




Changes in cardiovascular risk factors among children and young adults with type 1 diabetes during the COVID-19 pandemic compared to previous years—Results from the German DPV registry

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Abstract

Background: The diverse stages of the COVID-19 pandemic led to several social circumstances that influenced daily life and health behavior.

Purpose: To evaluate changes in cardiovascular risk factors and physical activity among children and young adults with type 1 diabetes (T1D) during the COVID-19 pandemic in Germany compared to previous years.

Methods: A total of 32 785 individuals aged 6–21 years at baseline with T1D from the German diabetes patient follow-up (DPV) registry contributed data on 101 484 person-years between 2016 and 2021. The first treatment year of each

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individual within this period was considered as baseline. Based on trends from 2016 to 2019, we estimated differences in body mass index-SD score (BMI-SDS), blood pressure (BP-SDS), and lipid levels (non-high-density lipoprotein [non-HDL]) between observed and predicted estimates for the years 2020 and 2021 using linear regression analysis standardized for age, diabetes duration, sex, and migratory background. The proportion doing organized sports and smoking cigarettes was analyzed using multivariable logistic regression models.

Results: BMI-SDS increased constantly from 2016 to 2021 without a significant increase above expected values for 2020/2021. Systolic BP-SDS (difference observed vs. expected with 95% confidence interval, 2020: 0.10 [0.07–0.14], 2021: 0.17 [0.14–0.20]) and non-HDL (2020: 2.7 [1.3–4.1] mg/dl, 2021: 4.1 [2.7–5.5] mg/dl) were significantly increased (all $p < .001$) in both pandemic years. The proportion of subjects participating in organized sports was reduced from over 70% in prepandemic years to 35%–65% in diverse stages/waves of the COVID-19 pandemic. The percentage smoking cigarettes did not change.

Conclusions: We describe an increase in BP and atherogenic lipid levels coinciding with a reduction in physical activity but no acceleration of the prepandemic increases in BMI-SDS among young people with T1D during the COVID-19 pandemic.

KEYWORDS

blood pressure, cholesterol, coronavirus, lipid, physical activity, sports

Highlights

- Cardiovascular risk factors worsened during COVID-19 in young people with type 1 diabetes.
- Blood pressure and atherogenic lipid levels were higher in 2020/2021 than expected.
- No further boost in 2020 and 2021 of the preexisting increase in body mass index-SD score.
- A reduction in organized sports but no change in smoking behavior was observed.

1 | INTRODUCTION

Physical activity during childhood and adolescence is inversely associated with several cardiovascular risk factors. There is evidence that in children aged 4–18 years, systolic blood pressure (BP), waist circumference, triglycerides (TG), and high-density lipoprotein (HDL) can benefit from moderate to vigorous physical activity.¹ In children and adolescents with type 1 diabetes (T1D), physical activity can improve low-density lipoprotein (LDL), TG, diastolic BP, and hemoglobin A1c (HbA1c).² Smoking is another important lifestyle factor related to cardiovascular risk in children and adolescents, especially in those with diabetes.^{3,4}

The COVID-19 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reached Germany in February 2020, leading to a first nationwide lockdown from March to May and subsequent additional governmental health measures to contain the pandemic. The incidences of COVID-19 fell during the summer months (June to September), but increased dramatically in a second (October 2020 to February 2021) and consecutive third wave (March to May 2021). Again, during summer 2021 the COVID-19 incidence was relatively low and increased again since October 2021.^{5,6}

The fear of infection with COVID-19 as well as the temporary closure of schools, sports clubs, and other public institutions led to isolation and lifestyle changes,



especially a reduction of physical activity in children and adolescents worldwide, most pronounced especially during the first lockdown in 2020.^{7–9} According to a recent meta-analysis, a reduction in physical activity during the COVID-19 pandemic was observed in several countries.¹⁰ This could have led to long-lasting health issues such as an increase in cardiovascular risk factors. However, in Germany, only organized sports were reduced during the first lockdown, together with an increase in sedentary time and the use of media during leisure time, but higher physical activity due to unorganized sports such as playing outdoors was observed in children.¹¹ Further, there seemed to be remarkable differences regarding socioeconomic factors enabling children with better housing situations to engage in more habitual physical activity.¹²

Children and adolescents with T1D are particularly at risk for hypertension, dyslipidemia, increased periaortic fat thickness,¹³ and accelerated atherosclerosis.¹⁴ Many studies concentrated on glycemic control in children and adolescents with T1D during the COVID-19-related lockdown, reporting worse or stable HbA1c,^{15,16} but data on cardiovascular risk, especially on BP and lipids during the pandemic, are still scarce.

The aim of this study was to evaluate changes in BP, serum lipids, physical activity, and smoking behavior in young individuals with T1D during the COVID-19 pandemic in Germany compared to previous years, based on data from a German diabetes patient registry.

2 | MATERIALS AND METHODS

2.1 | Data collection

This analysis is based on data from the prospective, multi-center diabetes patient follow-up registry (DPV, Diabetes-Patienten-Verlaufsdokumentation), which is a standardized electronic health record developed at the Institute of Epidemiology and Medical Biometry, Ulm University, Germany.¹⁷ The initiative and the analysis of anonymized data was approved by the Ethics Committee of Ulm University (approval number: 314/21) as well as by local review boards.

A total of 512 diabetes centers from Germany, Austria, Switzerland, and Luxembourg provided pseudonymized data on diabetes treatment and outcome to the registry until March 2022. Because of differences in societal responses among countries, only 300 German centers were included in this report, representing an estimated coverage of about 90% of children with diabetes in Germany.¹⁸ The transmitted data are checked for inconsistency or implausibility and reported back to the respective centers for correction, if necessary.

2.2 | Participants and evaluation periods

German individuals recorded in the DPV initiative were included if they had documented data at least in 1 year between 2016 and 2021 (Figure 1). The first year of each individual during this time frame was considered as baseline. The six treatment years were further divided into four periods according to the course of the COVID-19 pandemic and associated policy measures in 2020 and 2021 in Germany to allow detailed analysis of lifestyle factors and treatment with antihypertensive or lipid-lowering medication. Therefore, January and February were defined as period 1, before COVID-19 in 2020. March to May was determined as period 2, representing the first wave of COVID-19 and the first lockdown in 2020; June to September was defined as period 3 (summer) with lower COVID-19 cases in both years; October to December was set as period 4, representing the increasing COVID-19 incidences in Germany in both years.

