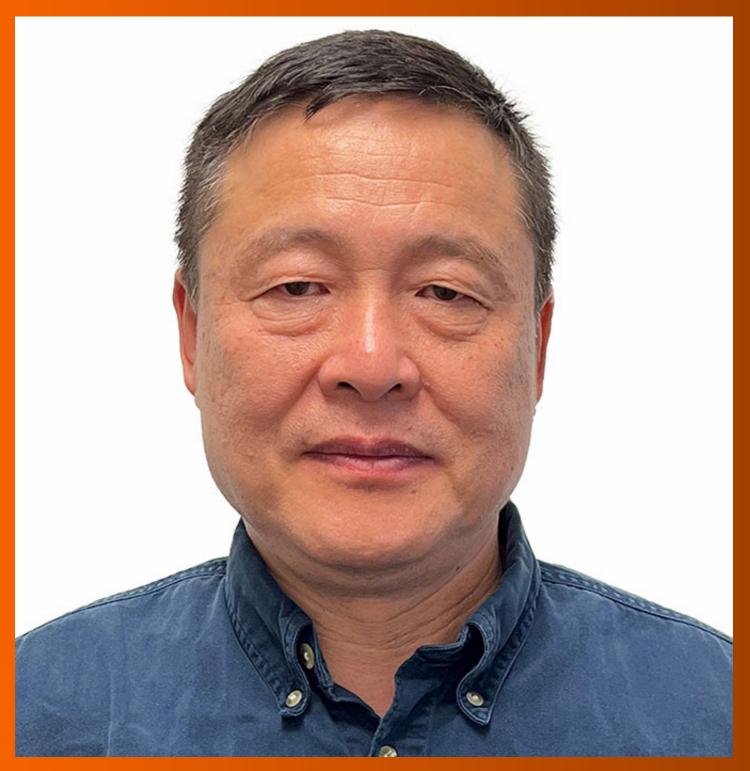
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ABOUT COVER

Editorial Board Member of World Journal of Diabetes, Guo-Xun Chen, PhD, Associate Professor, Director, Department of Nutrition, The University of Tennessee, Knoxville, TN 37909, United States. gchen6@utk.edu

AIMS AND SCOPE

The primary aim of World Journal of Diabetes (WJD, World J Diabetes) is to provide scholars and readers from various fields of diabetes with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WID mainly publishes articles reporting research results and findings obtained in the field of diabetes and covering a wide range of topics including risk factors for diabetes, diabetes complications, experimental diabetes mellitus, type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes, diabetic angiopathies, diabetic cardiomyopathies, diabetic coma, diabetic ketoacidosis, diabetic nephropathies, diabetic neuropathies, Donohue syndrome, fetal macrosomia, and prediabetic state.

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MINIREVIEWS

Multiple influences of the COVID-19 pandemic on children with diabetes: Changes in epidemiology, metabolic control and medical care

Stefano Zucchini, Andrea Scozzarella, Giulio Maltoni

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Stefano Zucchini, Andrea Scozzarella, Giulio Maltoni, Department of Pediatric, IRCCS AOU di Bologna, Bologna 40138, Italy

Corresponding author: Stefano Zucchini, MD, PhD, Adjunct Associate Professor, Department of Pediatric, IRCCS AOU di Bologna, 9 Via Massarenti, Bologna 40138, Italy. stefano.zucchini@aosp.bo.it

Abstract

The coronavirus disease 2019 (COVID-19) pandemic has heavily affected health worldwide, with the various forms of diabetes in children experiencing changes at various levels, including epidemiology, diabetic ketoacidosis rates and medical care. Type 1 diabetes showed an apparent increase in incidence, possibly owing to a direct damage of the virus to the β -cell. Diabetic ketoacidosis also increased in association with the general fear of referring patients to the hospital. Most children with diabetes (both type 1 and type 2) did not show a worsening in metabolic control during the first lockdown, possibly owing to a more controlled diet by their parents. Glucose sensor and hybrid closed loop pump technology proved to be effective in all patients with type 1 diabetes during the pandemic, especially because the downloading of data allowed for the practice of telemedicine. Telemedicine has in fact grown around the world and National Health Systems have started to consider it as a routine activity in clinical practice. The present review encompasses all the aspects related to the effects of the pandemic on the different forms of diabetes in children.

Key Words: Diabetes; COVID-19; Children; Diabetic ketoacidosis; Telemedicine

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Core Tip: Children with diabetes were significantly affected by the pandemic. There was a significant incidence increase of type-2 diabetes whereas conflicting results were found in type-1 diabetes. Metabolic control was not affected in the two types of the disease, whereas diabetic ketoacidosis incidence increased significantly, Telemedicine was very helpful in the period of social restrictions and significantly developed during the pandemic.

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INTRODUCTION

In 2020, humanity went through one of the most dangerous pandemics in human history, as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus spread worldwide, causing national lockdowns, national health systems to overload, as well as continuous uncertainties. By October 11th 2022, 620 million confirmed cases and more than 6.54 million deaths had been reported globally[1]. After the first outbreak in China, Italy was one of the first countries to be significantly affected by the pandemic^[2]. The healthcare crisis forced all countries worldwide to adopt emergency measures labeled as social restrictions, such as working remotely, wearing facemasks as protection, avoiding close social contacts.

Patients with most forms of diabetes may be considered a vulnerable population and were often negatively affected by the pandemic. Adult patients with type 2 diabetes (T2D), for example, experienced higher rates of hospitalization and more deaths, since obesity, hypertension and diabetes itself are known to be risk factors for severe SARS-CoV-2-related pneumonia[3,4]. Furthermore, the forced reduction in physical activities caused a significant increase in obesity rates at all ages, making the whole population more prone to develop T2D[5]. The limited availability of the emergency departments and of the national healthcare systems in general was associated with an increase in the acute and chronic complications of diabetes [6,7].

Moving to the pediatric population, SARS-CoV-2 infections have affected patients' health and care in many ways. A change in epidemiology occurred, affecting both T1D and T2D patients for various reasons, different rates of diabetic ketoacidosis (DKA) were described and there may have been a worsening of metabolic control in both T1D and T2D patients. Treatment mainstay for patients with T1D, for example, requires a fine-tuned balance between insulin doses on the one hand and food intake, glucose concentrations, and daily activities on the other. Finally, the general emergency forced the national healthcare services to adapt and, as expected, telemedicine health care was implemented around the world.

The present review encompasses the various changes that may have affected children with diabetes in the past two years, ranging from the epidemiology of both T1D and T2D, to the occurrence of DKA, the changes in metabolic control and general well-being and finally the development of telemedicine.

EPIDEMIOLOGY OF TYPE 1 DIABETES

T1D, the most prevalent form of diabetes in children, is an autoimmune disease whose trigger is currently under debate and may be different from patient to patient[8]. Nevertheless, virus infections have long been considered elicitors of autoimmune response in genetically susceptible patients, rather than the direct killer of the β -cells[9,10]. However, the possibility that viruses may directly damage β cells has never been totally excluded; with past viruses they have also been isolated in pancreatic tissues from diabetic patients 11,12. Since the outbreak of the pandemic, it has been stated that SARS-CoV-2 binds to angiotensin-converting enzyme 2 (ACE2) receptors in the pancreas, possibly damaging islet cells and reducing insulin release^[13], the description of viral infiltration in pancreatic autopsies in patients deceased owing to SARS-CoV-2 infections raised great concern^[14,15]. On the other hand, it has been proven that SARS-CoV-2 enters other cells of the endocrine system, such as the thyroid and the gonads, as the ACE2 receptor is also expressed in these tissues [16]. The selective destruction of the β cells was initially seen as a contributing factor in the worsening of metabolic control of many diabetic patients during the SARS-CoV-2 infection: In other words, the severe DKA that were observed during and after the infection in adult diabetic patients was supposed to be a clinical indicator of a lack of insulin due to β -cell loss or malfunction[17,18]. As reported in recent clinical studies[19,20], the initial question was whether the virus directly penetrates β -cells, potentially leading to endocrine dysregulation and in the end to autoantibody-negative T1D. Alternatively, SARS-CoV-2 infections may be a



precipitating factor of T1D clinical onset. Luckily, in July 2021, the national data coming from the German Diabetes Prospective Follow-up Registry (DPV) was published, which found no evidence that the pandemic was causing a significant increase in the number of new autoantibody-negative cases of T1D in children, adolescents and young adults[21]. According to the authors, the direct diabetogenic effects of the virus seemed highly unlikely. No other data coming from registry studies has been published thus far, therefore the phenomenon is currently under investigation.

