nature medicine

Article

https://doi.org/10.1038/s41591-024-02975-y

Equitable implementation of a precision digital health program for glucose management in individuals with newly diagnosed type 1 diabetes

Received: 27 September 2023

Accepted: 3 April 2024

Published online: 3 May 2024

Check for updates

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Few young people with type 1 diabetes (T1D) meet glucose targets. Continuous glucose monitoring improves glycemia, but access is not equitable. We prospectively assessed the impact of a systematic and equitable digital-health-team-based care program implementing tighter glucose targets (HbA1c < 7%), early technology use (continuous glucose monitoring starts <1 month after diagnosis) and remote patient monitoring on glycemia in young people with newly diagnosed T1D enrolled in the Teamwork, Targets, Technology, and Tight Control (4T Study 1). Primary outcome was HbA1c change from 4 to 12 months after diagnosis; the secondary outcome was achieving the HbA1c targets. The 4T Study 1 cohort (36.8% Hispanic and 35.3% publicly insured) had a mean HbA1c of 6.58%, 64% with HbA1c < 7% and mean time in the range (70–180 mg dl^{-1}) of 68% at 1 year after diagnosis. Clinical implementation of the 4T Study 1 met the prespecified primary outcome and improved glycemia without unexpected serious adverse events. The strategies in the 4T Study 1 can be used to implement systematic and equitable care for individuals with T1D and translate to care for other chronic diseases. ClinicalTrials.gov registration: NCT04336969.

Most adults (60%)[1] and 20% of young people[2] live with chronic medical conditions. To help prepare the health system for the growing population of individuals with chronic diseases, the American College of Physicians proposed the Chronic Care Model in 1998 (ref. 3). The five key components of the Chronic Care Model are: (1) well-developed processes and incentives for making changes in the healthcare system; (2) self-management support that increases an individual's confidence and skills to improve self-management; (3) reorganize team function and systems to meet the needs of individuals with chronic diseases; (4) develop and implement evidence-based guidelines and support them through provider education, reminders and interaction between primary care providers and specialists; and (5) improve information systems to facilitate the development of disease registries, tracking systems and reminders to give feedback on performance. Twenty-five

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https://doi.org/10.1038/s41591-024-02975-y

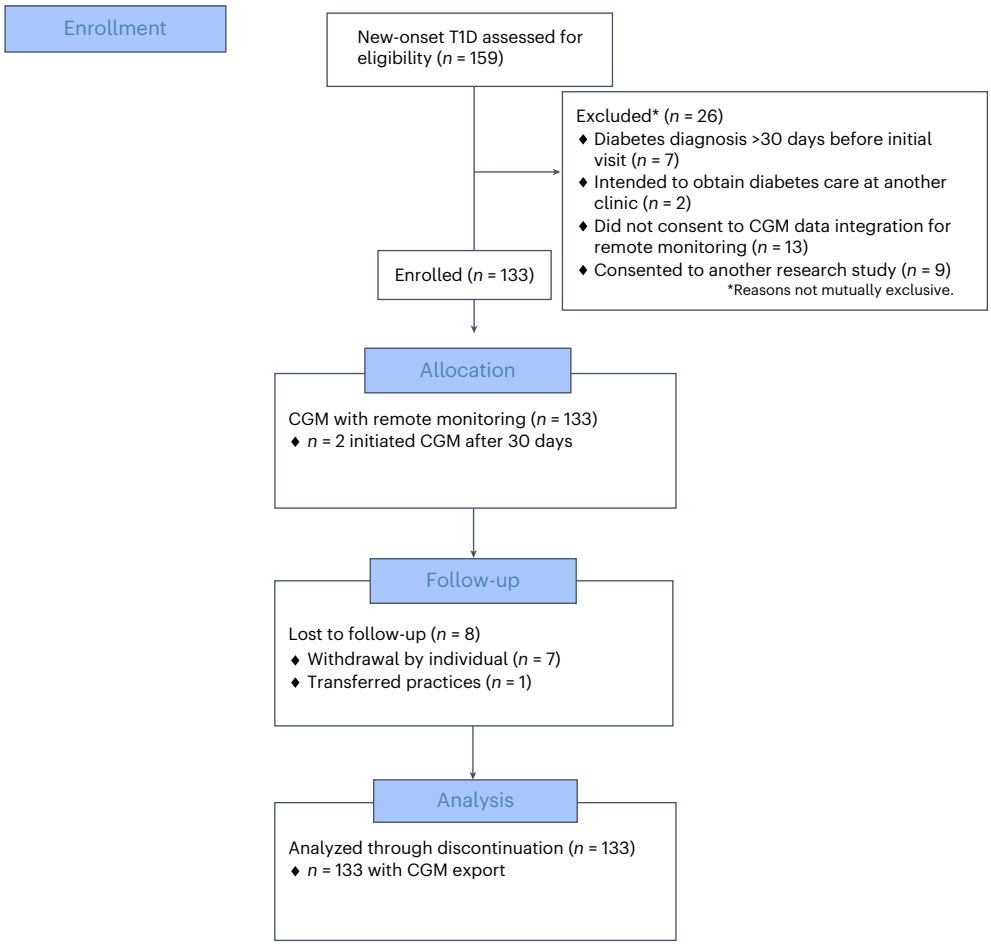


Fig. 1 | CONSORT diagram of participants in 4T Study 1. Consolidated standards of reporting trials for the 4T Study 1.

years later, healthcare systems have not consistently implemented these principles; the management of young people with diabetes is one example.

