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Title: Earlier Life Exposure to Environmental Determinants Over Time and Risk of Type 2 Diabetes Mellitus among Adults: A Systematic Review

Yannick Wilfried Mengue Mengue
yannick.mengue.1@ulaval.ca

Université Laval

Pierre Paul Audate
University of Montreal

Alexandre Lebel
Université Laval

Systematic Review

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Abstract

Background

This systematic review examined how long-term earlier life exposure to various physical (pollution, built environment) and social (area-level deprivation) environmental determinants (EDs) influences the risk of developing type 2 diabetes mellitus (T2DM) in adulthood using a comprehensive methodology not previously envisaged.

Methods

The search strategy encompassed six databases (PubMed Central, Embase, Elsevier, CINAHL Plus, Web of Science, EBSCOhost) and grey literature. We screened studies with full-text available and participants aged 18 or older. A risk of bias (RoB) assessment was performed, and a narrative synthesis was produced.

Results

A total of 169 studies were included as follows: area-level socioeconomic deprivation (18.9%), cultural norms related to land management (LM) (13.6%), food landscape (3%), built environment related to physical activity (PA) (3.6%), chemical pollution (56.8%), noise pollution (2.4%), and light pollution (1.8%). None of the studies were classified as 'low risk', 11 were rated 'high risk', and 158 were rated 'moderate risk'. No consistent evidence linked built environment PA with T2DM, whereas positive longitudinal associations were with food landscape (Adj_ES between 1.03 and 3.12), chemical pollution (Adj_ES between 1.01 and 9.26), light pollution (Adj_ES between 1.01 and 1.30), and noise pollution (Adj_ES between 1 and 1.05). In contrast, negative longitudinal associations were found with area-level socioeconomic deprivation (Adj_ES between 0.62 and 0.99) and cultural norms LM (Adj_ES between 0.97 and 0.99). Rural (Adj_ES between 1.25 and 1.37) and urban (Adj_ES between 1.16 and 1.29) differences, as well as differences between women (Adj_ES between 1.17 and 1.31) and men (Adj_ES between 1.06 and 1.20), were observed for chemical pollution. Meanwhile, sex/gender differences regarding cultural norms LM were inconclusive.

Discussion

This review corroborated the substantial role of earlier life EDs (excluding built environment PA) in T2DM risk among adults over time, as highlighted in previous reviews. However, caution is advised in interpretation due to biases and issues of generalizability. Research in this field should be encouraged in various income countries and among diverse ethnic populations, using improved cohort study designs before implementing cross-sectional interventions in public health and land management.

Introduction

The number of adults aged 20 to 79 living with diabetes worldwide increased from 151 million in 2000 to approximately 537 million in 2021 [1]. Projections suggest an additional 247 million cases by 2045 [1]. This growing burden is primarily driven by type 2 diabetes mellitus (T2DM), which accounts for about 90% of global diabetes cases [2]. Those most affected are predominantly men [1, 15], individuals living in urban areas of high-income countries, and populations of countries transitioning from low- to middle-income [1, 36]. The prevalence of T2DM also varies by race and ethnicity [8]. T2DM is a complex metabolic disorder mainly characterised by chronic hyperglycaemia [3–5], insufficient insulin production from adulthood onwards [6], and insulin resistance, which may appear up to 15 years earlier, often preceding β-cell failure [7]. T2DM often leads to severe consequences, including reduced quality of life, work limitations, increased risk of death, increased demand for healthcare resources, and substantial societal costs [8–14, 57]. Self-management education [12, 13] remained the primary strategy for preventing T2DM, although research highlighted area-level (physical and social) barriers or constraints [23] to its practical implementation. Some of these area-level (physical and social) constraints were examined previously as environmental determinants (EDs) of T2DM [31–34, 36–56, 87].

A growing body of research shows that T2DM has multiple causes and complex mechanisms of action [2–7, 15–26, 28–56], involving both physical (e.g. chemical, light, noise pollution, and various built environment aspects such as accessibility of healthy/ unhealthy food stores, green spaces/amenities or zoning norms, pleasant places to walk or accessibility to exercise facilities) [31–34, 36–51, 87] and social (e.g. various area-level social deprivation aspects such as social cohesion, safety, violence, adverse housing conditions, socioeconomic inequalities) [31, 52–55] EDs. These EDs represent long-term constraints, through various scales (e.g., family, neighbourhood, regional, or global), on positive health behaviours to which individuals were exposed across the period of life preceding the onset of hyperglycaemia (earlier life) [22, 23, 29]. So, there is a growing recognition that healthy residential environments are associated with a decreased risk of T2DM whereas worse residential environments are associated with an increased risk of T2DM with mediation of some individual-level (physical activity, diet, sleep) characteristics, independent of prominent confounders (age, sex/gender, race/ethnicity, country income level, urbanization, individual socioeconomic status, and family history of diabetes,) [15, 31–34, 36–56, 87, 255].

Previous studies found that living in residential environments with higher levels of pleasant places to walk and green amenities is associated with lower T2DM risk [56] whereas higher levels of socioeconomic deprivation [31], chemical (NO_2, $PM_{2.5}$, persistent organic pollutants or POPs, arsenic and mercury) [56, 255] and noise pollution [56] were associated with increased T2DM risk. Characteristics of studies such as racial and ethnic minorities, low-income adult populations in the United States of America (U.S.A) [31], and urbanisation [255] showed disproportionately higher risk. However, findings across studies often differ markedly regarding the size of effect estimates and sometimes contradict each other concerning the strength of evidence or the direction of the association, depending on the exposure assessment, populations, contexts, and methods used [31, 36, 41, 56, 198, 249–263]. Specifically, food store accessibility and the built environment related to physical activity sometimes showed mixed or limited evidence [56]. These limitations, which inhibit interventions and policy relevance, remain unaddressed in previous reviews with a comprehensive, methodologically rigorous analysis and critical assessment, as we envisage in this review.