As for incidence, the published studies have thus far yielded conflicting results (Table 1). The initial studies led in Italy, which experienced an early spread of the infection, seemed to confirm an increase in overall incidence in children: Mameli et al^[22] described, in fact, an incidence increase in the Lombardy region above all during the second wave of the infection, while Schiaffini et al [23] reported a 22%-35% increase in the Lazio region. During the first wave at the beginning of 2020, most children were forced to stay at home and were marginally affected by the pandemic^[24], making the influence of the SARS-CoV-2 virus on T1D incidence highly unlikely. This was again confirmed by the DPV registry [25], which found a non-significant increase in incidence between the years 2019 and 2020 (22.2 vs 23.4/100000 0-14 years). Opposite findings were published by the CDC in the US Morbidity and Mortality Weekly Report, which showed an increased risk of pediatric diabetes with the SARS-CoV-2 infection[26]. Heavy criticism was immediately raised based on the results^[27], including the possible mixture of T1D and T2D cases, the lack of data on insured children (1/3rd of all United States children) and others. A more accurate analysis on possible relations between the SARS-CoV-2 infection and T1D incidence was published by Scottish authors[28]. They studied the cause-effect link between infection and T1D onset by also considering the time distance between the 2 phenomena and found no significant association, despite an apparent increase in incidence. Like the DPV studies, they concluded that the SARS-CoV-2 infection itself was not the cause of this increase. A more conclusive result was reached by the Sweet consortium^[29], which analyzed data from 17280 cases of T1D diagnosed between 2018 and 2021 from 92 worldwide centers and focused on seasonality. They failed to prove strong direct virus-related effects, and only described a change in seasonality reflecting the spread of the pandemic: A delay in the usual winter peak in Northern Europe and North America, in fact, and a stronger peak during the summer and autumn months were described.

The conclusion of the ISPAD guidelines on epidemiology helps summarize this debated issue[30]: An increased incidence of pediatric T1D onset occurring at the same time as the pandemic has been reported in Germany and the United States, which may be due to a concurrent illness precipitating the clinical diagnosis of T1D rather than a change in the risk of developing T1D, as this often take years. Therefore, one must wait more years before drawing definitive conclusions on the matter.

EPIDEMIOLOGY OF TYPE 2 DIABETES

The magnitude of the pandemic's effects on the incidence of diabetes was stronger for T2D than for T1D. The main reason for this is that both adults and adolescents suffering from obesity gained weight while social restrictions were in force[5,31], causing a bidirectional impact between the two pathological conditions. Obesity is a known predisposing factor of T2D, and about three quarters of children with T2D are obese[32]. Furthermore, the possible role of a direct damage of the β -cells by the virus ought to be considered as a precipitating factor also for T2D.

The more precise data on T2D incidence comes from the countries where T2D is frequent, for example the United States (Table 1). As an example, its incidence increased in Florida from 14.6/100000 prepandemic to 16.9/100000 in the first quarter of 2020[33]. There was a 293% increase in Illinois[34] and a 225% increase in Wisconsin[35] compared to the pre-pandemic mean. As expected, the increase was greater among certain racial and ethnic subgroups, particularly among the Hispanic and Black population. The cause-effect mechanism between the two diseases is even more difficult to establish compared to T1D, since the precise start of T2D is often uncertain and it is impossible to know whether the SARS-CoV-2 infection occurred prior to a patient's presentation and ultimately increased their risk of diabetes.

However, the recent meta-analysis by Lai *et al*[36] seems to provide conclusive data on the subject, by collecting data of 8 consistent studies which found a general increased relative risk of T2D equal to 1.78. Unsurprisingly, the subcategory of patients aged 0-18 years showed a similar increased risk (RR 1.74). Although their conclusion was that the SARS-CoV-2 infection was associated with an increased risk of overall diabetes, the authors themselves wisely reported that the conclusions drawn at the moment may change over time as the pandemic continues, the virus mutates, and treatment strategies improve.

DIABETIC KETOACIDOSIS

Above all during the first wave of the pandemic, the necessary initiatives such as social distancing and limitations of non-essential services limited the access to healthcare services. Furthermore, people were reluctant to go to the hospital lest they contract the infection or struggle to obtain medical advice. These



Table 1 Conflicting results of type 1 diabetes and type 2 diabetes incidence in the studies examined led in diffe	lifferent countries
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Ref.	Region	Increased incidence	Period of observation	Diabetes type	Patient source	Results
Mameli <i>et al</i> [<mark>22</mark>], 2022	Lombardy (Italy)	Yes and no	March-December 2020	1	Local network	Incidence $16.0/100000$ higher in the 3 previous years but not vs 2019
Schiaffini <i>et al</i> [23], 2022	Lazio (Italy)	Yes	2020-2021	1	Local cohort	Peak of incidence in the last 4 months of 2021, above all in children < 12 yr
Tittel <i>et al</i> [25], 2020	Germany	No	13 March-13 May 2020	1	DPV registry	Incidence 23.4/100000 not different from prediction
Barrett <i>et al</i> [26], 2022	United States	Yes	March 2020-February 2021 (IQVA) and June 2021 (HealthVerity)	1 and 2	MMWR (CDC)	Hazard Ratio 2.66 (IQVA) and 1.31 (Health Verity)
McKeigue <i>et al</i> [28], 2022	Scotland	Yes and no	March 2020-November 2021	1	Scottish registry	Incidence 2020-2021 was 20% higher than the 7-yr average, but no association with COVID infection
Reschke <i>et al</i> [29], 2022	Worldwide (47 countries)	No	2018-2021	1	Sweet registry	Change in seasonality only in the Northern hemisphere (no winter peak)
Guo <i>et al</i> [<mark>33</mark>], 2022	Florida (United States)	Yes	January 2017-June 2021	1 and 2	Local network	Increased incidence for both T1D and T2D from May 2021
DeLacey <i>et al</i> [34], 2022	Illinois (United States)	Yes	May 1 st 2020-April 30 th 2021	2	Local cohort	Increase of 293% (490% in Hispanic and Black patients) <i>vs</i> pre-pandemic
Ansar <i>et al</i> [<mark>35</mark>], 2022	Wisconsin (United States)	Yes	March 2020-December 2021	1 and 2	Local cohort	T1D incidence increased by 69%, T2D incidence by 225%

T1D: Type 1 diabetes; T2D: Type 1 diabetes.

