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REVIEW ARTICLE

Is socio-economic status associated with risk of childhood type 1 diabetes? Literature review

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Abstract

Aims: Studies of social inequality and risk of developing type 1 diabetes are inconsistent. The present review aimed to comprehensively review relevant literature and describe what has been reported on socio-economic status or parental occupation and risk of type 1 diabetes in children.

Methods: We searched for publications between 1 January 1970 and 30 November 2021. We focused on the most recent and/or informative publication in cases of multiple publications from the same data source and referred to these as primary studies.

Results: Our search identified 69 publications with relevant data. We identified eight primary cohort studies with individual-level data, which we considered the highest quality of evidence. Furthermore, we identified 13 primary case–control studies and 14 semi-ecological studies with area-level socio-economic status variables which provided a weaker quality of evidence. Four of eight primary cohort studies contained data on maternal education, showing non-linear associations with type 1 diabetes that were not consistent across studies. There was no consistent pattern on the association of parental occupation and childhood-onset type 1 diabetes.

Conclusions: There is a need for more high-quality studies, but the existing literature does not suggest a major and consistent role of socio-economic status in the risk of type 1 diabetes.

KEYWORDS

environmental factors, incidence, parental education, parental occupation, public health, socio-economic status, type 1 diabetes

1 | INTRODUCTION

The incidence of childhood-onset type 1 diabetes varies widely between countries and the disease tends to be more common in wealthier countries.[1] The incidence has doubled during two to three decades in many countries.[2] Environmental factors, probably operating in early life, are therefore more likely to be involved in the aetiology.[3]

Lower parental socio-economic status has been consistently associated with a variety of lifestyles and exposures hypothesized to be linked to the risk of childhood-onset type 1 diabetes such as maternal and child obesity, smoking in pregnancy, lack of breastfeeding, childhood infections.[4–6] Studies describing risk of developing type 1 diabetes according to socio-economic status can therefore shed light on the aetiology of type 1 diabetes.

The literature linking socio-economic status or parental occupation and risk of type 1 diabetes is sporadic and is rarely mentioned in reviews of risk factors for the disease. A 1982 review suggested higher risk of type 1 diabetes in children from families with higher socio-economic status.[7] In contrast, a 2010 review of type 1 diabetes epidemiology emphasized that there were inconsistent methods and results across studies,[8] and a 2014 review of socio-economic status and autoimmune disease briefly covered type 1 diabetes.[9] An updated review of this topic is lacking.

We, therefore, aimed to comprehensively review relevant literature on the relationship between socio-economic status or parental occupation and the risk of childhood onset type 1 diabetes.

What's new?

- Socio-economic status has been associated with a variety of exposures, but the influence on type 1 diabetes risk is unclear.
- Our search identified eight high-quality and several lower quality studies, mostly using socio-economic status as a confounder. There was no consistent association between socio-economic status and risk of childhood type 1 diabetes. No conclusions could be drawn for specific parental occupations.
- While there is a need for more high-quality studies, the existing literature does not suggest a major and consistent role of socio-economic status in the risk of type 1 diabetes.

2 | METHODS

2.1 | Search strategy and inclusion criteria

We carried out a literature review of socio-economic status and the potential association with incidence of childhood-onset type 1 diabetes. We searched PubMed for publications between 1 January 1970 and 30 November 2021. We searched PubMed using the following search terms: (type 1 diabetes [Title] OR Insulin Dependent Diabetes [Title] OR Insulin-Dependent [Title] OR IDDM [Title] OR childhood diabetes [Title] OR juvenile onset diabetes [Title]) AND (incidence [Title/Abstract] OR incident [Title/Abstract] OR new cases [Title/Abstract]) AND (social class [Title/Abstract] OR socio-economic [Title/Abstract] OR socio-economic [Title/Abstract] OR socio-demographic [Title/Abstract] OR social [Title/Abstract] OR education [Title/Abstract] OR maternal education* OR parental education* OR occupation [Title/Abstract] OR deprivation [Title/Abstract]). We focused on the most recent and/or informative publications in cases of multiple publications from the same data source and referred to these as primary studies. We excluded all studies evaluating the socio-economic consequences of type 1 diabetes. Including pre-existing cases of type 1 diabetes was considered a methodological weakness, especially if socio-economic status variables were only available after diagnosis, because having a child with type 1 diabetes may influence parental socio-economic status. We excluded studies of own specific occupation in relation to development of adult-onset type 1 diabetes, and studies that used parental occupations as indicators of social contact, without showing data for either specific occupations or occupation-based socio-economic status.