This systematic review examines how long-term earlier life exposure to environmental determinants influences the risk of developing T2DM in adulthood. More specifically, it aims: (1) to identify and describe the characteristics and methodological quality of the studies that meet the inclusion criteria, including their design, general characteristics, and risk of bias; and (2) to evaluate the robustness, consistency, and heterogeneity of the associations reported between earlier life environmental exposures and later T2DM risk, in order to assess the overall strength of the evidence, identify potential sources of bias, and clarify policy implications and future research directions.

Methods

Data sources and Searches

Methods for this review are described in greater detail in the protocol prospectively registered on PROSPERO (CRD42023392073) and published [27] following established guidelines: the Joanna Briggs Institute guidelines (JBI), the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA), and the synthesis without meta-analysis (SWiM) framework. A summary of the methods used is provided in the following sections.

Selection Criteria

Previous studies mentioned above support the idea that for EDs to have an impact on T2DM risk, participants must have been exposed to them for several years (up to 15 years) across the life-course, from the foetal stage to adulthood in some cases. Therefore, included studies had to meet the following criteria (1) peer-reviewed or grey literature that reported participants aged 18 or older (this is to avoid confusion with type 1 diabetes, which is more prevalent among the population under 18); (2) at least one ED exposure mentioned in the rationale; (3) at least one relevant outcome (T2DM prevalence or incidence), and a risk estimator as the measure of association. Valid measurement of T2DM prevalence or incidence included clinical diagnosis (fasting plasma glucose – FPG –, glycosylated haemoglobin–A1C–tests, oral glucose tolerance test – OGTT –, 2-hour plasma glucose test–2hPG –, homoeostatic model assessment of insulin resistance levels – HOMA-IR –); diagnostic codes derived from administrative health data (for example, E110 to E119 of the 10th revision of the International Statistical Classification of Diseases and Related Health Problems–ICD-10–);and self-reported T2DM physician diagnosis with concordance analysis published in a peer-reviewed journal [27]. And finally, studies were excluded if no EDs were assessed, the full text was unavailable, or the study was not in French or English.

Search Strategy

References were retrieved from PubMed, Embase, CINAHL Plus, Web of Science, EBSCOhost, and grey literature sources via Laval University Library from January 23 to February 7, 2023, in March 2024, and April 2025. The search strategy, reviewed by three experienced information specialists, combined keywords related to T2DM and EDs (see Supplementary File, Sheet 7) [27]. Two independent reviewers screened all articles (through the title, abstract, and full-text screening stages), and disagreements were resolved by a third reviewer.

Data Extraction Process

One reviewer extracted data in Covidence® using a data extraction table validated by all reviewers (see the section on author contributions below) [27].

Outcome

The primary outcome was T2DM prevalence or incidence, defined as insulin deficiency or hyperglycaemia based on administrative health data, clinical diagnosis or self-reported physician diagnosis with concordance analysis.

Exposures

Given the complexity of EDs, this review attempted to categorise the exposure investigated in included studies based on residential environment dimensions, such as physical environment (characteristics of natural and built environment) and social environment (characteristics of demographic, social and economic environment) [27, 264, 265] as well as exposure assessment methods. This categorisation distinguished exposures such as area-level socioeconomic deprivation [31, 250], cultural norms related to land management [36, 41, 56, 253, 249, 257], food environment, built environment related to physical activity [31, 41, 56, 249, 253], and chemical [56, 198, 249, 252, 254, 255, 258, 261, 262], noise [260], or light pollution [263]. Studies frequently included multiple exposures with different measurement approaches. So, several available effect estimates and evidence-strength indicators were extracted.

Exposures were also categorised according to assessment methods: an objective approach (GIS-based measures, administrative data, or biomonitoring specifically for chemical pollution) and a self-reported approach (survey data on qualitative aspects such as preferences, perceptions, experiences, or feelings).

Other characteristics of studies

For study design, longitudinal associations were defined as those meeting the temporality principle between ED exposure and T2DM [200]. Therefore, it was also stated that the P-value indicates the level of strength of the evidence. Effect measure refers to the adjusted effect estimate. It means the risk of developing insulin deficiency or hyperglycaemia (clinical diagnosis of T2DM). The risk estimator value indicates the level of robustness of the association, as defined by established knowledge [27, 200]. T2DM risk estimators, such as odds ratio (OR), risk ratio (RR), hazard ratio (HR), and prevalence ratio (PR), are the most widely used statistical measures of association in this field of research.

Additional extracted characteristics included author names, language (English, French), publication year (2000–2011, 2011–2021, 2021–2025), source of evidence (peer-reviewed, research report, thesis), study design (Case control, longitudinal, cross-sectional, randomised controlled trial), study area (rural, urban, both or not considered), country income level (high, upper-middle, lower-middle, lower-middle & Low, Low, worldwide), participants, gender (men, women, both or not considered), exposure, exposure assessment (objective, self-reported, both), outcome (incidence, prevalence, both), outcome assessment (administrative health data, clinical diagnosis, SRPD&concordStudy), statistical models (cox, logistic, logistic multilevel, poisson), strength of evidence, and effect measure.

Study Risk of Bias Assessment

A risk of bias (RoB) assessment was carried out in Covidence ® using a 45-item checklist with ‘yes’ or ‘no’ questions, combining the criteria of two recognised, complementary bias assessment tools: the ‘Effective Public Health Practice Project’ (EPHPP) [266] and the ‘Risk of Bias in Non-randomised Studies – of Exposures’ (ROBINS-E) [267, 268]. The EPHPP criteria are more suitable for non-experimental and quasi-experimental studies, while the ROBINS-E criteria are more suitable for observational epidemiological studies. These tools were selected for their complementary coverage of selection, causality, information, confounding, analytical, and inferential biases.

The risk of bias classification of the studies selected for this review was assigned as follows, according to the Public Health Agency of Canada (PHAC) [65], to minimise subjective commentary by reviewers:

—High risk: fewer than 21 positive responses (< 47%).

—Moderate risk: if the study recorded between 21 and 35 positive responses (47–78%).

—Low risk: if the study recorded 35 or more positive responses (≥ 78%).