Data were aggregated for each individual and year for analysis of the main outcomes body mass index (BMI), BP, and lipid values. Additionally, data were aggregated for each individual, year and the aforementioned period to analyze lifestyle factors. Therefore, all participants contributed data in 1–6 years and in 1–24 observation intervals (years*periods) to this analysis. Further inclusion criteria were a clinical diagnosis of T1D, age at baseline $6 \leq 21$ years and available data on systolic/diastolic BP, BMI, and organized sports in at least 1 year (Figure 1). If an individual had data on all outcomes for some, but not all years/observation intervals, observation intervals with missing data were omitted. A subgroup of individuals with available data on lipid values (total cholesterol [TC], TG, LDL, HDL) in at least 1 year was built for a separate analysis (Figure 1).

2.3 | Patient data

For height, weight, BMI, and BP, SD scores (SDS) based on German reference values were used (anthropometry: AGA (Consortium of Obesity in Childhood and Adolescence as part of the German Obesity),¹⁹ blood pressure: KiGGS (German Health Interview and Examination Survey for Children and Adolescents).²⁰ Lipid values were converted to mg/dl. Non-HDL was calculated as TC minus HDL and remnant cholesterol (RC) as TC minus LDL and HDL. HbA1c values were standardized to the Diabetes Control and Complications Trial reference range of 4.05%–6.05% (20.7–42.6 mmol/mol) using the multiple of the mean transformation method to account

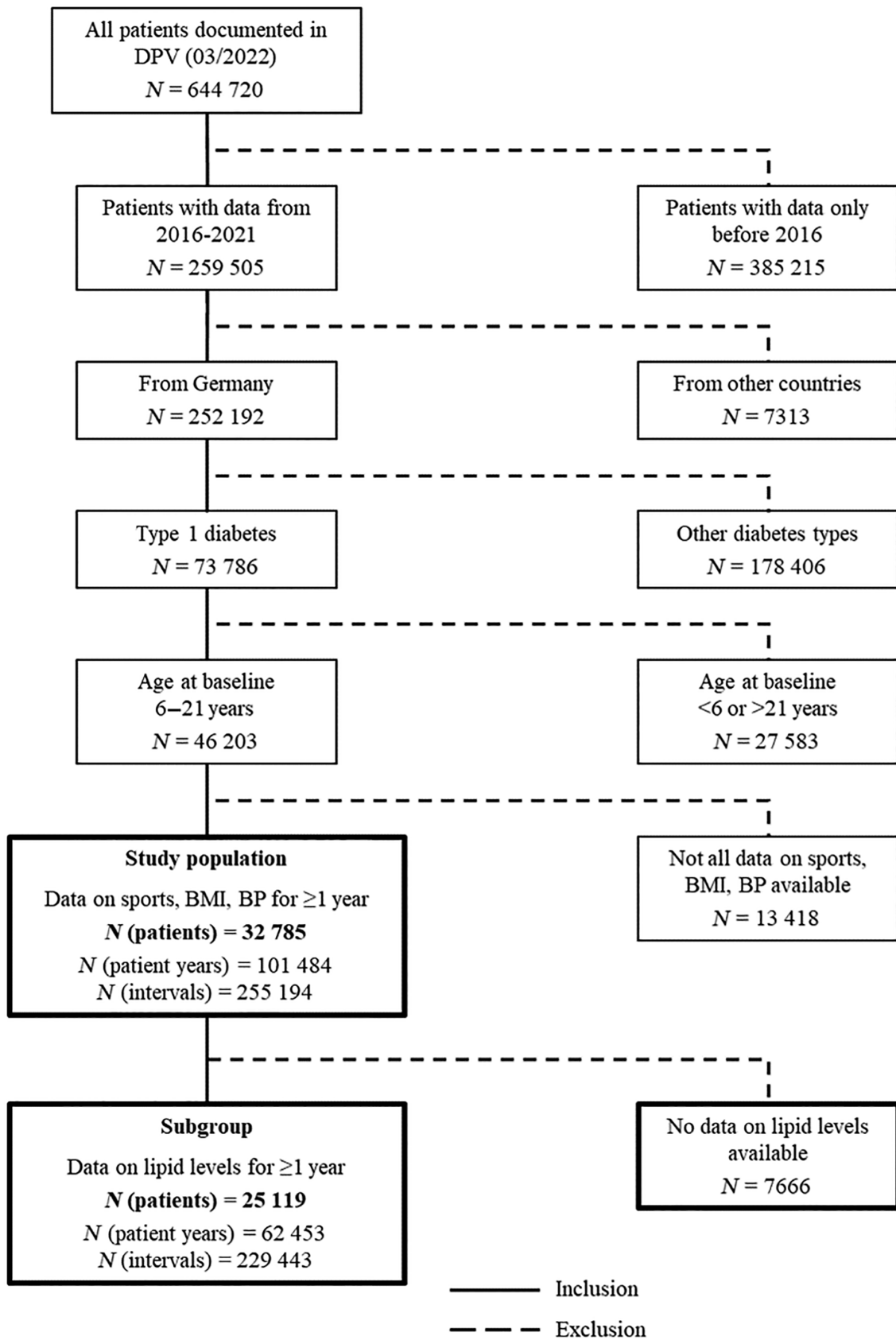


FIGURE 1 Legend on next page.



for different laboratory methods.²¹ Physical activity was defined as organized/club sports (individual exercise at home was not included).²² Unfortunately, data on the sedentary time and the use of media was not available. Smoking was defined as current smoking of cigarettes (yes/no). Missing data were set as no smoking. Migratory background was defined as the patient or at least one of his/her parents born outside of Germany.

2.4 | Statistical analysis

All statistical analyses were generated using SAS (Statistical Analysis Software, SAS Institute Inc., Cary, NC, USA) Version 9.4, Built M7, on a Windows Server 2016 mainframe. Descriptive statistics were performed for all patients at baseline. The results are shown as median with quartiles for continuous variables and as proportions for binary variables.

