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RESEARCH ARTICLE

Relative poverty is associated with increased risk of diabetic ketoacidosis at onset of type 1 diabetes in children. A Swedish national population-based study in 2014–2019

Johan H. Wersäll[1] | Jan Ekelund[2] | Karin Åkesson[3] | Ragnar Hanas[4] | Peter Adolfsson[4] | Sven-Erik Ricksten[1] | Gun Forsander[4]

[1]Institute of Clinical Sciences, Department of Anaesthesiology and Intensive Care, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

[2]Centre of Registers, Gothenburg, Sweden

[3]Division of Paediatrics, Department of Biomedical and Clinical Sciences, Linköping University, Linköping, Sweden

[4]Institute of Clinical Sciences, Department of Paediatrics, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

Correspondence
Johan H. Wersäll, Institute of Clinical Sciences, Department of Anaesthesiology and Intensive Care, The Sahlgrenska Academy, University of Gothenburg, 413 45 Gothenburg, Sweden.
Email: johan.wersall@gu.se

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Abstract

Aims: The aim of the study was to estimate the effect of household relative poverty on the risk of diabetic ketoacidosis at diagnosis of children with type 1 diabetes using an international standard measurement of relative poverty.

Methods: A national population-based retrospective study was conducted. The Swedish National Diabetes Register (NDR) was linked with data from Sweden's public statistical agency (Statistics Sweden). Children who were diagnosed with new-onset type 1 diabetes in the period of 2014–2019 were common identifiers. The definition of diabetic ketoacidosis was venous pH <7.30 or a serum bicarbonate level <18 mmol/L. The exposure variable was defined according to the standard definition of the persistent at-risk-of-poverty rate used by the statistical office of the European Union (Eurostat) and several other European public statistical agencies. Univariate and multi-variable analyses were used to calculate the effect of relative poverty on the risk of diabetic ketoacidosis.

Results: Children from households with relative poverty had a 41% higher risk of diabetic ketoacidosis (1.41, CI 1.12–1.77, $p = 0.004$) and more than double the risk of severe diabetic ketoacidosis (pH <7.10) (RR 2.10, CI 1.35–3.25, $p = 0.001$), as compared to children from households without relative poverty.

Conclusions: Relative poverty significantly increases the risk of diabetic ketoacidosis at onset of type 1 diabetes in children, even in a high-income country with publicly reimbursed health care.

KEYWORDS
children, education level, ketoacidosis, new-onset diabetes, socio-economic status, type 1 diabetes

1 | INTRODUCTION

Diabetic ketoacidosis is a preventable acute complication of type 1 diabetes. If insulin treatment is initiated at a sufficiently early stage, diabetic ketoacidosis will not develop. Public awareness, a low threshold for glucose tests when seeking medical attention, and early referral among general practitioners can potentially decrease the incidence of diabetic ketoacidosis at the onset of type 1 diabetes.[1,2] This has been shown in some studies.[3]

Socio-economic status (SES) has been associated with health and disease in various publications.[4–6] Several studies have demonstrated associations between low SES and a higher risk of diabetic ketoacidosis and higher HbA1c levels.[6–8] However, as there is no clear and universal definition of SES, it should rather be regarded as an umbrella term for various aspects of the economic, social, demographic and other coping resources that an individual has in Society, for example disposable income and education level. Economic status at the individual or household level can be measured in several ways.[9] Many public agencies, such as Eurostat (the European Union's statistical office), the Office for National Statistics (United Kingdom) and Statistics Sweden (Sweden's public statistical agency), use the term 'persistent risk of poverty' or similar terms to describe a household whose equivalised (weighted) household disposable income is less than 60% of the national median during an index year and during at least two of the three preceding years.[10–12] This is a relative measurement and does not imply that a household or an individual necessarily lives in absolute poverty. However, it facilitates comparisons between countries and populations, and a persistent risk of poverty as defined above has been associated with adverse health status in various publications.[13,14]

Sweden is one of the countries with the highest incidence of type 1 diabetes worldwide. Approximately one-fifth of all children with new-onset type 1 diabetes have diabetic ketoacidosis at the time of diagnosis, and this proportion has been relatively stable for the last two decades.[15] Sweden is also one of the countries with the highest gross domestic product (GDP) per capita, with totally reimbursed public health care for all children. Economic inequalities are usually presumed to be low. Nonetheless, nearly 10% of the population lives with a persistent risk of poverty during a given year since 2014.[11]

The aim of this study was to estimate the effect of an international standard measurement of relative poverty on the risk of diabetic ketoacidosis for children with new-onset type 1 diabetes.

what's new?