unforeseen consequences delayed medical care in people, especially those with non-SARS-CoV-2 diseases, such as children with type T1D, with potential damaging effects. The early detection T1D symptoms is pivotal for a prompt diagnosis and prevention of DKA. As feared, various studies from countries hit by the first wave of the pandemic showed an increase in DKA in patients with T1D. Table 2 shows the studies dealing with DKA incidence. Gera et al[37] described that the increased incidence of DKA during the early phase of the pandemic in Ohio (March-June 2020) was ultimately due to the higher proportion of secondary DKA compared to the same period in 2019 (secondary DKA 84% vs 52%). Rabbone et al[38] published a national survey on the changes in new diabetes diagnoses and its acute complications in Italy from February to April 2020. The authors found fewer new cases of T1D compared to those in 2019 (as social distancing resulted in a low exposure to viruses), but with a higher rate of severe DKA (44.0% vs 36.1%), as an expression of a delayed diagnosis. No changes in the incidence of secondary DKA were found. Goldman et al[39] reported data from a national collaboration in Israel on the evaluation of DKA during the first wave of the pandemic: The DKA incidence was significantly higher than in 2019, 2018 and 2017 (58.0% vs 38.9%, 40.5% and 44.2% respectively), especially owing to severe forms in patients aged 6-11 years (19.9% vs 13.3%, 9.2% and 9.2% respectively). Another national survey in the United Kingdom[40] confirmed that the proportion of DKA at diabetes onset was higher than previously reported before COVID-19, above all for the cases of severe DKA (51% vs 28%). All these reports from countries hit since the very first months of the pandemic linked the increase in DKA cases to diagnostic delays due to inability to contact or access healthcare providers and/or fear of contracting the infection in a hospital/medical setting. A metaanalysis of observational studies[41] confirmed that the risks of DKA and severe DKA were 35% and 76% higher in the during-pandemic group compared to the prior-pandemic group, respectively. The delay in seeking medical attention and care was suggested as causative by various studies hypothesizing a longer duration of symptoms.

However, other studies reported that the duration of symptoms during the pandemic were comparable to the duration prior to the pandemic, speculating that the delay in diagnosing was not the only reason behind an increased risk of DKA[42,43]. A subsequent meta-analysis by Rahmati et al[44] was performed to compare the relative risk of T1D and DKA among pediatric patients with T1D between the pre-pandemic and pandemic periods. Compared with the pre-pandemic period, the number of worldwide pediatric new-onset T1D, DKA, and severe DKA during the first year of the pandemic increased by 9.5%, 25.0%, and 19.5%, respectively.

A reduction in the frequency of DKA would have been expected if its increase were only due to parental fear of contracting the virus and the containment measures that reduced access to healthcare services. However, some authors reported that the increase of DKA at diabetes onset or in children with established diabetes was not documented only during the first wave of pandemic.



Table 2 Increase of the rate of diabetic ketoacidosis in patients with type 1 diabetes during the pandemic in studies led in different countries

Ref.	Country	COVID-19 period	No. patients	DKA (%)	Severe DKA (%)	Pre-COVID-19 period	No. patients	DKA (%)	Severe DKA (%)
Gera <i>et al</i> [37], 2021	Ohio (United States)	1 Mar-30 Jun, 2020	64	73 ¹	45 ^a	1 March-30 Jun, 2019	64	47 ¹	23 ^a
Rabbone <i>et al</i> [<mark>38</mark>], 2020	Italy	20 Feb-14 Apr, 2020	160	41.3	16.9 ¹	20 Feb-14 Apr, 2019	208	38.1	14.9 ¹
Goldman <i>et al</i> [<mark>39</mark>], 2022	Israel	15 Mar-30 June, 2020	146	58.2 ^a	19.9	15 Mar-30 Jun, 2017 15 Mar-30 Jun, 2018-15 Mar-30 Jun, 2019	120; 131; 113	44.2 ^a , 40.5 ^a , 38.9 ^a	9.2 ^a , 9.2 ^a , 13.3 ^a
Ng et al[<mark>40</mark>], 2020	United Kingdom	1 Mar-30 Jun, 2020	88	51	28	/	/	/	/
HO <i>et al</i> [42] , 2021	Canada	17 Mar-31 Aug, 2020	107	68.2 ^a	27.1 ^a	17 Mar-31 Aug, 2019	114	45.6 ^a	13.2 ^a
Unsworth <i>et al</i> [43], 2020	United Kingdom	23 Mar-4 Jun, 2020	33	72.7	36.3	/	/	/	/
Cherubini <i>et al</i> [<mark>45</mark>], 2022	Italy	1 Jan-31 Dec, 2020	1169	39.6 ^{a,2}	14.2 ^{a,2}	2017-2019	3068	35.7 ^a	10.4 ^a

^aP value < 0.05

¹P 0.03 for proportion of diabetic ketoacidosis (DKA) patients with severe DKA.

²In the text data are subdivided by periods of restrictions during COVID-19 pandemic.

DKA: Diabetic ketoacidosis; T1D: Type 1 diabetes; T2D: Type 1 diabetes.

In fact, Cherubini *et al*^[45] found a concerning increase in DKA and severe DKA in children newly diagnosed with T1D during the pandemic in 2020 compared with the three previous years (DKA rate 35.7% in 2017-2019 vs 39.6% in 2020, and severe DKA rate 10.4% in 2017-2019 vs 14.2% in 2020). The authors concluded that the reason behind the increased frequency of DKA was a delay in diabetes diagnosis, albeit not fully understood considering all the time periods in 2020.

Moving to the other form of diabetes, some studies focused on the impact of the pandemic on the clinical presentation also at T2D onset. In fact, T2D accounts for a significant proportion of diabetes onsets, especially in certain populations at risk, and T2D can sometimes occur with DKA as first presentation[46]. Chao et al[47] reported a retrospective single-center medical record of pediatric subjects presenting new-onset of T2D between March and August of 2018 to 2020. They found that the prevalence of DKA increased from less than 10% in 2018–2019 to 20% in 2020. Like in the previous cited studies, they concluded that orders imposed because of the pandemic may have delayed the diagnoses as patients and families were afraid of seeking medical care until the clinical presentation was extremely severe. In another study on the incidence and clinical presentation of T2D in youths during the pandemic, Marks et al [48] found that incident cases of youths with T2D increased by 182%, consistent with the cases of DKA (5.8% vs 23.4%). The authors found no cases of hyperglycemic hyperosmolar syndrome (HHS). However, hyperosmolar DKA, defined by the same glucose and plasma osmolality values of HHS with a pH \leq 7.25 or bicarbonate \leq 15.00 mmol/L, showed a significant increase in the study period.

METABOLIC CONTROL

Quite surprisingly, pediatric patients with both T1D and T2D did not show, as a whole, a worsening in metabolic control during the pandemic. Both forms may have been negatively affected by the pandemic for different reasons.

Starting from the most prevalent form in children, *i.e.*, T1D, the ideal glucose pattern in normal daily life is obtained through the fine-tuned balance between the correct insulin dose and food intake, glucose concentrations, and physical activity. Therefore, all these adjustments may have been undermined both by changes to one's daily routine and by the typical psychological stress of that time. A first study published by Di Dalmazi et al[49], which included both children and adults with T1D and wearing a glucose sensor, showed that in children, significantly lower glucose SD and time below range were detected after lockdown, whereas in adolescents metrics were comparable before and during lockdown. Adult patients obtained the same positive results as children. The limitation of having enrolled a wellselected cohort of patients was highlighted, *i.e.*, those under continuous glucose monitoring (CGM) monitoring with sensor use of > 70% during the study period. In fact, the adolescents showed mean



HbA1c levels of 6.8%, consistent with the levels of motivated patients. Subsequent studies conducted in Italy focused on the same subject during the first lockdown and yielded similar results [50-54].