We imported the identified articles to the software Covidence© and duplicates were characterized and excluded. We also included articles from our personal reference lists from a previous review[10] and references from review articles from 2010 and 2014.[8,9] In addition, we assessed studies included in previous systematic reviews on risk factors of type 1 diabetes.[11,12] We included studies with data on socio-economic variables and incident type 1 diabetes during childhood (age < 18 years) and focused on the most recent and/or informative publications in cases of multiple publications from the same data source. The reference lists from publications with a main aim of investigating socio-economic status in relation to risk of type 1 diabetes were screened for additional publications. Studies with a minimum of 100 cases of incident type 1 diabetes were included. Both authors screened the articles, and we resolved any disagreements through discussion. Key information was extracted and tabulated as shown in the Tables.

2.2 | Study designs and quality of evidence

Factors influencing quality of non-randomized studies include study design, selection of participants (including controls), measurement of exposure and outcome, and control of confounding. We considered study design most important. Study designs were categorized based on whether individual level childhood socio-economic status or area-based socio-economic status was available, and on whether the study design was cohort, case–control, ecological, or other. Cohort studies with detailed individual level information were considered the highest-level evidence, particularly if based on complete population-based registries. Case–control studies nested within registries, without need for active participation in an interview or

returning a questionnaire, were considered equal level evidence to that of a cohort design. Traditional case–control studies have a number of potential limitations, and even more so for ecological studies (see discussion section). Ecological study designs were considered the lowest quality of evidence. A study was labelled ecological if socio-economic status was only available at area level of residence (even if type 1 diabetes cases were available at the individual level). More details on other aspects of study quality are detailed in the Supporting Information.

3 | RESULTS

After screening 240 titles/abstracts from the PubMed search and excluding the majority due to lack of relevant data, 35 publications with relevant data were assessed in detail. We added 34 additional publications from other sources to a total of 69 publications with relevant data (Figure 1).

Eight primary publications used cohort design (including one large-scale registry-based case–control study considered to be of equivalent quality as cohort) with individual level data on socio-economic status (Table 1). Thirteen primary case–control studies are presented in Table 2. All case–control studies had individual level socio-economic status data (two had area-based socio-economic status in addition). Fourteen primary ecological studies are presented in Table S1.

The majority of studies had not accounted for ethnicity or country of origin, which may lead to confounding. Most cohort and case–control studies included socio-economic status as an adjustment variable, not as a primary study variable. A summary of study quality is presented in the Supporting Information, results section. A meta-analysis was not possible due to heterogeneity of the socio-economic indicators, but major studies were tabulated and characterized in terms of main characteristics and direction of association.[13]

3.1 | Maternal or paternal education in relation to risk of type 1 diabetes

Four of eight primary *cohort studies* contained data on maternal education in relation to risk of type 1 diabetes, showing non-linear associations with the highest risk of childhood-onset type 1 diabetes in the mid (or highest)

