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RESEARCH ARTICLE

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Stuttering in adolescence and the risk for dysglycemia in early adulthood

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Abstract

Aims: To investigate the association between stuttering during adolescence and the onset of dysglycemia (prediabetes or type 2 diabetes) in early adulthood among men and women.

Materials and Methods: This cohort study included Maccabi Health Services members assessed for mandatory military service at ages 16–19 during 1990–2019 and followed until 31 December 2020. Stuttering status was recorded in the baseline medical evaluation. Incident cases of dysglycemia were identified systematically using prediabetes and diabetes registries. Cox proportional hazard models were applied for men and women separately, adjusting for sociodemographics and medical status.

Results: The study cohort comprised 866,304 individuals (55% men; 0.21% with stuttering) followed for a total of 12,696,250 person-years. During the study period, 7.6% (n = 36,603) of men and 9.0% (n = 34,723) of women were diagnosed with dysglycemia. The mean ages at diagnosis were 34 and 32 years for men and women, respectively. Women with stuttering exhibited the highest dysglycemia incidence rate (102.3 per 10,000 person-years) compared with the other groups (61.4, 69.0, and 51.9 per 10,000 person-years for women without stuttering, men with stuttering, and men without stuttering, respectively). For both men and women, those with stuttering showed an increased risk of being diagnosed with dysglycemia compared with those without (adjusted hazard ratios 1.18 [1.01–1.38] and 1.61 [1.15–2.26], respectively). The associations persisted in extensive sub-analyses.

Conclusions: Stuttering in adolescence is associated with a higher risk of dysglycemia in early adulthood for men and women. Screening and targeted prevention in this population, especially women, may be beneficial.

KEYWORDS
adolescence, prediabetes, screening, type 2 diabetes, young adult

Avishai M. Tsur and Gilad Twig contributed equally to this work as senior co-authors.

1 | INTRODUCTION

The increasing incidence of early onset type 2 diabetes (diagnosed before age 40 years) has become a pressing public health concern, particularly in Western nations.[1] Approximately one-quarter of young adults are affected by prediabetes,[2] which progresses to type 2 diabetes in up to 70% of those affected.[3] Regardless of the progression, prediabetes poses a significant economic and health burden, including increased risks of cardiovascular morbidity and mortality.[4,5]

Stuttering, a speech fluency disorder characterised by repetitions, prolongations, and pauses in speech,[6] affects 1.99% of children in the United States,[7] and 0.27% of adolescents aged 16–20 years[8] The exact aetiology of stuttering is unknown but believed to be a combination of genetic, neurological, and environmental factors. Stuttering has been linked to aberrant dopaminergic activity,[9] and this aberration has also been linked to altered glucose metabolism.[10] However, further investigations of a possible link between stuttering and any metabolic sequela are scarce.[8] We reported a higher risk of developing type 2 diabetes in young adulthood among men with stuttering. However, we lacked the statistical power to determine the risk for women, as stuttering is four times less common in women than in men, and diabetes in young women is uncommon.[11]

This study aimed to determine the association between adolescent stuttering and incident dysglycemia among men and women in early adulthood. To this end, we linked data of adolescents with and without stuttering, evaluated at age 17 years, as part of mandatory screening, to the prediabetes and diabetes registries of the second-largest health maintenance organisation in Israel.

2 | MATERIAL AND METHODS

2.1 | Design

This retrospective cohort study linked medical evaluations from adolescents assessed for mandatory service in the Israel Defense Forces (IDF) with prediabetes and diabetes registries maintained by Maccabi Health Services (MHS). MHS is Israel's second-largest health maintenance organisation, encompassing approximately 25% of the general population and 40% of individuals eligible for military conscription. The IDF Medical Corps and MHS institutional review boards approved this study and waived the requirement for informed consent.

