MONICA [35] PCS | 8269 (2.27%) | 50.1/49.9 | 25–75 | Germany | 7.5 | Age, educational level, parental history of diabetes, smoking, alcohol consumption, hypertension, physical activity, history of angina pectoris, BMI, and dyslipidemia | Sleep DIS No | 1.0 1.10 (0.59–2.03) |
| [83] 2005 | SHHS [84] CSS | 1486 | 48.6/ 51.4 | 53–93 | United States | – | Age, sex, ethnicity, waist girth, and apnea-hypopnea index | Sleep (Hours) | ≤5 1.47 (1.03–2.09) 6 1.08 (0.80–1.47) 7 1.09 (0.83–1.43) 8 1.52 (1.06–2.17) 9 (W) 2.9 (0.6–15.0) |
| [52] 2005 | RS PCS | 1170 (7.52%) | 47/53 | 45–65 | Swedish | 12 | Age, marital status, living conditions, hypertension, obesity, smoking, alcohol use, snoring and depression | Sleep (Hours) | ≤5 1.71 (0.81–3.59) 6 1.95 (1.06–3.58) 7 1.40 (0.78–2.54) 8 3.03 (1.44–6.37) 9 ≥9 3.03 (1.44–6.37) |
| [50] 2005 | RS PCS | 1462 (8.62%) | 0/100 | 38–60 | Swedish | 32 | Age, subcutaneous skin-fold thickness, serum lipid values, blood pressure, resting heart rate, physical activity, education and socio-economic status | Sleep (Hours) | ≤5 1.71 (0.81–3.59) 6 1.95 (1.06–3.58) 7 1.40 (0.78–2.54) 8 3.03 (1.44–6.37) 9 ≥9 3.03 (1.44–6.37) |
| [85] 2006 | MMAS [86] PCS | 1139 (7.9%) | 100/0 | 40–70 | Blacks and Whites (USA) | 17 | Age, hypertension, smoking, self rated health status, waist circumference, education, testosterone, and cortisol | Sleep (Hours) | ≤5 1.71 (0.81–3.59) 6 1.95 (1.06–3.58) 7 1.40 (0.78–2.54) 8 3.03 (1.44–6.37) 9 ≥9 3.03 (1.44–6.37) |
| [87] 2007 | NHANES I [88] PCS | 8992 (4.78%) | 37.5/ 62.5 | 32–86 | Whites and Non-whites (USA) | 10 | Physical activity, depression, alcohol consumption, ethnicity, education, marital status, age, obesity and hypertension | Sleep (Hours) | ≤5 1.71 (0.81–3.59) 6 1.95 (1.06–3.58) 7 1.40 (0.78–2.54) 8 3.03 (1.44–6.37) 9 ≥9 3.03 (1.44–6.37) |

(continued on next page)
| Work Year | Study Design | Sample size (%DM) | %M/W | Age (Years) | Ethnicity | Follow-up duration (Years) | Adjusted variables | Findings |
|-----------|--------------|-------------------|------|-------------|-----------|---------------------------|-------------------|----------|
| 2007 QFS [90] | CSS | 740 | 43.65/ 56.35 | 21–64 | Europid race | 12 | Age, marital status, employment status, educational level, annual income, physical activity, alcohol intake, coffee intake, hypertension, heart disease and waist circumference | Sleep (Hours) | OR 5–6: 2.09 (1.34–2.98) 7–8: 1.0 9–10: 1.58 (1.13–2.31) |
| 2007 HIPOP-OHP [91] | PCS | 6509 (3.53%) | 78.4/21.6 | 32–86 | Japanese | 4.2 | Age, sex, BMI, history of smoking, history of hypertension, history of high cholesterol, history of diabetes and physical activity | DIS No | HR 1.42 (1.05–1.91) |
| 2008 FIN-D2D [93] | CSS | 2770 | 48.2/51.8 | 45–74 | Finland | 1 | Age, BMI, medication for sleep, antidepressants, smoking, sleep apnea probability, and physical activity | Sleep (Hours) | RR 5–6: 2.42 (1.49–3.33) 7–8: 1.0 9–10: 2.31 (1.41–3.15) |
| 2009 QFS [90] | PCS | 274 | 42.7/ 57.3 | 21–64 | Europid race | 6 | Age, smoking habits, employment status, annual household income, shift working history, resting metabolic rate, coffee intake, waist circumference and physical activity | Sleep (Hours) | OR 5–6: 2.36 (1.11–5.99) 7–8: 2.15 (0.50–9.30) 9–10: 0.63 (0.14–2.90) |
| 2009 IRAS [95] | – | 900 (16.22%) | 43.5/56.7 | 40–69 | Non-Hispanic Whites, Hispanics, and African-Americans | 5 | Age, sex, glucose tolerance, hypertension, family history of diabetes, smoking, educational level, BMI, insulin sensitivity, and acute insulin response | Sleep (Hours) | OR 5–6: 2.36 (1.11–5.99) 7–8: 2.15 (0.50–9.30) 9–10: 0.63 (0.14–2.90) |
| 2009 RS | CSS | 1741 | 42.6/ 57.4 | ≥20 | Pennsylvania | - | Age, race, sex, BMI, smoking, alcohol consumption, depression and sleep disordered breathing | Sleep (Hours) | RR 5–6: 2.95 (1.2–7.0) 5–6: 2.07 (0.68–6.4) |
| 2009 RS | – | 515 | 33/67 | 40–64 | Finland | 7 | Age, sex, BMI, study center, smoking, alcohol intake, hypertension medication, leisure time physical activity, and 1 year change in body weight | Sleep (Hours) | OR 5–6: 2.95 (1.2–7.0) 5–6: 2.07 (0.68–6.4) |
| 2010 NIH-AARP [99] | PCS | 174344 | 56.8/43.2 | 50–71 | Whites and non-whites (USA) | 8 | Age, race, sex, educational level, marital status, smoking, coffee intake, alcohol intake, calorie intake, BMI, and physical activity | Day napping (Hours) | OR 0: 1.0 1: 1.23 (1.18–1.29) 2: 1.55 (1.45–1.66) |
| 2011 RS | CSS | 3470 (5.2%) | 61.8/ 38.2 | ≥25 | Taiwan | - | BMI, WHR, family history of diabetes, family history of hypertension, smoking, alcohol consumption and coffee intake | Sleep (Hours) | OR 5–6: 1.55 (1.07–2.24) 7–8: 1.0 9–10: 2.83 (1.19–6.73) |
| 2012 EPIC-Potsdam [101] | PCS | 23620 (3.6%) | 38.63/ 61.37 | 35–65 | Germany | 7.8 | Age, sex, sleeping disorders, alcohol intake, smoking, walking, cycling, sports, employment status, education, BMI, WHR, hypertension, caffeinated beverages, life satisfaction, health satisfaction, and intake of antidepressants | Sleep (Hours) | OR 6–7: 1.06 (0.80–1.40) 7–8: 0.94 (0.78–1.14) 8–9: 1.0 9–10: 0.92 (0.77–1.10) 9–10: 1.05 (0.82–1.33) |
| Work Year | Study Design | Sample size (%DM) | Sample age (%M/W) | Ethnicity (years) | Follow-up duration (years) | Adjusted variables | Findings |
|-----------|--------------|-------------------|-------------------|------------------|---------------------------|--------------------|----------|
| [102] 2012 RS PCS 3570 | 35–55 Japan | 4 | Age, sex, fasting plasma glucose level, education, working hours, shift work, rate of sedentary work, occupational stress, smoking, alcohol intake and physical exercise | Sleep (Hours) | 5.37 (1.38–20.91) 1.38 (0.50–3.79) 1.57 (0.64–3.83) |
| [53] 2012 NHIS [103] CSS 29818 | 18–85 Blacks and whites (USA) | 10 | Age, sex, income, hypertension, heart disease, depression and obesity | Sleep (Hours) | 1.0 1.0 1.0 1.0 1.0 |
| [104] 2013 IHHP [105] CSS 12514 | ≥19 – – | - | Age, sex, BMI, and waist circumference | Sleep (Hours) | 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 |
| [106] 2013 MC [107] PCS 47093 (1.85%) 74.4/ 25.6 Mean 34.9 USA | 6 | Age, sex, BMI, education and race | Sleep (Hours) | 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 |
| [54] 2013 NHIS [103] CSS 130943 (10.12%) 99.75/ 0.25 Mean 50.6 Blacks and whites (USA) | 7 | Age, sex, household income, poverty status, education, occupation, employment status, alcohol consumption, smoking, leisure time physical activity, marital status, heart disease, hypertension, and BMI | Sleep (Hours) | 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 |
| [108] 2013 45 and up [109] PCS 156902 | 50–82 Australia | - | Age, sex, education, marital status, residential remoteness, alcohol consumption, smoking status, health insurance status, income, BMI, physical activity and baseline health | Sleep (Hours) | 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 |

DIS-Difficulty Initiating Sleep, DMS-Difficulty Maintaining Sleep, EPIC-European Prospective Investigation into Cancer and Nutrition, FIN D2D-Finnish type 2 Diabetes, HIPOP-OHP-High risk and Population Strategy for Occupational Health Promotion, IHHP-Isfahan Healthy Heart Program, IRAS-Insulin Resistance Atherosclerosis Study, M-Men, MC-Millennium Cohort, MMAS-Massachusetts Male Aging Study, MONICA-Multinational MONitoring of trends and determinants in Cardiovascular disease, MPP-Malmo Preventive Project, NHANES-National Health and Nutrition Examination Survey, NHIS-National Health Interview Survey, NHS-Nurse Health Study, NHW-Non Hispanic Whites, NIH AARP-National Institutes of Health American Association of Retired Persons Diet and Health Study, QFS-Quebec Family Study, RS-Random Sample, SHHS-Sleep Heart Health Study, W-Women, PCS-Prospective Cohort Study, CSS-Cross-Sectional Study.
Table 3
Characteristics and findings of the studies examining the association between smoking and type 2 diabetes.