What is already known?

- Socio-economic factors are associated with metabolic control in children with type 1 diabetes.

What has this study found?

- Household relative poverty, measured with an established international standard, is associated with a 41% increase in the risk of diabetic ketoacidosis at diabetes diagnosis.

What are the implications of the study?

- Active support from the diabetes team is important for economically vulnerable families. External, international validation of the findings is warranted, to increase understanding of the risk factors for diabetic ketoacidosis in cases of new-onset diabetes type 1 and to identify ways to lower the rates of this complication.

2 | METHODS

2.1 | Ethics statement

Permission for conducting this study was granted by the Swedish Ethical Review Authority (no. 2019–03600), which also granted a complete waiver of informed consent. Statistics Sweden substituted personal identification data with random-generated numbers for each individual. Identifiers for personal data are retained by Statistics Sweden, and the data used in this study were anonymised for the researchers.

2.2 | Study design

This was a retrospective cohort study of children (age range, 9 months to <18 years) with new-onset type 1 diabetes registered in Sweden between 1 January 2014 and 31 December 2019. Two databases were linked using the Swedish personal identity numbers to match children from both databases. The longitudinal integrated database for health insurance and labour market studies (LISA) was used to acquire data on parental education level, household equivalised (weighted) disposable income, parental cohabitation and foreign or Swedish background of the child.[16] The Swedish National Diabetes Register (NDR) was used to obtain data on sex, age, venous pH level, serum bicarbonate level and the date of diagnosis of diabetes.

2.3 | Eligibility for participation

Inclusion criteria were children aged 9 months to <18 years with new-onset type 1 diabetes in Sweden and hospital admission registered in the NDR between 1 January 2014 and 31 December 2019. The start date was chosen because the current method for calculating equivalised disposable income is valid from 2011 and onwards, and the study design required economic data from 3 years preceding the year of diagnosis. The end date was chosen to avoid uncontrolled confounding effects from the SARS-CoV-2 pandemic. The exclusion criteria were missing pH levels and serum bicarbonate values. Figure 1 presents a flow chart that shows the inclusion and exclusion procedures used for the study.

2.4 | Variables

2.4.1 | Diabetic ketoacidosis (Outcome variable)

Diabetic ketoacidosis was defined as venous pH <7.3 or serum bicarbonate level <18 mmol/L in the case of missing pH values, according to the current definition listed in the Clinical Practice Consensus Guidelines from the International Society for Pediatric and Adolescent Diabetes (ISPAD).[17]

2.4.2 | Relative poverty (Exposure variable)

The exposure variable had two categories (relative poverty or no relative poverty) and was defined according to the standard definition of the term 'persistent at-risk-of-poverty'(synonymously called 'persistent risk of poverty') used by Statistics Sweden, Eurostat, and the Office for National Statistics.[10–12,18] This term describes an equivalised disposable household income that was less than 60% of the national median during an index year, and during at least 2 of the 3 years preceding the index year. The term 'equivalised' means weighting for additional household members.

In this study, a child was considered to live in relative poverty if the equivalised household income was less than 60% of the national median for the entire time during the 3 years preceding the year of diagnosis of type 1 diabetes. If the parents were living in separate households, the equivalised disposable incomes from each household were summed and divided by two, under the assumption that parents in Sweden generally contribute equally to the support and welfare of their children. Disposable incomes for the period of 2011–2018 were adjusted for inflation with the index year set to 2019.