The recent meta-analysis by Han et al^[55], which collected data of 2106 pediatric patients including the afore-mentioned studies, confirmed that, as a whole and compared with the pre-lockdown period, glucose had significantly decreased both during and after lockdown. Furthermore, the improvement was also found for many metrics, *i.e.*, time in range, time above range, time below range and coefficient of variation during and post-lockdown.

To a certain extent, T2D is a more aggressive disease in children than T1D, both in terms of compliance to treatment, comorbidities and complication rates. Furthermore, depression is not rare in adolescents with T2D and the social isolation caused by lockdown may have had detrimental effects on the degree of obesity and metabolic control of these patients. In the first study conducted in Malaysia and published in 2021[56] metabolic control had worsened (HbA1c increased from 8.5% to 9.9%) only in the 30 patients with T2D (not in those with T1D). Despite this preliminary data, most studies published subsequently fortunately reported an unchanged metabolic pattern. There is an agreement between the two recent study by Schmitt et al^[57] and the data collection from the Italian study group of pediatric diabetology[58]: The first was conducted in Alabama (United States) and found no changes in HbA1c levels in 642 patients, the second reached similar conclusions in 61 patients. The obesity rates of the two studies [body mass index (BMI) around + 3 SDS in the United States and + 2 in Italy] did not change before and after lockdown. Similarly to what happened with children with T1D, the lack of changes in clinical and metabolic data may be explained by the increased attention of parents towards their children during the lockdown period. The Pittsburgh study by Vajravelu et al[59] simultaneously evaluated both glucose (HbA1c) and BMI z-score (BMIZ) trajectories through the pandemic, to identify high-risk subgroups of adolescents with both T1D (1322 patients) and T2D (59 patients). They found that the pandemic was not associated with an increase in BMIZ, but rather a decrease during the lockdown period that coincided with worsening glycemic control in the T1D patients in the high-risk group (initial poor control). In addition, for both T1D and T2D patients, there were significant racial and socio-economic disparities in the combined glucose and BMIZ trajectories from pre-pandemic to the pandemic period, with black youths belonging to low-income classes being more penalized. On the other hand, T2D is a more heterogeneous diseases compared to T1D, and its course is heavily influenced by genetic and social factors.

TELEMEDICINE

The World Health Organization defines telemedicine as a tool for providing healthcare services through the use of electronic information technologies and telecommunication, including direct patient care, health education and population health management^[60]. Over the years, the digitalization of healthcare experienced a wide range of changes, with various studies showing that telemedicine is an effective method to prevent DKA in adolescents as well as an effective tool to treat diabetes[61-63]. Telemedicine became a necessary measure of infection prevention, given the drastic reduction of all health services. Therefore, one of the few advantages of the pandemic was the major acceleration in the modernization process of telemedicine, which experienced a widespread implementation[61,64].

Diabetes is one of the fields in medicine in which technology has brought in the past year a rapid development of the relevant technology. This is also driven by the use of tools such as continuous subcutaneous insulin infusion (CSII) and CGM, connected to online data-sharing platforms, which allow for remote interaction between doctor and patient[65]. The pandemic gave the opportunity to successfully overhaul children and adult outpatient clinics by using telemedicine and video consultations[66,67]. A further confirmation of its usefulness is given by the fact that instead of routine lifestyle changes, various studies reported that during lockdown T1D patients did not show a deterioration in metabolic control[49-54].

Table 3 summarizes the positive results on metabolic control and patient satisfaction obtained with telemedicine in various studies, both in patients with T1D and with T2D. The study by Russo et al[68] led in T2D patients showed that the group followed through telemedicine had a greater probability of displaying not only a better glycemic profile but also better metabolic parameters than the group followed with a face-to-face approach. Similarly, patients with T1D also seemed very satisfied with telemedicine during the pandemic, as reported in other studies [69,70]. In the first study [69], the results showed that not only T1D patients but also caregivers showed a high degree of satisfaction with telemedicine, an adequate degree of attention from healthcare professionals through this new assistance modality and, last but not least, everyone felt quite comfortable during their televisits. Furthermore, the same study showed that patients treated with CSII were more satisfied with the quality of the service than those treated with MDI. Moreover, as reported in the review of Chan et al[71], patients thus felt safer, as the professionals could constantly monitor their data.

The results obtained in the Italian survey on the impact of COVID-19 and the use of telemedicine[61] are significant, because although before the pandemic telemedicine was expanding in the monitoring of patients with diabetes [72], it was often carried out on a voluntary basis, without tracking and con-



Table 3 Positive outcome on metabolic control and on patient satisfaction obtained with telemedicine during the pandemic in the studies examined

Type of patients	Parameters evaluated	Outcome		
School and preschool age children with T1D	Time in range using hybrid closed loop pump	Improved		
Adults with T2D	Glycemic profile and metabolic control	Improved		
Children with T1D and caregivers	Degree of satisfaction of telemedicine	High rates of satisfaction		
Children and adults with both T1D and T2D	Satisfaction and utilization of telemedicine	High rates of satisfaction		
Children and adults with both T1D and T2D	HbA1c and quality of care	Improved metabolic control and quality of care		
Adults with T1D	Metabolic control through Flash Glucose Monitoring	Improved metabolic control		
	School and preschool age children with T1D Adults with T2D Children with T1D and caregivers Children and adults with both T1D and T2D Children and adults with both T1D and T2D	School and preschool age children with T1DTime in range using hybrid closed loop pumpAdults with T2DGlycemic profile and metabolic controlChildren with T1D and caregiversDegree of satisfaction of telemedicineChildren and adults with both T1D and T2DSatisfaction and utilization of telemedicineChildren and adults with both T1D and T2DHbA1c and quality of careAdults with T1DMetabolic control through Flash Glucose		

T1D: Type 1 diabetes; T2D: Type 1 diabetes.

sequently on a non-refundable basis[50].

Telemedicine also shows limitations: Firstly, the uploading of glucose monitoring data itself and HbA1c point of care data are a limitation for those who lack the required equipment. Furthermore, the physical examination that includes the measurement of weight and blood pressure is obviously missing, and also major micro-macrovascular complications cannot be monitored. This ought to be taken into account for the future implementation of telemedicine programs[73]. A further limitation is equity. In Italy and in many other countries not everyone has the same sources of information, such as an internet connection and quality digital devices^[74]. Lastly, the cultural barrier and lack of mediation services may be an obstacle for speakers of a foreign language. Although telemedicine is an excellent support tool for diabetic patients, it must be integrated in a structured way into the daily care of diabetic patients.

CONCLUSION

The pandemic has also significantly affected children and adolescents with both forms of diabetes, determining a change in epidemiology, DKA rates and medical care. The implementation of telemedicine is probably the only positive consequence of the pandemic: Social inequalities must therefore be tackled, adequate training for physicians with appropriate knowledge and skills must be provided, and infrastructure in the age of technological development must be enhanced.

FOOTNOTES

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Country/Territory of origin: Italy

ORCID number: Stefano Zucchini 0000-0003-1184-7170; Giulio Maltoni 0000-0002-2526-5588.