2.2 | Study population

MHS members aged 16–19 who underwent medical assessment for military service between 1 January 1990 and 31 December 2019 were included. The external validity of this cohort to the general Israeli population was previously exemplified.[12] We excluded members with a history of dysglycemia at study entry (i.e., any history of abnormal serum glucose level or glucosuria) or missing body mass index (BMI) data, and those who died before 2000 (when the MHS prediabetes registry was established). BMI values below 12 or above 48 kg/m^2 were considered missing.

2.3 | Definition of stuttering

Before recruitment to the IDF military service, each examinee underwent a medical evaluation to determine medical fitness. A physician conducted the assessment, usually 1 year before recruitment, at around age 17 years. It included a review of medical history (medical records and health history provided by the examinee's family physician), a detailed interview, and a physical examination. If indicated, the physician referred the examinee for further evaluation by tests or board-certified physicians. The established diagnosis was documented in the examinee's military medical record as one or more medical classification codes. The diagnosis of stuttering was recorded using a specific diagnostic code (ICD-10: F80.81) and confirmed by a speech-language pathologist who also evaluated stuttering severity.

2.4 | Definitions of dysglycemia, prediabetes and diabetes

The study's primary outcome was dysglycemia, defined as prediabetes or type 2 diabetes, recorded on the validated computerised registries for prediabetes and diabetes of MHS.[13,14]

Prediabetes was defined in individuals who did not meet the criteria for diabetes and were diagnosed with prediabetes (by their family physicians) or who had an abnormal laboratory result that met the criteria of prediabetes. The latter included at least two glucose measurements >100 mg/dL (documented within 3 years or less and not performed in an emergency department setting), a single measurement of HbA1c ≥ 5.7% (39 mmol/mol), or a 2-h plasma oral glucose tolerance test level of 140 mg/dL or above. The entry date to the prediabetes registry was determined by the earliest of the three dates. These included the date of diagnosis, the date of the first abnormal HbA1c or glucose measurement, and the date of the first purchase of an oral medication.

Diabetes was defined by documented diagnosis, abnormal laboratory findings (glucose or HbA1c), and the purchase of diabetes medications (oral or insulin). This definition required the presence of at least one of the following: (a) a documented diagnosis of diabetes, with HbA1c ≥ 6.5% (48 mmol/mol) or two glucose measurements of ≥126 mg/dl (one of them at least 6 months before or after the diagnosis); (b) an HbA1c result of at least 7.25% (56 mmol/mol); (c) at least two glucose measurements of ≥200 mg/dl (not performed in an emergency MHS centre, with a minimal 30-day interval between the measurements); (d) at least two recorded purchases (on different occasions) within 3 months, of oral diabetes medications, and at least one glucose measurement of ≥125 mg/dl or HbA1c ≥ 6.5% (48 mmol/mol); (e) at least two recorded purchases of insulin within

3 months (the patient is removed from the registry if the purchase is stopped for six consecutive months or the patient does not fall under any other criteria). Type 2 diabetes was defined as diabetes currently treated with oral medications for at least 3 years (before initiating or after stopping insulin treatment if prescribed). Examinees who met the criteria for gestational, type 1, or unspecified diabetes were not classified as having type 2 diabetes. Notably, a metformin prescription without abnormal glucose levels did not meet the dysglycemia criteria.

2.5 | Study variables

Sociodemographic information was based on data items routinely reported to IDF authorities by governmental ministries. The country of birth, retrieved from the Israeli Ministry of Interior, was dichotomised to those born in and out of Israel. Socioeconomic status (SES) was based on residential locality at the time of examination and was obtained from the Israeli Ministry of Interior records. Residential SES was coded on a 1–10 scale developed by the Israeli Central Bureau of Statistics. This was grouped into low (SES 1–4) and high (SES 5–10).[11] Years of education at the time of IDF recruitment, as recorded in the registry, were based on data from the Israeli Ministry of Education. The two categories were full (12 years or more) and partial (11 years or less) education. Cognitive performance was based on a general intelligence score recorded during prerecruitment. This test is associated with the intelligence quotient and is dichotomised to below- and above-average categories.[11] BMI was calculated based on weight and height measurements by trained medics, with the examinee barefoot and wearing underwear. It was classified as > 85th percentile (high) and ≤85th percentile (not high).[15]