Type 1 diabetes (T1D) is one of the most common chronic medical conditions in young people, and effective and sustainable models of care are lacking[4]. Unfortunately, most young people with T1D do not achieve the glycemic targets[5–8] set by the American Diabetes Association (ADA)[9] and the International Society for Pediatric and Adolescent Diabetes (ISPAD)[10]. The Type 1 Diabetes Exchange (T1DX) registry in the United States reported increasing HbA1c in young people with T1D from 2010–2012 to 2016–2018 (ref. 6). Newer diabetes technology, including continuous glucose monitoring (CGM), insulin pumps and automated insulin delivery (AID) systems improve HbA1c[11–16] and hold the potential to improve outcomes in young people with T1D. These devices are now the standard of care for all young people with T1D[9,17–19]. However, in the United States, the introduction of technology often benefits those of higher socioeconomic status and non-minoritized ethnicity[20]. This widens disparities, as has been documented in the T1DX registry compared to the German–Austrian Diabetes Prospective Follow Up (DPV) registry[21–23].

While translating research into practice has been estimated to take 17 years[24], the Diabetes Control and Complications Trial (DCCT), which established the benefit of lower HbA1c on reducing vascular complications through intensive management[25], including team-based care and frequent insulin dose adjustments, has yet to be implemented 30 years later because of many challenges. With the widespread use of smartphones and connected diabetes technology, it may be possible to mimic the frequency of patient–healthcare team interaction in the DCCT through the use of CGM-based remote patient monitoring (RPM). However, much as in other chronic medical conditions, developing RPM in diabetes care has been challenging because of inadequate clinic staffing and reimbursement for care, as well as gaps in Internet access and digital literacy for patients[26]. In addition, a major challenge in medical care delivery, especially care involving digital health, is developing equitable, translational programs of proven research therapies.

The Teamwork, Targets, Technology, and Tight Control (4T) Study is a real-world pragmatic research study designed to deliver team-based clinical care with tighter glucose targets and equitable access to diabetes technology soon after T1D diagnosis[27–29]. The principles of this program are consistent with the Chronic Care Model. The 4T program used evidence-based guidelines to redesign the management of T1D in the first year of diabetes diagnosis by implementing a team-based approach to uniform technology access and unified glycemic target setting to facilitate the development of self-management skills by the young people and their caregivers. The team incorporated RPM to tighten glucose control through more frequent engagement in education and for insulin dose adjustments. Information systems were developed to track CGM data and a dashboard was built to provide clinical decision support to help identify young people who would most benefit from intervention through electronic health record (EHR) messaging. The Pilot 4T study used a team-based approach to glycemic and HbA1c targets (<7.5%) based on the 2018 ADA guidelines (time of study initiation)[30]. To facilitate tight glucose control, young people were started on CGM during the first month of diabetes diagnosis with a subset receiving RPM. Compared to historical controls (diagnosed June 2014 to December 2016, $n = 272$)[31], young people in the Pilot 4T study

(diagnosed July 2018 to June 2020, $n = 135$)[27] had a 0.5% improvement in HbA1c at 12 months after diagnosis[27]. While this approach did not completely eliminate outcome gaps in individuals from minoritized groups, all groups benefited similarly from this intervention[32]. Early CGM initiation was positively accepted by families of children with new-onset T1D[33,34]. In the 4T Study, we focused on ensuring that our interventions were equitable. We approached all young people with new-onset T1D to enroll in this study. For those who did not have insurance coverage for CGM, we provided access to CGM for 1 year. For those without a compatible smartphone to share data, we provided iPod Touch devices. Care was provided in the preferred language of the young people or their caregivers.

In this article, we report data from the 4T Study 1, which refined the teamwork approach from the Pilot 4T study and lowered the HbA1c target to <7% (and related glucose targets based on current ADA[9] and ISPAD[10] guidelines) and ensured early CGM initiation with RPM for the entire study population. We hypothesized that the 4T Study 1 approach would improve HbA1c and CGM metrics in the first year of T1D diagnosis compared to historical controls and the 4T Pilot study. We assert that these methods can scale to other clinics caring for young people with T1D and these team-based digital health concepts can translate broadly to other chronic health conditions[26].