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REFERENCES

- 1 World Health Organization. WHO Coronavirus (COVID-19) Dashboard. [cited 10 January 2023]. Available from: https://covid19.who.int/
- Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, 2 Wu G, Gao GF, Tan W; China Novel Coronavirus Investigating and Research Team. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med 2020; 382: 727-733 [PMID: 31978945 DOI: 10.1056/NEJMoa2001017]
- Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW; the Northwell COVID-19 Research Consortium, Barnaby DP, Becker LB, Chelico JD, Cohen SL, Cookingham J, Coppa K, Diefenbach MA, Dominello AJ, Duer-Hefele J, Falzon L, Gitlin J, Hajizadeh N, Harvin TG, Hirschwerk DA, Kim EJ, Kozel ZM, Marrast LM, Mogavero JN, Osorio GA, Qiu M, Zanos TP. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA 2020; 323: 2052-2059 [PMID: 32320003 DOI: 10.1001/jama.2020.6775]
- Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, Huang H, Zhang L, Du C, Zhang Y, Song J, Wang S, Chao Y, Yang Z, Xu J, Chen D, Xiong W, Xu L, Zhou F, Jiang J, Bai C, Zheng J, Song Y. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med 2020; 180: 934-943 [PMID: 32167524 DOI: 10.1001/jamainternmed.2020.0994]
- Kapoor N, Kalra S, Al Mahmeed W, Al-Rasadi K, Al-Alawi K, Banach M, Banerjee Y, Ceriello A, Cesur M, Cosentino F, Firenze A, Galia M, Goh SY, Janez A, Kempler P, Lessan N, Lotufo P, Papanas N, Rizvi AA, Sahebkar A, Santos RD, Stoian AP, Toth PP, Viswanathan V, Rizzo M; CArdiometabolic Panel of International experts on Syndemic COvid-19 (CAPISCO). The Dual Pandemics of COVID-19 and Obesity: Bidirectional Impact. Diabetes Ther 2022; 13: 1723-1736 [PMID: 36030317 DOI: 10.1007/s13300-022-01311-2]
- Birkebaek NH, Kamrath C, Grimsmann JM, Aakesson K, Cherubini V, Dovc K, de Beaufort C, Alonso GT, Gregory JW, White M, Skrivarhaug T, Sumnik Z, Jefferies C, Hörtenhuber T, Haynes A, De Bock M, Svensson J, Warner JT, Gani O, Gesuita R, Schiaffini R, Hanas R, Rewers A, Eckert AJ, Holl RW, Cinek O. Impact of the COVID-19 pandemic on longterm trends in the prevalence of diabetic ketoacidosis at diagnosis of paediatric type 1 diabetes: an international multicentre study based on data from 13 national diabetes registries. Lancet Diabetes Endocrinol 2022; 10: 786-794 [PMID: 36202118 DOI: 10.1016/S2213-8587(22)00246-71
- Gregg EW, Sophiea MK, Weldegiorgis M. Diabetes and COVID-19: Population Impact 18 Months Into the Pandemic. 7 Diabetes Care 2021; 44: 1916-1923 [PMID: 34244333 DOI: 10.2337/dci21-0001]
- Storling J, Overgaard AJ, Brorsson CA, Piva F, Bang-Berthelsen CH, Haase C, Nerup J, Pociot F. Do post-translational 8 beta cell protein modifications trigger type 1 diabetes? Diabetologia 2013; 56: 2347-2354 [PMID: 24048671 DOI: 10.1007/s00125-013-3045-3]
- Lowdell M, Bottazzo GF. Autoimmunity and insulin-dependent diabetes. Lancet 1993; 341: 1378-1379 [PMID: 8098796 DOI: 10.1016/0140-6736(93)90947-f]
- Filippi CM, von Herrath MG. Viral trigger for type 1 diabetes: pros and cons. Diabetes 2008; 57: 2863-2871 [PMID: 10 18971433 DOI: 10.2337/db07-10231
- Menser MA, Forrest JM, Bransby RD. Rubella infection and diabetes mellitus. Lancet 1978; 1: 57-60 [PMID: 74564 DOI: 11 10.1016/s0140-6736(78)90001-6
- Andréoletti L, Hober D, Hober-Vandenberghe C, Belaich S, Vantyghem MC, Lefebvre J, Wattré P. Detection of coxsackie 12 B virus RNA sequences in whole blood samples from adult patients at the onset of type I diabetes mellitus. J Med Virol 1997; 52: 121-127 [PMID: 9179756 DOI: 10.1002/(sici)1096-9071(199706)52:2<121::aid-jmv1>3.0.co;2-5]
- Fignani D, Licata G, Brusco N, Nigi L, Grieco GE, Marselli L, Overbergh L, Gysemans C, Colli ML, Marchetti P, Mathieu 13 C, Eizirik DL, Sebastiani G, Dotta F. SARS-CoV-2 Receptor Angiotensin I-Converting Enzyme Type 2 (ACE2) Is Expressed in Human Pancreatic β-Cells and in the Human Pancreas Microvasculature. Front Endocrinol (Lausanne) 2020; 11: 596898 [PMID: 33281748 DOI: 10.3389/fendo.2020.596898]
- 14 Müller JA, Groß R, Conzelmann C, Krüger J, Merle U, Steinhart J, Weil T, Koepke L, Bozzo CP, Read C, Fois G, Eiseler T, Gehrmann J, van Vuuren J, Wessbecher IM, Frick M, Costa IG, Breunig M, Grüner B, Peters L, Schuster M, Liebau S, Seufferlein T, Stenger S, Stenzinger A, MacDonald PE, Kirchhoff F, Sparrer KMJ, Walther P, Lickert H, Barth TFE, Wagner M, Münch J, Heller S, Kleger A. SARS-CoV-2 infects and replicates in cells of the human endocrine and exocrine pancreas. Nat Metab 2021; 3: 149-165 [PMID: 33536639 DOI: 10.1038/s42255-021-00347-1]
- 15 Ben Nasr M, D'Addio F, Montefusco L, Usuelli V, Loretelli C, Rossi A, Pastore I, Abdelsalam A, Maestroni A, Dell'Acqua M, Ippolito E, Assi E, Seelam AJ, Fiorina RM, Chebat E, Morpurgo P, Lunati ME, Bolla AM, Abdi R, Bonventre JV, Rusconi S, Riva A, Corradi D, Santus P, Clark P, Nebuloni M, Baldi G, Finzi G, Folli F, Zuccotti GV, Galli M, Herold KC, Fiorina P. Indirect and Direct Effects of SARS-CoV-2 on Human Pancreatic Islets. Diabetes 2022; 71: 1579-1590 [PMID: 35499468 DOI: 10.2337/db21-0926]
- Gnocchi M, D'Alvano T, Lattanzi C, Messina G, Petraroli M, Patianna VD, Esposito S, Street ME. Current evidence on the 16 impact of the COVID-19 pandemic on paediatric endocrine conditions. Front Endocrinol (Lausanne) 2022; 13: 913334 [PMID: 35992140 DOI: 10.3389/fendo.2022.913334]
- Li J, Wang X, Chen J, Zuo X, Zhang H, Deng A. COVID-19 infection may cause ketosis and ketoacidosis. Diabetes Obes 17 Metab 2020; 22: 1935-1941 [PMID: 32314455 DOI: 10.1111/dom.14057]
- 18 Goldman N, Fink D, Cai J, Lee YN, Davies Z. High prevalence of COVID-19-associated diabetic ketoacidosis in UK secondary care. Diabetes Res Clin Pract 2020; 166: 108291 [PMID: 32615280 DOI: 10.1016/j.diabres.2020.108291]
- 19 Marchand L, Pecquet M, Luyton C. Type 1 diabetes onset triggered by COVID-19. Acta Diabetol 2020; 57: 1265-1266 [PMID: 32653960 DOI: 10.1007/s00592-020-01570-0]
- Hollstein T, Schulte DM, Schulz J, Glück A, Ziegler AG, Bonifacio E, Wendorff M, Franke A, Schreiber S, Bornstein SR, 20 Laudes M. Autoantibody-negative insulin-dependent diabetes mellitus after SARS-CoV-2 infection: a case report. Nat Metab 2020; 2: 1021-1024 [PMID: 32879473 DOI: 10.1038/s42255-020-00281-8]
- 21 Kamrath C, Rosenbauer J, Tittel SR, Warncke K, Hirtz R, Denzer C, Dost A, Neu A, Pacaud D, Holl RW. Frequency of