2.4.3 | Parental education level

In the LISA database, education level is comparable to the World Health Organization's ISCED standard.[16] The LISA database registers nine different levels, where: Level 1, <9 years of primary school; Level 2, 9 years of primary

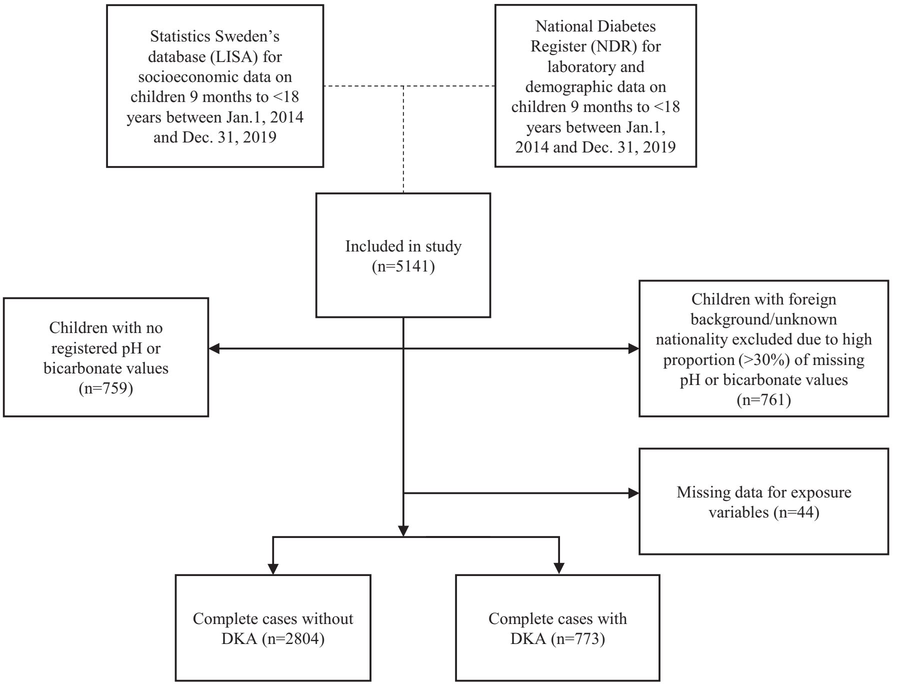

FIGURE 1 Flow chart describing the inclusion and exclusion procedures for analysis of the effect of persistent risk of poverty on the probability of diabetic ketoacidosis for children with new-onset type 1 diabetes. Data were collected for children aged 9 months to <18 years registered for type 1 diabetes between 1 January 2014 and 31 December 2019.

school; Levels 3–4, secondary school; Levels 5–8, tertiary education (university, military academy, college, doctoral studies, etc.); and Level 9, data not retrieved. In this study, educational background was aggregated into three categories: Levels 1–2, primary; Levels 3–4, secondary; Levels 5–8. tertiary. Level 9 was assigned as missing information. The parent with the highest education level was designated as the highest parental education level.

2.4.4 | Cohabiting parents

In the LISA database, parents share the same Family ID if they live at the same address. Therefore, cohabiting parents were defined as those consecutively sharing the same Family ID for the 3 years preceding the year of diagnosis of type 1 diabetes. It was not possible from the data to determine with whom the child lived if the parents were not cohabiting. However, a survey conducted in 2019 by Statistics Sweden estimated that approximately one third of all children with non-cohabiting parents spend equal amounts of time with both parents ('shared parenting').[19]

2.4.5 | Age of the child at diagnosis

Age was available as a continuous variable in years and months. However, it is known that the rate of diabetic ketoacidosis at onset of type 1 diabetes is highest in the youngest children (aged 9–24 months), while children aged 2–4 years have comparatively low rates.[15] In this study, age was therefore divided into the same categories as used by the NDR (9–24 months, 2–4 years, 5–9 years, 10–14 years, 15–17 years).[15]

2.4.6 | Foreign background

The Swedish formal definition of foreign background is birth outside Sweden, or both parents born outside Sweden.[20] Socio-economic heterogeneity was anticipated to a large extent in this group of children, since 'foreign' by definition can mean any country outside Sweden.

2.5 | Missing data

Assumptions were made regarding the mechanisms underlying the missing outcome data. In principle, these mechanisms were defined as: Missing Completely At Random (MCAR; missing data for a random subset of the population); Missing At Random (MAR, missingness related to one or more observed explanatory variables); Missing Not at Random (MNAR; the outcome itself is a source of missingness).[21] The a priori assumption was that the missing outcome values would be of the MCAR type. A complete cases analysis was planned, as low rates of missing data were expected for all the exposure variables due to the high-level coverage of the data from Statistics Sweden.