| Work Year | Study | Design | Sample Size (%DM) | %M/W | Age (Years) | Ethnicity | Follow-up Duration (Years) | Adjusted Variables | Findings |
|-----------|-------|--------|-------------------|------|-------------|-----------|----------------------------|--------------------|----------|
| 1989      | ZS    | PCS    | 841 (6.9%)        | 100/0| 40-59       | Dutch     | 25                        | Age, subscapular skin-fold, resting heart rate, cigarette use, alcohol intake and energy intake | Cigarettes/day 0 20 | HR 1.0 3.3 (1.4-7.9) |
| 1993      | NHS [80] | PCS | 114247 (2.04%)   | 0/100| 30-55       | USA       | 12                        | Age, BMI, family history of diabetes, menopause, postmenopausal hormone use, oral contraceptive use, alcohol consumption, and physical activity | Cigarettes/day 0 1-14 15-24 >25 Ex-smoker | RR 1.0 0.90 (0.68-1.19) 1.20 (0.96-1.50) 1.41 (1.19-1.87) 1.17 (1.02-1.35) |
| 1995      | HPFS  | PCS    | 41810 (1.22%)    | 100/0| 40-75       | USA       | 62                        | Age, BMI, family history of diabetes, alcohol consumption and physical activity | Cigarettes/day 0 1-14 15-24 >25 Ex-smoker | RR 1.0 1.37 (0.77-2.43) 2.38 (1.57-3.59) 1.94 (1.25-3.03) 1.29 (1.05-1.57) |
| 1997      | RS    | PCS    | 2312 (1.77%)     | 100/0| -           | Japanese  | 8                         | -                                | Cigarettes/day 0 1-15 16-25 >26 | HR 1.0 1.33 (0.40-4.39) 3.59 (1.32-9.76) 2.68 (0.88-8.05) |
| 1997      | SOF [113] | CSS | 9435 (7%)        | 0/100| ≥65         | Non-black (USA) | -                          | Age, resting heart rate, BMI, education level, alcohol intake, energy expenditure, WHR, and postmenopausal hormone use | Cigarettes/day 0 <10 ≥10 Ex-smoker | OR 1.0 0.55 (0.30-0.99) 1.21 (0.87-1.71) 0.99 (0.82-1.19) |
| 1999      | OHS   | PCS    | 6250 (7.2%)      | 100/0| 25-60       | Japan     | 16                        | Age, BMI, alcohol consumption, physical activity, fasting plasma glucose, total cholesterol, and triglycerides | Cigarettes/day 0 1-20 21-30 ≥30 | RR 1.0 1.40 (1.05-1.86) 1.71 (1.02-1.93) 173 (1.20-2.48) |
| 2000      | PHS [115] | PCS | 21068 (3.65%)   | 100/0| 40-84       | USA       | 12.10                      | Age, BMI, physical activity, history of hypertension, history of high cholesterol, parental history of myocardial infarction, and alcohol consumption | Cigarettes/day 0 <20 ≥20 Ex-smoker | RR 1.0 1.5 (1.0-2.2) 1.7 (1.3-2.3) 1.1 (1.0-1.4) |
| 2001      | RS    | CSS    | 3718             | 19.2-80.0 | 12-88     | Chinese  | -                         | Age, BMI, alcohol consumption, and family history of diabetes | Smoking No Yes | OR 1.0 1.705 (1.106-2.630) |
| 2001      | BRHS [117] | PCS | 7124 (4.07%)   | 100/0| 40-59       | UK        | 16.8                       | Age, BMI, physical activity, alcohol intake, social class, heart disease and antihypertensive treatment | Smoking No Yes Pipe/cigar Ex-smoker (15 yrs.) Ex-smoker (10 yrs.) | OR 1.0 1.61 (1.05-2.46) 2.15 (1.24-3.70) 1.45 (0.95-2.21) 2.03 (1.22-3.37) |
| 2001      | CPS-I [118] | PCS | 709827 (3.6%) | 38.8/61.2 | ≥30       | Whites and Blacks (USA) | 13                        | Age, BMI, alcohol consumption, race, amount of exercise, education level, and intakes of fats and carbohydrates | Cigarettes/day 0 <20 (M) ≥20 (W) 20-39 (M) 20-39 (W) ≥40 (M) ≥40 (W) Ex-smoker (M) Ex-smoker (W) | OR 1.0 1.05 (0.98-1.12) 0.98 (0.93-1.03) 1.19 (1.13-1.26) 1.21 (1.14-1.29) 1.45 (1.34-1.57) 1.74 (1.49-2.03) 1.07 (1.02-1.13) 1.07 (0.99-1.15) |
| 2001      | NHS [80] | PCS    | 84941 (3.9%)     | 0/100| 30-55       | USA       | 16                        | Age, family history of diabetes, menopausal status, postmenopausal hormone use, fat intake, and physical activity | Cigarettes/day 0 1-14 ≥15 | OR 1.0 1.14 (0.85-1.54) 1.40 (1.14-1.71) |
| 2002      | NCDS [121] | -    | 15396            | M/W   | -           | UK        | 33                        | Maternal smoking during pregnancy, sex, mother’s age at the time of giving birth, age at which mother left school, family social class at birth, birth weight, own smoking at the age of 16, and BMI at the week of birth | Cigarettes/week Self 0 <1 1-9 10-19 20-29 ≥30 Mother Non-smoker Medium-smoker Medium to heavy-smoker Heavy-smoker | OR 1.0 2.07 (0.25-17.19) 1.92 (0.52-7.10) 2.48 (0.52-11.97) 1.61 (0.20-12.96) 3.62 (1.42-9.24) 1.01 (0.23-4.53) 3.53 (0.88-14.38) 4.02 (1.14-14.14) |
| Work Year Study | Design | Sample Size (%DM) | %M/W | Age (Years) | Ethnicity Follow-up Duration (Years) | Adjusted Variables | Findings |
|----------------|--------|-------------------|------|-------------|--------------------------------------|-------------------|----------|
| 2004 RIH CSS   | 27777  | 45/55             | 20-69| France      | Age, BMI, WHR, and alcohol consumption | Smoked No Yes | OR 1.49 (1.13-1.96) 0.89 (0.54-1.39) 1.31 (1.01-1.70) 1.46 (0.92-2.22) |
| 2004 NTHS [123]| 38805  | 46.9/53.1         | ≥20  | Norwegian   | Age, BMI, and sex                    | Cigarettes/day | RR 1.64 (1.12-2.39) |
| 2005 IRAS [95] | 906 (25%)| 43.3/56.7        | 40-69| Non-Hispanic Whites, Hispanics, and African-Americans | Age, sex, ethnicity, BMI, WHR, glucose tolerance status, HDL cholesterol level, triglyceride level and hypertension | Smoking No Ex-smoker | Current-smoker OR 1.31 (0.82-2.09) 2.66 (1.49-4.77) |
| 2006 KMIC [124]| 27635  | 100/0             | 35-44| Korea       | Age, baseline fasting serum, glucose, weight change, baseline BMI, family history of diabetes, alcohol consumption, and physical activity | Cigarettes/day | No <10 10-19 ≥20 Ex-smoker (≥8 yrs.) | Ex-smoker (7-7.9 yrs.) Ex-smoker (5-6.9 yrs.) OR 1.23 (1.86-1.77) 1.60 (1.28-2.00) 1.75 (1.35-2.27) 0.95 (0.72-1.25) 2.13 (1.51-3.00) |
| 2009 RS PCS    | -      | M/W               | 40-69| Ansung and Ansan Korean | Age, family history of diabetes, rural or urban area, waist, body fat, exercise, alcohol consumption, income, education, WBC, HDL cholesterol, triglyceride, systolic BP, HOMA IR, and HOMA beta | Smoking No Ex-smoker | Current-smoker OR 1.06 (1.35-3.16) 2.41 (1.48-3.93) 1.60 (1.07-2.39) |
| 2010 ARIC [36] | 10892 (11.51%) | 43.3/56.7 | 45-64| Whites and Non-whites (USA) | Race, sex, level of education, BMI, waist circumference, baseline age, physical activity, HDL cholesterol, triglycerides, and systolic BP | Smoking No Ex-smoker (9 yrs.) Ex-smoker (6-9 yrs.) Ex-smoker (3-6 yrs.) Ex-smoker (<3 yrs.) | Current-smoker HR 1.16 (0.99-1.36) 1.21 (0.89-1.65) 1.54 (1.10-2.14) 1.80 (1.44-2.25) 1.26 (1.08-1.46) |
| 2010 KORA S4/F4 [125] | 885 | 50.4/49.6 | 55-74| Germany | Age, sex, parental diabetes, socioeconomic status, alcohol intake, physical activity, intake of meat and sausage, intake of salad and vegetables, intake of whole grain bread, coffee consumption, waist circumference, blood pressure, hypertriglyceridemia, HDL cholesterol, log insulin and log adiponectin | Smoking No (passive+active) Passive Passive+prediabetes Active Active+prediabetes | OR 1.0 2.5 (1.15-5.6) 4.4 (1.5-13.4) 2.8 (1.3-6.1) 7.8 (2.4-25.7) |
| 2011 KCP S [126] | 1236443 | 63.7/36.3 | 30-95| Korea | Age, alcohol drinking, BMI, and physical exercise | Cigarettes/day | No Low passive High passive 1-14 15-24 ≥25 Ex-smoker | Ex-smoker (W) Ex-smoker (M) Ex-smoker (<5 yrs.) OR 1.30 (1.03-1.68) 1.37 (1.05-1.80) 1.82 (1.40-2.34) 2.43 (1.84-3.24) 1.68 (1.07-2.63) 2.84 (1.53-5.29) |
| 2011 NHS [80] | 100526 (5.36%) | 0/100 | 41-55| USA | Age, BMI, physical activity, husband’s education, family history of diabetes, total energy intake, alcohol intake, caffeine, total trans fat, total saturated fat, calcium, magnesium and vitamin D | Cigarettes/day | No Low passive Ex-smoker (W) | Ex-smoker (M) Ex-smoker (<5 yrs.) (W) OR 1.43 (1.16-1.76) 1.42 (1.03-1.94) 1.68 (1.07-2.63) 2.84 (1.53-5.29) |
| 2012 JPHC [127] | 59834 | 43.24/56.76 | Mean 55-57.9| Japanese | Age, BMI, history of hypertension, alcohol intake, family history of diabetes, weight change, study area, and leisure time physical activity | Smoking No Current-smoker (M) Current-smoker (W) Ex-smoker (<5 yrs.) (M) Ex-smoker (<5 yrs.) (W) | OR 1.41 (1.13-1.78) 1.42 (1.03-1.94) 1.68 (1.07-2.63) 2.84 (1.53-5.29) |

(continued on next page)
Table 3 (continued)

| Findings | Smoking No | Ex-smoker (<9 yrs) | Ex-smoker (6-9 yrs) | Ex-smoker (>9 yrs) | No Current-smoker | Current-smoker | Smoking No Ex-smoker (<3 yrs) | Ex-smoker (<3 yrs) | No Ex-smoker (>3 yrs) | Current-smoker | Ex-smoker (<3 yrs) | No Ex-smoker (>3 yrs) |
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Table 4
Characteristics and findings of the studies examining the association between depression and type 2 diabetes.