Autoantibody-Negative Type 1 Diabetes in Children, Adolescents, and Young Adults During the First Wave of the COVID-19 Pandemic in Germany. Diabetes Care 2021; 44: 1540-1546 [PMID: 33990377 DOI: 10.2337/dc20-2791]

- 22 Mameli C, Scaramuzza A, Macedoni M, Marano G, Frontino G, Luconi E, Pelliccia C, Felappi B, Guerraggio LP, Spiri D, Macellaro P, Chiara Redaelli F, Cardani R, Zampolli M, Calcaterra V, Sordelli S, Calzi E, Cogliardi A, Brambilla I, Pistone C, Rigamonti A, Boracchi P, Biganzoli E, Zuccotti GV, Bonfanti R. Type 1 diabetes onset in Lombardy region, Italy, during the COVID-19 pandemic: The double-wave occurrence. EClinicalMedicine 2021; 39: 101067 [PMID: 34430836 DOI: 10.1016/j.eclinm.2021.101067]
- Schiaffini R, Deodati A, Rapini N, Pampanini V, Cianfarani S. Increased incidence of childhood type 1 diabetes during the 23 COVID-19 pandemic. Figures from an Italian tertiary care center. J Diabetes 2022; 14: 562-563 [PMID: 35916392 DOI: 10.1111/1753-0407.13298]
- 24 Khemiri H, Ayouni K, Triki H, Haddad-Boubaker S. SARS-CoV-2 infection in pediatric population before and during the Delta (B.1.617.2) and Omicron (B.1.1.529) variants era. Virol J 2022; 19: 144 [PMID: 36076271 DOI: 10.1186/s12985-022-01873-4]
- Tittel SR, Rosenbauer J, Kamrath C, Ziegler J, Reschke F, Hammersen J, Mönkemöller K, Pappa A, Kapellen T, Holl RW; 25 DPV Initiative. Did the COVID-19 Lockdown Affect the Incidence of Pediatric Type 1 Diabetes in Germany? Diabetes Care 2020; 43: e172-e173 [PMID: 32826282 DOI: 10.2337/dc20-1633]
- 26 Barrett CE, Koyama AK, Alvarez P, Chow W, Lundeen EA, Perrine CG, Pavkov ME, Rolka DB, Wiltz JL, Bull-Otterson L, Gray S, Boehmer TK, Gundlapalli AV, Siegel DA, Kompaniyets L, Goodman AB, Mahon BE, Tauxe RV, Remley K, Saydah S. Risk for Newly Diagnosed Diabetes >30 Days After SARS-CoV-2 Infection Among Persons Aged <18 Years -United States, March 1, 2020-June 28, 2021. MMWR Morb Mortal Wkly Rep 2022; 71: 59-65 [PMID: 35025851 DOI: 10.15585/mmwr.mm7102e2]
- Gujral J, Tamborlane W, Nally L. Commentary on CDC data showing an increased risk for pediatric diabetes with COVID-19 infection. J Diabetes 2022; 14: 630-632 [PMID: 36073304 DOI: 10.1111/1753-0407.13311]
- 28 McKeigue PM, McGurnaghan S, Blackbourn L, Bath LE, McAllister DA, Caparrotta TM, Wild SH, Wood SN, Stockton D, Colhoun HM. Relation of Incident Type 1 Diabetes to Recent COVID-19 Infection: Cohort Study Using e-Health Record Linkage in Scotland. Diabetes Care 2022; dc220385 [DOI: 10.2337/figshare.20001458.v1]
- 29 Reschke F, Lanzinger S, Herczeg V, Prahalad P, Schiaffini R, Mul D, Clapin H, Zabeen B, Pelicand J, Phillip M, Limbert C, Danne T; SWEET Study Group. The COVID-19 Pandemic Affects Seasonality, With Increasing Cases of New-Onset Type 1 Diabetes in Children, From the Worldwide SWEET Registry. Diabetes Care 2022; 45: 2594-2601 [PMID: 36166593 DOI: 10.2337/dc22-0278]
- 30 ISPAD Clinical Practice Consensus Guidelines 2014 Compendium: Type 2 diabetes in the child and adolescent. Pediatr Diabetes 2015; 16: 392 [PMID: 26153026 DOI: 10.1111/pedi.12239]
- Maltoni G, Zioutas M, Deiana G, Biserni GB, Pession A, Zucchini S. Gender differences in weight gain during lockdown 31 due to COVID-19 pandemic in adolescents with obesity. Nutr Metab Cardiovasc Dis 2021; 31: 2181-2185 [PMID: 33994065 DOI: 10.1016/j.numecd.2021.03.018]
- Cioana M, Deng J, Nadarajah A, Hou M, Qiu Y, Chen SSJ, Rivas A, Banfield L, Toor PP, Zhou F, Guven A, Alfaraidi H, Alotaibi A, Thabane L, Samaan MC. The Prevalence of Obesity Among Children With Type 2 Diabetes: A Systematic Review and Meta-analysis. JAMA Netw Open 2022; 5: e2247186 [PMID: 36520430 DOI: 10.1001/jamanetworkopen.2022.47186]
- Guo Y, Bian J, Chen A, Wang F, Posgai AL, Schatz DA, Shenkman EA, Atkinson MA. Incidence Trends of New-Onset Diabetes in Children and Adolescents Before and During the COVID-19 Pandemic: Findings From Florida. Diabetes 2022; 71: 2702-2706 [PMID: 36094294 DOI: 10.2337/db22-0549]
- 34 DeLacey S, Arzu J, Levin L, Ranganna A, Swamy A, Bianco ME. Impact of SARS-CoV2 on youth onset type 2 diabetes new diagnoses and severity. J Diabetes 2022; 14: 532-540 [PMID: 36040204 DOI: 10.1111/1753-0407.13301]
- Ansar A, Livett T, Beaton W, Carrel AL, Bekx MT. Sharp Rise in New-Onset Pediatric Diabetes During the COVID-19 35 Pandemic. WMJ 2022; 121: 177-180 [PMID: 36301642]
- 36 Lai H, Yang M, Sun M, Pan B, Wang Q, Wang J, Tian J, Ding G, Yang K, Song X, Ge L. Risk of incident diabetes after COVID-19 infection: A systematic review and meta-analysis. Metabolism 2022; 137: 155330 [PMID: 36220361 DOI: 10.1016/j.metabol.2022.155330
- 37 Gera S, Longendyke RL, Minich NM, Malay S, Wood JR. The COVID-19 pandemic and associated worsening of diabetic ketoacidosis presentation in youth. Diabet Med 2021; 38: e14610 [PMID: 34053098 DOI: 10.1111/dme.14610]
- Rabbone I, Schiaffini R, Cherubini V, Maffeis C, Scaramuzza A; Diabetes Study Group of the Italian Society for Pediatric 38 Endocrinology and Diabetes. Has COVID-19 Delayed the Diagnosis and Worsened the Presentation of Type 1 Diabetes in Children? Diabetes Care 2020; 43: 2870-2872 [PMID: 32778554 DOI: 10.2337/dc20-1321]
- Goldman S, Pinhas-Hamiel O, Weinberg A, Auerbach A, German A, Haim A, Zung A, Brener A, Strich D, Azoulay E, 39 Levy-Khademi F, Ludar H, Koren I, Rachmiel M, Yackobovitch-Gavan M, Zuckerman-Levin N, David O, Halloun R, Cahn R, Ben-Ari T, Yeshayahu Y, Landau Z, Phillip M, Lebenthal Y. Alarming increase in ketoacidosis in children and adolescents with newly diagnosed type 1 diabetes during the first wave of the COVID-19 pandemic in Israel. Pediatr Diabetes 2022; 23: 10-18 [PMID: 34865288 DOI: 10.1111/pedi.13296]
- 40 Ng SM, Woodger K, Regan F, Soni A, Wright N, Agwu JC, Williams E, Timmis A, Kershaw M, Moudiotis C, Drew J. Presentation of newly diagnosed type 1 diabetes in children and young people during COVID-19: a national UK survey. BMJ Paediatr Open 2020; 4: e000884 [PMID: 34192183 DOI: 10.1136/bmjpo-2020-000884]
- Alfayez OM, Aldmasi KS, Alruwais NH, Bin Awad NM, Al Yami MS, Almohammed OA, Almutairi AR. Incidence of 41 Diabetic Ketoacidosis Among Pediatrics With Type 1 Diabetes Prior to and During COVID-19 Pandemic: A Meta-Analysis of Observational Studies. Front Endocrinol (Lausanne) 2022; 13: 856958 [PMID: 35355556 DOI: 10.3389/fendo.2022.856958]
- Ho J, Rosolowsky E, Pacaud D, Huang C, Lemay JA, Brockman N, Rath M, Doulla M. Diabetic ketoacidosis at type 1 diabetes diagnosis in children during the COVID-19 pandemic. Pediatr Diabetes 2021; 22: 552-557 [PMID: 33745226 DOI: 10.1111/pedi.13205]