The coexistence of chronic morbidities was defined as any medical condition requiring medical follow-up, the use of regular medications, or a history of major surgery or cancer. Psychiatric disorders were documented following a structured screening process previously described in detail,[16] beginning with a framed interview by trained individuals to assess for behavioural disturbances. If specific criteria were met and a suspicion of psychiatric disorder arose, the examinee was referred to an in-depth psychological assessment by a clinical social worker. A board-certified psychiatrist evaluated and approved examinees referred by the clinical social worker or any examinees with pre-existing diagnoses, a history of treatment by mental health professionals, or prior hospitalisations. He then recorded a diagnosis using specific International Classification of Disease codes.[16] The onset of prediabetes and diabetes, treatment with metformin, smoking status (active or past), and mortality were obtained from the MHS database.

2.6 | Statistical analysis

All the analyses were conducted separately for men and women due to a previously identified interaction between stuttering, sex, and diabetes.[11] Kaplan-Meier curves were used to demonstrate the crude incidence of dysglycemia among men and women with and without stuttering. Hazard ratios (HR) and 95% confidence intervals (CIs) for dysglycemia in young adulthood were determined using Cox proportional hazard models in which adolescents without stuttering comprised the reference group. E-values were computed for point estimates and their corresponding CIs that were closer to the null.[17,18] Follow-up began at the baseline medical examination and ended at dysglycemia diagnosis, death, or 31 December 2020 (whichever came first). The proportional hazard assumption was visually confirmed. We have adjusted the model to pre-specified sociodemographic and clinical variables that were available to us and have been associated with early onset type 2 diabetes in prior research,[19–21] and were consistently used in previous studies from this cohort to identify risk factors for early onset type 2 diabetes.[11,22] The prespecified adjusted model included the year of birth, country of birth, and several variables assessed at study entry. The latter included age at the first examination, BMI, residential SES, level of education, cognitive performance, and the presence of chronic morbidities or psychiatric disorders. Smoking status was the only data item added to the model based on status in adulthood.

We conducted several additional analyses to further explore the relationship between stuttering and dysglycemia. To mitigate confounding effects of coexisting illnesses, we performed an analysis limited to adolescents with unimpaired health at baseline apart from stuttering (excluding those on chronic medical treatment, under regular medical follow-up, or with a history of cancer or major surgeries).[11] For the same purpose, we conducted a separate analysis that excluded individuals with any history of psychiatric background; these conditions may have overlapped in part with those relating to the previous subanalysis. We performed a sensitivity analysis based on the study entry period (1990–1999) to reflect individuals with sufficient follow-up. To better characterise dysglycemia risk among people with stuttering, we defined the outcome as the onset of dysglycemia at several ages (before age 40, 35, 30, and 25 years). We performed a subanalysis based on stuttering severity to explore the severity-dependent relationship between stuttering and dysglycemia. We also examined the association between stuttering and type 2 diabetes to confirm our previous findings.[11] A p-value of <0.05 was considered statistically significant, and all tests were two-tailed. Statistical analyses were performed using IBM SPSS version 27.0, and R version 4.0.2 (R Core Team, Vienna, Austria).

3 | RESULTS

A total of 866,304 examinees were included in the final study: 479,140 men and 387,164 women (Figure 1). Stuttering diagnoses were reported in 0.34% (n = 1616) of men and 0.06% (n = 220) of women. Table 1 shows the population characteristics stratified by sex and stuttering status. Individuals with stuttering diagnoses were more likely to be born outside of Israel and to have chronic or psychiatric morbidities. They were less likely to have completed high