| Work | Year | Study | Design | Sample size (%DM) | %M/W | Age (Years) | Ethnicity | Follow-up Duration (Years) | Adjusted variables | Findings |
|------|------|-------|--------|-------------------|------|-------------|-----------|-----------------------------|-------------------|----------|
| [137] | 1991 | RS    | PCS    | 2380 (1.72%)      | 100/0| 18          | Japanese | 8                           | Age              | Depression (SDS score) HR 1.0 1.07 (0.53–2.13) 2.32 (1.06–5.08) |
| [155] | 1996 | ECAPS |        | 1715 (5.2%)       | 37.8/62.2 | 18   | USA      | 13                     | Depression No Yes | OR 2.23 (0.90–5.55) |
| [157] | 2003 | NHANES I | PCS | 6190 | 45.7/54.3 | 25–74 | Whites and Non-whites (USA) | 15.6 | Age, sex and race, Depression No Yes | RR 1.0 1.24 (0.91–1.70) 2.52 (1.73–3.67) |
| [158] | 2004 | ARIC  | PCS    | 11615 | 44.85/55.15 | 48–67 | Whites and Non-whites (USA) | 6 | Age, sex, race, study site, fasting insulin, fasting glucose, HDL cholesterol, BMI, WHR, systolic BP, physical activity, total calorie intake, smoking status, and education | Depression No Low MILD Major | OR 1.12 (0.90–1.39) 1.03 (0.81–1.31) 1.31 (1.04–1.64) |
| [136] | 2004 | SWAN  | PCS    | 2662 (3.64%)      | 0/100 | 42–52       | Caucasian, African-American, Hispanic, Japanese-American and Chinese-American Norwegians | 3 | Age, study site, race, education, and medication use | Depressed African-Americans are 2.56 times more likely to have diabetes. |
| [160] | 2007 | NTHS  | PCS    | 37291 | 47.2/52.8   | 29    | Norwegian | 10 | Age, sex, education, smoking, physical activity, BMI, WHR, waist circumference, and marital status | Depression No Yes | OR 1.40 (1.16–1.69) |
| [138] | 2007 | CHS   | PCS    | 4681 | 40.8/59.2   | 65    | USA      | 8 | Age, race, sex, educational level, marital status, physical activity, smoking, alcohol consumption, BMI, and reactive protein level | Depression (CES-D score) | OR 1.57 (1.07–2.29) |
| [139] | 2014 | RBHCDS| -      | 971 | 43/57 | 50 | California | 8 | Age, sex, BMI and exercise | Depression (BDI score) | OR 2.50 (1.29–4.87) |

RS-Random Sample, SDS-Self rating Depression Scale, ECAPS-Epidemiologic Catchment Area Program Survey, NHANES-National Health and Nutrition Examination Survey, ARIC-Atherosclerosis Risk in Communities, RNH-RegistratieNet Huisarts Praktijken, SWAN-Study of Women’s Health Across the Nation, NTHS-Nord Trondelag Health Study, CHS-Cardiovascular Health Study, CESD-Center for Epidemiological Studies Depression Scale, RBHCDS-Rancho Bernardo Heart and Chronic Disease Study, BDI-Beck Depression Inventory, M-Men, W-Women, PCS-Prospective Cohort Study, CSS-Cross-Sectional Study.
decreases with an increase in cessation duration. The association between smoking cessation and the incidence of type 2 diabetes is more in women than men [78].

In summary, both active and passive smoking are strongly associated with the incidence of type 2 diabetes. The association is more in men compared to women. Moreover, the association remains significant in ex-smokers during first the 5–10 years of smoking. After 10 years of smoking cessation, the risk of incidence type 2 diabetes is the same as that in a non-smoker. Women ex-smokers are at a higher risk of developing diabetes compared to men ex-smokers.

3.4. Depression

Depression is a mood disorder that negatively affects the way a person feels, thinks and acts [130]. It can be due to a family history of depression, early childhood trauma, brain structure, medical conditions, drug use or surrounding environment. Depression is associated with multiple health conditions including diabetes [131]. It elevates the sympathetic nervous system activities and hypothalamic–pituitary–adrenal axis activities [132]. Elevated sympathetic nervous system activities lead to an increase in catecholamines and inflammation, and eventually causing insulin resistance [133]. On the other hand, elevated adrenal axis activities lead to an increase in cortisol and eventually blood sugar level [134]. Both insulin resistance and increased blood sugar levels develop type 2 diabetes. The characteristics and findings of the work in the literature examining the association between depression and the incidence of type 2 diabetes are presented in Table 4.

The results show that depression is highly associated with the incidence of type 2 diabetes. In the context of gender, depressed men are at higher risk of incidence type 2 diabetes, whereas depression in women is not associated with type 2 diabetes [135]. Moreover, compared to Caucasian, Hispanic, Japanese-American and Chinese-American, depressed African-Americans are at 2.56 times higher risk of incidence type 2 diabetes [136]. Based on self rating depression scale (SDS) score, an individual having a score of 48–80 is at higher risk of developing diabetes compared to an individual having a score of 20–39 [137]. Similarly, an individual having a score ≥ 11 using center for epidemiological studies depression scale (CES-D) or a score ≥ 8 using beck depression inventory (BDI) is at higher risk of incidence type 2 diabetes [138,139].

In summary, depression is associated with type 2 diabetes. However, the association is different in men and women. Moreover, the study by Yu et al. [140] show that depression itself is not a risk factor for diabetes, rather the activities related to depression such as physical inactivity, poor diet, and obesity lead to diabetes. In addition, the medical drugs used to treat depression also have an association with the incidence of type 2 diabetes. Consequently, similar to high-level serum uric acid, depression is not an independent risk factor but it emphasizes the impact of other independent risk factors such as gender, ethnicity, physical inactivity, and obesity.

3.5. Cardiovascular disease

Increased heart rate and cardiovascular disease can elevate the blood pressure in the arteries. As a result, the body’s glucose uptake decreases leading to insulin resistance condition. Consequently, a person suffering from heart disease is at a higher risk of developing type 2 diabetes. However, this association is still obscure. Few studies argue that a history of cardiovascular disease leads to the incidence of type 2 diabetes [141], while others claim that type 2 diabetes increases the risk of cardiovascular disease [142–144]. Yeung et al. [141] examined the association between family history of coronary heart disease (CHD) and type 2 diabetes (Table 5). The authors concluded that a high family CHD score is associated to the incidence of type 2 diabetes in individuals who have a positive history of family diabetes. For the individuals having a negative family history of diabetes, this association was nonsignificant. In summary, it is debatable whether cardiovascular disease is a risk factor for type 2 diabetes or not.

3.6. Dyslipidemia

Dyslipidemia refers to an abnormal level of lipids, such as triglycerides and cholesterol. It is characterized by high triglyceride levels, increased low-density lipoproteins (LDL) levels and decreased high-density lipoproteins (HDL) levels [145]. Elevated LDL and lowered HDL levels lead to beta-cell dysfunction inhibiting insulin secretion and consequently type 2 diabetes [146,147]. Table 6 shows the characteristics and findings of the work in the literature studying the association between dyslipidemia and type 2 diabetes.

Dietary fats, that raise the total cholesterol and LDL levels, are considered significant in the development of type 2 diabetes [148]. Substituting saturated fatty acid with polyunsaturated fatty acid and animal fat with vegetable fat can help lower blood cholesterol and eventually type 2 diabetes. This is because both polyunsaturated fatty acid and vegetable fat are inversely related to the risk of incidence type 2 diabetes with RR 0.84 (95% CI 0.71–0.98) and RR 0.78 (95% CI 0.67–0.91) respectively for the highest quintile of intake [148]. Tajima et al. [149] also confirmed the association between high cholesterol diet intake (>273 mg/day) and type 2 diabetes (RR 1.25, 95% CI 1.16–1.36) compared to low cholesterol intake (<185 mg/day).

In order to reduce elevated LDL level, LDL lowering therapy and drugs are suggested. However, these drugs and therapy are found to be associated with a higher risk of type 2 diabetes [150]. Individuals having familial hypercholesterolemia, a genetic disorder that results in high LDL levels, are less likely to have type 2 diabetes.

| Work Year | Study Design | Sample size (%DM) | Age (Years) | Ethnicity | Follow-up duration (Years) | Adjusted variables | Findings |
|-----------|--------------|-------------------|-------------|-----------|---------------------------|-------------------|----------|
| [141] 2007 | ARIC PCS | 11297 (11.5%) | M/W 45–64 Blacks and Whites (USA) | 9 | Age, sex, race, smoking, alcohol consumption, educational level, leisure index, BMI, WHR, systolic and diastolic pressure, triglycerides, HDL, glucose, hypertension, WBC count, and fibrinogen | CHD risk score | HR |

ARIC-Atherosclerosis Risk in Communities, CDH-Coronary Heart Disease, M-Men, W-Women, PCS-Prospective Cohort Study.
compared to individuals having high LDL levels due to dietary patterns [151]. Zhang et al. [152] in their analysis found that the ratio of non-HDL and LDL levels is an independent risk factor for incidence diabetes. They show that an individual having a ratio of 3.1 is at 40% increased risk of incidence diabetes (OR 1.4, 95% CI 1.1–1.8) compared to an individual having a ratio of 1.4. Elevated non-HDL and lowered HDL levels are significantly associated with incidence diabetes [153].

On the contrary to studies confirming the association between low-HDL levels and the incidence of type 2 diabetes, Haase et al. [154] in their study concluded that a life-long reduction in HDL levels are not associated with an increased risk of type 2 diabetes. They found that the association is most likely reverse causation, i.e., type 2 diabetes leads to low HDL levels.

### 3.7. Hypertension

Hypertension, also known as high blood pressure, is a medical condition in which the blood pressure in the arteries is persistently elevated. Hypertension elevates the sympathetic nervous system activity leading to a decrease in the body’s glucose uptake. This causes the condition of insulin resistance and eventually type 2 diabetes. Hypertension elevates sympathetic nervous system activities leading to impaired vasodilation of skeletal muscles. Consequently, muscle glucose uptake decreases with the eventual impairment of insulin sensitivity. This association is dependent on obesity and hypertension medications. Hypertension medications are considered to increase the risk of diabetes depending on the type of medication [167]. For instance, hypertensive individuals taking thiazide diuretics and angiotensin-converting-enzyme medications are at lower risk of diabetes compared to the hypertensive individuals not taking any medication. However, those taking beta-blockers or calcium channel blockers are at 28% higher risk of incidence type 2 diabetes (HR 1.28, 95% CI 1.04–1.57) [167]. The association between hypertension and the incidence of type 2 diabetes is significant in women as well [168]. Women having hypertension are at 2 times increased risk of developing diabetes (HR 2.03, 95% CI 1.77–2.32) compared to women having normal blood pressure (<120/75 mmHg) [168]. The association is more in overweight and obese women. Irrespective of gender, prehypertension (HR 2.17, 95% CI 0.9–1.5) and hypertension (HR 2.93, 95% CI 1.59–5.41) are associated with increased risk of incidence type 2 diabetes [169]. In the context of obesity, whites individuals having hypertension are at higher risk of developing diabetes (HR 1.25, 95% CI 1.03–1.53), but no such association is seen in African American hypertensive individuals (HR 0.92, 95% CI 0.70–1.22) [170].