- 43 Unsworth R, Wallace S, Oliver NS, Yeung S, Kshirsagar A, Naidu H, Kwong RMW, Kumar P, Logan KM. New-Onset Type 1 Diabetes in Children During COVID-19: Multicenter Regional Findings in the U.K. Diabetes Care 2020; 43: e170e171 [PMID: 32816997 DOI: 10.2337/dc20-1551]
- 44 Rahmati M, Keshvari M, Mirnasuri S, Yon DK, Lee SW, Il Shin J, Smith L. The global impact of COVID-19 pandemic on the incidence of pediatric new-onset type 1 diabetes and ketoacidosis: A systematic review and meta-analysis. J Med Virol 2022; 94: 5112-5127 [PMID: 35831242 DOI: 10.1002/jmv.27996]
- 45 Cherubini V, Marino M, Scaramuzza AE, Tiberi V, Bobbio A, Delvecchio M, Piccinno E, Ortolani F, Innaurato S, Felappi B, Gallo F, Ripoli C, Ricciardi MR, Pascarella F, Stamati FA, Citriniti F, Arnaldi C, Monti S, Graziani V, De Berardinis F, Giannini C, Chiarelli F, Zampolli M, De Marco R, Bracciolini GP, Grosso C, De Donno V, Piccini B, Toni S, Coccioli S, Cardinale G, Bassi M, Minuto N, D'Annunzio G, Maffeis C, Marigliano M, Zanfardino A, Iafusco D, Rollato AS, Piscopo A, Curto S, Lombardo F, Bombaci B, Sordelli S, Mameli C, Macedoni M, Rigamonti A, Bonfanti R, Frontino G, Predieri B, Bruzzi P, Mozzillo E, Rosanio F, Franzese A, Piredda G, Cardella F, Iovane B, Calcaterra V, Berioli MG, Lasagni A, Pampanini V, Patera PI, Schiaffini R, Rutigliano I, Meloni G, De Sanctis L, Tinti D, Trada M, Guerraggio LP, Franceschi R, Cauvin V, Tornese G, Franco F, Musolino G, Maltoni G, Talarico V, Iannilli A, Lenzi L, Matteoli MC, Pozzi E, Moretti C, Zucchini S, Rabbone I, Gesuita R. The Silent Epidemic of Diabetic Ketoacidosis at Diagnosis of Type 1 Diabetes in Children and Adolescents in Italy During the COVID-19 Pandemic in 2020. Front Endocrinol (Lausanne) 2022; 13: 878634 [PMID: 35784550 DOI: 10.3389/fendo.2022.878634]
- Glaser N, Fritsch M, Priyambada L, Rewers A, Cherubini V, Estrada S, Wolfsdorf JI, Codner E. ISPAD clinical practice 46 consensus guidelines 2022: Diabetic ketoacidosis and hyperglycemic hyperosmolar state. Pediatr Diabetes 2022; 23: 835-856 [PMID: 36250645 DOI: 10.1111/pedi.13406]
- Chao LC, Vidmar AP, Georgia S. Spike in Diabetic Ketoacidosis Rates in Pediatric Type 2 Diabetes During the COVID-19 Pandemic. Diabetes Care 2021; 44: 1451-1453 [PMID: 33905347 DOI: 10.2337/dc20-2733]
- Marks BE, Khilnani A, Meyers A, Flokas ME, Gai J, Monaghan M, Streisand R, Estrada E. Increase in the Diagnosis and 48 Severity of Presentation of Pediatric Type 1 and Type 2 Diabetes during the COVID-19 Pandemic. Horm Res Paediatr 2021; 94: 275-284 [PMID: 34564073 DOI: 10.1159/000519797]
- 49 Di Dalmazi G, Maltoni G, Bongiorno C, Tucci L, Di Natale V, Moscatiello S, Laffi G, Pession A, Zucchini S, Pagotto U. Comparison of the effects of lockdown due to COVID-19 on glucose patterns among children, adolescents, and adults with type 1 diabetes: CGM study. BMJ Open Diabetes Res Care 2020; 8 [PMID: 33115820 DOI: 10.1136/bmjdrc-2020-001664]
- Tornese G, Ceconi V, Monasta L, Carletti C, Faleschini E, Barbi E. Glycemic Control in Type 1 Diabetes Mellitus During 50 COVID-19 Quarantine and the Role of In-Home Physical Activity. Diabetes Technol Ther 2020; 22: 462-467 [PMID: 32421355 DOI: 10.1089/dia.2020.0169]
- Predieri B, Leo F, Candia F, Lucaccioni L, Madeo SF, Pugliese M, Vivaccia V, Bruzzi P, Iughetti L. Glycemic Control 51 Improvement in Italian Children and Adolescents With Type 1 Diabetes Followed Through Telemedicine During Lockdown Due to the COVID-19 Pandemic. Front Endocrinol (Lausanne) 2020; 11: 595735 [PMID: 33424771 DOI: 10.3389/fendo.2020.595735]
- Schiaffini R, Barbetti F, Rapini N, Inzaghi E, Deodati A, Patera IP, Matteoli MC, Ciampalini P, Carducci C, Lorubbio A, 52 Schiaffini G, Cianfarani S. School and pre-school children with type 1 diabetes during Covid-19 quarantine: The synergic effect of parental care and technology. Diabetes Res Clin Pract 2020; 166: 108302 [PMID: 32623034 DOI: 10.1016/j.diabres.2020.108302]
- Minuto N, Bassi M, Montobbio C, Vinci F, Mercuri C, Perri FN, Cabri M, Calevo MG, d'Annunzio G, Maghnie M. The 53 Effect of Lockdown and Physical Activity on Glycemic Control in Italian Children and Young Patients With Type 1 Diabetes. Front Endocrinol (Lausanne) 2021; 12: 690222 [PMID: 34326814 DOI: 10.3389/fendo.2021.690222]
- Tinti D, Savastio S, Grosso C, De Donno V, Trada M, Nugnes M, Bertelli E, Franceschi L, Marchisio M, Pozzi E, Tappi E, 54 Felici E, De Sanctis L, Rabbone I. Impact of lockdown during COVID-19 emergency on glucose metrics of children and adolescents with type 1 diabetes in Piedmont, Italy. Acta Diabetol 2021; 58: 959-961 [PMID: 33721077 DOI: 10.1007/s00592-021-01702-0]
- 55 Han Y, Chen Y, Sun C, Zhou Z. The impact of COVID lockdown on glycaemic control in paediatric patients with type 1 diabetes: A systematic review and meta-analysis of 22 observational studies. Front Endocrinol (Lausanne) 2022; 13: 1069559 [PMID: 36531473 DOI: 10.3389/fendo.2022.1069559]
- Cheng HP, Wong JSL, Selveindran NM, Hong JYH. Impact of COVID-19 lockdown on glycaemic control and lifestyle 56 changes in children and adolescents with type 1 and type 2 diabetes mellitus. Endocrine 2021; 73: 499-506 [PMID: 34244903 DOI: 10.1007/s12020-021-02810-1]
- Schmitt JA, Ashraf AP, Becker DJ, Sen B. Changes in Type 2 Diabetes Trends in Children and Adolescents During the 57 COVID-19 Pandemic. J Clin Endocrinol Metab 2022; 107: e2777-e2782 [PMID: 35377436 DOI: 10.1210/clinem/dgac209]
- Zucchini S, Iafusco D, Cherubini V, De Sanctis L, Maltoni G, Lenzi L, Mozzillo E, Calcaterra V, Gallo F, Arnaldi C, 58 Delvecchio M, Rabbone I, Minuto N, Predieri B, Zanfardino A, Piscopo A, Tiberi V, Tinti D, Rapini N, Toni S, Schiaffini R; Diabetes Study Group of the ISPED. COVID-19 forced restrictions did not affect metabolic control in youth with T2D in Italy. Nutr Metab Cardiovasc Dis 2023; 33: 232-233 [PMID: 36404240 DOI: 10.1016/j.numecd.2022.10.012]
- 59 Vajravelu ME, Mani I, Malik S, Hewitt B, Peyyety V, Arslanian S. Race and Neighborhood-Related Disparities Spanning the COVID-19 Pandemic: Trajectories of Combined Glycemic Control and Body Mass Index in Youth With Diabetes. Diabetes Care 2022; dc221439 [DOI: 10.2337/figshare.21663827]
- World Health Organization. A Health Telematics Policy in Support of WHO's Health-for-All Strategy for Global Health 60 Development: Report of the WHO Group Consultation on Health Telematics. [cited 10 January 2023]. Available from: https://apps.who.int/iris/handle/10665/63857
- Tornese G, Schiaffini R, Mozzillo E, Franceschi R, Frongia AP, Scaramuzza A; Diabetes Study Group of the Italian Society for Pediatric Endocrinology and Diabetes. The effect of the COVID-19 pandemic on telemedicine in pediatric diabetes centers in Italy: Results from a longitudinal survey. Diabetes Res Clin Pract 2021; 179: 109030 [PMID: 34461140] DOI: 10.1016/j.diabres.2021.109030]
- Buonsenso D, Onesimo R, Valentini P, Chiaretti A, Gatto A, Attinà G, Conti G, Vento G, Cambieri A, Mercuri E, Zampino 62