The proportions of individuals doing organized sports, smoking cigarettes, with prescribed antihypertensive or lipid-lowering medication as well as the proportion with overweight or obesity (BMI-SDS \geq 90th percentile, representing an SDS value \geq 1.28) and with obesity (BMI-SDS \geq 97th percentile, representing an SDS value \geq 1.88) by year and period were analyzed using multivariable logistic regression models adjusted for age groups (6–11, >11–16, >16–21 years at baseline), sex, diabetes duration groups (\leq 2, >2–6, >6 years at baseline), and migratory background. To consider repeated measurements of individuals that contributed more than one observation interval, a random effect (random residual for each subject) for the period*year-interaction was implemented with a first-order autoregressive covariance structure and an optimization technique of Newton–Raphson with ridging.

To analyze deviations of the respective outcome during the COVID-19 pandemic (years 2020 and 2021) compared to predicted levels based on the prepandemic years (2016–2019), we first applied multivariable linear trend regression models from 2016 to 2019 for BMI, systolic and diastolic BP, and lipid levels (TC, LDL, HDL, non-HDL, RC, and TG). Independent variables were treatment year (continuous), age groups, and diabetes duration groups at baseline, sex, and migratory background. Again, repeated measurements of individuals with data from more than 1 year were considered with a

random effect of each subject for treatment years. Based on these trend models, we predicted the outcomes for 2016 to 2021, standardized for the aforementioned confounders. Second, a linear regression model with the same standardization, but the year as a categorical term was used to estimate the observed outcome levels for each year (2016–2021). Third, a linear regression model that included a binary variable indicating observed and predicted data as independent variables was applied to compare the observed with the predicted outcome levels. As a measure of deviation, the difference between these observed and predicted outcome levels was estimated as the standardized difference with the corresponding 95% confidence intervals (CI) and two-sided *p* values from the Wald test. Sensitivity analysis was conducted with further adjustment for BMI-SDS groups ($</\geq$ 90th percentile) and the proportion with antihypertensive medication (for systolic and diastolic BP) or the proportion with lipid-lowering medication (for lipid levels). We additionally analyzed non-HDL only in individuals with good glycaemic control (HbA1c $<$ 7.5%). Two-sided *p* $<$.05 indicated a significant difference.

3 | RESULTS

3.1 | Study population

Among all individuals registered in DPV, 32 785 were aged $6 \leq 21$ years at baseline, had a diagnosis of T1D, were from Germany, and fulfilled the inclusion criteria. These individuals provided a total of 101 484 patient-years. Figure 1 gives an overview on the inclusion criteria and the number of patients and observation intervals.

Included individuals had a median age at baseline of 12.8 [9.5; 15.5] years with 53% being male and 25% having a migratory background, and 76% were physically active. Table 1 displays further characteristics at baseline.

3.2 | Cardiovascular risk factors by treatment year

Yearly analysis of cardiovascular risk factors showed an ongoing trend in BMI-SDS increase from 2016 to 2021, but no further worsening during the COVID-19

FIGURE 1 Inclusion and exclusion criteria of study population. Intervals = number of all observation intervals included in the analysis (1–24 per participant); lipid levels include total cholesterol, low-density lipoprotein, high density lipoprotein (HDL), non-HDL, remnant cholesterol, triglycerides. Baseline = first treatment year per patient from 2016–2021. BMI, body mass index (as SD score). BP, blood pressure (systolic and diastolic, as SD score). DPV, Diabetes-Patienten-Verlaufsdokumentation.

Characteristic	Missing (N)	%	Median	Q1	Q3
Sex (% male)		52.8			
Age (years)			12.8	9.5	15.5
Diabetes duration (years)			2.9	0.8	6.2
Height-SDS			0.1	-0.6	0.7
Weight-SDS			0.4	-0.2	1.1
BMI-SDS			0.4	-0.2	1.1
Doing organized sports		76.1			
Smoking cigarettes		3.2			
HbA1c (%)	280		7.4	6.6	8.2
HbA1c (mmol/mol)	280		57	49	66
Systolic BP (mmHg)			115	107	124
Systolic BP (SDS)			0.7	-0.0	1.4
Diastolic BP (mmHg)			68	62	74
Diastolic BP (SDS)			0.3	-0.4	1.0
Hypertension		3.8			
Antihypertensive medication		1.4			
Total cholesterol (mg/dl)	14 206		170	151	192
LDL (mg/dl)	15 181		94	77	113
HDL (mg/dl)	15 116		62	52	72
Non-HDL (mg/dl)	15 439		106	89	127
Remnant cholesterol (mg/dl) ^a	15 664		12	6	19
Triglycerides (mg/dl)	14 915		89	62	129
Fasting triglycerides (mg/dl)	29 506		76	54	115
Proportion TG fasting ^b	14 915	18.4			
Dyslipidemia	13 834	24.3			
Non-HDL > 140 mg/dl	15 439	15.4			
Lipid-lowering medication		0.4			

TABLE 1 Patient characteristics at baseline, $N = 32\ 785$.

Abbreviations: BMI, body-mass index; BP, blood pressure; HbA1c, Hemoglobin A1c; HDL, high density lipoprotein; LDL, low density lipoprotein; Q1, lower quartile; Q3, upper quartile; SDS, SD score, reference AGA (height, weight, BMI) or KIGGS (systolic/diastolic blood pressure); TG, triglycerides.

^aRemnant cholesterol = Total cholesterol - (LDL + HDL).

^bProportion of TG measurements that were performed fasting.

pandemic in 2020 or 2021 (Figure 2A). Nevertheless, systolic BP was higher in 2020 and in 2021 than expected (standardized difference with 95% CI, observed vs. expected: 2020: 0.10 [0.07; 0.14], $p = .001$ and 2021: 0.17 [0.14; 0.20], $p = .001$). This implies an increase of 15% (2020) and 25% (2021) compared to the expected systolic BP. Similar results could be observed for diastolic BP with an increase of 13%/12% compared to expected diastolic BP in 2020 and 2021, despite a previously increasing trend since 2016 (Figure 2B,C and Table 2). This increase in BP was still significant, even with further adjustment for BMI-SDS and for antihypertensive treatment (Figure S1).