2.6 | Statistics

The Stata statistical software release 17 (StataCorp LLC, College Station, TX, USA) was used for all tables, analyses and calculations. For descriptive purposes, *N* and % were presented for the categorical variables. The aim was to estimate the risk of diabetic ketoacidosis for children in relative poverty, as compared to children not in relative poverty, for all children admitted to hospital for new-onset type 1 diabetes. Towards this aim, the average treatment effect (ATE) for all the subjects was estimated and generalised linear models for the binomial distribution with a log link were built for calculations of relative risks, with associated 95% confidence intervals and *p*-values using a robust estimate of the variance.[22] The assumed causal relationships are described in Figure S1. All tests were two-tailed, and the significance level was set to 0.05.

3 | RESULTS

The total number of children registered with a diagnosis of type 1 diabetes during the study period was 5141, of whom 4190 (81.5%) had registered venous pH levels and/or serum bicarbonate values. Of the children with registered values, 954 (22.8%) had diabetic ketoacidosis. Children with non-foreign and foreign backgrounds differed considerably regarding the proportion of missing values for the primary outcome (16.5% vs 30.4%). The assumption that the missing values for the primary outcome were MCAR in the whole study population was abandoned because foreign background likely caused MAR (missing values associated with foreign background). Children with foreign background were excluded from further analyses, after which the assumption of MCAR as the mechanism for missing values was retained for the remainder of the population. The missing data for children with non-foreign background are listed in Table S1. A flow chart of the inclusion and subsequent exclusion steps is presented in Figure 1.

The background characteristics across the exposure variable are presented in Table 1. For the sex and age categories, no clear differences were seen between

TABLE 1 Background demographic characteristics of the Swedish children aged 9 months to <18 years with persistent risk of poverty[a] registered in Sweden with new-onset diabetes type 1 between 1 January 2014 and 31 December 2019. Children with foreign background[b] are excluded.

	Subjects with persistent risk of poverty, *N* (%)		
	No	**Yes**	**Total**
N	4045 (94.2)	248 (5.8)	4293 (100.0)
Sex			
Male	2222 (56.4)	122 (50.6)	2344 (56.1)
Female	1718 (43.6)	119 (49.4)	1837 (43.9)
Age category			
9 months–1 year	177 (4.4)	7 (2.8)	184 (4.3)
2–4 years	579 (14.3)	33 (13.4)	612 (14.3)
5–9 years	1272 (31.5)	93 (37.7)	1365 (31.8)
10–14 years	1516 (37.5)	86 (34.8)	1602 (37.3)
15–17 years	499 (12.3)	28 (11.3)	527 (12.3)
Parental education level			
Primary	50 (1.2)	31 (12.5)	81 (1.9)
Secondary	1443 (35.7)	141 (56.9)	1584 (36.9)
Tertiary	2549 (63.1)	76 (30.6)	2625 (61.2)
Parents cohabiting			
No	852 (21.2)	113 (45.9)	965 (22.6)
Yes	3168 (78.8)	133 (54.1)	3301 (77.4)

[a]Persistent risk of poverty is defined as a household with weighted disposable income <60% of the national median for the 3 years preceding the year of diagnosis of type 1 diabetes.

[b]Foreign background is formally defined as being born outside Sweden and/or having all parents born outside Sweden.

children with or without relative poverty. Parental education level and parental cohabitation showed substantial between-group differences. There was a numerically higher proportion of children with relative poverty in households with lower levels of education (primary education level): 12.5% versus 1.2%. The proportion of children with non-cohabiting parents were numerically higher in the group with relative poverty: 46% versus 21%.

The background data across the outcome (diabetic ketoacidosis vs non-diabetic ketoacidosis) are presented in Table 2. Assumptions as to the causal pathways for these children are illustrated in Figure S1. The proportion of diabetic ketoacidosis across the sex and age categories followed the patterns seen in the annual reports from the NDR, that is no differences noted between males and females, the largest proportion of diabetic ketoacidosis being seen for children aged 9 months to <2 years (41.4%), and the smallest proportion of diabetic ketoacidosis being seen in children aged 2 to <5 years (10.1%) (Table 2).

Diabetic ketoacidosis appeared more frequently among children from households with the lowest parental education level (28.6%), as compared to children from households with the highest parental education level (21.2%) (Table 2).

Furthermore, diabetic ketoacidosis was observed more commonly for children from households with non-cohabiting parents (24.8%) than for children from households with cohabiting parents (20.6%). (Table 2).