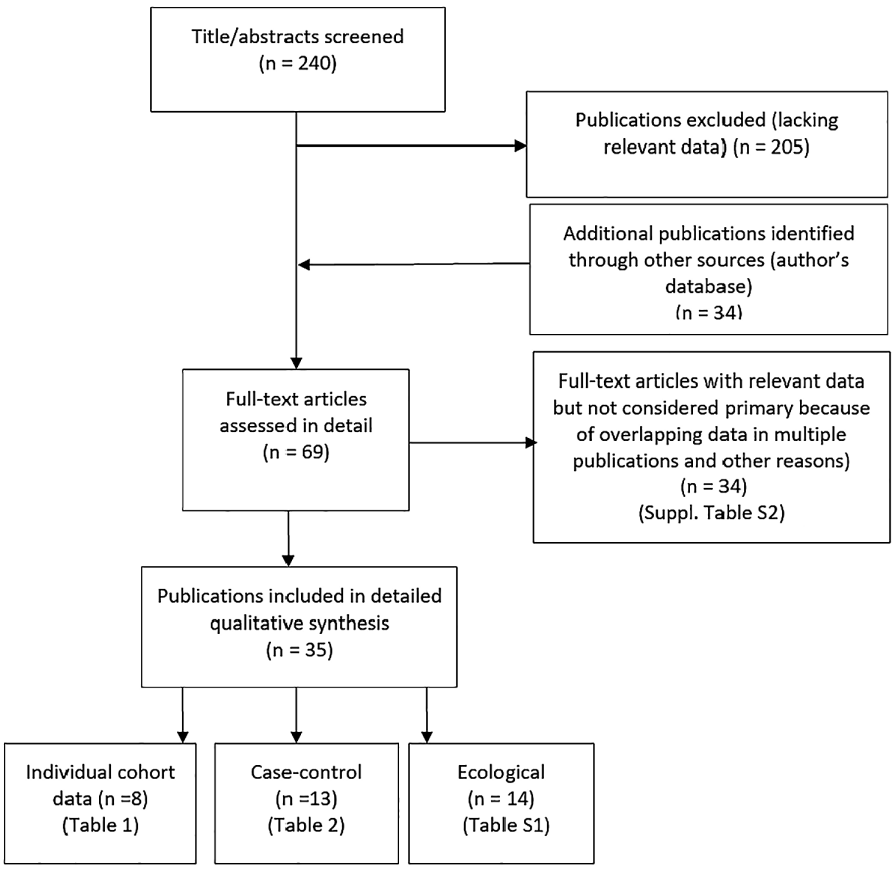

FIGURE 1 Flowchart of literature review.

TABLE 1 Literature review: primary cohort studies of individual level socio-economic status and incidence of type 1 diabetes.[a]

First author, year published (reference)	Period T1D diagnosed	No. w/T1D (age)[b]	Place	SES variables[c]	Direction of association[d]	Results[d]	Comments
Begum 2020[32]	2002–2014	333 (<11 y)	South Australia	Parental employment status, public/private hospital (+ area-based)	+	Both parents employed vs. none: uRR = 1.3 (unclear statistical significance)	Only unadjusted associations shown
Bengtsson 2020[14]	1980–2015	8335 (<35 y)	Denmark	Family poverty (5.5% of cohort), parental long-term unemployment (25% of cohort)	No clear association	RRs 0.94–1.05, not significant	SES part of 'adversities' before age 18, as time-varying
Syrjälä 2019[33]	1996–2018	188 (<15 y)	Finland (Oulu and Tampere)	Maternal education	Non-linear	uRR for highest to lowest mat educ., 1.00, 0.63 (upper vocational), 0.55 (vocational)	Cohort with genetically susceptible children
Clausen 2016[34]	1997–2012	1503 (<15 y)	Denmark	Mat. and pat. educ. at child's birth (incl vocational/occupation)	Non-linear	Highest risk in mid of 3 categories for mat.educ (uRR = 1.13, 95%CI 0.99–1.29), no assoc. with paternal education	Ordering of levels not obvious[e]
Khashan 2015[35]	1973–2009	13,944 (<15 y)	Sweden	Maternal education	Non-linear	Highest risk in mid cat vs. low: uRR = 1.1; high vs. low: uRR = 0.9 (both significant).	uRR calculated from Table 1
Bruno 2013[31]	1984–2007	274 (<15 y)	Italy (city of Turin)	Parental education, crowding	+ (non-linear)	Age 4-14 y: high vs. low par. educ.: RR = 1.67 (mid vs. low: uRR = 0.99). Low vs. high h.hold crowding: RR = 0.83 (95%CI: 0.56–1.22) (educ. and crowding mutually adjusted)	Other ages studied but no significant parental educ. × age interaction
D'Angeli 2010[36]	1992–2005	899 (<19 y)	US (Washington State)	Maternal education	+ (non-linear)	Mat. educ. high (>=13 y) vs. low (<12 y): aRR = 1.9 ($p < 0.05$). Mid (12 y) vs. low: aRR = 1.8.	Assoc. adj. for maternal age and marital status. Mat educ. only for births after 1992
Ievins 2007[37]	1963–1999	348 (<15 y)	UK (Oxfordshire, West Berkshire)	Maternal social class	No clear association	High (I and II) vs. low (IV and V): uRR = 1.2, not significant	20% missing data