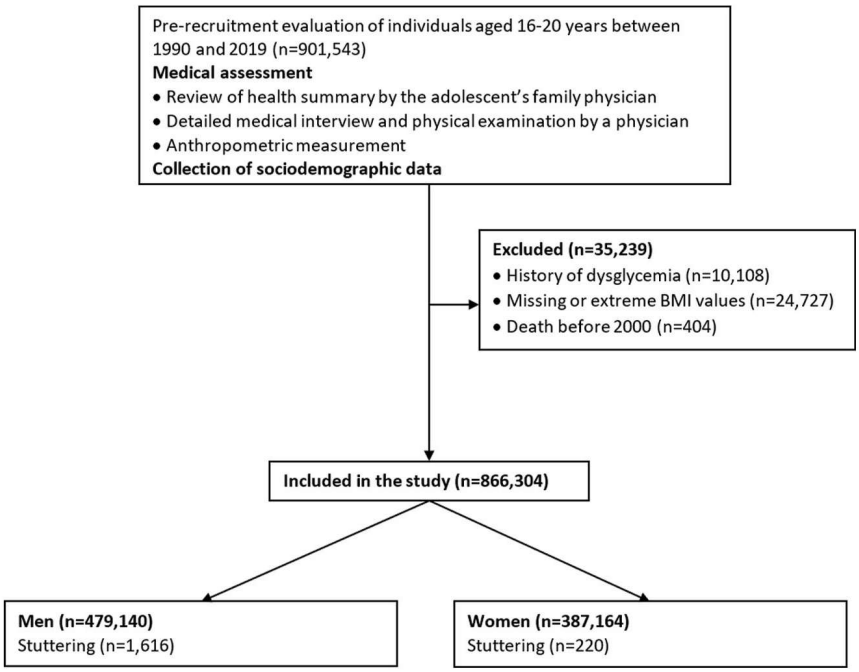

FIGURE 1 Study design and outcomes.

school or to have average or above cognitive performance. Men with stuttering were more likely to have a lower residential SES status.

Dysglycemia was diagnosed in 7.6% (n = 36,603) of men and 9.0% (n = 34,723) of women during a cumulative follow-up of 7,045,602 and 5,650,648 person-years, respectively (Table 2). The mean age at diagnosis was 34 years for men and 32 years for women. Prediabetes was documented before type 2 diabetes in 61.4% (n = 1727) of men and 81.4% (n = 935) of women. The mean interval between documentations was 4.4 ± 3.7 years in men and 6.1 ± 4.6 years in women. Metformin was prescribed in 2.4% (n = 817) of men and 6.3% (n = 2118) of women with prediabetes. Type 2 diabetes was diagnosed in 0.6% (n = 2812) of men and 0.3% (n = 1149) of women. Among the adolescents with stuttering, 171 (10.6%) and 34 (15.5%) men and women, respectively, developed dysglycemia; and 17 (1.1%) and 3 (1.4%), respectively, developed type 2 diabetes.

Women with stuttering had a higher incidence of dysglycemia (102.3 per 10,000 person-years) than the other groups (61.4, 69.0, and 51.9 per 10,000 person-years for women without stuttering, men with stuttering, and men without stuttering, respectively) (Table 2). Kaplan-Meier analysis showed earlier separation (increased dysglycemia incidence) among women (at 5 years, Figure 2B) than among men (at 10 years, Figure 2A). Kaplan-Meier analysis for type 2 diabetes exhibited similar findings but was based on a relatively limited number of cases (Figure S1).

There was no interaction of stuttering with sex (p = 0.13) or with any of the other study covariates. The unadjusted HRs for dysglycemia among men and women with stuttering were 1.31 [1.13–1.53] and 1.65 [1.18–2.31], respectively (Figure 2C). Adjustment to age, BMI, residential SES, level of education, cognitive performance, the presence of chronic morbidities or psychiatric disorders, year of birth and country of birth, and smoking status marginally affected point estimates for dysglycemia: HR_{men} 1.18 [1.01–1.38] and HR_{women} 1.61 [1.15–2.26]. Point estimates were also marginally affected in a sensitivity analysis that restricted the population to those with a minimum follow-up of 20 years (i.e., those who entered the study during 1990–1999). The adjusted HR_{men} was 1.25 [1.04–1.49], the adjusted HR_{women} was 1.54 [1.00–2.36], $p < 0.05$.