The proportion of children with new-onset type 1 diabetes and diabetic ketoacidosis was substantially larger in households in relative poverty. Thus, the proportion of children in relative poverty and diabetic ketoacidosis at hospital admission was 30.0%, as compared to 21.1% for the children not living in relative poverty.

The assumption of causal relationships depicted in Figure S1 was retained after tabulations of the background variables across the exposure variable (Table 1) and the background variables across the outcome variable (Table 2), which indicated possible confounding effects from: age at diagnosis, parental education level and parental cohabitation status.

Complete cases analyses were performed. A univariate analysis showed an association between relative poverty and diabetic ketoacidosis (RR 1.41, CI 1.13–1.76, $p = 0.002$). In the multi-variable analysis with adjustments for sex, age, parental level of education and parental cohabitation, the risk of diabetic ketoacidosis at diagnosis was 41% higher for children living in relative poverty than for those not in relative poverty (RR 1.41, CI 1.12–1.77, $p = 0.004$). The interaction between parental education level and poverty status was not statistically significant ($p = 0.72$).

A sensitivity analysis was performed, comparing the complete cases multi-variable model with a model that included the International Classification of Diseases (ICD) codes E10.0 (type 1 diabetes with coma) and E10.1 (type 1 diabetes with acidosis), to complement the diabetic ketoacidosis cases. Cases that were not categorised as diabetic ketoacidosis in the NDR and that were not coded E10.0 or E10.1 were categorised as non-diabetic ketoacidosis, and missing data for the exposure variables were included as categories in the equation. No substantial differences were seen between this model and the complete cases model (Table S2).

Among the children from households with relative poverty, the risk of moderate to severe diabetic ketoacidosis (pH <7.20 or serum bicarbonate <10 mmol/L) was 76% higher (RR 1.76, CI 1.31–2.37, $p = 0.001$), and the risk of severe diabetic ketoacidosis (pH <7.10 or serum bicarbonate <5 mmol/L) was more than double (RR 2.10, CI 1.35–3.25, $p = 0.001$), compared to children not in relative poverty.

	Subjects, N (%)		
	Without diabetic ketoacidosis	With diabetic ketoacidosis	Total
N	2871 (78.5)	787 (21.5)	3658 (100.0)
Sex			
Male	1599 (78.3)	442 (21.7)	2041 (100)
Female	1272 (78.7)	345 (21.3)	1617 (100)
Age category			
9 months–1 year	95 (58.6)	67 (41.4)	162 (100)
2–4 years	465 (89.9)	52 (10.1)	517 (100)
5–9 years	987 (84.6)	179 (15.4)	1166 (100)
10–14 years	992 (72.6)	374 (27.4)	1366 (100)
15–17 years	331 (74.2)	115 (25.8)	446 (100)
Parental education level			
Primary	50 (71.4)	20 (28.6)	70 (100)
Secondary	1051 (78.3)	291 (21.7)	1342 (100)
Tertiary	1768 (78.8)	476 (21.2)	2244 (100)
Parents cohabiting			
No	601 (75.2)	198 (24.8)	799 (100)
Yes	2213 (79.4)	575 (20.6)	2788 (100)
Persistent risk of poverty[b]			
No	2675 (78.9)	717 (21.1)	3392 (100)
Yes	145 (70.0)	62 (30.0)	207 (100)

[a]Foreign background is formally defined as being born outside Sweden and/or having all parents born outside Sweden.

[b]Persistent risk of poverty is defined as a household with weighted disposable income <60% of the national median for the 3 years preceding the year of diagnosis of type 1 diabetes.

TABLE 2 Background demographic characteristics of the children aged 9 months to <18 years without and with diabetic ketoacidosis at onset of type 1 diabetes, registered in Sweden between 1 January 2014 and 31 December 2019. Children with foreign background[a] are excluded.

3.1 | Children with foreign background

In the study cohort, there were 440 children with foreign background, 33% of whom had diabetic ketoacidosis at hospital admission. No difference was seen in the proportions of children with diabetic ketoacidosis between households in relative poverty (31%, $N=42$) and those not in relative poverty (30%, $N=58$). Diabetic ketoacidosis was more common in households with primary education level (39%, $N=30$), less common in households with secondary education level (33%, $N=45$) and least common in households with tertiary level of education (29%, $N=56$). There were only small differences in the proportions of children with diabetic ketoacidosis between households with cohabiting (32%, $N=96$) and non-cohabiting parents (29%, $N=21$).