Note: u/aRR: Unadjusted (u) or adjusted (a) relative risk (or odds ratio, incidence rate ratio or hazard ratio) comparing higher versus lower socio-economic status. H.hold: Household.

[a]One register-based, large-scale nested case–control study was considered of equal quality as cohort design (D'Angeli 2010). Bruno 2013 was the only publication where investigation of socio-economic status (SES) as a risk factor for type 1 diabetes (T1D) was the main aim, while socio-economic status was only a covariate in Syrjälä 2019, Khashan 2015, and Ievins 2007. The following had accounted for ethnicity by adjustment or restriction: Bengtsson 2020, D'Angeli 2020 and possibly Begum 2020.

[b]Age (years) at diagnosis of type 1 diabetes (T1D) <15 years unless otherwise specified. Cases with available data on socio-economic status are reported.

[c]Socio-economic (SES) variables. Parental educ (education) or occupation refers to highest level within the pair of maternal or paternal education, as opposed to separate data for mat. (maternal) or pat. (paternal) educ.

[d]Comparing higher versus lower socio-economic status (SES). +: increased socio-economic status was associated with higher risk of type 1 diabetes. –: Increased socio-economic status was associated with lower risk of type 1 diabetes. For socio-economic status variables such as deprivation and unemployment mean low socio-economic status. Socio-economic status based on occupation typically used in the United Kingdom is often labelled with roman number I for high social class and III, IV or V refers to lower socio-economic status.

[e]The three levels of maternal and paternal education in Clausen 2016 were labelled 'Elementary school/high school', 'Short education/skilled worker' and 'Medium/long education'. It is not obvious whether skilled worker refers to education or actual occupation, and the ordering of these categories is not entirely obvious.

TABLE 2 Characteristics of 13 primary case–control studies of socio-economic status and T1D.[a]