The results also generally persisted for the onset of dysglycemia after age 25 years (Figure S2). In a subanalysis that further stratified stuttering by its severity (Figure S3), HRs for dysglycemia were higher for those with severe versus mild stuttering among men but not women (adjusted HR of 1.39 [1.07–1.79] vs. 1.09 [0.90–1.32]). Nonetheless, the number of cases for this subanalysis was small (110 and 61 cases of dysglycemia for mild and severe stuttering, respectively).

4 | DISCUSSION

We report a higher risk for developing dysglycemia in young adulthood among adolescents with than without stuttering. The HRs were 1.31 and 1.65 for men and women, respectively. This association was independent of sociodemographic characteristics, comorbidities, and adolescent BMI.

The incidence rate of type 2 diabetes in our study was similar to worldwide reports,[23] and dysglycemia incidence was slightly lower than in other studies.[24–26] The 20%–40% cumulative incidence of dysglycemia in our cohort compares to 32%–47% reported among Canadian immigrants aged 20–85.[27] The prevalence of stuttering among male adolescents in Western countries has been reported in the range of 0.27%–1.15%, yet the means of assessment vary.[8] Our prevalences of 0.34% and 0.06% for males and females, respectively, are similar to those of 0.3% and 0.1% reported in a German study

TABLE 1 Baseline characteristics of the study population.

Characteristic	Men		Women	
	Without stuttering (n = 477,524)	With stuttering (n = 1616)	Without stuttering (n = 386,944)	With stuttering (n = 220)
Age at examination (years)	17.3 ± 0.5	17.5 ± 0.6	17.2 ± 0.4	17.4 ± 0.6
Born in Israel	389,233 (81.5)	1103 (68.3)	319,657 (82.6)	142 (64.5)
Socioeconomic status				
Low	107,950 (22.6)	415 (25.7)	64,396 (16.6)	42 (19.1)
High	366,695 (76.8)	1189 (73.6)	320,096 (82.7)	178 (80.9)
Complete high school education	416,644 (87.3)	1349 (83.5)	358,168 (92.6)	183 (83.2)
Cognitive performance				
Below average	138,918 (29.1)	630 (39.0)	111,353 (28.8)	115 (52.3)
Average and above	333,229 (69.8)	956 (59.2)	271,995 (70.3)	101 (45.9)
Height (cm)	174.5 ± 6.8	174.4 ± 7.0	162.4 ± 6.2	162.0 ± 7.2
Weight (kg)	67.5 ± 12.7	67.0 ± 13.2	57.7 ± 10.4	57.7 ± 11.3
Adolescent BMI (kg/m^2)	21.7 ± 3.8	21.6 ± 4.0	21.4 ± 3.7	21.5 ± 4.0
BMI category				
Not high	397,535 (83.2)	1330 (82.3)	331,894 (85.8)	191 (86.8)
High	79,989 (16.8)	286 (17.7)	55,050 (14.2)	29 (13.2)
Smoker[a]	132,611 (27.8)	424 (26.2)	104,752 (27.1)	55 (25.0)
Period of birth				
1970–1979	125,530 (26.3)	466 (28.8)	102,172 (26.4)	62 (28.2)
1980–1989	147,903 (31.0)	535 (33.1)	118,848 (30.7)	68 (30.9)
1990–2003	204,091 (42.7)	615 (38.1)	165,923 (42.9)	90 (40.9)
Period of study entry				
1990–1999	163,956 (34.3)	617 (38.2)	133,862 (34.6)	86 (39.1)
2000–2009	149,706 (31.4)	478 (29.5)	121,649 (31.4)	68 (30.9)
From 2010 onwards	163,862 (34.3)	521 (32.2)	131,433 (34.0)	66 (30.0)
No chronic morbidities	382,726 (80.2)	1091 (67.5)	299,966 (77.5)	125 (56.8)
No psychiatric disorders	450,583 (94.4)	1367 (84.5)	375,575 (97.1)	199 (90.5)

Note: The data are presented as means ± SD or as n (%).