Data Synthesis and Analysis

A narrative synthesis was performed following the ‘Synthesis Without Meta-Analysis’ (SWiM) guidelines [64, 66, 67]. This review used a T2DM conceptual framework to examine the interconnectedness between EDs, T2DM and some intermediate variables (Study area and Sex/gender) (see the protocol [27]) to describe the association investigated in this review. Therefore, descriptive methods were applied to underscore the reliability of the selection process, the quality of data distribution, and the assessment of associations, using RStudio 2024.12.0 + 467 for graphs, IBM SPSS Statistics 30.0.0.0 (172), and Microsoft Excel and Word 365 for tables.

Description of the selection process

A PRISMA selection flow diagram was extracted from Covidence® to present the number of included studies and to assess whether the selection process was transparent, reproducible, and scientifically credible.

Description of Studies

The distribution of included studies across different characteristics underscores an overview of the circumstances surrounding the evidence. It contributes to establishing the consistency of the association between EDs and T2DM and to interpreting the evidence. To this end, the

characteristics that could affect evidence interpretation or reliability were considered based on previous research and plausibility and presented as frequencies (percentages) in a table by exposure. These characteristics included language, year of publication, source of evidence, study design, exposure assessment, the study area, country income level, gender, outcome, outcome assessment, and statistical model. This table could highlight inequalities, unusual trends, and outliers in data distribution.

Description of risk of bias (RoB)

The RoB statement for included studies contributes to establishing the reliability of the findings. Therefore, the distribution of frequencies (percentages) and pictograms indicating the specific and global RoB statements of the included studies by exposure were used to assess the reliability of the findings.

Assessment of Longitudinal Associations Between EDs and T2DM

Only associations with complete data on robustness (T2DM risk estimator values) and strength of evidence (P-values) were analysed. When the P-value is less than 0.05 (null threshold), the association is considered statistically significant. Otherwise, the association is considered nonsignificant. In addition, T2DM risk estimators (OR, RR, HR, PR) greater than 1 (the null threshold) indicate a positive association, whereas values less than 1 indicate an inverse association.

Then, statistically significant associations by exposures, study design (association type, such as longitudinal and others) and risk of bias (RoB) were presented as frequencies to highlight consistency and reliable evidence. The number in bold indicates the total number of associations, and the number in brackets indicates the study reference number.

Sensitivity Analyses

A sensitivity analysis using descriptive methods (forest plots, clustered, and box plots) [64, 66] and a critical interpretation of the evidence was provided. The purpose was to understand how the dispersion of the P-value and the adjusted effect estimate (Adj_ES) change when using longitudinal rather than cross-sectional associations.

Results

Characteristics of included studies

A total of 169 studies met the inclusion criteria out of 17,755 records initially identified. Overall, 6,339 duplicates were removed, 10,830 records were excluded during the first screening stages (title and abstract), and 412 were excluded at the full-text screening stage (see Fig. 1). Table 1 presents the included studies as frequencies (percentages) according to the main exposures investigated (noting that several studies examined more than one exposure) and the primary study characteristics described above. This table highlights key elements that may influence the consistency or reliability of the evidence. A more detailed description of each characteristic is available in sheet 1 of the Supplementary File.

Firstly, the main exposures investigated among included studies were chemical pollution (56.8%), area-level socioeconomic deprivation (18.9%), cultural norms LM (13.6%), the food landscape (3%), the built environment related to PA (3.6%), noise pollution (2.4%) and light pollution (1.8%). Secondly, the study descriptions also reveal that relatively few studies were conducted specifically in rural (4.1%) or urban (5.9%) residential settings, and that sex-specific analyses remain uncommon, with only 3.5% of studies focusing on women and 0.6% on men.

The distribution of included studies across other characteristics was non-random. Several variables showed marked polarisation, which may have implications for the consistency or the interpretation of the overall evidence.

The first of these concerns relates to the income level of the study setting [68]. Most studies were from high- and upper-middle-income countries (89.9%), particularly those focusing on chemical pollution. The second pattern concerns study design: longitudinal designs predominated among the included studies, particularly in research focusing on pollution, the built environment, and the food landscape (see Table 1). Longitudinal designs with a time-varying [248] outcome and a fixed exposure (VO-FE) were more common. In contrast, studies with a time-varying outcome and a time-varying exposure (VO-VE) were observed only among studies using a geographic information system (GIS)-based exposure assessment. However, most of that group of longitudinal studies were carried out on the same data such as the FinnGen Study [237, 210, 228]; the National Health and Nutrition Examination Survey (NHANES) [237, 102, 158]; the Multi-Ethnic Study of Atherosclerosis (MESA) [236, 106, 99]; the Henan Rural Cohort Study [165, 174, 136, 141, 143, 167, 93]; the UK Biobank [116, 237, 86, 207, 139, 210, 89, 214, 161, 241, 164]; the Maastricht Study [225, 122, 126]; and the Dongfeng-Tongji cohort [131, 132, 176, 135, 213, 133]).

Description of Exposure Metrics of Included Studies

Table 2 presents the distribution of studies by the main exposures investigated and the types of exposure metrics used. Overall, exposure assessments were predominantly (over 50%) based on objective data, including non-georeferenced administrative data, GIS measures, or clinical

diagnoses. In contrast, self-reported data, derived from surveys capturing qualitative aspects such as preferences, perceptions, or experiences, were used less frequently.

Risk of Bias in Studies

Figure 2 describes findings of the RoB assessment. Polarisation is evident in the classification, highlighting several key points. First, no study achieved a 'Low risk' classification. In contrast, eleven studies were classified as 'high risk', particularly those examining the chemical pollution [166, 185, 228, 230, 247] and area-level socioeconomic deprivation [70, 113, 122, 128], indicating room for improvement in rigour in future research. Second, most studies (93.5%) were rated as having a 'moderate risk', particularly those examining the chemical pollution, area-level socioeconomic deprivation, and cultural norm LM, highlighting several areas where interventional adjustments could significantly strengthen future findings. Lastly, among the 'high-risk' studies, the most frequent limitations were biases in information, selection, inference, analysis, and confounding. Similarly, in studies with 'moderate risk', the predominant limitations were biases in inference and analysis.

Information biases include classification and missing data in inferential statistics. Regarding classification, exposure indicators derived from participants' self-reported data may introduce misclassification bias. Although objective exposure assessment is increasing to overcome classification biases and improve the reliability of findings, subjective exposure assessment remains widely used due to its qualitative nature.

