pronounced trends were found among HIV-positive MSM. No studies reported on other outcomes of interest, such as acquisition or transmission of other STIs or complications of tertiary syphilis or neurosyphilis.

One fair-quality study (n = 361) addressed the performance of risk assessment methods (KQ2).[5] Allan-Blitz et al developed and evaluated an online risk calculator for predicting future syphilis among high-risk individuals (eg, individuals living with HIV or who have a history of syphilis infection) seeking STI testing or treatment. The final model for predicting syphilis incidence within the next 3 months demonstrated an area under the curve of 0.69 and included the following risk factors: current HIV infection, history of syphilis infection, number of male sex partners, and receptive sex role in anal sex in the past 3 months.

One fair-quality study (n = 1097) addressed potential harms of screening for syphilis (KQ3).[6] Reynolds et al examined factors associated with emotional stress just before and after syphilis testing. Factors that were associated with stress at pretest were injection drug use, Black race, and less than a high school education. Factors associated with stress at posttest included less than a high school education and single marital status. The results suggested that emotional stress may be a common experience for individuals, although the study did not directly compare changes in levels of emotional stress pretest vs posttest.

Discussion | The findings of this targeted evidence update are generally consistent with those from the prior systematic review that supported the USPSTF 2016 statement recommending screening for syphilis in at-risk adolescents and adults. Limitations of this review include that only studies in English, conducted in very high-income and high-income countries, and conducted in settings and with tests applicable to current practice in the US were included. Further research on novel screening approaches, how to best identify persons most likely to benefit from screening, and the effectiveness of specific screening intervals among different risk populations is still needed.

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Editorial Disclaimer: This evidence report is presented as a document in support of the accompanying USPSTF recommendation statement. It did not undergo additional peer review after submission to *JAMA*.

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SARS-CoV-2 Infections and Presymptomatic Type 1 Diabetes Autoimmunity in Children and Adolescents From Colorado, USA, and Bavaria, Germany

An increased incidence of clinical diabetes has been reported in children with previous COVID-19.[1,2] It is plausible that the virus may trigger autoimmune response to the islets or

hasten metabolic decompensation in persons with already established islet autoimmunity. We tested the hypothesis that previous SARS-CoV-2 infection was associated with autoimmunity, which predicts future type 1 diabetes.

Methods | In 2020 and 2021, a cross-sectional screening for islet autoantibodies and SARS-CoV-2 antibodies was offered to children and adolescents aged 1 to 18 years participating in the Autoimmunity Screening for Kids (ASK)[3] in Colorado, US, and to children aged 1 to 10.9 years enrolled in the Fr1da study[4] in Bavaria, Germany. In addition, in Bavaria, autoantibody-negative children were followed up after detection of SARS-CoV-2 antibodies with blood sample collection every 3 months. Screening was approved by the respective institutional review boards. Written informed consent was obtained from parents of each study participant. The race and ethnicity of participants were reported by parents using the US Census categories and included to control for possible confounding.

Supplemental content

Past SARS-CoV-2 infection was defined by the presence of antibodies to both SARS-CoV-2 receptor binding domain and nucleocapsid proteins,[5,6] with similar detection thresholds for positivity as assessed by the World Health Organization international standard. Autoantibodies to insulin, glutamic acid decarboxylase, islet antigen 2, and zinc transporter 8 autoantibodies were measured using comparable methods (eMethods in the Supplement). Study outcomes included the presence of multiple or single high-affinity islet autoantibodies that carry, respectively, a 50% and 30% risk of progression to clinical diabetes in 5 years.

Statistical analyses were performed using R version 4.1.2 (R Core Team). Multivariable logistic regression was used to assess independent associations between previous SARS-CoV-2 infection and islet autoimmunity as well as testing for interactions by study site. Standardized assessments of exposure and outcomes permitted multivariable logistic regression analysis of combined data to maximize statistical power. Covariates included age, sex, family history of type 1 diabetes, and race and ethnicity. Sensitivity analyses were performed excluding siblings and offspring of