First author, year published (reference)	Period T1D diagnosed	No. w/T1D (age)[b]	Place	SES variables[c]	Direction of association[d]	Results	Comments
Liese 2012[38]	2003–2006	507 (10-22 y)	US (2 centres)	Parental educ. and income, area characteristics	+	Parental high vs. low educ: uRR = 2.1; high vs. low income uRR = 4.9	Response in eligible controls: ca 20%
Karavanaki 2008[39]	1999–2000	107 (<16 y)	Greece (Athens)	Mat. and pat. educ. and occup	–	Mat. university vs. elem. uRR = 0.1; Pat. univ vs. elem uRR = 0.51, n.s.) Occup socio-economic status not consistent (n.s.)	Also reported socio-economic status but not defined. Small study
Svensson 2005[40]	1996–1999	490 (<15 y)	Denmark	Maternal white collar worker or not	–	Mat. white collar worker (high socio-economic status) vs. not (low): aRR = 0.82 (95%CI: 0.64–1.05)	Response: 81% in cases and ca 48% om controls
Sipetic 2004[41]	1994–1997	105 (<16 y)	Serbia (Belgrade)	Mat. and pat. educ. and occupation	+ (non-linear)	Mat. educ high vs. low: uRR = 1.1 (n.s.) Pat. educ. high vs. low uRR = 1.6 (sign.). Highest T1D risk in mid cat.	Controls hospitalized. Small study. Pat educ. sign. after adjustment in Sipetic 2005[42]
Stene 2003[26]	1997–2000	545 (<15 y)	Norway	Mat. educ.	(−)	Mat.educ highest vs. lowest: aRR = 0.60 (CI: 0.32–1.10)	Response: cases 73%, controls 56%.
Wadsworth 1997[43]	1992	218 (<5 y)	UK and Ireland	Mat. and pat. soc. class	No clear assoc.	Mat. class high vs. low: uRR = 0.89 (n.s.); pat class: uRR = 0.80 (n.s.)	Only <5-year-old children
McKinney 1997[44]	1993–1994	196 (<15 y)	UK (Yorkshire)	Mat. educ. and occup. soc. status	No clear assoc.	Mat educ vs. none: high: RR = 0.84, basic: RR = 0.79 (n.s.). No assoc with mat occup	Nothing to comment
Verge 1994[45]	1990–1991	235 (<15 y)	Australia (New South Wales)	Mat. educ.	–	Mat. educ high vs. none: uRR ca 0.6, p(trend) = 0.06	Response 92% in cases, 55% in controls
Soltesz 1994[46]	1990	130 (<15 y)	Hungary	Mat. educ.	–	Mat educ university vs. not: uOR = 0.59 (p = 0.07)	Friends as controls matched for socio-economic status to some extent
Patterson 1994[47]	1975–1988	529 (<15 y)	N. Ireland and Scotland	Pat. occup. (soc. class)	Inconsistent	High pat. occup. soc. class- > higher T1D in N. Ireland, but n.s. lower T1D in Scotland.	Nothing to comment
Lawler-Heavner 1994[48]	1978–1988	221 (<15 y)	US (Colorado)	Mat. educ., fam. income	–	Mat >high school vs. high school or less: uRR = 0.63 (p = 0.03). fam. income high vs. low: uRR = 0.49 (p[trend] < 0.001)	Results seems inconsistent with overlapping data in Mayer 1988 (Table S2).

(Continues)

TABLE 2 (Continued)

First author, year published (reference)	Period T1D diagnosed	No. w/T1D (age)[b]	Place	SES variables[c]	Direction of association[d]	Results	Comments
Virtanen 1991[49]	1988–1989	103 (<7y)	Finland	Mat. educ.	–	>13 y of educ vs. <=13 y: uRR = 0.51, $p = 0.04$	Response 95% in cases, 54% in controls. Small study.
Blom 1989[50]	1985–1986	339 (<15y)	Sweden	Mat. and pat. educ. and occup.	–	Mat university vs. elementary: uRR = 0.66 ($p < 0.05$) (pat educ. similar but n.s.). Pat self-employed vs. manual: uRR ca 0.7–0.8	Response 86% in cases, 67% in controls

Note: u/aRR: Unadjusted (u) or adjusted (a) relative risk (or odds ratio, incidence rate ratio or hazard ratio) comparing higher versus lower socio-economic status (SES). Often calculated from characteristics tables in publications. Socio-economic status: Socio-economic status.

[a]Case–control studies where controls (and typically also cases) were invited to participate for data collection via questionnaire (10 studies) or interview (two studies: McKinney 1997 and Liese 2012). Patterson 1994 used information from health records. All studies typically have less than complete participation, and lower participation among controls than among cases was quite common.

[b]Age (years) at diagnosis of type 1 diabetes (T1D) <15 years unless otherwise specified. Cases with available data on socio-economic status are reported.