G; pedCOVID-team. Children's Healthcare During Corona Virus Disease 19 Pandemic: the Italian Experience. Pediatr Infect Dis J 2020; 39: e137-e140 [PMID: 32404790 DOI: 10.1097/INF.00000000002732]

- Umano GR, Di Sessa A, Guarino S, Gaudino G, Marzuillo P, Miraglia Del Giudice E. Telemedicine in the COVID-19 era: 63 Taking care of children with obesity and diabetes mellitus. World J Diabetes 2021; 12: 651-657 [PMID: 33995852 DOI: 10.4239/wjd.v12.i5.651]
- Iughetti L, Trevisani V, Cattini U, Bruzzi P, Lucaccioni L, Madeo S, Predieri B. COVID-19 and Type 1 Diabetes: 64 Concerns and Challenges. Acta Biomed 2020; 91: e2020033 [PMID: 32921727 DOI: 10.23750/abm.v91i3.10366]
- Boscari F, Avogaro A. Current treatment options and challenges in patients with Type 1 diabetes: Pharmacological, 65 technical advances and future perspectives. Rev Endocr Metab Disord 2021; 22: 217-240 [PMID: 33755854 DOI: 10.1007/s11154-021-09635-3
- Crossen S, Raymond J, Neinstein A. Top 10 Tips for Successfully Implementing a Diabetes Telehealth Program. Diabetes 66 Technol Ther 2020; 22: 920-928 [PMID: 32191141 DOI: 10.1089/dia.2020.0042]
- March CA, Flint A, DeArment D, Gilliland A, Kelly K, Rizzitano E, Chrisman A, Muzumdar RH, Libman IM. Paediatric 67 diabetes care during the COVID-19 pandemic: Lessons learned in scaling up telemedicine services. Endocrinol Diabetes Metab 2021; 4: e00202 [PMID: 33349799 DOI: 10.1002/edm2.202]
- Russo GT, Andreozzi F, Calabrese M, Di Bartolo P, Di Cianni G, Bruno Giorda C, Lapice E, Manicardi E, Giandalia A, 68 Lucisano G, Nicolucci A, Rocca A, Rossi MC, Spreafico E, Vespasiani G, Manicardi V; AMD Annals study group. Role of telemedicine during COVID-19 pandemic in type 2 diabetes outpatients: The AMD annals initiative. Diabetes Res Clin Pract 2022; 194: 110158 [PMID: 36400169 DOI: 10.1016/j.diabres.2022.110158]
- Bassi M, Strati MF, Parodi S, Lightwood S, Rebora C, Rizza F, d'Annunzio G, Minuto N, Maghnie M. Patient Satisfaction 69 of Telemedicine in Pediatric and Young Adult Type 1 Diabetes Patients During Covid-19 Pandemic. Front Public Health 2022; 10: 857561 [PMID: 35392480 DOI: 10.3389/fpubh.2022.857561]
- 70 Agbali R, Balas AE, Beltrame F, De Leo G. A review of audiovisual telemedicine utilization and satisfaction assessment during the COVID-19 pandemic. Int J Technol Assess Health Care 2021; 38: e2 [PMID: 34924067 DOI: 10.1017/S026646232100060X
- Chan CB, Popeski N, Hassanabad MF, Sigal RJ, O'Connell P, Sargious P. Use of Virtual Care for Glycemic Management 71 in People With Types 1 and 2 Diabetes and Diabetes in Pregnancy: A Rapid Review. Can J Diabetes 2021; 45: 677-688.e2 [PMID: 34045146 DOI: 10.1016/j.jcjd.2021.02.007]
- Tchero H, Kangambega P, Briatte C, Brunet-Houdard S, Retali GR, Rusch E. Clinical Effectiveness of Telemedicine in 72 Diabetes Mellitus: A Meta-Analysis of 42 Randomized Controlled Trials. Telemed J E Health 2019; 25: 569-583 [PMID: 30124394 DOI: 10.1089/tmj.2018.0128]
- 73 Bonora BM, Morieri ML, Avogaro A, Fadini GP. The Toll of Lockdown Against COVID-19 on Diabetes Outpatient Care: Analysis From an Outbreak Area in Northeast Italy. Diabetes Care 2021; 44: e18-e21 [PMID: 33127611 DOI: 10.2337/dc20-1872]
- Krisiunas E, Sibomana L. Benefits of Technology in the Age of COVID-19 and Diabetes. . . Mobile Phones From a 74 Rwanda Perspective. J Diabetes Sci Technol 2020; 14: 748-749 [PMID: 32460536 DOI: 10.1177/1932296820930032]





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