In summary, hypertension is associated with the development of type 2 diabetes in both men and women. However, the association is ethnicity-dependent. The selection of hypertension medications should be made properly as the medication impacts the medication of obesity and hypertension. For instance, hypertensive individuals taking thiazide diuretics and angiotensin-converting-enzyme medications are at lower risk of diabetes compared to the hypertensive individuals not taking any medication. However, those taking beta-blockers or calcium channel blockers are at 28% higher risk of incidence type 2 diabetes (HR 1.28, 95% CI 1.04–1.57) [167].

### 3.8. Aging

The number of elderly people (above 60 years) is increasing worldwide. The 900 million global elderly population in 2015 is expected to rise to 2 billion by 2050 [171]. Aging increases the risk of metabolic syndrome and chronic diseases including type 2 diabetes. Aging increases chronic inflammation in an elderly individual leading to insulin resistance [172]. In addition, lipid metabolism disorder due to aging increases the accumulation of body fat leading to elevated free fatty acids concentration in the body.

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Table 6 Characteristics and findings of the studies examining the association between dyslipidemia and type 2 diabetes.

| Work Year | Study | Design | Sample Size(’n) | %M/W | Age (Years) | Ethnicity | Follow-Up Duration (Years) | Adjusted Variables | Findings |
|-----------|-------|--------|----------------|-------|-------------|-----------|--------------------------|--------------------|---------|
| [148] 2001 LWHS [162] | PCS | 35988 | 0/100 | 55–69 | USA | 11 | | Age, total energy, WHR, BMI, physical activity, cigarette smoking, alcohol consumption, education, marital status, occupational status, area and hormone replacement therapy | |
| [154] 2015 CCHS [163] and CGPS [164] | PCS | 47627 | | | | | | Age, sex, BMI, hypertension, smoking, alcohol intake, physical inactivity, postmenopausal status and hormonal replacement therapy, lipid lowering therapy, and educational level | |
| [152] 2018 REACTION [165] | PCS | 4882 (14.42%) | 36.5/ 63.5 | | Chinese | 3 | | Non-HDL/HDL(m mol/L) | OR |

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| Work Year | Study Design | Sample size (%DM) | %M/W | Age (Years) | Ethnicity | Follow-up duration (Years) | Adjusted variables                                                                 | Findings                                                                 |
|-----------|--------------|-------------------|------|-------------|-----------|---------------------------|------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| 1999      | RS           | PCS 7594 (7.9%)   | 100/0| 30–65       | Japanese  | 16                        | Age, BMI, alcohol consumption, smoking habits, leisure time physical activity, and parental history of diabetes | Blood pressure in mmHg: 130/85, 139/89, RR 1.76 (1.43–2.16) |
| 2000      | ARIC [36]    | PCS 12550         | 44.39/55.61 | 45–64 | Blacks and Whites (USA) | 3 and 6 | Age, sex, race, BMI, WHR, educational level, smoking status, alcohol consumption, physical activity, systolic and diastolic blood pressure, fasting serum insulin concentration, history of hypercholesterolemia, cardiovascular diseases, pulmonary diseases, renal insufficiency, and family history of diabetes | Hypertension medication: None, RR 1.0, ACE inhibitor, RR 0.98 (0.72–1.34) |
| 2007      | WHS [185]    | PCS 38172 (4.38%) | 0/100 | 45          | USA       | 10.2                      | Blood pressure in mmHg: 120–129/75–84, 130–139/85–89, RR 1.76 (1.43–2.16) |
| 2011      | ARIC [36], CARDIA [186], and FHS [187] | PCS 10893 (9.45%) | 43/57 | 35–54       | African-American and Whites (USA) | Median 8.9 | Age, BMI, fasting glucose, DL cholesterol and triglycerids | Blood pressure in mmHg: 120–139/80–89, RR 2.03 (1.77–2.32) |
| 2012      | GPPS [189]   | PCS 7494 (12.02%) | 100/0 | 47–55       | Swedish   | 35                        | Blood pressure in mmHg: 120–139/80–89, RR 2.03 (1.77–2.32) |
| 2015      | KGES [190]   | PCS 7150 (14.7%)  | 47.46/52.54 | 40–69   | Korean    | 8                         | Blood pressure in mmHg: 120–139/80–89, RR 2.03 (1.77–2.32) |

RS-Random Sample, ARIC-Atherosclerosis Risk in Communities, WHS, Women’s Health Study, CARDIA-Coronary Artery Risk Development in Young Adults, FHS-Framingham Heart Study, GPPS-Gothenburg Primary Prevention Study, KGES-Korean Genome and Epidemiology Study, M-Men, W-Women, PCS-Prospective Cohort Study.
blood/plasma and eventually insulin resistance [173]. Consequently, an aged individual is at higher risk of developing type 2 diabetes. However, there is not much work concluding that aging is an independent risk factor for type 2 diabetes. Choi et al. [174] concluded that the risk of diabetes increases with aging only in overweight individuals, and the risk decreases with a moderate level of physical activity. Aging can be considered as triggering the association between independent risk factors and risk of diabetes, but more evidence and studies are required to examine the association between aging as an independent factor and diabetes.

3.9. Ethnicity

Ethnicity is associated with a range of health complications including diabetes because of the heterogeneity in the demographic environmental conditions and lifestyle. It is an independent risk factor which tends to be exacerbated by the social disadvantage and the affluent way of living. Table 8 shows the characteristics and findings of the work in the literature studying the association between ethnicity and type 2 diabetes. Compared to white individuals, type 2 diabetes is more prevalent in Pacific Islanders (OR 3.1, 95% CI 1.4–6.8), followed by Blacks (OR 2.3, 95% CI 2.1–2.6), Native Americans (OR 2.2, 95% CI 1.6–2.9), Hispanics (OR 2.0, 95% CI 1.8–2.3), and Multiracial (OR 1.8, 95% CI 1.5–2.9) [175]. In another study by Shai et al. [176], it was found that compared to whites, Asians (RR 1.94, 95% CI 1.46–2.58), Hispanics (RR 1.70, 95% CI 1.28–2.26), and Blacks (RR 1.36, 95% CI 1.14–1.63) are at higher risk of incidence type 2 diabetes.

A study by Zimmet et al. [177] showed that type 2 diabetes is 10 times more prevalent in rural Indians compared to rural Melanesians, and 2 times more prevalent in urban Indians compared to urban Melanesians. They also revealed that the prevalence is 5 times more in urban Melanesians compared to rural Melanesians. One of the reason could be that the rural residents have an increased amount of physical activity compared to the urban ones, leading to decreased risk of diabetes [178]. It should thus important to have a moderate amount of physical activity as a therapy for diabetes prevention. Compared to Europeans, type 2 diabetes is 3.8 times more prevalent in Indians, and the prevalence increases to 5 times for 40–64 years old individuals [179]. In another comparison between Asian and non-Asian ethnicity, it is found that the prevalence of type 2 diabetes in Bangladeshis (Asians) is more [180]. Furthermore, the prevalence is high in women (5.75 times) compared to that in men (2.2 times). However, ethnicity can not be considered as an independent risk factor for this association as Bangladeshi had higher smoking rates and a lower ratio of polysaturated fatty acids to saturated fatty acids. Consequently, ethnicity, smoking and dyslipidemia all contributed to the risk of incidence type 2 diabetes. Simmons et al. [181] also confirmed in their study that the prevalence is more in Asians compared to Whites. However, in contrast to the results obtained by [180], Simmons et al. [181] found that the prevalence is more in men compared to women. This inconsistency should be examined further.

In summary, ethnicity is associated with the incidence of type 2 diabetes. However, there is no definite explanation of why individuals of a particular ethnicity are at higher risk of type 2 diabetes compared to the others. One possible explanation can be the ethnicity-dependent relation between BMI and body fat. For instance, Asians have around 3–4 kg/m² lower BMI compared to Caucasians for a given percentage of body fat [182]. Another reason could be ethnicity-based insulin sensitivity. Studies show that Asians, Blacks and Mexican Americans are less insulin sensitive compared to non-Hispanic Whites [183,184].

3.10. Family history of diabetes

Family history information can serve as a useful tool for prognosis/diagnosis and public health. Family history of diabetes reflects both genetic as well as environmental factors and can lead to better prediction of incidence type 2 diabetes than only genetic factors and environmental factors alone [192]. Table 9 shows the characteristics and findings of the work in the literature studying the association between family history of diabetes and type 2 diabetes. A study by Tsenkova et al. [193] revealed that a family history of diabetes is strongly associated with incidence diabetes (OR 2.77, 95% CI 2.03–3.78). Another study also shows that parental history of diabetes is an independent risk factor for diabetes (OR 1.73, 95% CI 1.29–2.33) [194]. However, the association becomes weaker in men free of cardiovascular disease (OR 1.63, 95% CI 1.18–2.24). Moreover, the association is much higher in 45–54 years old men (OR 1.99, 95% CI 1.38–2.89) compared to 55–68 years old men (OR 1.33, 95% CI 0.70–2.52). Furthermore, the prevalence of type 2 diabetes is stronger in men compared to women [195]. This indicates that parental history of diabetes in combination with other risk factors such as aging, gender and cardiovascular diseases, increases the risk of incidence type 2 diabetes.

Rodriguez-Moran et al. [196] showed that a family history of diabetes in first degree of relative (parents, offspring and siblings) is a strong and independent risk factor for the prevalence of impaired fasting glucose (prediabetes) (OR 11.7, 95% CI 9.5–21.2) in children and adolescents. This is in the absence of obesity. The results reveal that it is important to consider the parental history of diabetes while screening for diabetes children and adolescents. This is because only obesity-based screening could lead to underestimation. Valdez et al. [197] also showed that the family history of diabetes in at least two first-degree relatives or one first-degree and at least two second-degree relatives is significant for prevalence of type 2 diabetes. However, it can not be denied that the presence of a family history of diabetes can make the association between obesity and diabetes stronger [198]. Given a BMI ≥ 35, an individual with a family history of diabetes is at a higher risk of incidence diabetes (OR 26.7, 95% CI 14.4–49.4) compared to the one without a family history of diabetes (OR 6.1, 95% CI 3.4–11.2). Furthermore, ethnicity is also considered an important factor in an obese individual with a family history of diabetes [199,200].

An individual having a family history of diabetes can have an early onset of diabetes compared to the ones without a family history. However, it is hard to conclude that which among the maternal, paternal and both maternal and paternal family history of diabetes is more significant for incidence/prevalence of type 2 diabetes as the results in the literature are inconsistent [195,201–205].