For lipid levels, we detected higher observed vs. expected values for total cholesterol, non-HDL (difference observed vs. expected in 2020: 2.7 [1.3; 4.1] mg/dl, $p < .001$ and in 2021: 4.1 [2.7; 5.5] mg/dl, $p < .001$), and RC (Figure 2E/H/I and Table 2) but not for TG or LDL (Figure 2D,F and Table 2). HDL was also significantly increased in both years (Figure 2G and Table 2). Again, these results persisted with further adjustment for BMI-SDS and lipid-lowering medication (Figure S1). An increase in non-HDL was also detected in a subgroup with well-controlled HbA1c (<7.5%, Figure S1H). Figure 2 and Table 2 show the trend from 2016 to 2019 as well as the standardized differences between observed and expected values for all outcomes.

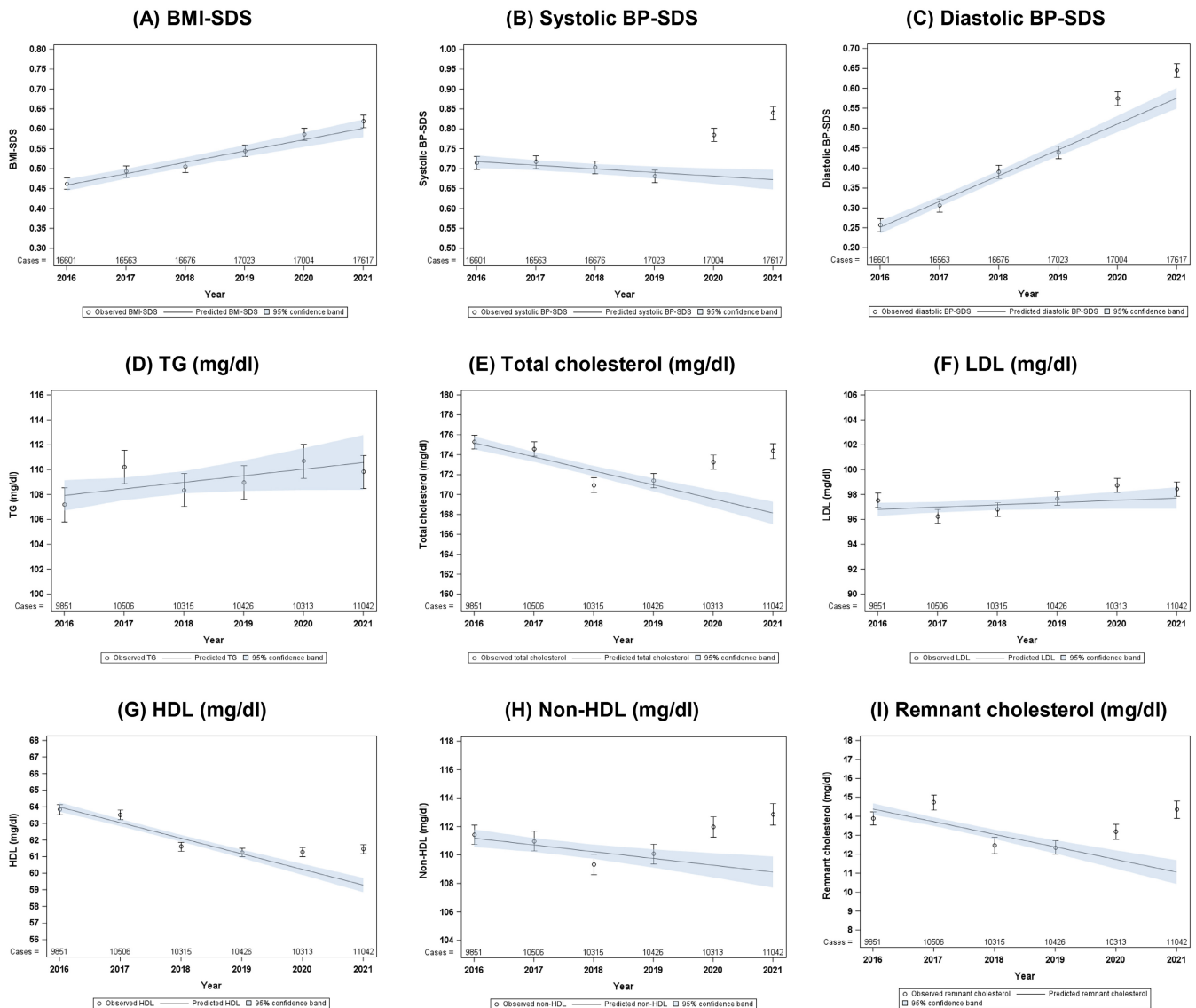


FIGURE 2 Cardiovascular risk factors, observed and predicted values from 2016 to 2021. Circles with vertical bars represent standardized estimates with 95% CI, solid lines with bands represent standardized trend estimates with 95% CI estimated from linear trend regression models. All models were standardized for age at baseline, sex, diabetes duration at baseline and migration background. BMI, body mass index; BP, blood pressure; CI, confidence interval; HDL, high density lipoprotein; LDL, low density lipoprotein; SDS, SD score; TG, triglycerides.

3.3 | Results by year and period

The analysis by year and period revealed a significant (all $p < .001$) decrease in the proportion of children and adolescents doing organized sports at least once per week starting in March 2020, from constantly over 70% in the pre-pandemic observation periods to 35%–65% during the diverse periods of the COVID-19 pandemic in 2020 and 2021 (Figure 3A). The proportion of children and young adults smoking cigarettes stayed relatively stable since 2016; only during summer 2021, an increase was observed (Figure 3B). The percentage with prescribed antihypertensive and lipid-lowering

medication (Figures 3C,D) as well as the proportions of individuals with overweight and with obesity (Figures 3E,F) constantly increased from 2016 to 2021 without a clear acceleration in the two pandemic years.

4 | DISCUSSION

We found significantly elevated systolic and diastolic blood pressure and higher atherogenic lipid levels during the COVID-19 pandemic in Germany compared to the expected values based on trend analyses from the

TABLE 2 Cardiovascular risk factors, trend 2016–2019 and standardized difference between observed and expected values for 2020 and 2021.