Additionally, measuring the frequency of the exposure outcome can introduce reverse causality and classification bias when time is not considered, as is the case in most studies on T2DM prevalence (see Table 1). Finally, 1098 missing P-values and Adj_ES were recorded among 2014 associations. The presence of missing essential inferential statistics may be interpreted as a systematic failure to disclose essential information or reporting bias.

Participant selection bias concerns participation rates. Studies identified in the various exposures investigated very often (except for case-control design studies) either did not report participation rates or reported participation rates below 70%. Among them, several did not discuss the implications of this limitation or possible adjustments (e.g. weighting or sensitivity analyses). This bias is partly likely due to the frequent use of secondary data (Such as the FinnGen Study [237, 210, 228]; the National Health and Nutrition Examination Survey – NHANES – [237, 102, 158]; the Multi-Ethnic Study of Atherosclerosis – MESA – [236, 106, 99]; the Henan Rural Cohort Study [165, 174, 136, 141, 143, 167, 93]; the UK Biobank [116, 237, 86, 207, 139, 210, 89, 214, 161, 241, 164]; the Maastricht Study [225, 122, 126]; the Dongfeng-Tongji cohort [131, 132, 176, 135, 213, 133]). Furthermore, the databases mentioned above were predominantly Chinese or white and from high-income or upper-middle-income countries, suggesting that data production costs may be a prominent factor affecting data availability. This data choice generally affected the participation rate and limited generalisability to other ethnic groups or countries with different income levels.

The reverse causality bias refers to the misinterpretation of associations as causation due to a lack of research on interventions targeting environmental determinants (EDs). It concerns all relationships analysed in observational designs (e.g. cross-sectional or case-control studies), as they do not provide certainty that exposure to an environmental determinant preceded the onset of T2DM, particularly the food landscape. After all, according to spatial commercial logic [199], food retailers, including fast-food outlets, most likely choose to locate where demand is.

Inferential bias concerns statistical models (e.g. logistic regression without a multilevel approach) that involve relatively more ecological or atomistic fallacies, which are most common in studies. In observational studies focusing on complex phenomena, as is the case for most studies included in this review, the research community agrees that the statistical model with the fewest ecological or atomistic fallacies is the multilevel approach [200]. However, in this review, other statistical models that involve relatively more ecological or atomistic fallacies were used in most studies (see Table 1).

Confounding biases and analytical biases concern overestimating or underestimating the effect estimate due to uncontrolled confounding or misuse of interaction terms. In general, and particularly among studies with a high overall risk of bias, it was observed that, except for environmental deprivation, the other exposures investigated in this review were not considered as confounding factors. This bias can lead to overestimating or underestimating the importance of exposure in a model, as was observed in most statistically significant cross-sectional associations.

Association between EDS and T2DM

Table 3 describes the findings regarding associations (robustness and strength of evidence). Complete information is available in Sheet2 of the Supplementary File. The second column of this table shows that 2,014 associations were identified. The third column shows that 279 statistically significant associations remain after excluding 1,098 due to missing data (missing information on adjusted effect estimates or P-values) and 637 due to nonsignificant P-values. The fourth column shows that among statistically significant associations, 69 were longitudinal, while 210 were from other study designs.

Longitudinal Association Between EDS and T2DM

Among longitudinal statistically significant associations, four from two studies [83, 69] were related to the area-level socioeconomic deprivation, three from one study [86] were related to cultural norms LM, four from three studies [69, 84, 108] were related to the food landscape, 44 from 12

studies [76, 140, 151, 161, 177, 186, 207, 214, 223, 238, 242, 246] were related to chemical pollution, five from two studies [241, 242] were related to light pollution, and nine from one study [161] were related to noise pollution. All were rated as having a moderate risk of bias (see Table 3).

Cultural Norms Related to Land Management

It comprises built environmental aspects that preserve human health and well-being, such as green spaces/amenities, or zoning norms that promote the availability, accessibility, and adequacy of these aspects [86]. In this review, as cross-sectional associations (10 among eight studies), three longitudinal associations from one study of the United Kingdom (UK Biobank) [86], showed that long-term exposure to elevated levels of cultural norms related to land management (defined as residential green space) was associated with a lower risk of incident T2DM (HR = 0.984 [0.976–0.992] P-value = 0.001) (see Table 3).

Area-level Socioeconomic Deprivation

Area-level socioeconomic deprivation encompasses aggregate-level measures of socioeconomic characteristics (SEC), such as cohesion, problems, safety, and violence, that may contribute to T2DM through stress, transmission of negative health behaviours, and a lack of social support [69, 83]. Four longitudinal associations from two studies [69, 83] corroborated cross-sectional associations (32 from 10 studies). Longitudinal associations from the first one study showed that exposure over time to higher area-level socioeconomic deprivation (defined as neighbourhood social cohesion) was inversely associated with the incidence of type 2 diabetes mellitus (T2DM) (HR = 0.78, [0.62–0.99] P-value = 0.044) among African American, aged 21–94 years, regardless of gender (the Jackson Heart Study, a USA cohort study) [69]. In addition, longitudinal associations of the second one study, using three associations, showed that increase of cumulative exposure over time to area-level socioeconomic deprivation (defined as safety & social cohesion environment), built environment related to PA (defined as neighbourhood PA resources) and food landscape (defined as neighbourhood healthy food resources) was inversely associated with T2DM incidence among individuals from low-income households (HR = 0.84 [0.70–1.01, P-value = 0.03) or intermediate-income households (HR = 0.97 [0.81–1.15] P-value = 0.03) and positively associated with T2DM incidence among individuals from high-income households (HR = 1.22, [0.98–1.50] P = 0.03). Associations of this second study were observed among individuals aged 45–84 years who self-identified as white, black, Hispanic or Chinese, regardless of gender, in the Multi-Ethnic Study of Atherosclerosis (MESA), a USA cohort study [83]. This study [83] goes beyond the findings of the first [69] by specifying that individuals from low- and intermediate-income households are most sensitive to area-level deprivation.