[a]Active or past smoking.

that applied a similar assessment method.[28] This similarity in prevalence and the stability of point estimates following adjustment to various socioeconomic variables supports the generalisability of our findings to other Western countries.

We are unaware of studies that linked stuttering with dysglycemia or prediabetes. Among 2628 children with stuttering, 1.3% (n = 35) were reported to have comorbidities, including diabetes.[29] In another study, children with stuttering were reported to be more likely to have diabetes than those without stuttering (0.49% vs. 0.25%).[30] Using data from 2 million adolescents from the Israeli National Diabetes Registry, we reported a positive association between stuttering and type 2 diabetes in young men but lacked the statistical power to demonstrate an association in women.[11] The current study provides a more comprehensive investigation, including associations of stuttering with prediabetes and dysglycemia in women and men and temporal data regarding screening timing.

The American Diabetes Association recommends screening for prediabetes and type 2 diabetes at age 35 years. However, we found non-negligible dysglycemia rates among adolescents with stuttering much earlier, especially in women. This implies a possible benefit of earlier screening in this population. The transition from prediabetes to diabetes is preventable with lifestyle modifications and medications, of which metformin is the most common. Data from the Diabetes Prevention Programme Outcome Study showed that the

TABLE 2 Time-to-event summary.

	Men		Women	
	Without stuttering (*n* = 477,524)	**With stuttering (*n* = 1616)**	**Without stuttering (*n* = 386,944)**	**With stuttering (*n* = 220)**
Mean follow-up, dysglycemia (years)	14.7 ± 8.7	15.3 ± 8.5	14.6 ± 8.7	15.1 ± 8.7
Mean follow-up, type 2 diabetes (years)	15.1 ± 8.8	15.9 ± 8.7	15.2 ± 8.9	15.9 ± 8.9
Incidence of dysglycemia	36,432 (7.6)	171 (10.6)	34,689 (9.0)	34 (15.5)
Incidence of prediabetes[a]	33,637 (7.0)	154 (9.5)	33,543 (8.7)	31 (14.1)
Incidence of type 2 diabetes	2795 (0.6)	17 (1.1)	1146 (0.3)	3 (1.4)
Cumulative follow-up, dysglycemia (person-years)	7,020,822	24,780	5,647,324	3324
Cumulative follow-up, type 2 diabetes (person-years)	7,211,483	25,690	5,866,688	3515
Dysglycemia per 10,000 person-years	51.9	69.0	61.4	102.3
Type 2 diabetes per 10,000 person-years	3.9	6.6	2.0	8.5

Note: The data are presented as means ± SD, *n* (%). Dysglycemia—prediabetes or type 2 diabetes.

[a]This refers to prediabetes that did not progress to type 2 diabetes during the follow-up.

subpopulation that most benefitted from metformin-based primary prevention therapy was young women (aged <45 years).[31]

The mechanisms underlying the association between stuttering and dysglycemia are unclear. Common pathophysiological pathways of the two conditions exist, including dopamine, oestrogen, and cortisol abnormalities. Evidence of dopamine excess as a factor related to stuttering includes increased dysfluency with L-dopa treatment of Parkinson's disease and a demonstrated benefit of anti-dopaminergic drugs on stuttering.[9] Several haplotypes and single nucleotide polymorphisms of dopaminergic genes were found to be more prevalent among people with than without stuttering.[32] Dopamine may also affect glucose homoeostasis by affecting appetite, lipid accumulation, and food reward.[10]

A second putative cellular site relates to serum G-protein coupled receptor-1 (GPER-1), a 7-transmembrane receptor involved in rapid oestrogen signalling.[33] A paediatric study showed higher levels of GPER-1 among those with than without stuttering.[34] In knockout studies in mice, GPER-1 was shown to be involved in beta cell survival and responsiveness to insulin.[33] In a pilot study, serum GPER-1 was higher among individuals with diabetes mellitus, especially those with diabetic retinopathy, and positively correlated with oxidative markers.[35]