Results

Participant demographics

From 13 June 2020 to 5 March 2022, a total of 159 young people were newly diagnosed with T1D and 133 (84%) were enrolled in 4T Study 1 (Fig. 1). The median age at diagnosis was 11 years (interquartile range (IQR) = 6–14 years), 55.6% male, 39.1% non-Hispanic white, 84.2% English-speaking and 62.4% on private insurance. The mean HbA1c at diabetes diagnosis was 12.2 ± 2.4%, which was similar to the Pilot 4T cohort but higher than the historical cohort (Table 1). The overall demographics across the historical, Pilot 4T and 4T Study 1 cohorts were similar with the exception of a higher percentage of individuals with public insurance in the 4T Study 1 cohort. All except two participants in the 4T Study 1 cohort started CGM within 1 month of insulin initiation, with a median time to CGM initiation of 10 days (IQR = 6–18 days), compared to 100 days (IQR = 50–172 days) among the 37.5% of young people who initiated in the historical cohort and 7 days (IQR = 5–11 days) among the 97.8% who initiated in the Pilot 4T cohort. A greater percentage of 4T Study 1 participants initiated insulin pumps within 1 year (49.6% in the 4T Study 1 cohort compared to 32.7% in the historical cohort and 35.6% in the Pilot 4T cohort). Time to 1-year insulin pump initiation in the Pilot 4T (142 days, IQR = 91–256 days) and 4T Study 1 (162 days, IQR = 86–255 days) cohorts was not substantially different but lower than in the historical cohort (178 days, IQR = 111–250 days).

A total of 1,564 RPM messages triggered by 1,901 metric alerts (average 11.8 messages per participant) were sent, with most messages triggered by low time in range (TIR) (63%), hypoglycemia (39%), decline in TIR (13%) or insufficient CGM wear time (7%) (Supplementary Table 1; some messages were due to multiple metric alerts). The median frequency of contact among participants in the Pilot 4T study was 8 (IQR = 3–18) messages per participant and 10 (IQR = 4–17) messages per participant in the 4T Study 1.

Early technology use and tight targets improve glycemia

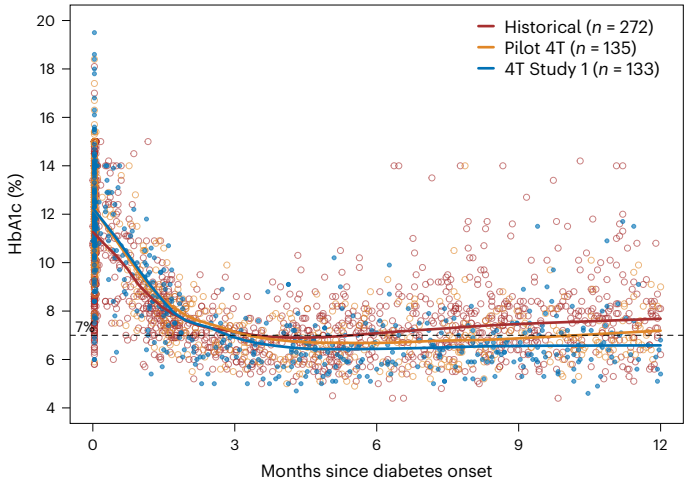
For all three cohorts, HbA1c was highest at diabetes diagnosis and decreased to a nadir at 4 months after diabetes diagnosis (Fig. 2). While those in the historical cohort had the lowest HbA1c at diagnosis, they had the highest HbA1c at the nadir. Although HbA1c at diagnosis was similar in the Pilot 4T and 4T Study 1 cohorts, participants in the 4T Study 1 cohort reached a lower nadir at 4 months after diagnosis. All three groups had an increase in their HbA1c starting at 5 months after diagnosis. This rise was fastest in the historical cohort and slowest in the 4T Study 1 cohort. For those in the 4T Study 1 cohort, the locally estimated scatterplot smoothing (LOESS)-based mean at 12 months after diagnosis was 6.58%, an improvement of 0.61% compared to the Pilot 4T cohort (mean = 7.19%) and 1.1% compared to the historical cohort (mean = 7.68%). LOESS-based differences at 6, 9 and 12 months after