Table 1. Baseline Characteristics of the Study Population

	Previous SARS-CoV-2 infection, No. (%)			
	Colorado (n = 4717)		Bavaria (n = 47 253)	
Characteristic	Yes (n = 1524)	No (n = 3193)	Yes (n = 2862)	No (n = 44 391)
Autoantibodies present				
Multiple islet autoantibodies	7 (0.46)	14 (0.44)	8 (0.28)	133 (0.31)
Single high-affinity islet autoantibody	11 (0.74)	15 (0.47)	4 (0.14)	50 (0.11)
Sex				
Female	767 (50.3)	1607 (50.3)	1410 (49.3)	21 670 (48.8)
Male	757 (49.7)	1586 (49.7)	1452 (50.7)	22 721 (51.2)
Age group, y				
1.0-4.9	381 (25.0)	868 (27.2)	1610 (56.3)	29 537 (66.5)
5.0-11.9	651 (42.7)	1473 (46.1)	1252 (43.7)	14 854 (33.5)
12.0-18.0	492 (32.3)	852 (26.7)	NA	NA
First-degree relative with type 1 diabetes				
Yes	49 (3.2)	188 (5.9)	111 (3.9)	1555 (3.5)
No	1475 (96.8)	3005 (94.1)	2751 (96.1)	42 836 (96.5)
Race and ethnicity[a]				
African American	114 (7.5)	208 (6.5)		
American Indian or Alaska Native	27 (1.8)	47 (1.5)		
Asian American	23 (1.5)	99 (3.1)		
Hispanic	1004 (65.9)	1198 (37.5)		
Native Hawaiian and Other Pacific Islander	4 (0.3)	7 (0.2)		
Non-Hispanic White	287 (18.8)	1400 (43.8)		
Other	43 (2.8)	138 (4.3)		
Unknown	22 (1.4)	55 (1.7)		
Received SARS-CoV-2 vaccine (before or after COVID-19 infection)				
Yes	192 (12.6)	345 (10.8)		
No	1317 (86.4)	2844 (89.1)	None has received vaccine	
Unknown	15 (1.0)	4 (0.1)		

Abbreviation: NA, not applicable.

[a] "Other" was one of the categories from which parents could choose in the survey. Race and ethnicity were not collected in Bavaria.

Table 2. Results of Multivariable Logistic Regression for an Association Between Autoantibodies and SARS-CoV-2 Antibody Status, Colorado and Bavaria (N = 51 970)

	All participants		Excluded siblings and offspring of people with type 1 diabetes		Excluded youths vaccinated against SARS-CoV-2	
Covariate[a]	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Multiple islet autoantibodies						
SARS-CoV-2 infection	1.06 (0.59-1.80)	.83	0.90 (0.44-1.65)	.74	1.37 (0.46-3.71)	.55
Sex (male)	1.05 (0.77-1.43)	.38	1.12 (0.80-1.59)	.51	0.69 (0.26-1.70)	.42
Age/y	1.02 (0.97-1.08)	.76	1.03 (0.97-1.09)	.34	1.00 (0.90-1.11)	>.99
First-degree relative with type 1 diabetes	6.34 (4.22-9.25)	<.001	NA	NA	4.65 (1.29-13.33)	.02
Racial and ethnic minority group[b]	0.50 (0.20-1.20)	.12	0.75 (0.28-2.13)	.58	0.46 (0.17-1.19)	.11
Study site (Colorado)	1.79 (0.91-3.23)	.09	1.53 (0.62-3.22)	.33	NA	NA
Single high-affinity islet autoantibody						
SARS-CoV-2 infection	1.34 (0.70-2.44)	.36	1.45 (0.75-2.67)	.25	1.61 (0.66-3.79)	.29
Sex (male)	0.66 (0.42-1.02)	.06	0.68 (0.43-1.07)	.10	0.90 (0.39-2.07)	.81
Age/y	1.10 (1.03-1.17)	.004	1.10 (1.03-1.17)	.005	1.07 (0.97-1.17)	.16
First-degree relative with type 1 diabetes	1.30 (0.39-3.14)	.63	NA	NA	2.11 (0.33-7.40)	.37
Racial and ethnic minority group[b]	0.99 (0.44-2.37)	.98	0.99 (0.43-2.49)	.99	1.05 (0.44-2.70)	.91
Study site (Colorado)	2.76 (1.18-5.78)	.02	2.60 (1.06-5.66)	.04	NA	NA

Abbreviation: NA, not applicable.

[a] Covariates included age, sex, family history of type 1 diabetes, and race and ethnicity (in Colorado).

[b] Racial and ethnic minority was defined as race or ethnicity other than non-Hispanic White.

people with type 1 diabetes and separately excluding youths vaccinated against SARS-CoV-2. Two-tailed *P* values less than .05 were considered significant.