Outcome	Trend 2016–2019 (change per year)	Difference observed vs. expected, 2020	Difference observed vs. expected, 2021
BMI-SDS	0.03 (0.02; 0.03), $p < .001$	0.01 (−0.02; 0.04), $p = .308$	0.02 (−0.01; 0.05), $p = .308$
Systolic BP-SDS	−0.009 (−0.015; −0.003), $p = .005$	0.10 (0.07; 0.14), $p < .001$	0.17 (0.14; 0.20), $p < .001$
Diastolic BP-SDS	0.06 (0.06; 0.07), $p < .001$	0.06 (0.03; 0.10), $p < .001$	0.07 (0.04; 0.10), $p < .001$
TG (mg/dl)	0.5 (−0.1; 1.1), $p = 0.075$	0.7 (−2.1; 3.4), $p = .999$	−0.7 (−3.4; 2.0), $p = .999$
Total cholesterol (mg/dl)	−1.4 (−1.7; −1.1), $p < .001$	3.7 (2.2; 5.2), $p < 0.001$	6.2 (4.8; 7.7), $p < .001$
LDL (mg/dl)	−0.18 (−0.04; −0.40), $p = .102$	1.2 (0.1; 2.3), $p = .028$	0.7 (−0.3; 1.8), $p = .121$
HDL (mg/dl)	−0.9 (−1.1; −0.8), $p < .001$	1.1 (0.5; 1.6), $p < .001$	2.2 (1.7; 2.7), $p < .001$
Non-HDL (mg/dl)	−0.5 (−0.8; −0.2), $p < .001$	2.7 (1.3; 4.1), $p < .001$	4.1 (2.7; 5.5), $p < .001$
Remnant cholesterol (mg/dl)	−0.7 (−0.8; −0.5), $p < .001$	1.5 (0.7; 2.3), $p < .001$	3.3 (2.5; 4.1), $p < .001$

Note: The trend 2016–2019 describes the estimated change per year in the respective unit (SDS or mg/dl), standardized for age groups at baseline, sex, diabetes duration at baseline, and migration background. Estimated differences between observed and expected (based on trend 2016–2019) values are presented in the same unit and standardized for the same variables.

Abbreviations: BMI, body-mass index; BP, blood pressure; HDL, high density lipoprotein; LDL, low density lipoprotein; SDS, SD score; TG, triglycerides.

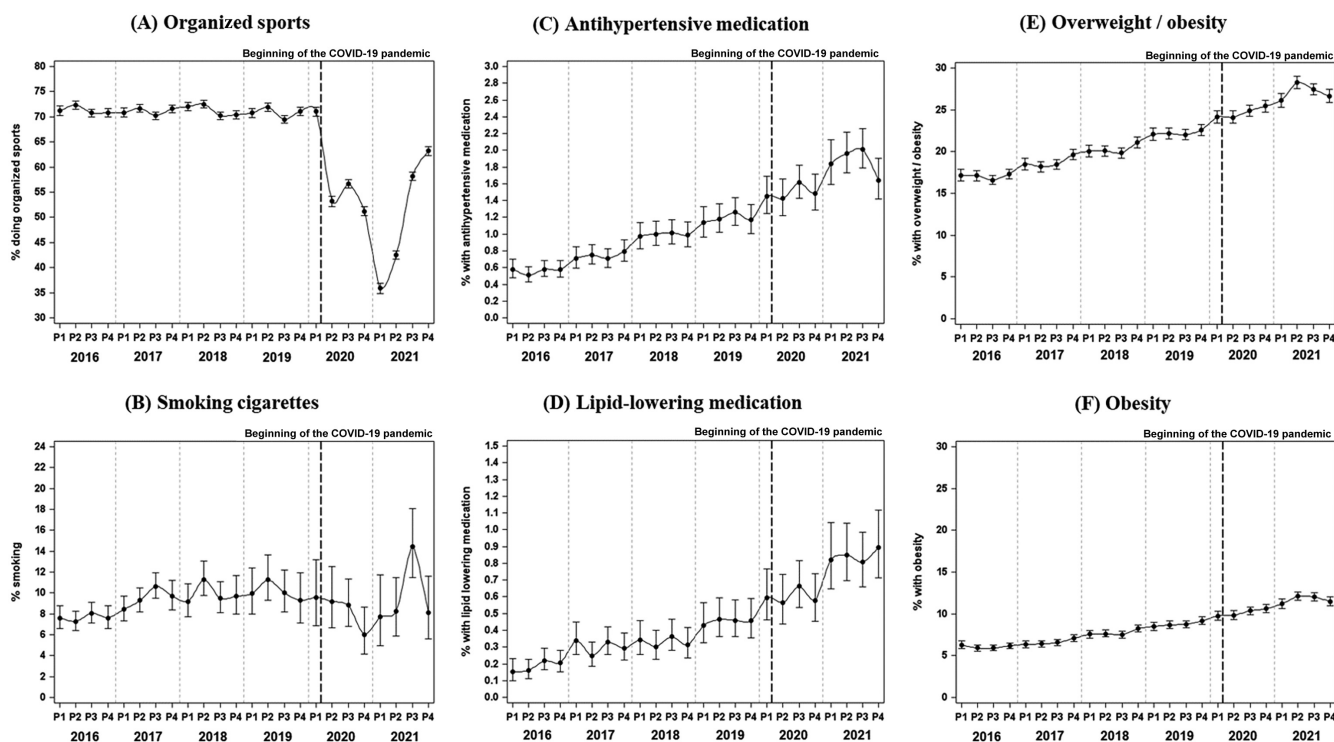


FIGURE 3 Proportion (%) of lifestyle factors and prescribed medication by year and period. Shown are results from multivariable regression models, adjusted for age, sex, diabetes duration, and migratory background, with random effect for repeated measurements. Outcomes are (A) organized sports, (B) smoking cigarettes, (C) with prescribed antihypertensive medication, (D) with prescribed lipid-lowering medication, with overweight or obesity defined as BMI-SDS ≥ 90 th percentile (E), with obesity defined as BMI-SDS ≥ 97 th percentile (F). Missing values on smoking were assumed as no smoking. Excluding these missing data provided similar results, data not shown). BMI-SDS, body mass index-SD score.

years 2016–2019. This increase coincided with a reduction in the proportion of children and young adults with T1D doing organized sports, but no remarkable

differences in the proportion smoking cigarettes and no acceleration of the prepandemic increase in BMI-SDS.