Food Landscape

The food landscape comprises favourable (low-fat products or fresh fruits and vegetables) [69, 84, 108] and unfavourable (fast food, bakery products, candy/nuts, ice cream, alcohol, and other convenience store products) [69, 108, 109] food stores in the residential environment. In this review, as in one cross-sectional association [109], four significant longitudinal associations from three studies with moderate risk of bias [69, 84, 108] corroborated the prominent role of the food landscape in T2DM risk, regardless of area deprivation status. The first one study with one [69] association investigated was among the participants of the Jackson Heart Study, a USA cohort study mentioned above, the second one [84] with two associations investigated was among the participants of the Multi-Ethnic Study of Atherosclerosis or MESA, a USA cohort study also mentioned above, and the last one with one [108] association investigated was among the participants of three waves (2005, 2007/2008, 2009/2010) combined, of the Canadian community health survey (CCHS) aligned with the timeframe of the 2008 retail food data, the 2006 area-level material deprivation data, and the 2009 walkability data. Findings highlighted that, long-term exposure to neighbourhoods with healthy foods resources assessed using survey -based measures may decrease the risk of developing T2DM (HR = 0.63 [0.42–0.93] P-value = 0.02) [84] while long-term exposure to neighbourhoods with greater density of unfavourable food stores (HR = 1.34 [1.12–1.60] P-value = 0.001) [69] or high number (≥ 3) of fast-food restaurants in neighbourhoods (HR = 1.79 [1.03–3.12] P-value = 0.039) [108] assessed using GIS-based measures may increase the risk of developing T2DM, even though that the first study was among African Americans only [69] while the last one went beyond the first by using a multi-ethnic sample data.

Chemical Pollution

Chemical pollution encompasses never smokers exposed to other people's tobacco smoke [76, 214], chemical air pollutants (contaminants) [140, 177, 186, 223, 242, 246], or a complex mixture of chemical air pollutants [151, 161, 207, 238] measures which are well recognised as major contributors to the T2DM epidemic through various biological mechanism disorders such as metabolic dysregulation, prompt vascular endothelial dysfunction, and insulin resistance. As in cross-sectional associations (166 associations across 44 studies), this review underscored consistent longitudinal associations for chemical air pollutants, environmental tobacco smoke (ETS), and chemical drinking water pollutants (see Table 3 and sheet 2 of the Supplementary File). Most studies assessed exposure using an objective-based method (e.g. GIS or biomonitoring).

Thirty-six longitudinal associations from nine studies using the UK Biobank [151, 161, 207] and Chinese cohort studies [140, 177, 223, 238, 242, 246] found positive associations between chemical air pollutants and T2DM incidence, with Adj_ES ranging from 1.01 to 9.26.

Seven longitudinal associations of two studies using the China Kadoorie Biobank (CKB) [76] and the UK Biobank [214] reported positive associations between the highest levels of ETS and T2DM incidence, with Adj_ES ranging from 1.07 to 1.25.

Lastly, one longitudinal association from the prospective San Luis Valley Diabetes Study (SLVDS) in the USA, among Hispanic and non-Hispanic white participants, found positive associations between chemical drinking water pollutants and T2DM incidence, with Adj_ES ranging from 1.02 to 1.64.

Light Pollution

Light pollution is documented as the average level of nighttime and/or daytime light to which an individual was exposed, based on their one-week light recording [241, 242]. In this review, two studies found that the highest levels of light exposure over time were associated with an increased risk of diabetes. The first one from a cohort established in Yinzhou District, China, showed that increasing exposure to outdoor light at night (LAN) over time was associated with an increased risk of T2DM (HR = 1.22 [1.15–1.30], P-value = 0.001) [242]. The latter study, which used the UK Biobank, goes beyond the first study by including daylight exposure and by combining indoor and outdoor measures in the associations investigated. Findings showed that increasing indoor/outdoor day and night light exposure over time was also associated with an increased risk of T2DM (HR = 1.03 [1.01–1.06], P-value = 0.017) [242].

Noise Pollution

Noise pollution is defined as a weighted average of 24-hour noise, primarily from road traffic, with a 5 and 10 dB penalty applied to evening and nighttime, respectively (Lden) [161]. In this review, as in one cross-sectional association [245], longitudinal associations investigated in the UK Biobank showed that increasing 24-hour road traffic noise (Lden) exposure over time was associated with an increased risk of T2DM (HR = 1.03 [1.00-1.05], P-value = 0.02) [161].

Longitudinal Association Between EDS and T2DM in an Urban Area

According to the study area, 22 studies investigated the urban – rural location differences in several associations between EDs and the occurrence of T2DM (see sheet 2 of the Supplementary File). Fifteen studies found statistically nonsignificant associations, while nine found statistically significant associations, including one study with a longitudinal association [140] and eight with cross-sectional associations [91, 102, 130, 141, 143, 166, 174, 240] (see Table 3). As other associations (except cadmium and Zinc exposure in rural China [166]), finding showed positive longitudinal association between chemical air pollutants exposure and T2DM incidence among participants living in urban area (HR = 1.22 [1.16–1.29] P-value = 0.02) and more among those living in rural area (HR = 1.31 [1.25–1.37], P-value = 0.02) [140]. In contrast, no longitudinal association corroborated cross-sectional findings regarding urban-rural differences in cultural norms related to land management exposure [91]. In addition, no statistically significant longitudinal association was found concerning other exposures (see sheet 2 of the Supplementary File).

Sex or Gender Difference in Longitudinal Association Between EDS and T2DM

Forty studies examined differences between men and women in several associations between EDs and T2DM (see sheet 2 of the Supplementary File). Thirty-six studies found statistically nonsignificant associations, while fourteen found statistically significant associations, including longitudinal [86, 76, 140, 161, 177] and other [70, 102, 115, 122, 174, 189, 205, 232, 235] studies (see Table 3). Findings showed a similar negative longitudinal association between cultural norm-related land management exposure (green space availability) and T2DM incidence among men (HR = 0.99 [0.97–1], P-value = 0.004) and women (HR = 0.98 [0.97–1], P-value = 0.009) participants [86]. Meanwhile, a difference between men (Adj_ES ranging from 1.06 to 1.20) [161, 140] and women (Adj_ES ranging from 1.17 to 1.31) [177, 140] regarding positive longitudinal associations between exposure to chemical air pollutants (mainly atmospheric pollutants) and T2DM incidence was underscored, as in other associations. In contrast, no longitudinal association corroborated cross-sectional findings regarding sex or gender differences in area-level deprivation exposure [70, 115, 122] (see sheet 2 of the Supplementary File).