Results | Prior SARS-CoV-2 infections were identified in 1524 (32.3%) of 4717 Colorado youths (median age, 8.6 years; 50.3% female) and in 2862 (6.1%) of 47 253 Bavarian children (median age, 3.9 years; 48.9% female) (**Table 1**). Multiple islet autoantibodies were detected in 21 Colorado youths (0.45%) and in 141 Bavarian children (0.30%). In addition, 26 (0.55%) and 54 (0.11%) Colorado and Bavarian youths, respectively, were positive for a single high-affinity islet autoantibody. The prevalence of multiple or single high-affinity islet autoantibodies did not significantly differ between youths with vs without previous SARS-CoV-2 infection in Colorado (1.18% vs 0.91%, *P* = .43) or Bavaria (0.42% vs 0.41%, *P* = .88). Previous SARS-CoV-2 infection was not significantly associated with the presence of multiple islet autoantibodies (odds ratio, 1.06 [95% CI, 0.59-1.80]; *P* = .83) or a single high-affinity islet autoantibody (odds ratio, 1.34 [95% CI, 0.70-2.44]; *P* = .36) controlling for confounders (**Table 2**).

There was no significant interaction between the study site and the association with SARS-CoV-2 infection, sex, age, or family history of type 1 diabetes. Sensitivity analyses excluding siblings and offspring of people with type 1 diabetes or vaccinated youths yielded similar results (Table 2). In Bavaria, 465 children were followed up longitudinally after first detection of SARS-CoV-2 antibodies for a median of 8.9 months (IQR, 3.4-10.3) and up to 2 years. None of these children developed islet autoantibodies.

Discussion | Screening of more than 50 000 youths in diverse populations of Colorado and Bavaria found no association of SARS-CoV-2 infection with autoimmunity related to development of type 1 diabetes. Study limitations include the low prevalence of autoantibodies, limiting the power to detect an increase in risk associated with SARS-CoV-2 infection. Moreover, the cross-sectional design did not allow determination of whether autoantibodies developed before or after SARS-CoV-2 infection. Long-term follow-up of persons with preexisting autoimmunity is necessary to determine whether SARS-CoV-2 accelerates progression to clinical diabetes.

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COMMENT & RESPONSE

Ischemic Stroke in Patients With Asymptomatic Severe Carotid Stenosis Without Surgical Intervention

To the Editor In a recent study[1] of the clinical outcomes of 3737 adults with asymptomatic severe carotid stenosis who did not undergo carotid revascularization, the 5-year ipsilateral stroke rate was 4.7%. The authors concluded that "these findings may inform decision-making regarding surgical and medical treatment for patients with asymptomatic severe carotid artery stenosis." A multicenter randomized prospective trial[2] from 2021 reported similar 5-year stroke rates for 3625 patients with asymptomatic severe carotid stenosis who underwent carotid endarterectomy. Based on these studies,[1,2] one could come to the conclusion that results of medical and surgical therapy for patients with severe carotid stenosis are similar.

However, even if not specified, the patients in this study[1] were probably not considered candidates for surgery because of severe comorbidities; the authors stated that "patients not receiving intervention tended to be older, female, and with a larger overall comorbidity burden." This was confirmed by the short life expectancy of the cohort: only 43 patients (1%) were alive at the end of the study (mean follow-up, 4.1 years).

Analysis of the optimal form of therapy to reduce stroke in asymptomatic carotid artery stenosis has proven difficult over the last decade with the introduction of new forms of medical and surgical endovascular treatments. Guidelines from the Society for Vascular Surgery and the American Heart Association/American Stroke Association[3,4] recommend carotid endarterectomy for asymptomatic carotid artery stenosis if a patient's minimum life expectancy is 3 to 5 years. According to those guidelines, most patients in this study[1] were not candidates for surgery, and they were followed up with noninvasive imaging. Indeed, 40% of the patients underwent carotid surgery during a relative short follow-up, presumably because of transient ischemic attack or severe progression of occlusive disease.

The results of this study[1] demonstrate the importance of a wise therapeutic approach for patients with asymptomatic severe carotid disease and reduced life expectancy, as suggested by the Society for Vascular Surgery and the American Heart Association, rather than as a comparison with the results of surgery. The study also highlights the importance of a close collaboration between physicians and surgeons in choosing the optimal therapy for a heterogeneous group of patients and the need for accurate noninvasive follow-up and appropriate medical therapy.[5]

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