A third mechanism for the association between stuttering and dysglycemia relates to abnormalities in the hypothalamic-pituitary-adrenal axis. Stuttering is also associated with increased stress levels and chronic anxiety.[36] Chronic anxiety is an independent risk factor for type 2 diabetes.[37] In this regard, salivary cortisol levels were higher during stressful stimuli among adults with than without stuttering.[38] The persistence of the association after limiting the analysis to people without psychiatric morbidities, such as anxiety and depression, does not exclude this mechanistic route.

Lastly, stuttering possibly influences lifestyle choices among women.[39] Considering the inverse association between physical activity and type 2 diabetes risk,[40] the negative impact of stuttering on physical activity might be a complementary explanation for the association of stuttering with dysglycemia.

Several limitations of this study should be acknowledged. First, the databases lacked longitudinal data on risk factors for dysglycemia, BMI, and stuttering status. Smoking status was a qualitative measure that was categorised only as active or past smoking. Second, data regarding glucose tests were unavailable to us. Such data could have highlighted the differences between men and women (earlier Kaplan-Meier separation). Given that people with stuttering tend to avoid medical encounters,[41] this caveat is expected to underestimate the association. Third, we lacked lifestyle data, specifically regarding physical activity. Adults with stuttering were described as favouring avoidant behaviour and different lifestyle choices than those without,[39] including 70% fewer social group activities and 40% fewer individual activities.[42] Finally, because of specific characteristics regarding obligatory military service, the study's cohort population is under-representative of some non-Jewish minorities and Orthodox and ultra-orthodox Jewish women. The strengths of our study include a large unselected cohort with systematic and careful assessment of health status at adolescence, quality assurance of stuttering diagnosis, use of well-established prediabetes and diabetes registries, and the collection of several socio-demographic variables.

In summary, adolescents of both sexes with stuttering were shown to have a higher risk for developing dysglycemia (prediabetes or type 2 diabetes) in young adulthood. This population should be encouraged to maintain a metabolically favourable lifestyle, including a healthy diet and physical activity, and be medically followed to mitigate type 2 diabetes risk in young adulthood.