Sensitivity Analyses

Regarding the comparison of the dispersion of adjusted effect estimates and P-values between longitudinal associations and cross-sectional associations, the sensitivity analysis of the robustness of the association, according to the type of association (FigureS.4.1 in Sheet4 of the supplementary files), shows that the adjusted effect estimate tends to be higher in cross-sectional associations. Similarly, the sensitivity analysis of the strength of the evidence, according to the type of association (FigureS.4.2 in Sheet4 of the supplementary files), shows that the strength of the evidence dispersion tends to be more clustered around 0 in cross-sectional associations and more spread out towards the null threshold in longitudinal associations.

Concerning the identification of whether other study characteristics, beyond biases, also impact the dispersion of adjusted effect estimates and P-values, an examination of the most influential characteristics of studies on the dispersion of the P-value (Sheet 5 of the supplementary files) and the adjusted effect estimate (Sheet 6 of the Supplementary File) was conducted. Overall, the results show greater asymmetry in the dispersion of the P-values than in the adjusted effect estimates. Specifically, findings regarding P-values revealed that more recurrent asymmetric distributions of the strength of the evidence were observed for the outcome, the outcome assessment, the country income level, the study area, and the statistical model used across all exposures investigated, particularly for longitudinal associations. Similarly, findings on adjusted effect estimates showed more recurrent asymmetric distributions for the statistical model, gender, study area, country income level, and the outcome used across all exposures studied, particularly among other association types.

In brief, this result reveals that the dispersion of the adjusted effect estimate and the P-value vary with the distribution of the study characteristics, regardless of the exposure investigated. However, the adjusted effect estimate is less sensitive to study characteristics than the P-value, mainly among longitudinal associations.

Discussion

General interpretation of the results

This systematic review aimed to explore how exposure to the main EDs affects the risk of developing T2DM over time in adults. Accordingly, 169 studies were systematically searched, synopsised, assessed, and analysed following established guidelines (JBI, PRISMA, and SWiM), risk of bias assessment tools (EPHPP, ROBINS-E), and applications (Covidence, RStudio 2024.12.0 + 467, IBM SPSS Statistics 30.0.0.0–172–, Excel and Word from Microsoft365).

Findings from this review of the longitudinal association between T2DM incidence and EDs (except built environment PA) did not contrast with those of previous reviews on the same relationship [31, 36, 41, 56, 198, 249–263]. Previous reviews highlighted the positive longitudinal association between incidence of T2DM and built environment related to food or physical activity [31, 41, 56, 249, 253], chemical pollution [56, 198, 249, 252, 254, 255, 258, 261, 262], light pollution [263], and noise pollution [260]. These previous reviews also highlighted a negative longitudinal association between T2DM incidence and area-level socioeconomic deprivation, mainly among low-income adult populations, women, ethnic or other demographic minorities in high-income countries [31, 250], as well as cultural norms related to land management [36, 41, 56, 253, 249, 257]. Similarly, in this review, longitudinal (and cross-sectional) findings contributed to reinforcing the consistency of previous reviews evidence of this relationship concerning exposures such as cultural norms LM [86], food landscape [69, 84, 108], chemical pollution [76, 140, 151, 161, 177, 186, 207, 214, 223, 238, 242, 246], light pollution [241, 242], noise pollution [161], and area-level socioeconomic deprivation [69, 83]. Socioeconomic deprivation is not only a crucial determinant of health disparities but also a matter of social justice. It highlights the inequities in access to resources that can lead to a higher burden of diabetes, particularly in marginalised communities. The observed extreme Adj_ES size of up to 9.26 regarding chemical air pollutants exposure may raise concerns about its plausibility or the presence of an artefact. However, this association is supported by biological plausibility: higher levels of pollution correlate with more severe health effects [254, 259]. In contrast, no statistically significant association was found regarding the built environment related to physical activity. Regarding the study area and sex/gender differences, three key points were highlighted. A difference was found between participants living in rural areas (HR = 1.31 [1.25–1.37], P-value = 0.02) and those living in urban areas (HR = 1.22 [1.16–1.29], P-value = 0.02) regarding a positive longitudinal association between exposure to chemical air pollutants and T2DM [140]. Another difference between men (Adj_ES ranging from 1.06 to 1.20) [161, 140] and women (Adj_ES ranging from 1.17 to 1.31) [177, 140] regarding positive longitudinal associations between exposure to chemical air pollutants (mainly atmospheric pollutants) and T2DM incidence was underscored. Similar findings were previously underscored [15]. In contrast, no difference was found between men and women regarding the negative longitudinal association between green space availability in the residential environment and T2DM incidence (Adj_ES ranging from 0.98 to 0.99) [86]. Several other statistically nonsignificant associations between exposure to EDs and T2DM incidence or prevalence [41, 56, 250, 252, 256, 260], but without an overall comprehensive quantitative synthesis like this one. However, most of all longitudinal associations were carried out using the same observational data (NHANES, MESA, the Henan Rural Cohort Study, the UK Biobank, the Maastricht Study, the Dongfeng-Tongji cohort) predominantly from Chinese or White participants in high- and upper-middle-income countries, which limits generalisability to other ethnic groups or other income level countries. So, readers of this review should exercise caution regarding the limitations mentioned above when interpreting the results of this study.

Strengths and Limitations

Strengths of this review include adherence to established methodological guidelines (JBI, PRISMA, SWIM), the use of established risk-of-bias assessment tools (EPHPP and ROBINS-E), and a comprehensive synthesis of the evidence. They lend credibility to the methods and findings. Specifically, thanks to the flexibility of its methods (e.g. cross-tabulations, forest plots, box-and-whisker plots), SWIM has enabled summarising and analysing studies with different designs. However, several limitations remain, which can be grouped into two broad categories: limitations of the evidence included in the review (See risk of bias assessment section) and limitations of the review processes used.