BMI-SDS rose constantly from 2016 to 2021, but there was no significantly higher increase in 2020 or 2021 than expected from the previous years. Therefore, no additional deterioration due to the lockdown periods and the pandemic itself on BMI-SDS can be postulated by now. A study on children with T1D from India found no worsening in BMI *z* scores as well,²³ whereas another study found increased body weight and BMI in pediatric T1D already during the first lockdown.¹⁵ However, these studies did not account for the preexisting trend and only compared BMI at a certain point of time before the pandemic and during the lockdown. This approach seems to be problematic as we discovered an increase in BMI-SDS in young individuals with diabetes that occurred even before the beginning of COVID-19. A Korean study group analyzed this BMI-SDS trend over 15 years in children (with no regard to diabetes) and detected a constant increase in BMI-SDS over this time span but the increase from 2019 to 2020 was smaller than the prepandemic increases per year²⁴ which supports our results on a preexisting trend. Another limitation in the evaluation of BMI prepandemic and during the pandemic that must be kept in mind is the definition of BMI itself. Because BMI is only the ratio of body weight and squared body height, there could have been body fat independent changes, for example, lower muscle mass due to the decrease in physical activity, that might have limited the increase in body weight and therefore BMI during the COVID-19 period, which does not exclude a worse body fat percentage or composition.

Higher BP (systolic and diastolic) in 2020 and 2021 compared to previous years goes parallel with the decrease in the proportion of individuals being physically active during the COVID-19 pandemic so far. This is not surprising because physical activity can improve BP within hours²⁵ as well as reduce hypertension in children with obesity.²⁶ Therefore, inactivity might lead to higher BP in the long term. It is even suggested that the positive effects of physical activity on BP can be negated with excessive sedentary time.²⁷ Unfortunately, there are still only few studies describing the association of the COVID-19 pandemic with BP in children. A Chinese work group found elevated BP in children during the COVID-19 quarantine,²⁸ but studies on children with diabetes are scarce. It must be mentioned that other factors are likely to contribute to this increase in BP during the pandemic, such as stress, anxiety, or other psychological effects, as well as dietary habits that might have changed at least during the lockdown periods.

As TC, HDL, and non-HDL were significantly higher in 2020 and 2021 than expected from the previous trend since 2016, one might assume that the detrimental (non-

HDL) and beneficial (HDL) effects could negate each other. However, it is discussed in the literature that an increase in non-HDL as marker of the combined atherogenic lipids might be most important, especially in people with diabetes.^{29,30} It is further suspected that remnant cholesterol might be another important marker for cardiovascular risk independently from traditional risk factors such as LDL³¹ and that HDL might have a U-shaped – rather than a linear – association with cardiovascular risk.³² This is confirmed by a recent cohort study from the United Kingdom that identified very high HDL levels being associated with mortality in people with coronary artery disease.³³ We, therefore, assume that the elevated levels of non-HDL and RC could lead to a more atherogenic lipid profile during the COVID-19 pandemic, despite the potentially beneficial effect of increasing HDL. This effect seems to be independent of weight status, as neither BMI-SDS itself was higher than expected in 2020/2021 nor adjustment for BMI-SDS changed these results. This would be in line with another observational study that found higher lipid values, but no significant changes in BMI *z*-scores in young people with T1D aged 2–21 years.³⁴ The shown development of hypertension and dyslipidemia depicts the need for early detection and adequate treatment of these cardiovascular risk factors in young people with T1D, because it is known that the management, especially of dyslipidemia, is suboptimal in adults with type 1 and type 2 diabetes.^{35,36} The increase of atherogenic lipid levels, namely non-HDL, was although to a lower extent than in the whole study cohort also present in well controlled individuals with HbA1c <7.5% suggesting that this development does not only affect children and adolescents with worse glycemic control.

Owing to the closure of schools and sports clubs, the proportion of children and young adults with T1D doing organized sports decreased from over 70% in previous years to 35% at the beginning of 2021, recovering to about 65% at the end of 2021. Several previous studies have reported a worrying decline in physical activity in children and adolescents with and without diabetes.^{8,37,38} In regard to a recent meta-analysis we have to assume that not only the percentage of individuals doing organized sports but also the amount of physical activity, especially with high intensity, was lower.¹⁰ As in the DPV registry, only club sports are accurately documented, children might have played outdoors to a higher extent, adolescents and young adults could have performed at-home exercises or increased their habitual physical activity as suggested by a study on children during the first lockdown in Germany.³⁹ However, mostly children with good socioeconomic status had the opportunity to compensate the loss of organized sports by being habitually active.¹² It is known that during summer 2020, some sports

facilities in European countries reopened occasionally, but most of them closed again in winter 2020/2021 resulting in an even higher decline in physical activity.⁴⁰ This is in line with our findings on a short recovery in the proportion of doing organized sports from June to September 2020, followed by the lowest proportion in January and February 2021.

Smoking behavior did not reveal remarkable differences during the COVID-19 pandemic compared to previous years. Other studies found quite varying lifestyle changes during the first wave of COVID-19.^{41,42} It might be individually different how to respond to a challenging situation with fear of infection and reduced peer interaction due to social distancing but also the possibility to structure one's life in a healthier way, for example, because of more control over smoking behavior of the children and better dietary habits because the parents worked partly at home and therefore had more time to provide healthier food.

The strength of this study was that >30 000 children and young adults with T1D, providing data on over 100 000 patient years between 2016 and 2021, could be analyzed, and therefore, reliable results were generated on the change in markers for cardiovascular risk, physical activity and lifestyle factors during the COVID-19 pandemic compared to previous years. It is an important approach to take the preexisting trends of these risk factors into account to minimize error-prone interpretations that could emerge when only a single time point before the pandemic is compared with a second time point within the COVID-19 pandemic. Nevertheless, there are some limitations: In this diabetes patient registry, only data on organized sports were accurately documented. It is, therefore, possible, that some individuals conducted exercises at home as a reaction to the closure of sport clubs. For this reason, we confined ourselves to analyzing the proportion of children and young adults reporting any physical activity by period as documented in the DPV data set. Unfortunately, no data on sedentary time and use of media were available. Further, some patients might not (or less frequently) have seen their diabetologists during the pandemic, which might have led to bias in the population before and within the pandemic. We tried to consider this by analyzing aggregated data per year for the main outcomes, as it is likely that children and young adults with diabetes had at least one visit per year, even during the two pandemic years. It must be stated that our data cannot provide causality; we can only speculate about underlying reasons.