[c]Socio-economic (SES) variables. Parental educ (education) or occupation refers to highest level within the pair of maternal or paternal education, as opposed to separate data for mat. (maternal) or pat. (paternal) educ.

[d]+: increased socio-economic status was associated with higher risk of type 1 diabetes. –: Increased socio-economic status was associated with lower risk of type 1 diabetes. Lower level of deprivation and unemployment means higher socio-economic status. Socio-economic status based on occupation typically used in the United Kingdom is often labelled with roman number I for high social class and III, IV or V refers to lower socio-economic status.

of three categories of maternal education in one, and a U-shaped association in one study (Table 1).

Of 14 primary *case–control studies*, nine contained data on maternal education, two on paternal education and one on parental education (highest of maternal or paternal education). Of the nine studies with maternal education, six reported inverse association, and the remaining showed no clear association. Of two studies with paternal education, one showed a positive and the other no significant association with type 1 diabetes (Table 2).

3.2 | Parental income and risk of childhood onset type 1 diabetes

None of the primary *cohort studies* reported associations for parental income (main Table 2). Parental employment status (both parents working, only father, only mother or neither), use of public versus private hospital were reported by Begum et al. in South Australia, showing a slightly but significantly higher risk associated with higher socio-economic status. In a Danish study, family poverty (5.5% of cohort), parental long-term unemployment (25% of cohort) was not significantly associated with childhood-onset type 1 diabetes.[14]

Two of the 14 primary *case–control studies* contained data on parental or family income, both from the United States, and results showed associations in the opposite direction (Table 2).

3.3 | Area-based socio-economic status in relation to type 1 diabetes incidence

Details regarding methodological aspects and composite indices used in area-based studies are described in Supporting Information results section. Five of the 14 primary studies analysing area-based based socio-economic status in relation to type 1 diabetes incidence found a positive relation, while one found a clear inverse relation (Patterson 1991) and the remaining found no clearly significant associations or suggestive non-linear associations (Table S1).

3.4 | Occupation-derived socio-economic status and risk of childhood type 1 diabetes

One primary cohort study reported maternal social class based on occupation and found no significant association. Two studies of parental unemployment are reported in the section on parental income above.

Of the 14 primary case–control studies, six reported social class according to maternal occupation, and six according to paternal occupation, and there was no clear association with childhood-onset type 1 diabetes in these (Table 2).

A limited number of studies of specific maternal or paternal occupations or other socio-economic indices in relation to risk of type 1 diabetes are presented in the Supporting Information, results section.

4 | DISCUSSION

There were remarkably few high-quality studies relating socio-economic status or parental occupation to childhood onset type 1 diabetes. Many studies reported non-linear associations, and there was little or no consistency across studies, even among the highest quality studies.

Many health aspects are well known to be associated with low socio-economic status, including child mortality.[15] However, we should not take for granted that all aspects of health are caused by or predicted by low socio-economic status. Social inequality in child health represents separate methodological challenges, and it is important to differentiate between studies of objective health outcomes that are not likely to be influenced by parents' reports or behaviour that may influence the likelihood of their child receiving a diagnosis, which may create bias in studies of child health. A previous review of childhood leukaemia risk documented methodological weaknesses and inconsistencies in the literature similar to what we have documented here for type 1 diabetes.[16] It is possible that aspects of socio-economic status have context-dependent effects. A study of city dwellers in high-income European countries reported higher circulating levels of several environmental chemical contaminants in children and their mothers with higher socio-economic status.[17]

Childhood type 1 diabetes is a well-defined disease for which underdiagnosis is not a likely problem, at least in middle- and high-income settings. It is well documented that low socio-economic status is associated with suboptimal glycaemic outcomes and co-morbidities in people with type 1 diabetes.[18,19] However, the latter is an entirely different research question than what we have addressed in the current review.