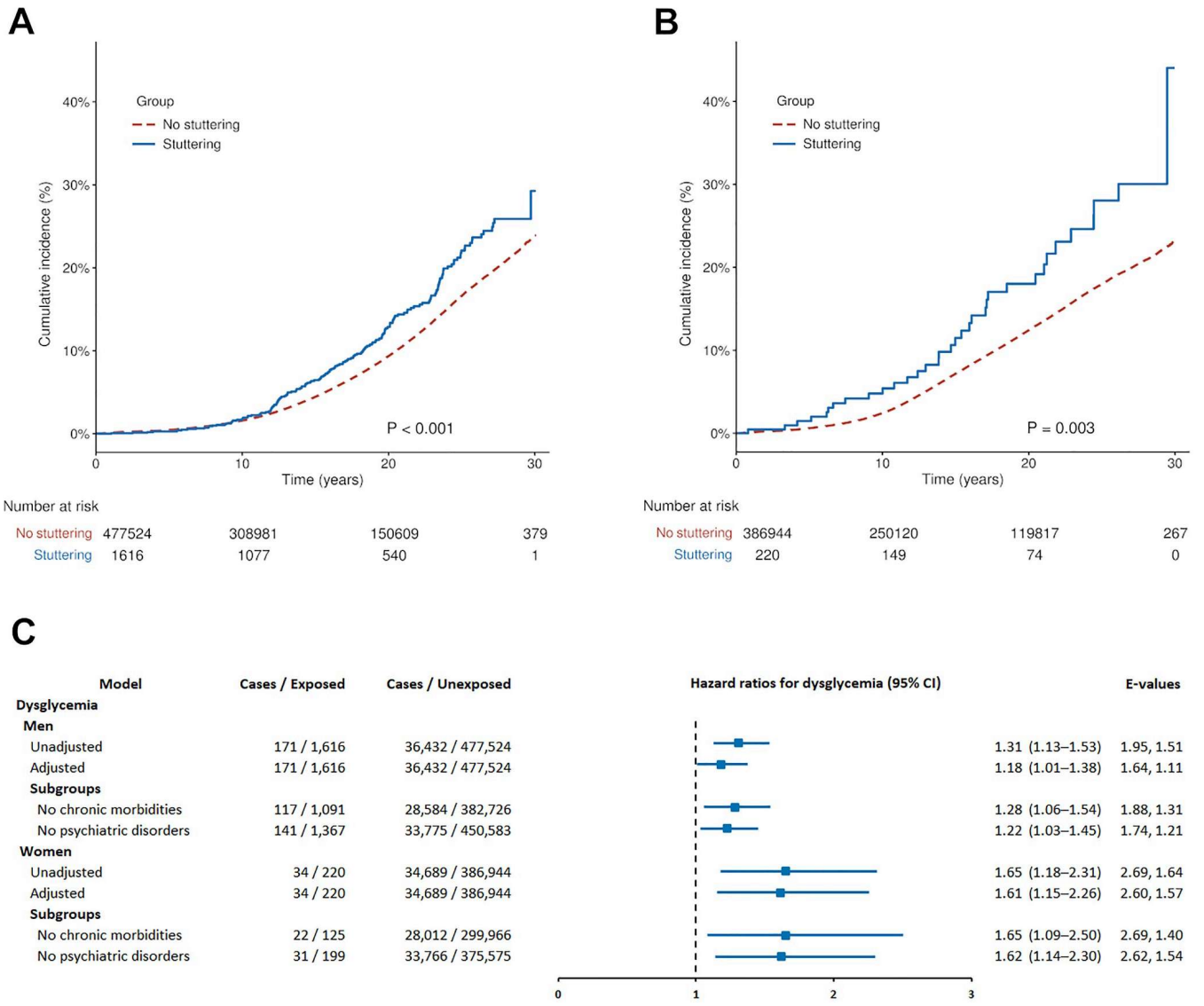

FIGURE 2 Kaplan-Meier curves for dysglycemia in men (A) and women (B) with and without stuttering ("No stuttering"). (C) Hazard ratios of stuttering in adolescence and incident dysglycemia in men. *p*-values of the log-rank test are presented accordingly in (A) and (B). (C) The model was adjusted for the year of birth, country of birth, and several variables assessed at study entry. The latter included: age at the first examination, BMI, residential socioeconomic status, level of education, cognitive performance, and the presence of chronic morbidities or psychiatric disorders. Smoking status was based on status in adulthood. The subgroup analyses were adjusted for all of the above in addition to the subgroup variable. *E*-values for point estimates and their corresponding confidence intervals, which are closer to the null, are delineated with a comma.

AUTHOR CONTRIBUTIONS

Alexandra Rabotin designed the study, statistically analysed and interpreted the data, and drafted and revised the manuscript. Gabriel Chodick acquired the data, contributed to the discussion, and critically revised the manuscript. Orit Pinhas-Hamiel, Ofer Amir, Yair Schwarz, and Arnon Afek contributed to the discussion and critically revised the manuscript. ED and DT acquired data and statistically analysed the data. Gilad Twig and Avishai M. Tsur designed and supervised the study, statistically analysed and interpreted the data, and drafted and revised the manuscript. All authors have read and approved the final manuscript.

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CONFLICT OF INTEREST STATEMENT

No potential conflicts of interest relevant to this article were reported.

DATA AVAILABILITY STATEMENT

The datasets generated and analysed during the current study are based on a military database with limited access. Summaries and aggregated data may be available upon reasonable request to the corresponding author.

ETHICS STATEMENT

The IDF Medical Corps and MHS institutional review boards approved this study (Protocols 18602017 and 11219, respectively) and waived the requirement for informed consent.

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PEER REVIEW

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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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