This review underscored two primary limitations of the evidence: the first is the predominance of missing data (in inferential statistics such as P-values and adjusted effect estimates), which may be interpreted as a selective reporting bias. Because of this limitation, 1098 associations were excluded from the quantitative synthesis among 2014 associations, which could impact the relevance of findings, specifically among studies focusing on exposures such as the built environment, the noise pollution, and the cultural norms LM, due to a reduction in the possibilities for conducting comparative studies. Moreover, the relatively low ethnic and socioeconomic diversity among study participants, combined with the exclusion of numerous studies due to these missing statistical inference data, may have limited the identification of statistically significant longitudinal studies examining the relationship between T2DM and EDs (excluding chemical pollution), as well as urban-rural or gender/sex differences. The last one is the predominance of studies with moderate or high risk of bias, while no study with low risk of bias was found, as mentioned in the risk of bias assessment section. According to epidemiological established knowledge [200], these biases are frequently observed in cross-sectional and longitudinal observational studies. They can lead to overestimating or underestimating the adjusted effect of the relationship

between EDs and T2DM as observed in the sensitive section. To reduce the impact of these biases, evidence was generated by comparing longitudinal and cross-sectional associations. No other corrective measures were applied to address these limitations in the evidence. We therefore recommend that readers exercise caution concerning the bias mentioned above when interpreting the results of this review.

The last category of limitations is those associated with the review process, including the search strategy and misuse of meta-analysis. They have been widely discussed in the published protocol of this systematic review [27]. First, regarding the search strategy, we observed during the exploration of the electronic databases (PubMed, Embase, CINAHL, Web of Science, EBSCO) that many authors prefer the keyword 'diabetes', although the outcome concerns T2DM. So, we added the keyword 'diabetes' in the search strategy. This change led to approximately 1,500 results per database. More time was allocated to the title and abstract screening stage to address this limitation. We also observed that the selection criteria regarding reliable definition of the outcome (administrative health data, clinical diagnosis or self-reported physician diagnosis with concordance analysis) and the choice of association measures that estimate risk (such as HR, OR, PR…etc.) led to the exclusion of several studies that focused on the relationship between T2DM and EDs at the full-text screening stage. These criteria likely favoured the selection of studies examining pollution exposure, as they are more accustomed to incorporating them into their methodologies. In contrast, studies on other exposures, which are less familiar with these criteria, may have been at a disadvantage during the full-text screening stage of selection. According to previous reviews [31, 56, 198, 254], this limitation is a significant constraint in this field of research. No corrective measures were applied to this limitation, so we recommend that readers exercise caution when interpreting the results of this review. Lastly, a meta-analysis was not included in this research because the methods of the selected studies (e.g. design, exposure, exposure assessments) differed too widely, as mentioned above. So, this review could not define a pooled adjusted effect size or a pooled P-value among the exposures investigated. To address this methodological limitation, we used the SWiM guidelines [66] to identify exposures with more homogeneous study characteristics. In addition, meta-analysis is envisaged as a complementary study among studies with homogeneous characteristics.

Overall, the findings of this systematic review indicate that the hypothesis that long-term earlier life exposure to EDs (such as area-level socioeconomic deprivation, cultural norms, food landscape, chemical pollution, light pollution, and noise pollution) increases T2DM risk is supported by strong evidence. However, it is important to qualify this conclusion by acknowledging that biases and issues of generalisability do temper the conclusiveness of such findings. While the evidence is compelling, caution is advised in interpretation.

How could findings help develop more effective prevention policies?

These findings underscore the crucial role of land management and public health in addressing the T2DM risk. Policymakers should develop cross-sectional interventions (public health and land management) to reduce T2DM risk, including EDs. One of these two directions can be pursued: the first focuses on policy changes that address area-level socioeconomic deprivation, chemical pollution, cultural norms related to land management, the food landscape, or light and noise pollution. For example, regarding chemical air pollutants, one immediate policy lever could be stricter PM2.5 standards. Such regulatory action is critical, as it could lead to significant health benefits by reducing the incidence of T2DM associated with air pollution exposure. The last one is targeted interventions in rural areas or among women regarding chemical air pollutant exposure.

Research Gaps and Research Needs

This review could not define a pooled adjusted effect size or a pooled P-value across all examined exposures, or generalise the significance of these results, due to biases and heterogeneity. Regarding research needs, studies that investigate the relationship between T2DM and long-term earlier life exposure to EDs should be encouraged in low- and middle-income countries, and among ethnic groups other than Chinese or white people, by research financing. More emphasis should be placed on study designs, such as cohort studies and cross-sectional interventions (that involve public health and land management). Concerning RoB assessment findings, convincing researchers to adopt multilevel modelling could enhance study designs by allowing simultaneous tests of associations between T2DM and both individual- and area-level exposures, thereby yielding more nuanced and reliable insights. Finally, meta-analysis studies are eventually hoped, before implementing cross-sectional interventions mentioned above, to provide further knowledge in exposures (area-level socioeconomic deprivation, chemical pollution, cultural norms, food landscape, light and noise pollution) with characteristics (statistical models and outcome assessment should be given special attention) that involve homogeneous robustness of associations or strength of evidence.

In summary, to sharpen focus on future research priorities, several urgent research questions and methodological enhancements should be addressed: First, develop standardised exposure metrics for consistent comparison across studies. Second, prioritise investigating the impacts of EDs across diverse ethnic and socioeconomic contexts, which are often underrepresented in current data. Third, formulate and test interventions in varied environmental and demographic settings to better understand effective preventive strategies. Fourth, foster cohort studies that capture both immediate and long-term EDs impact on T2DM incidence. Lastly, encourage the creation of a comprehensive database incorporating diverse population samples to improve generalisability and relevance.