3.11. Obesity

Obesity is a complex health condition that involves an excessive amount of body fat. It is defined by the BMI and further evaluated in terms of fat distribution via the waist-hip ratio. Abdominal fat in the body increases inflammation which decreases insulin sensitivity by disrupting the function of beta-cells. The insulin resistance condition then leads to the prevalence of type 2 diabetes. Table 10 shows the characteristics and findings of the work in the literature studying the association between obesity and type 2 diabetes. Ishikawa-Takata et al. [206] found that the risk of diabetes increases significantly for an individual having a BMI greater than 29 kg/m². The relative risk of diabetes increases up to 3.8 (95% CI 3.19–4.72) for an individual having a BMI greater than 34.9 kg/m² [119]. Furthermore, study shows that the association between obesity and incidence diabetes is gender-dependent [207]. For each
Table 8
Characteristics and findings of the studies examining the association between ethnicity and type 2 diabetes.

| Work Year | Study Design | Sample size (%DM) | %M/W | Age (Years) | Ethnicity | Follow-up duration (Years) | Adjusted variables | Findings |
|-----------|--------------|-------------------|------|-------------|-----------|---------------------------|-------------------|----------|
| 1983      | RS           | -                 | 2638 | 46.81/53.19 | ≥20       | Melanesians and Indians   | -                 | Age      |
|           |              |                   |      |             |           |                           |                   |          |
| 1985      | RS           | -                 | 61130 (1.87%) | M/W | All age      | Asians and Europeans      | -                 | Age      |
| 1988      | RS           | -                 | 253  | 65.6/34.4   | 35–69     | Bangladeshi and Non-Asian | -                 | Age      |
| 1989      | RS           | -                 | 4020 | 46.4/51.6   | 20–79     | Asian and White           | -                 | Age      |
| 2003      | BRFSS [174]  | -                 | 163584 | 46.8/51.4  | ≥30       | Asian, Black, Hispanic,   | -                 | Age, sex and BMI |
|           |              |                   |      |             |           | Native American, Pacific  |                   |          |
|           |              |                   |      |             |           | Islander, White, Other    |                   |          |
|           |              |                   |      |             |           | Multiracial               |                   |          |
| 2006      | NHS [80]     | PCS               | 78419 (4.90%) | 0/100      | 30–55     | White, Asian, Hispanic,   | 20                | Age, BMI, family history of |
|           |              |                   |      |             |           | Black                      |                   | diabetes, alcohol consumption, |
|           |              |                   |      |             |           |                           |                   | physical exercise, and smoking |

RS-Random Sample, BRFSS-Behavioral Risk Factor Surveillance System, NHS-Nurses’ Health Study, PCS-Prospective Cohort Study.
Table 9
Characteristics and findings of the studies examining the association between family history of diabetes and type 2 diabetes.

| Work Year | Study Design | Sample size | %M/W | Age (Years) | Ethnicity | Follow-up duration (Years) | Adjusted variables | Findings |
|-----------|--------------|-------------|------|-------------|-----------|----------------------------|-------------------|----------|
| [204] 1981 RS | - | 3177 | - | >5 | Pima Indians | - | Age and BMI | 1.0 | 2.3 | 3.9 |
| [195] 1993 SAHS | - | 4914 | 43/57 | Mean 42–44.8 | Mexicans, Americans and Non-Hispanics | 9 | Age and ethnicity | Family History No Mother/father both OR | 3.44 (2.32–5.12) | 3.49 (2.16–5.64) | 3.73 (1.72–8.08) |
| | | | | | | | | Family History No Mother father both OR (Men) | 2.03 (1.47–2.81) | 1.35 (0.83–2.19) | 2.59 (1.41–4.77) |
| | | | | | | | | Family History No Mother father both OR (Women) | 1.0 | 1.0 |
| | | | | | | | | Family History No | 1.0 |
| | | | | | | | | Family History No Mother | 1.0 |
| | | | | | | | | Family History No Father | 1.0 |
| | | | | | | | | Family History No Both | 1.0 |
| | | | | | | | | Family History Age at onset 40–49 | 1.0 |
| | | | | | | | | Family History Age at onset 40–49 No | 1.0 |
| | | | | | | | | Family History Age at onset 40–49 No Mother | 4.41 (1.71–10.13) |
| | | | | | | | | Family History Age at onset 40–49 No Father | 2.21 (0.25–8.86) |
| | | | | | | | | Family History Age at onset 50–59 | 1.0 |
| | | | | | | | | Family History Age at onset 50–59 No | 1.0 |
| | | | | | | | | Family History Age at onset 50–59 No Mother | 1.57 (0.40–4.41) |
| | | | | | | | | Family History Age at onset 50–59 No Father | 2.80 (0.54–9.07) |
| | | | | | | | | Family History Age at onset 50–59 No Both | 1.0 |
| | | | | | | | | Family History Age at onset ≥60 | 1.22 (0.38–3.05) |
| | | | | | | | | Family History Age at onset ≥60 No | 0.56 (0.01–3.31) |
| | | | | | | | | Family History Age at onset ≥60 No Mother | 1.73 (1.29–2.33) |
| | | | | | | | | Family History Age at onset ≥60 No Father | 1.0 |
| | | | | | | | | Family History Age at onset ≥60 No Both | 1.0 |
| | | | | | | | | Family History Age at onset ≥60 | 2.51 (1.55–4.07) |
| | | | | | | | | Family History Age at onset ≥60 No Mother | 1.41 (0.657–3.05) |
| | | | | | | | | Family History Age at onset ≥60 No Father | 3.96 (1.22–12.9) |

(continued on next page)
| Work Year | Study Design | Sample size | %M/W | Age (Years) | Ethnicity | Follow-up duration (Years) | Adjusted variables | Findings |
|-----------|--------------|-------------|------|-------------|-----------|----------------------------|-------------------|----------|
| 2000      | EPIC [101]   | CSS         | 6473 | 45.54/ 54.46| USA       | 22.5                       | Age and sex       | OR       |
|           |              |             |      |             |           |                            |                   | 1.0      |
|           |              |             |      | 22.5–24.9   | BMI       |                            |                   | 2.0 (1.2–3.1)|
|           |              |             |      | 27.5–29.9   | BMI       |                            |                   | 2.5 (1.6–4.0)|
|           |              |             |      | 30–34.9     | BMI       |                            |                   | 0.5 (1.3–11.3)|
|           |              |             |      | ≥35         | BMI       |                            |                   | 1.1 (0.2–5.1)|
|           |              |             |      | <22.4       | BMI       |                            |                   | 2.6 (1.3–5.3)|
|           |              |             |      | 22.5–24.9   | BMI       |                            |                   | 2.8 (1.5–5.3)|
|           |              |             |      | 25–27.4     | BMI       |                            |                   | 2.2 (1.1–4.6)|
|           |              |             |      | 27.5–29.9   | BMI       |                            |                   | 6.4 (3.6–11.3)|
|           |              |             |      | 30–34.9     | BMI       |                            |                   | 26.7 (14.4–49.4)|
| 2000      | FHS [187]    | -           | 2527 | M/W         | 26–82     | 40                         | Age               | OR       |
|           |              |             |      |             |           |                            |                   | 1.0      |
|           |              |             |      | 22.5–24.9   | BMI       |                            |                   | 3.4 (2.3–4.9)|
|           |              |             |      | 25–27.4     | BMI       |                            |                   | 3.5 (2.3–5.2)|
|           |              |             |      | ≥22.4       | BMI       |                            |                   | 6.1 (2.9–13.0)|
| 2001      | MONICA [35]  | CSS         | 12751| 49.6/ 50.4  | -         | -                          | Age and sex       | OR       |
|           |              |             |      |             |           |                            |                   | 1.0      |
|           |              |             |      | 4.9 (2.3–4.9)| BMI       |                            |                   | 3.5 (2.3–5.2)|
|           |              |             |      | 6.1 (2.9–13.0)| BMI     |                            |                   | 6.1 (2.9–13.0)|
| 2007      | NHANES [88]  | -           | 16388| 49.3/ 50.7  | ≥18       | 6                          | sex, race/ethnicity, age, BMI, hypertension, and household income | OR       |
|           |              |             |      |             |           |                            |                   | 1.0      |
|           |              |             |      | 2.9 (2.3–3.6)| BMI       |                            |                   | 2.8 (2.1–3.8)|
| 2009      | NHANES [88]  | CSS         | 10899| 48/ 52      | Mean 51.3–61| 5                          | Age and sex       | OR       |
|           |              |             |      |             |           |                            |                   | 1.0      |
|           |              |             |      | 2.3 (2.1–3.8)| BMI       |                            |                   | 5.6 (1.8–17.3)|
|           |              |             |      | 5.5 (1.8–17.3)| BMI     |                            |                   | 8.5 (3.8–19.4)|
| 2011      | RS           | CSS         | 3723 | 49.1/ 50.9  | 7–15      | 2                          | Age, sex, and BMI | OR       |
|           |              |             |      |             |           |                            |                   | 1.0      |
|           |              |             |      | 20.4 (6.5–64.5)| BMI     |                            |                   | 20.4 (6.5–64.5)|
|           |              |             |      | 14.0 (3.4–58.0)| BMI     |                            |                   | 14.0 (3.4–58.0)|
|           |              |             |      | 8.5 (3.8–19.4)| BMI     |                            |                   | 8.5 (3.8–19.4)|
| 2016      | MIDUS 1 and 2| -           | 978  | 45/ 55      | 34–84     | -                          | Age, sex, and socioeconomic status | OR       |
|           |              |             |      |             |           |                            |                   | 1.0      |
|           |              |             |      | 11.7 (9.5–21.2)| BMI     |                            |                   | 11.7 (9.5–21.2)|
|           |              |             |      | 2.77 (2.03–3.78)| BMI     |                            |                   | 2.77 (2.03–3.78)|

**Notes:** RS-Random Sample, SAHS-San Antonio Heart Study, MRFIT-Multiple Risk Factor Intervention Trial, MA-Meta Analysis, THHP-The Honolulu Heart Program, EPIC-European Prospective Investigation into Cancer, FHS-Framingham Heart Study, MONICA-Multinational MONItoring of trends and determinants in Cardiovascular disease, NHANES-National Health and Nutrition Examination Survey, PD-Prediabetes, IGF-Impaired Fasting Glucose, IGT-Impaired Glucose Tolerance, M-Men, W-Women, PCS-Prospective Cohort Study, CSS-Cross-Sectional Study.
Table 10
Characteristics and findings of the studies examining the association between obesity and type 2 diabetes.