4 | DISCUSSION

To the best of our knowledge, this is the first study to define the effect of an international standard measurement of relative poverty on the risk of diabetic ketoacidosis at diagnosis of new-onset type 1 diabetes in children. The findings suggest that low income is an important risk factor for developing diabetic ketoacidosis, also in a country such as Sweden with totally reimbursed health care for all children and a high degree of social transfers.

Socio-economic status (SES) is a multi-dimensional construct that includes social and economic factors that are assumed to increase coping resources within Society. Several studies have shown that SES is associated with disease and complications of disease.[4,5,14] A paediatric study from Germany analysed the association between SES and outcomes of diabetes care and found that despite the availability of free health care, including publicly reimbursed technical tools, low SES was associated with adverse diabetes HbA1c levels and an increased need for in-patient care.[23] Screening for low SES in relation to impaired glycaemic control is not generally part of routine care. A high prevalence of low SES has been found for children with poorly controlled type 1 diabetes, and these children had high rates of emergency healthcare utilisation.[6] Income is usually considered a major part of SES and access to modern technology depends on family income or insurance status in many countries.[24] Reduced access to these tools may lead to a higher risk of impaired glycaemic control for the child.[25]

Both parental education level and the child's age at diagnosis of diabetes likely confound the effect of a household's relative poverty as a risk factor for diabetic ketoacidosis. Education level has been associated with health outcomes in several studies and may be assumed to have a direct effect on the risk of diabetic ketoacidosis.[5,6] However, it is also likely that education level is associated with relative poverty in a causal sense, as indicated in Table 1, which in turn mediates the risk of diabetic ketoacidosis among children with new-onset type 1 diabetes.

Age at diagnosis is an important risk factor for diabetic ketoacidosis, as can be seen in Table 2. The high incidence of diabetic ketoacidosis in the youngest children is likely caused by a rapid progression to metabolic acidosis and difficulties linked to the interpretation of symptoms. However, just as in the case of education level, the age of the child/children may also affect the household economy. As examples of this, parental leave after term substantially reduces the level of disposable income in most families, and income may increase with age.

It can be assumed that children's economic standards generally do not improve after they are diagnosed with a chronic illness. A Swedish study describing the labour market consequences of childhood-onset type 1 diabetes has suggested an effect running from health to earnings that encompasses factors related to patient health and parental earnings.[26]

Studies that have pointed out a relationship between diabetic ketoacidosis at diagnosis and high long-term HbA1c levels have been carried out in countries where low economic standards can have obvious adverse consequences.[27]

Both direct and indirect effects of relative poverty may have influenced the findings of this study. Economic difficulties in themselves might contribute to a higher risk of parental delay in seeking healthcare evaluations for children. For example, parents in relative poverty might be reluctant to stay home from work when their children are ill, since no financial compensation is provided for the first day of sick leave in Sweden.

Children from immigrant backgrounds with type 1 diabetes could be a vulnerable group as indicated in studies from other countries.[23,28] Further research is warranted to determine the situation for this group of children in Sweden.

This study has certain limitations and strengths. As is the case for all retrospective register-based studies and indeed most observational studies, causal pathways are difficult to establish, and uncontrolled confounders may distort the risk estimates. Relatively recent methods, such as Mendelian randomisation, may ameliorate such problems in future studies.[29] Another limitation is that the findings are not generalisable to all children since those with foreign background were excluded.

The strengths of the study are that the data were collected for a relatively long period and that the NDR covers a very large proportion of children with type 1 diabetes.[30] The study had a national population-based design to which Statistics Sweden, a public agency, provided data on parental education and weighted disposable income that are directly comparable to international standards.

5 | CONCLUSION

Swedish children in relative poverty have an increased risk of diabetic ketoacidosis at the time of diagnosis of type 1 diabetes. Prospective studies to validate these results and to increase understanding of how diabetic ketoacidosis rates can be reduced are warranted.

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CONFLICT OF INTEREST STATEMENT

All the authors of this study declare that no relationships or activities might bias, or be perceived to bias, their work on the study.

ORCID

Johan H. Wersäll https://orcid.org/0000-0003-0875-7297
Peter Adolfsson https://orcid.org/0000-0001-7615-9737

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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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