4.1 | Interpretation

Socio-economic status variables may have different meanings and interpretations in different locations and at different times. For health outcomes in children, it is the parental socio-economic status that is relevant. Education, occupation and income have traditionally been the most frequently used measures in epidemiology.[20,21] Occupation has traditionally been used in some countries to categorize families into groups of social status. Specific parental occupations may serve as indicators of exposures, including prenatal exposures, that may provide clues to the aetiology of type 1 diabetes. For instance, studies in asthma and allergy have suggested that farm living is associated with a lower risk of these outcomes.[22] Teachers or health workers are typically frequently exposed to infections.[23,24] Industrial workers may be exposed to toxic chemicals.[25] Further studies in the field of parental occupational exposures are warranted.

4.2 | Methodological weaknesses in published studies

Several methodological weaknesses were apparent in most studies assessed. Registry-based case–control studies typically do not require consent or active participation, or at least consent and/or participation in data collection is done before the disease outcome and hence similarly for cases and controls. On the other hand, traditional case–control studies require active participation and usually involve collection of data at or after diagnosis of cases with type 1 diabetes. Participation is always lower than 100%, biased towards participants with higher socio-economic status and differentially so in cases and controls because of a typically lower participation among controls than cases.[26,27] Severe selection and/or recall bias is therefore often present in case–control studies of socio-economic status and type 1 diabetes. Many studies with a main aim of relating socio-economic status to type 1 diabetes had used area-based socio-economic status. Ecological studies are vulnerable to distinct biases that cannot be mitigated by adjustment for confounding.[28] The larger and more heterogeneous the geographical area on which an individual's socio-economic status is attributed, the larger the potential for very strong biases that may even reverse the direction of associations or causal effects existing at the individual level.

Only three of the eight cohort studies had accounted for immigration/ethnicity by restriction or adjustment. The general lack of adjustment for ethnicity and immigration status in most studies also represents an important problem when attempting to interpret the literature.[2] We excluded studies with prevalent type 1 diabetes, as development of type 1 diabetes in a childhood may influence parental socio-economic status.[29]

4.3 | Practical implications for future studies

Given the relatively weak and inconsistent associations between socio-economic status and risk of type 1 diabetes documented here and the many layers of methodological problems discussed above, additional ecological studies are not likely to advance the field. Future studies should aim for prospective designs, possibly registry-based studies with complete population coverage. Furthermore, large sample size is important for sufficient power to detect the likely weak to moderate strength of associations, or conclusively rule out associations. We further recommend to avoid categorizing indicators of socio-economic status too broadly, and to allow for potential non-linear associations in the analysis. Finally, use of clearly defined individual level socio-economic status indicators (area-based indicators) could be used together with individual level indicators in multilevel analyses.[30]

4.4 | Strengths and limitations of the review

We have comprehensively reviewed a broad literature that was scarce and sometimes difficult to identify because socio-economic status was not necessarily part of the main aim of the study. Most studies were from middle- or high-income countries. We limited our review to childhood-onset type 1 diabetes to make interpretation of parental socio-economic status most relevant. Type 1 diabetes may occur at any age, and socio-economic status may have different effects in young adults. While a few studies have also included young adults (e.g. Bruno[31]), the person's own indicator of socio-economic status may become increasingly relevant with increasing age. As opposed to a formal systematic review which usually requires searches in two or more literature databases, we limited our search to PubMed. While this provides a transparent and reproducible approach, we cannot exclude the possibility that a few studies may have been missed. Given the sparse and inconsistent literature we identified, we believe that missed studies are unlikely to severely influence our conclusions.

4.5 | Conclusion

We conclude that there is a need for more high-quality studies and that the existing literature does not suggest a major and consistent role of socio-economic status as a risk factor for the development of type 1 diabetes.

AUTHOR CONTRIBUTIONS

Lars C. Stene conceived the idea of the work. Lars C. Stene and Paz Lopez-Doriga Ruiz were involved in the acquisition, analysis and interpretation of the work and drafted the work.

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CONFLICT OF INTEREST STATEMENT

All authors declare no competing interests.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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