| Work Year | Study Design | Sample size (%DM) | %M/W | Age (Years) | Ethnicity | Follow-up duration (Years) | Adjusted variables | Findings |
|-----------|--------------|-------------------|------|-------------|-----------|-----------------------------|--------------------|----------|
| [206] 2002 PCS 4737 100/0 45–64 Japanese 4 | Age, smoking status, alcohol intake, family history, and baseline value of fasting blood glucose. | BMI (kg/m²) | RR | 1.0 | 5.16 (1.92–13.80) 5.25 (1.96–14.04) |
| [213] 2007 BWHS [214] 49766 (4.96%) 0/100 21–69 African-American (USA) 8 | Age, physical activity, family history of diabetes, cigarette smoking, years of education, and time period of data collection | BMI (kg/m²) | IRR | 1.0 | 23 (17–31) |
| [119] 2001 PCS 84941 (3.88%) 0/100 30–55 - 16 | Age (in five-year categories), time (eight periods), presence or absence of a family history of diabetes, menopausal status, and use or nonuse of postmenopausal hormone therapy | BMI (kg/m²) | RR | 1.0 | 2.67 (2.13–3.34) 7.59 (6.27–9.19) 20.1 (16.6–24.4) 38.8 (31.9–47.2) |
| [207] 2006 27 cohorts PCS + CSS 154989 (0.20%) 54/ 46 Mean 51 - Mean 8 | Age, sex, cohort, and smoking habit | 5.3 cm | Each 2 kg/m² lower BMI is associated with a 23% (15–30%) lower risk of total DM in men and 27% (23–31%) lower risk in women. In the Asian cohort, each 2 kg/m² lower BMI was associated with a 37% (26–46%) lower risk and in Australasian cohorts the same reduction in BMI was associated with 25% (21–29%) lower risk. |
| [208] 2006 RS 827 (7.86%) - - Japanese 10 | Age, sex, total cholesterol, systolic pressure, smoking and overall obesity | WC (cm) | RR | 2.07 (1.03–4.16) |
| [209] 2006 TLGS PCS 4479 (3.70%) 41.34/ 58.66 >3 Tehran 3.6 (mean) | Age, smoking, family history of diabetes, HTN, TG, HDL, and other anthropometric variables | WC (cm) | OR | 1.0 | 2.875 (1.987–4.160) |
| [210] 2009 RS 5071 37.80/ 62.2 ≥40 Chinese - | Educational level, age group, smoking and alcohol drinking | WC (cm) | OR | 1.0 | 2.308 (1.473–3.615) |
| [211] 2001 MAHES - 835 39.16/ 60.84 60–92 Hispanics and Non-Hispanics - | Age, physical activity and smoking | WC (cm) | OR | 1.0 | 2.1(1.2–3.9) 0.9 (0.3–3.1) 1.6 (1.0–2.8) 15.1 (1.9–117.6) |

SWHS-Shanghai Women’s Health Study, BWHS- Black Women’s Health Study, RS-Random Sample, WC-Waist Circumference, TLGS-Tehran Lipid and Glucose Study, MAHES-Massachusetts Hispanic Elderly Study, H-Hispanics, NH-Non Hispanics, M-Men, W-Women, PCS-Prospective Cohort Study, CSS-Cross-Sectional Study.
2 kg/m² lower BMI, men are at 23% (15–30%) lower risk of diabetes, whereas women are at 27% (23–32%) lower risk. Further, the association between obesity and diabetes is also dependent on ethnicity [207]. For each 2 kg/m² lower BMI, Asians are at 37% (26–46%) lower risk of diabetes, whereas Australians are at 25% (21–29%) lower risk.

Ohnishi et al. [208] found that compared to overall obesity, central obesity is highly associated with the risk of type 2 diabetes (RR 2.07, 95% CI 1.03–4.16). This association is more in elderly people (>60 years) (OR 3.8, 95% CI 1.8–7.7) [209]. The association between central obesity and the incidence of type 2 diabetes is found significant in both men and women. However, centrally obese women are at higher risk (OR 2.875, 95% CI 1.987–4.160) compared to centrally obese men (OR 2.308, 95% CI 1.473–3.615) [210]. The prevalence of type 2 diabetes in obese individual is ethnicity dependent [211]. Non-Hispanics centrally obese women are at higher risk of developing type 2 diabetes (OR 15.1, 95% CI 1.9–117.6) compared to centrally obese Hispanic women (OR 1.6, 95% CI 1.0–2.8). The centrally Hispanic men are also at risk of developing type 2 diabetes (OR 2.1, 95% CI 1.2–3.9). No such association is found in centrally obese Non-Hispanic men. However, all these studies examining the association between central obesity and the incidence of type 2 diabetes consider different definitions of central obesity. For instance, [208] defines central obesity as waist circumference (WC) ≥ 85 cm in men and ≥ 90 cm in women, whereas [211] defines it as WC ≥ 102 cm in men and ≥ 88 cm in women. Consequently, it is difficult to conclude the association between central obesity and the incidence of type 2 diabetes.

In summary, although obesity is a significant predictor, the association between obesity and diabetes is a factor of gender and ethnicity. Women with high BMI are at greater risk of diabetes compared to men. Moreover, the association is stronger in Asians compared to Australians. The association between central obesity and the incidence of type 2 diabetes is also found to be significant for the prevalence of type 2 diabetes. This association is the strongest in Non-Hispanics women. However, more studies are required to examine the association between central obesity and type 2 diabetes following one standard criterion defining central obesity.

### 3.12. Physical inactivity

An individual is considered physically inactive if he/she does not get the recommended 30–60 min of exercise three to four times a week. Physical inactivity decreases insulin sensitivity with progressive loss of beta-cells. This leads to impaired glucose tolerance and eventually type 2 diabetes. However, no work examines the association between physical inactivity as an independent factor and the prevalence of diabetes. One of the reasons that physical inactivity leads to type 2 diabetes can be that physical inactivity can cause obesity which in turn is a significant risk factor for type 2 diabetes.

### 4. Conclusion

Diabetes is a global crisis that is primarily driven by rapid urbanization, changing lifestyles, and uneven dietary patterns [215,216]. It is crucial to predict the prevalence of diabetes in an individual to reduce the risk of diabetes development and save lives. Diabetes is thought to prevail due to several risk factors such as high-level serum uric acid, sleep quality/quantity, smoking, depression, cardiovascular disease, dyslipidemia, hypertension, aging, ethnicity, family history of diabetes, physical inactivity, and obesity. Studies in the literature have examined the association between each of these risk factors and the risk of developing type 2 diabetes. In this review, we provide an analysis of the studies in the literature to deduce inferences on the relationship between the risk factors and incidence/prevalence of type 2 diabetes.

In conclusion, it can be observed that sleep quantity/quality, smoking, dyslipidemia, hypertension, ethnicity, family history of diabetes, obesity and physical inactivity are strongly associated with the development of type 2 diabetes. Both sleep quantity and quality are found to be strongly associated with the development of type 2 diabetes. The association is stronger in women sleeping for more hours and in men sleeping for fewer hours. However, the sleeping quantity and quality data in these studies are self-reported by the participants, and therefore, prone to errors. More studies are required that use measurement techniques for data collection to validate the association between sleep quantity/quality and type 2 diabetes. Smoking is also found to be a significant risk factor for type 2 diabetes. Both active and passive smokers are at higher risk of developing type 2 diabetes. Moreover, the risk for developing type 2 diabetes remains high in ex-smokers for the first 5–10 years of smoking cessation. Dyslipidemia is associated with the development of type 2 diabetes. Increased non-HDL and decreased HDL levels are strongly associated with type 2 diabetes. However, in the majority of these studies, the incidence or prevalence of type 2 diabetes is self-reported. Consequently, further studies are needed to validate this association between dyslipidemia and type 2 diabetes using standardized measurement techniques, such as A1C test [217]. Hypertension is a significant risk factor for type 2 diabetes and this is further elevated in obese individuals. Ethnicity strongly associates with the development of type 2 diabetes. This could be due to the fact that insulin sensitivity varies among individuals of different ethnicity. Family history of diabetes in first degree of relatives is strongly associated with the development of type 2 diabetes. In addition, family history of diabetes also signifies the association between obesity and type 2 diabetes. Obesity is found to a significant risk factor for incidence of type 2 diabetes and the association is stronger in women compared to men.

The association between serum uric acid and type 2 diabetes remains obscure. It can not be concluded that serum uric acid is an independent risk factor for type 2 diabetes or it only elevates the association between other independent risk factors such as obesity, hypertension, and dyslipidemia, and type 2 diabetes. Moreover, our analysis shows that there might be no association between serum uric acid and the development of type 2 diabetes, but rather there might be a reverse association, i.e., diabetes leads to elevated serum uric acid level. Similarly, based on the evidence in the literature, aging can not be considered as an independent risk factor for type 2 diabetes. Aging only emphasizes the association between obesity and type 2 diabetes. Depression as well is not found to an independent risk factor contributing to the development of type 2 diabetes. Rather, the activities related to depression such as physical inactivity, poor diet, and obesity leads to diabetes. There is no sufficient evidence to conclude the association between cardiovascular disease and type 2 diabetes. It is debatable whether cardiovascular disease leads to the development of type 2 diabetes. Consequently, more studies are required to study the direct association between these risk factors, i.e., serum uric acid, aging, depression, and cardiovascular disease, and incidence of type 2 diabetes.
Based on this study, we devise recommendations to different stakeholders leading to better patient care. In particular, we provide recommendations for allied healthcare professionals, individuals, and government institutions as follows:

- **Allied healthcare professionals:** The hypertensive medications and the LDL lowering therapy and drugs should be carefully prescribed as they are associated with increased risk of type 2 diabetes. In addition, overweight and obese adults should be screened for diabetes.

- **Individuals:** A healthy lifestyle, which involves intake of polyunsaturated fatty acids and vegetable fats, regular exercise, a healthy diet and proper sleep, is crucial. Individuals should avoid both active and passive smoking.

- **Government:** Physical activity in the nation should be promoted for a healthy nation. Law policies should be implemented to restrict public smoking as passive smoking significantly increases the risk of type 2 diabetes. For instance, designated smoking areas can be established to eliminate the risk of developing passive smokers. It would be beneficial to have periodic surveys that include the demographic and lifestyle features of the citizens and the surveys' results can then be used to develop a nation-wide diabetes prevention plan, in coordination with the allied health professionals.