Other information

Supplementary files:

Supplementary File (including sheets 1 to 8)

Abbreviations

A1C
Glycosylated haemoglobin tests
CINAHL
Cumulated Index to Nursing and Allied Health Literature EDs:Environmental determinations
Embase
Excerpta Medica Database
EPHPP
Effective Public Health Practice Project
ETS
Environmental Tobacco Smoke
FFR
Fast-food restaurants
FPG
Fasting plasma glucose
GIS
Geographic Information System
HOMA-IR
Homoeostatic model assessment of insulin resistance level
HR
Hazard ratio
ICD-10
10th revision of the International Statistical Classification of Diseases and Related Health Problems
IMD
Index of Multiple Deprivation
LAeqN or Lnight
Average night-time noise level
Lden
Average day – evening – night noise level
LST
Land Surface Temperature
MeSH
Medical Subject Headings
NF
Non-fasting
NO2
nitrogen dioxide, a chemical air pollutant
OR
Odds ratio
PA
Physical activity
PECOS
Population, exposure, comparator, outcome, and study designs
PM
Particulate matter (with a diameter of 1 μm or less, 2.5 μm or less, 10 μm or less)
POPs
Persistent organic pollutants
PR
Prevalence ratio
PRISMA
Preferred Reporting Items for Systematic reviews and Meta-Analyses
PROSPERO
The International Prospective Register of Systematic Reviews
RoB

Risk of bias
ROBINS-E
Risk of Bias in Non-randomised Studies of Exposures
RR
Risk ratio
SWiM
Synthesis without meta-analysis
T1DM
Type 1 diabetes Mellitus
T2DM
Type2 diabetes Mellitus
2hPG
2-hour plasma glucose test

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Consent for publication:

Not applicable

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The authors declare that they have no competing interests.

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Authors' contributions:

Yannick Wilfried Mengue (YWM), Alexandre Lebel (AL) and Pierre-Paul Audate (PPA) carried out the collection of bibliographical references, study selection, and quality assessment.

YWM conducted data extraction using a validated data extraction table, with all reviewers agreeing.

YWM, AL and PPA carried out data synthesis.

YWM produced tables and figures.

YWM, AL, and PPA designed and wrote the manuscript.

AL and PPA carried out the critical revision of the manuscript.

YWM, PPA, and AL are the guarantors of this work. They assume responsibility for the integrity of the work.

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Tables

Tables 1 to 3 are available in the Supplementary Files section.

Figures

Exposures	RoB, global statement		RoB, specific statement						N (%)
			A	B	C	D	E	F	
Area-level socioeconomic deprivation	High								4 (12.5)
Built environment PA									1 (16.7)
Food landscape									1 (20.0)
Chemical pollution									5 (5.2)
Total									11 (6.5)
Area-level socioeconomic deprivation	Moderate								28 (87.5)
Built environment PA									5 (83.3)
Cultural norms LM									23 (100.0)
Food landscape									4 (80.0)
Chemical pollution									91 (94.8)
Light pollution									3 (100.0)
Noise pollution									4 (100.0)
Total									158 (93.5)

RoB: Risk of bias
(A) Selection bias
(B) Causality bias
(C) Informatin bias
(D) Confounding bias
(E) Analytical or modelling bias
(F) Inferential bias
N: Frequencies (percent) of included studies

The average number of 'yes' answers is more than or equal to 78%.
The average number of 'yes' answers is less than 78% and more than or equal to 47%.
The average number of 'yes' answers is less than 47%.

Figure 1

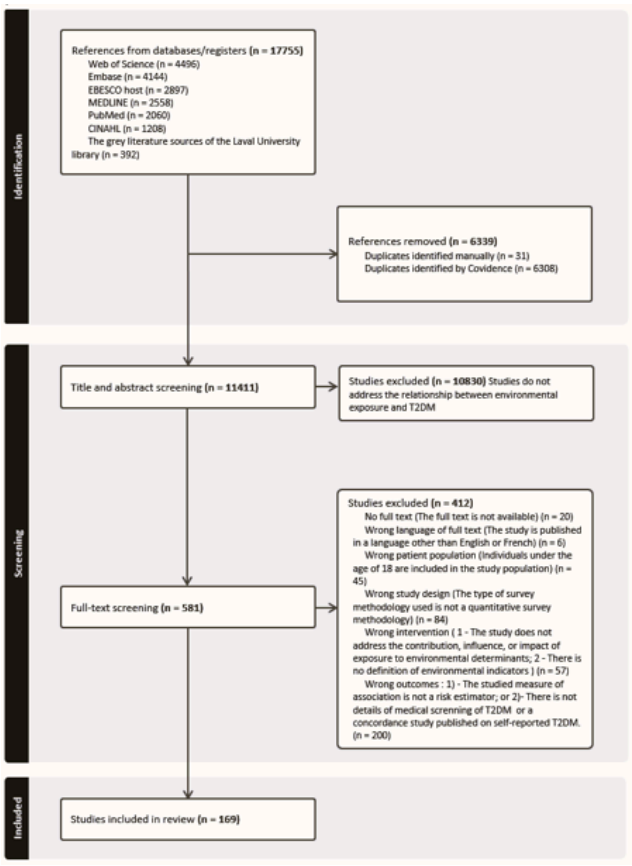


Figure 1

Prisma selection flow diagram

Exposures	RoB, global statement		RoB, specific statement						N (%)
			A	B	C	D	E	F	
Area-level socioeconomic deprivation	High								4 (12.5)
Built environment PA									1 (16.7)
Food landscape									1 (20.0)
Chemical pollution									5 (5.2)
Total									11 (6.5)
Area-level socioeconomic deprivation	Moderate								28 (87.5)
Built environment PA									5 (83.3)
Cultural norms LM									23 (100.0)
Food landscape									4 (80.0)
Chemical pollution									91 (94.8)
Light pollution									3 (100.0)
Noise pollution									4 (100.0)
Total									158 (93.5)

RoB: Risk of bias
(A) Selection bias
(B) Causality bias
(C) Informatin bias
(D) Confounding bias
(E) Analytical or modelling bias
(F) Inferential bias
N: Frequencies (percent) of included studies

The average number of 'yes' answers is more than or equal to 78%.
The average number of 'yes' answers is less than 78% and more than or equal to 47%.
The average number of 'yes' answers is less than 47%.

Figure 2

Distribution of specific and global risk of bias statement

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryFiles.xlsx
- Tables.docx