Taken together, we assume that there is a worsening in BP and lipid profile present over a period of 2 years by now in this already vulnerable and young population with T1D. This deterioration in cardiovascular risk

factors seems to be independent of the ongoing increase in BMI-SDS. Cigarette smoking is assumingly not strongly associated with the increase in BP and lipid values during the COVID-19 pandemic. The reduced physical activity together with increased sedentary time, dietary habits, and psychological as well as socioeconomic aspects might be more important for this development. Although organized sports seemed to go back to near normal availability by the end of 2021, the differences between observed and predicted BP and non-HDL were even higher in 2021 than in 2020. Therefore, it will be important to follow these individuals in future studies to investigate how cardiovascular outcomes develop during the ongoing pandemic.

AUTHOR CONTRIBUTIONS

Alexander J. Eckert analyzed the data and wrote the first draft of the paper. Reinhard W. Holl conceived and coordinated the study and reviewed the article critically. Joachim Rosenbauer helped with statistical analysis and reviewed the article critically. The authors Sabine Linke, Karl-Otfried Schwab, Thekla von dem Berge, Eckhard Schönau, Ibrahim Duran, Axel Dost, Christine Joisten, Heike Bartelt, and Katarina Braune participated in the DPV initiative by providing data and reviewed the article critically.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

- Ekelund U, Luan J, Sherar LB, et al. Moderate to vigorous physical activity and sedentary time and cardiometabolic risk factors in children and adolescents. *JAMA*. 2012;307:704-712.
- Herbst A, Kordon O, Schmidt F, Holl RW, DPV Initiative of the German Working Group for Pediatric Diabetology Germany. Impact of physical activity on cardiovascular risk factors in children with type 1 diabetes: a multicenter study of 23,251 patients. *Diabetes Care*. 2007;30:2098-2100.
- Hofer SE, Rosenbauer J, Grulich-Henn J, Naeke A, Fröhlich-Reiterer E, Holl RW. Smoking and metabolic control in adolescents with type 1 diabetes. *J Pediatr*. 2009;154:20-23.e1.
- Schwab KO, Doerfer J, Hallermann K, et al. Marked smoking-associated increase of cardiovascular risk in childhood type 1 diabetes. *Int J Adolesc Med Health*. 2008;20:285-292.
- Robert Koch Institut Aktueller Lage-/Situationsbericht des RKI zu COVID-19. Accessed Jul 26, 2022. https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/Situationsberichte/Gesamt.html.
- World Health Organization Coronavirus disease (COVID-19) Weekly Epidemiological Update and Weekly Operational Update. Accessed Jul 26, 2022. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>.
- Deutsches Ärzteblatt Lockdown: Hälfte der Kinder kann nicht trainieren. Accessed Jul 06, 2021. <https://www.aerzteblatt.de/nachrichten/121432/Lockdown-Haelfte-der-Kinder-kann-nicht-trainieren>.
- Lopez-Bueno R, Lopez-Sanchez GF, Casajus JA, Calatayud J, Tully MA, Smith L. Potential health-related behaviors for pre-school and school-aged children during COVID-19 lockdown: a narrative review. *Prev Med*. 2021;143:106349.
- Pietrobelli A, Pecoraro L, Ferruzzi A, et al. Effects of COVID-19 lockdown on lifestyle behaviors in children with obesity living in Verona, Italy: a longitudinal study. *Obesity (Silver Spring)*. 2020;28:1382-1385.
- Neville RD, Lakes KD, Hopkins WG, et al. Global changes in child and adolescent physical activity during the COVID-19 pandemic: a systematic review and meta-analysis. *JAMA Pediatr*. 2022;176:886-894.
- Schmidt SCE, Burchartz A, Kolb S, et al. (2021) Zur Situation der körperlich-sportlichen Aktivität von Kindern und Jugendlichen während der COVID-19 Pandemie in Deutschland: Die Motorik-Modul Studie (MoMo).
- Schmidt SCE, Burchartz A, Kolb S, Niessner C, Oriwol D, Woll A. Influence of socioeconomic variables on physical activity and screen time of children and adolescents during the COVID-19 lockdown in Germany: the MoMo study. *Ger J Exerc Sport Res*. 2021;52:362-373.
- Akyurek N, Atabek ME, Eklioglu BS, Alp H. Evaluation of the relationship between cardiovascular risk factors and periaortic fat thickness in children with type 1 diabetes mellitus. *Diabetes Metab*. 2015;41:338-341.
- Schwab KO, Doerfer J, Hecker W, et al. Spectrum and prevalence of atherogenic risk factors in 27,358 children, adolescents, and young adults with type 1 diabetes: cross-sectional data from the German diabetes documentation and quality management system (DPV). *Diabetes Care*. 2006;29:218-225.
- Al Agha AE, Alharbi RS, Almohammadi OA, Yousef SY, Sulimani AE, Alaama RA. Impact of COVID-19 lockdown on glycemic control in children and adolescents. *Saudi Med J*. 2021;42:44-48.
- Iughetti L, Trevisani V, Cattini U, et al. COVID-19 and type 1 diabetes: concerns and challenges. *Acta Biomed*. 2020;91:e2020033.
- Hofer SE, Schwandt A, Holl RW, Austrian/German DPV Initiative. Standardized documentation in pediatric Diabetology: experience from Austria and Germany. *J Diabetes Sci Technol*. 2016;10:1042-1049.
- Karges B, Schwandt A, Heidtmann B, et al. Association of Insulin Pump Therapy vs insulin injection therapy with severe hypoglycemia, ketoacidosis, and glycemic control among children, adolescents, and young adults with type 1 diabetes. *JAMA*. 2017;318:1358-1366.
- Kromeyer-Hauschild K, Moss A, Wabitsch M. Referenzwerte für den Body-Mass-Index für Kinder, Jugendliche und Erwachsene in Deutschland. Anpassung der AGA-BMI-Referenz im Altersbereich von 15 bis 18 Jahren. *Adipositas*. 2015;9:123-127.
- Neuhauser H, Schienkiewitz A, Rosario AS, Dortschy R, Kurth BM. Referenzperzentile für anthropometrische Maßzahlen und Blutdruck aus der Studie zur Gesundheit von Kindern und Jugendlichen in Deutschland (KiGGS). In: *Beiträge Zur Gesundheitsberichterstattung Des Bundes*. Robert Koch-Institute; 2013 (2. Erweiterte Auflage).
- Rosenbauer J, Dost A, Karges B, et al. Improved metabolic control in children and adolescents with type 1 diabetes: a trend analysis using prospective multicenter data from Germany and Austria. *Diabetes Care*. 2012;35:80-86.
- Bohn B, Herbst A, Pfeifer M, et al. Impact of physical activity on glycemic control and prevalence of cardiovascular risk factors in adults with type 1 diabetes: a cross-sectional multicenter study of 18,028 patients. *Diabetes Care*. 2015;38:1536-1543.
- Shah N, Karguppikar M, Bhor S, Ladkat D, Khadilkar V, Khadilkar A. Impact of lockdown for COVID-19 pandemic in Indian children and youth with type 1 diabetes from different socio-economic classes. *J Pediatr Endocrinol Metab*. 2020;34:217-223.
- Kim MJ, Lee KH, Lee JS, et al. Trends in body mass index changes among Korean adolescents between 2005-2020, including the COVID-19 pandemic period: a national representative survey of one million adolescents. *Eur Rev Med Pharmacol Sci*. 2022;26:4082-4091.
- Carpio-Rivera E, Moncada-Jimenez J, Salazar-Rojas W, Solera-Herrera A. Acute effects of exercise on blood pressure: a meta-analytic investigation. *Arq Bras Cardiol*. 2016;106:422-433.
- Aguilar-Cordero MJ, Rodriguez-Blanque R, Leon-Rios X, Exposito Ruiz M, Garcia Garcia I, Sanchez-Lopez AM. Influence of physical activity on blood pressure in children with overweight/obesity: a randomized clinical trial. *Am J Hypertens*. 2020;33:131-136.
- Garcia-Hermoso A, Hormazabal-Aguayo I, Gonzalez-Calderon N, et al. Exercise program and blood pressure in children: the moderating role of sedentary time. *J Sci Med Sport*. 2020;23:854-859.
- Qiu N, He H, Qiao L, et al. Sex differences in changes in BMI and blood pressure in Chinese school-aged children during the COVID-19 quarantine. *Int J Obes (Lond)*. 2021;45:2132-2136.
- Carr SS, Hooper AJ, Sullivan DR, Burnett JR. Non-HDL-cholesterol and apolipoprotein B compared with LDL-