### Table A1

| Risk factor                      | Search string                                                                 |
|----------------------------------|-----------------------------------------------------------------------------|
| Serum uric acid                  | (risk OR “risk factor” OR etiology OR association OR development OR progression OR incidence) AND (“uric acid” OR uric-acid OR hyperuricemia OR “serum uric acid” OR gout) AND (diabetes OR “diabetes mellitus” OR “type 2 diabetes” OR “type II diabetes” OR “non-insulin dependent diabetes” OR “non insulin dependent diabetes” OR “noninsulin dependent diabetes”) |
| Sleep quantity/quality           | (risk OR “risk factor” OR etiology OR association OR development OR progression OR incidence) AND (“sleep hour” OR “sleeping hour” OR “hours of sleep” OR “sleep duration” OR “sleep time” OR “sleep length” OR “sleep period” OR “sleeping time” OR “sleep span” OR nap OR napping OR “daytime sleep” OR sleep quality OR “sleep disturbance” OR “sleep apnea” OR insomnia OR “sleep deprivation”) AND (diabetes OR “diabetes mellitus” OR “type 2 diabetes” OR “type II diabetes” OR “non-insulin dependent diabetes” OR “non insulin dependent diabetes” OR “noninsulin dependent diabetes”) |
| Smoking                          | (risk OR “risk factor” OR etiology OR association OR development OR progression OR incidence) AND (smoking OR “smoking cessation” OR cigarette OR “cigarette smoking” OR “passive smoking” OR “secondhand tobacco smoke”) AND (diabetes OR “diabetes mellitus” OR “type 2 diabetes” OR “type II diabetes” OR “non-insulin dependent diabetes” OR “non insulin dependent diabetes” OR “noninsulin dependent diabetes”) |
| Depression                       | (risk OR “risk factor” OR etiology OR association OR development OR progression OR incidence) AND (“depressive disorder” OR depression OR “dysthmic disorders”) AND (diabetes OR “diabetes mellitus” OR “type 2 diabetes” OR “type II diabetes” OR “non-insulin dependent diabetes” OR “non insulin dependent diabetes” OR “noninsulin dependent diabetes”) |
| Cardiovascular disease           | (risk OR “risk factor” OR etiology OR association OR development OR progression OR incidence) AND (“cardiovascular disease” OR stroke OR “heart disease”) AND (diabetes OR “diabetes mellitus” OR “type 2 diabetes” OR “type II diabetes” OR “non-insulin dependent diabetes” OR “non insulin dependent diabetes” OR “noninsulin dependent diabetes”) |
| Dyslipidemia                     | (risk OR “risk factor” OR etiology OR association OR development OR progression OR incidence) AND (cholesterol OR “cholesterol intake” OR “cholesterol consumption” OR diet OR fat OR “density lipoprotein” OR density-lipoprotein OR dyslipidemia) AND (diabetes OR “diabetes mellitus” OR “type 2 diabetes” OR “type II diabetes” OR “non-insulin dependent diabetes” OR “non insulin dependent diabetes” OR “noninsulin dependent diabetes”) |
| Hypertension                     | (risk OR “risk factor” OR etiology OR association OR development OR progression OR incidence) AND (“high blood pressure” OR “blood pressure” OR hypertensi OR “Hypertension-”) AND (diabetes OR “diabetes mellitus” OR “type 2 diabetes” OR “type II diabetes” OR “non-insulin dependent diabetes” OR “non insulin dependent diabetes” OR “noninsulin dependent diabetes”) |
| Aging                            | (risk OR “risk factor” OR etiology OR association OR development OR progression OR incidence) AND (age OR aging OR old OR elderly) AND (diabetes OR “diabetes mellitus” OR “type 2 diabetes” OR “type II diabetes” OR “non-insulin dependent diabetes” OR “non insulin dependent diabetes” OR “noninsulin dependent diabetes”) |
| Ethnicity                        | (risk OR “risk factor” OR etiology OR association OR development OR progression OR incidence) AND (ethnicity OR race OR “rac” OR community) AND (diabetes OR “diabetes mellitus” OR “type 2 diabetes” OR “type II diabetes” OR “non-insulin dependent diabetes” OR “non insulin dependent diabetes” OR “noninsulin dependent diabetes”) |
| Family history of diabetes       | (risk OR “risk factor” OR etiology OR association OR development OR progression OR incidence) AND (“family history” OR “parental history” OR “parental diabetes” OR “parental transmission” OR paternal OR maternal) AND (diabetes OR “diabetes mellitus” OR “type 2 diabetes” OR “type II diabetes” OR “non-insulin dependent diabetes” OR “non insulin dependent diabetes” OR “noninsulin dependent diabetes”) |
| Physical inactivity              | (risk OR “risk factor” OR etiology OR association OR development OR progression OR incidence) AND (“physical inactivity”) AND (diabetes OR “diabetes mellitus” OR “type 2 diabetes” OR “type II diabetes” OR “non-insulin dependent diabetes” OR “non insulin dependent diabetes” OR “noninsulin dependent diabetes”) |
| Obesity                          | (risk OR “risk factor” OR etiology OR association OR development OR progression OR incidence) AND (“body mass index” OR BMI OR “body fat distribution” OR “over weight” OR overweight OR obesity OR “weight change” OR “weight gain” OR “central obesity”) AND (diabetes OR “diabetes mellitus” OR “type 2 diabetes” OR “type II diabetes” OR “non-insulin dependent diabetes” OR “non insulin dependent diabetes” OR “noninsulin dependent diabetes”) |

### CRediT authorship contribution statement

- **Leila Ismail:** Conceptualization, Methodology, Investigation, Writing - original draft, Writing - review & editing.
- **Huned Materwala:** Investigation, Writing - original draft.
- **Juma Al Kaabi:** Validation, Writing - review & editing.

### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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### Appendix A


## Table A2
Quality assessment of the included studies according to the Quality assessment tool for observational cohort and cross-sectional studies.

| Work | Q1 | Q2 | Q3 | Q4 | Q5 | Q6 | Q7 | Q8 | Q9 | Q10 | Q11 | Q12 | Q13 | Q14 | Quality |
|------|----|----|----|----|----|----|----|----|----|-----|-----|-----|-----|-----|----------|
| [14] | Yes| Yes| Yes| No| Yes| Yes| Yes| Yes*| NR| NR| Yes| Yes| Good|
| [21] | Yes| Yes| NR| No| CD| No| No| NR| No| CD| NR| No| Yes| Poor|
| [23] | No| No| NR| NR| No| Yes| CD| No| NR| Yes| NR| NR| No| Poor|
| [15] | No| Yes| NR| Yes| No| Yes| Yes| Yes| Yes| Yes| Yes| NR| NR| Yes| Good|
| [24] | No| Yes| NR| Yes| No| Yes| Yes| Yes| Yes| NR| Yes| NR| Yes| Good|
| [16] | Yes| Yes| NR| No| Yes| Yes| Yes| NR| NR| No| NR| NR| Yes| Fair|
| [25] | Yes| Yes| NR| No| Yes| Yes| No| Yes| Yes| Yes| NR| NR| Yes| Fair|
| [27] | Yes| No| NR| CD| No| Yes| Yes| No| Yes| Yes| Yes| NR| NR| Yes| Fair|
| [30] | No| Yes| NR| Yes| No| No| Yes| NR| Yes| NR| NR| Yes| Fair|
| [79] | Yes| Yes| NR| Yes| No| Yes| Yes| No| Yes| Yes| NR| NR| Yes| Fair|
| [50] | Yes| Yes| NR| No| Yes| Yes| Yes| Yes| No| No| Yes| NR| NR| Yes| Fair|
| [83] | No| Yes| NR| No| No| No| Yes| No| NR| Yes| NR| NR| Yes| Fair|
| [52] | Yes| Yes| NR| Yes| No| Yes| Yes| No| No| No| Yes| NR| Yes| Fair|
| [85] | Yes| Yes| NR| Yes| No| Yes| Yes| Yes| Yes| No| NR| No| Yes| Fair|
| [87] | Yes| Yes| NR| Yes| No| Yes| Yes| Yes| No| No| No| NR| Yes| Fair|
| [59] | Yes| Yes| NR| Yes| No| Yes| Yes| Yes| No| No| No| NR| No| Yes| Fair|
| [89] | Yes| Yes| NR| Yes| No| Yes| Yes| Yes| No| Yes| Yes| NR| NR| Yes| Fair|
| [92] | Yes| Yes| NR| Yes| No| Yes| Yes| Yes| No| Yes| Yes| NR| NR| Yes| Fair|
| [94] | Yes| Yes| NR| Yes| No| Yes| Yes| No| Yes| No| NR| Yes| NR| Yes| Fair|
| [55] | Yes| Yes| No| Yes| No| Yes| Yes| No| Yes| No| NR| Yes| NR| Yes| Fair|
| [96] | CD| Yes| No| No| No| Yes| No| Yes| No| NR| Yes| NR| CD| Yes| Fair|
| [97] | Yes| Yes| NR| Yes| No| Yes| Yes| Yes| No| Yes| NR| Yes| NR| Yes| Fair|
| [98] | Yes| Yes| NR| No| Yes| Yes| Yes| No| No| No| Yes| NR| Yes| Fair|
| [100] | Yes| Yes| NR| CD| No| No| Yes| No| Yes| No| NR| Yes| NR| Yes| Fair|
| [51] | No| Yes| CD| Yes| No| Yes| No| Yes| No| Yes| No| NR| Yes| NR| Yes| Fair|
| [102] | Yes| Yes| NR| Yes| No| Yes| Yes| Yes| No| No| Yes| NR| Yes| Yes| Fair|
| [53] | Yes| Yes| NR| No| No| No| Yes| No| No| No| NR| No| NR| Yes| Fair|
| [104] | Yes| Yes| NR| CD| No| No| Yes| No| Yes| No| NR| Yes| NR| Yes| Fair|
| [106] | Yes| Yes| Yes| Yes| No| Yes| Yes| No| Yes| No| Yes| Yes| NR| No| Yes| Good|
| [54] | Yes| Yes| NR| No| No| Yes| Yes| No| Yes| No| No| NR| NR| Yes| Fair|
| [108] | Yes| Yes| No| Yes| No| Yes| NR| No| No| No| NR| No| NR| Yes| Poor|
| [110] | No| Yes| NR| Yes| No| Yes| Yes| No| Yes| No| NR| Yes| NR| NR| Yes| Fair|
| [67] | No| Yes| NR| NR| No| Yes| Yes| Yes| NA| Yes| Yes| Yes| NR| Yes| NR| Yes| Fair|
| [68] | Yes| Yes| NR| Yes| No| Yes| Yes| Yes| NA| Yes| Yes| No| Yes| NR| Yes| Good|
| [112] | No| No| Yes| Yes| No| Yes| Yes| Yes| NA| Yes| Yes| NR| Yes| NR| Yes| Fair|
| [73] | CD| Yes| NR| Yes| No| No| Yes| NA| NR| No| Nr| Yes| FAIR| Poor|
| [114] | Yes| Yes| NR| Yes| No| Yes| Yes| Yes| NA| Yes| Yes| NR| Yes| NR| Yes| Good|
| [69] | Yes| Yes| NR| Yes| No| Yes| Yes| Yes| NA| Yes| Yes| NR| No| Yes| NR| Yes| Good|
| [116] | No| Yes| NR| Yes| No| No| No| No| NA| NR| No| NR| NR| Yes| Poor|
| [65] | Yes| Yes| NR| Yes| No| Yes| Yes| No| NA| Yes| Yes| NR| Yes| Yes| Fair|
| [63] | Yes| Yes| NR| Yes| No| Yes| Yes| NA| NR| CD| No| NR| Yes| Fair|
| [119] | No| Yes| No| Yes| No| Yes| Yes| NA| Yes| Yes| Yes| NR| Yes| NR| Yes| Good|
| [120] | No| CD| NR| CD| No| Yes| Yes| Yes| NA| Yes| Yes| NR| NR| NR| Yes| Fair|
| [74] | Yes| Yes| NR| CD| No| No| No| No| NA| Yes| No| Yes| NR| NR| Yes| Fair|
| [122] | Yes| Yes| Yes| No| Yes| Yes| No| NA| No| Yes| No| NR| Yes| NR| Yes| Good|
| [70] | Yes| Yes| No| Yes| No| Yes| Yes| No| NA| No| Yes| NR| Yes| NR| Fair|
| [77] | Yes| Yes| NR| Yes| No| Yes| Yes| Yes| NA| Yes| Yes| NR| CD| Yes| Good|
| [71] | Yes| CD| Yes| Yes| No| Yes| Yes| Yes| NA| Yes| Yes| NR| Yes| NR| Yes| Good|
| [75] | Yes| Yes| NR| Yes| No| Yes| Yes| Yes| NA| Yes| Yes| NR| Yes| NR| Yes| Good|
| [66] | No| Yes| Yes| No| Yes| Yes| No| NA| No| Yes| NR| No| Yes| NR| No| Yes| Fair|
| [64] | Yes| Yes| NR| Yes| No| Yes| Yes| Yes| NA| Yes| Yes| CD| No| Yes| NR| Yes| Fair|
| [72] | Yes| No| NR| CD| No| Yes| Yes| Yes| NA| Yes| Yes| NR| Yes| Yes| Good|
| [78] | Yes| Yes| Yes| Yes| No| Yes| No| NA| Yes| Yes| NR| Yes| NR| Yes| Good|
| [76] | Yes| Yes| NR| Yes| No| Yes| Yes| Yes| NA| Yes| Yes| NR| Yes| Yes| Good|
| [128] | No| Yes| NR| Yes| No| Yes| Yes| No| NA| NR| No| NR| NR| Yes| Fair|
| [137] | Yes| Yes| Yes| No| Yes| Yes| Yes| Yes| Yes| No| Yes| NR| Yes| Yes| Good|
| [155] | No| Yes| NR| Yes| No| Yes| Yes| No| Yes| No| NR| No| NR| Yes| Fair|
| [157] | Yes| Yes| NR| Yes| No| Yes| Yes| No| No| No| NR| No| NR| Yes| Fair|
| [158] | Yes| Yes| NR| Yes| No| Yes| Yes| Yes| NR| Yes| NR| Yes| NR| Yes| Fair|
| [136] | Yes| Yes| NR| Yes| No| Yes| Yes| Yes| NR| Yes| NR| CD| Yes| Fair|
| [160] | Yes| Yes| Yes| Yes| No| Yes| No| Yes| Yes| Yes| NR| Yes| NR| Yes| Good|
| [138] | No| Yes| NR| Yes| No| Yes| No| Yes| No| CD| NR| Yes| NR| Yes| Fair|
| [139] | No| Yes| NR| Yes| No| Yes| No| Yes| No| NR| Yes| NR| Yes| Fair|

**High-level serum uric acid**

**Sleep quantity/quality**

**Smoking**

**Depression**
| Work | Q1 | Q2 | Q3 | Q4 | Q5 | Q6 | Q7 | Q8 | Q9 | Q10 | Q11 | Q12 | Q13 | Q14 | Quality |
|------|----|----|----|----|----|----|----|----|----|-----|-----|-----|-----|-----|---------|
| [141]| No | Yes| NR | Yes| No | Yes| Yes| Yes| Yes| Yes| NR | NR | Yes| Good |
| [148]| Yes| Yes| NR | Yes| No | Yes| Yes| Yes| CD | CD | No | NR | No | Yes| Fair |
| [154]| Yes| Yes| NR | Yes| No | Yes| Yes| Yes| NR | NR | NR | NR | Yes| Yes| Fair |
| [152]| No | Yes| NR | Yes| No | Yes| CD | Yes| Yes| Yes| No | NR | NR | Yes| Fair |
| [166]| Yes| Yes| NR | Yes| No | Yes| Yes| Yes| NR | Yes| NR | Yes| NR | Yes| Good |
| [167]| Yes| Yes| NR | Yes| No | Yes| Yes| Yes| Yes| No | Yes| NR | NR | Yes| Good |
| [168]| Yes| Yes| NR | Yes| No | Yes| Yes| Yes| No | Yes| NR | NR | Yes| NR | Good |
| [170]| Yes| Yes| NR | No | No | No | NA | NA | NA | NA | NR | NR | NR | Yes| Fair |
| [179]| No | Yes| No | Yes| No | Yes| No | NA | NA | NA | NR | NR | Yes| Poor |
| [180]| No | Yes| No | No | No | No | NA | NA | NA | No | NR | NR | Yes| Fair |
| [181]| Yes| Yes| Yes| CD | No | No | NA | NA | No | Yes| NR | NR | Yes| Fair |
| [175]| Yes| Yes| Yes| No | No | No | NA | NR | No | NR | NR | Yes| Poor |
| [176]| Yes| Yes| NR | No | Yes| Yes| NA | NA | Yes| NR | NR | Yes| Good |
| [204]| No | No | NR | CD | No | Yes| NR | No | Yes| NA | Yes| NR | NR | Yes| Fair |
| [195]| Yes| Yes| Yes| No | No | No | Yes| No | Yes| No | NA | Yes| NR | Yes| Fair |
| [200]| Yes| Yes| Yes| No | Yes| Yes| Yes| Yes| No | No | NR | NR | Yes| Fair |
| [205]| No | Yes| No | NR | No | No | Yes| CD | Yes| NR | NA | NR | NR | Yes| Poor |
| [194]| No | Yes| No | Yes| No | Yes| CD | No | NR | NA | Yes| NR | Yes| NR | Yes| Good |
| [201]| Yes| Yes| Yes| No | Yes| Yes| Yes| CD | NA | Yes| NR | Yes| Yes| Good |
| [198]| Yes| Yes| NR | No | Yes| No | No | No | No | NA | Yes| NR | NR | Yes| Poor |
| [202]| No | Yes| NR | No | Yes| Yes| Yes| Yes| No | Yes| NR | NR | Yes| Good |
| [203]| Yes| Yes| Yes| No | No | No | Yes| No | Yes| No | NA | No | NR | Yes| Fair |
| [177]| No | Yes| Yes| No | No | No | No | No | No | Yes| NR | NR | Yes| Good |
| [179]| No | Yes| No | Yes| No | No | No | NA | NA | NR | NR | NR | NR | Yes| Poor |
| [180]| No | Yes| No | No | No | No | No | NA | NA | No | NR | NR | Yes| Poor |
| [181]| Yes| Yes| Yes| CD | No | No | NA | NA | No | Yes| NR | NR | Yes| Fair |
| [175]| Yes| Yes| Yes| No | No | No | NA | NR | No | NR | NR | Yes| Poor |
| [176]| Yes| Yes| NR | No | Yes| Yes| NA | NA | Yes| NR | NR | Yes| Good |
| [204]| No | No | NR | CD | No | Yes| NR | No | Yes| NA | Yes| NR | NR | Yes| Fair |
| [195]| Yes| Yes| Yes| No | No | No | Yes| No | Yes| No | NA | Yes| NR | Yes| Fair |
| [200]| Yes| Yes| Yes| No | Yes| Yes| Yes| No | No | NR | NR | Yes| NR | Yes| Fair |
| [205]| No | Yes| No | NR | No | No | Yes| CD | Yes| NR | NA | NR | NR | Yes| Poor |
| [194]| No | Yes| No | Yes| No | Yes| CD | No | NR | NA | Yes| NR | Yes| NR | Yes| Good |
| [201]| Yes| Yes| Yes| No | Yes| Yes| Yes| CD | NA | Yes| NR | Yes| Yes| Good |
| [198]| Yes| Yes| NR | No | Yes| No | No | No | No | NA | Yes| NR | NR | Yes| Poor |
| [202]| No | Yes| NR | No | Yes| Yes| Yes| Yes| No | Yes| NR | NR | Yes| Good |
| [203]| Yes| Yes| Yes| No | No | No | Yes| No | Yes| No | NA | No | NR | Yes| Fair |
| [177]| No | Yes| Yes| No | No | No | No | No | No | Yes| NR | NR | Yes| Good |
| [179]| No | Yes| No | Yes| No | No | Yes| No | Yes| No | NA | NR | NR | Yes| Fair |
| [180]| No | Yes| No | No | No | No | No | NA | NA | No | NR | NR | Yes| Poor |
| [181]| Yes| Yes| Yes| CD | No | No | NA | NA | No | Yes| NR | NR | Yes| Fair |
| [175]| Yes| Yes| Yes| No | No | No | NA | NR | No | NR | NR | Yes| Poor |
| [176]| Yes| Yes| NR | No | Yes| Yes| NA | NA | Yes| NR | NR | Yes| Good |
| [193]| Yes| Yes| Yes| No | Yes| CD | NR | No | No | NA | Yes| NR | NR | Yes| Fair |
| [206]| Yes| Yes| NR | Yes| No | Yes| Yes| Yes| Yes| Yes| Yes| Yes| NR | NR | Yes| Good |
| [213]| Yes| Yes| NR | No | Yes| No | Yes| Yes| Yes| Yes| Yes| Yes| NR | NR | Yes| Fair |
| [119]| No | Yes| No | No | No | Yes| Yes| Yes| Yes| Yes| Yes| Yes| NR | NR | Yes| Good |
| [207]| No | No | NR | CD | No | Yes| Yes| Yes| NR | Yes| NR | NR | NR | Yes| Fair |
| [208]| No | Yes| NR | No | Yes| No | Yes| No | Yes| No | NR | NR | NR | Yes| Fair |
| [209]| Yes| Yes| Yes| No | Yes| No | Yes| No | Yes| NR | Yes| No | NR | Yes| Good |
| [210]| Yes| Yes| Yes| NR | No | Yes| CD | NR | No | Yes| NR | NR | Yes| NR | Yes| Good |
| [211]| Yes| Yes| NR | Yes| No | Yes| CD | No | Yes| NR | Yes| NR | Yes| NR | Yes| Fair |

Q1. Was the research question or objective in this paper clearly stated?.
Q2. Was the study population clearly specified and defined?.
Q3. Was the participation rate of eligible persons at least 50%?.
Q4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?.
Q5. Was a sample size justification, power description, or variance and effect estimates provided?.
Q6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?.
Q7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?.
Q8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?.
Q9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?.
Q10. Were the exposure(s) assessed more than once over time?.
Q11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?.
Q12. Were the outcome assessors blinded to the exposure status of participants?.
Q13. Was loss to follow-up after baseline 20% or less?.
Q14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?.
CD—Cannot be Determined; NA—Not Applicable; NR—Not Reported.

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