- cholesterol in atherosclerotic cardiovascular disease risk assessment. *Pathology*. 2019;51:148-154.
30. Sone H, Nakagami T, Nishimura R, Tajima N, MEGA Study Group. Comparison of lipid parameters to predict cardiovascular events in Japanese mild-to-moderate hypercholesterolemic patients with and without type 2 diabetes: subanalysis of the MEGA study. *Diabetes Res Clin Pract*. 2016;113:14-22.
 31. Quispe R, Martin SS, Michos ED, et al. Remnant cholesterol predicts cardiovascular disease beyond LDL and ApoB: a primary prevention study. *Eur Heart J*. 2021;42:4324-4332.
 32. Feng M, Darabi M, Tubeuf E, et al. Free cholesterol transfer to high-density lipoprotein (HDL) upon triglyceride lipolysis underlies the U-shape relationship between HDL-cholesterol and cardiovascular disease. *Eur J Prev Cardiol*. 2020;27:1606-1616.
 33. Liu C, Dhindsa D, Almuwaqqat Z, et al. Association between high-density lipoprotein cholesterol levels and adverse cardiovascular outcomes in high-risk populations. *JAMA Cardiol*. 2022;7:672-680.
 34. Shah N, Khadilkar V, Oza C, et al. Impact of decreased physical activity due to COVID restrictions on cardio-metabolic risk parameters in Indian children and youth with type 1 diabetes. *Diabetes Metab Syndr*. 2022;16:102564.
 35. Shah VN, Grimsman JM, Foster NC, et al. Undertreatment of cardiovascular risk factors in the type 1 diabetes exchange clinic network (United States) and the prospective diabetes follow-up (Germany/Austria) registries. *Diabetes Obes Metab*. 2020;22:1577-1585.
 36. Bramlage P, Lanzinger S, Rathmann W, et al. Dyslipidaemia and its treatment in patients with type 2 diabetes: a joint analysis of the German DIVE and DPV registries. *Diabetes Obes Metab*. 2017;19:61-69.
 37. Dunton GF, Do B, Wang SD. Early effects of the COVID-19 pandemic on physical activity and sedentary behavior in children living in the U.S. *BMC Public Health*. 2020;20:1351-1353.
 38. Telford DM, Signal DM, Hofman PL, Gusso S. Physical activity in adolescents with and without type 1 diabetes during the New Zealand COVID-19 pandemic lockdown of 2020. *Int J Environ Res Public Health*. 2021;18:4475. doi:10.3390/ijerph18094475
 39. Schmidt SCE, Anedda B, Burchartz A, et al. Physical activity and screen time of children and adolescents before and during the COVID-19 lockdown in Germany: a natural experiment. *Sci Rep*. 2020;10:21780-21784.
 40. Kovacs VA, Brandes M, Suesse T, et al. Are we underestimating the impact of COVID-19 on children's physical activity in Europe?-a study of 24 302 children. *Eur J Public Health*. 2022;32:494-496.
 41. Jordan S, Starker A, Krug S, et al. Health behaviour and COVID-19: initial findings on the pandemic. *J Health Monit*. 2020;5:2-14.
 42. Rubin R. Alcohol-related diseases increased as some people drank more during the COVID-19 pandemic. *JAMA*. 2021;326:209-211.

SUPPORTING INFORMATION

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

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