Table 1 | Characteristics of the historical, Pilot 4T and 4T Study 1 cohorts

Characteristic	Historical cohort	Pilot 4T cohort	4T Study 1 cohort
n	272	135	133
Baseline characteristics			
Age in years at T1D diagnosis, median (Q1, Q3)	10 (7, 13)	10 (7, 13)	11 (6, 14)
Sex, *n* (%)			
Male	137 (50.4)	71 (52.6)	74 (55.6)
Female	135 (49.6)	64 (47.4)	59 (44.4)
Ethnicity, *n* (%)			
Non-Hispanic white	120 (44.1)	53 (39.3)	52 (39.1)
Non-Hispanic Black	5 (1.8)	0 (0)	1 (0.8)
Hispanic	69 (25.4)	29 (21.5)	49 (36.8)
Asian or Pacific Islander	25 (9.2)	19 (14.1)	11 (8.3)
American Indian or Alaska Native	1 (0.4)	0 (0)	0 (0)
Other	21 (7.7)	19 (14.1)	17 (12.8)
Unknown or declined to state	31 (11.4)	15 (11.1)	3 (2.3)
Diabetic ketoacidosis at diagnosis, *n* (%)	94 (34.7)	67 (49.6)	72 (54.1)
HbA1c (%) at diagnosis, mean (s.d.)	10.9 (2.5)	12.3 (2.1)	12.2 (2.4)
Insurance type, *n* (%)			
Private	197 (73.0)	104 (77.0)	83 (62.4)
Public	73 (27.0)	31 (23.0)	47 (35.3)
Both	0 (0)	0 (0)	2 (1.5)
No insurance	0 (0)	0 (0)	1 (0.8)
Primary language, *n* (%)			
English	245 (90.1)	117 (86.7)	112 (84.2)
Non-English	27 (9.9)	18 (13.3)	21 (15.8)
Follow-up characteristics			
CGM initiation within 1 year, *n* (%)	102 (37.5)	132 (97.8)	133 (100)
Initiated CGM ≤30 days, *n* (%)	6 (2.2)	124 (91.9)	131 (98.5)
Days to CGM initiation, median (Q1, Q3)	100 (50, 172)	7 (5, 11)	10 (6, 18)
CGM wear time[a] (%), median (Q1, Q3)	N/A	90.7 (55.8, 96.0)	96.4 (89.3, 97.9)
Insulin pump use within 1 year, *n* (%)	89 (32.7)	48 (35.6)	66 (49.6)
Predictive low-glucose suspend	2 (0.7)	2 (1.5)	2 (1.5)
Open loop	66 (24.3)	30 (22.2)	34 (25.6)
Hybrid closed loop	21 (7.7)	17 (12.6)	33 (24.8)
None	183 (67.0)	87 (64.4)	67 (50.4)
Days to pump initiation, median (Q1, Q3)	178 (111, 250)	142 (91, 256)	162 (86, 255)

[a]Percentage of time CGM was worn out of eligible hours of device wear.

https://doi.org/10.1038/s41591-024-02975-y



	Month 3	Month 6	Month 9	Month 12
Historical	7.17%	7.07%	7.46%	7.68%
Pilot 4T	7.17%	6.68%	6.87%	7.19%
4T Study 1	6.96%	6.44%	6.56%	6.58%

Fig. 2 | Participants in 4T Study 1 had lower LOESS based means compared to those in the Pilot 4T Study and the historical cohort. HbA1c trajectories in the first 12 months of diabetes diagnosis in the historical, Pilot 4T and 4T Study 1 cohorts. Mean HbA1c was higher in the Pilot 4T and 4T Study 1 cohorts. Young people in the 4T Study 1 cohort had the lowest nadir 4 months after diabetes diagnosis and remained on a lower HbA1c trajectory throughout the first year of diabetes diagnosis.

diagnosis between the 4T Study 1 and historical cohort (with bootstrapped 95% confidence intervals (CIs) from 1,000 resamples on the participant level) were −0.64% (−0.88 to −0.37), −0.90% (−1.18 to −0.63) and −1.10% (−1.55 to −0.65). The LOESS-based differences between the 4T Study 1 cohort and Pilot 4T cohort at 6, 9 and 12 months after diagnosis were −0.25% (−0.55 to 0.03), −0.31% (−0.61 to −0.01) and −0.61% (−1.10 to −0.12).

Regression analysis examining the change in HbA1c from 4 months to 12 months after diagnosis showed that participants in 4T Study 1 experienced an average increase in HbA1c of 1.44 (95% CI = 1.34–1.54). This was statistically lower ($P < 0.001$) than the increase in HbA1c of 1.60 (95% CI = 1.52–1.68) in the historical cohort, but not statistically different ($P = 0.583$) from that in the Pilot 4T cohort (1.47, 95% CI = 1.37–1.57). Results were not materially changed under multiple imputations. To understand the contribution of AID, we censored our follow-up analysis at AID initiation. Resulting estimates of 4–12-month change in HbA1c and their 95% intervals from the mixed-effects regression model were within 0.02 of the estimates from our main model that considered the full 12-month follow-up (Supplementary Table 2). As inference remained unchanged, we considered the primary analysis robust to AID usage.

As HbA1c data at 12 months was available for only a subset of participants, we calculated the glucose management indicator (GMI). The average GMI at 12 months after diagnosis was 7.25% in the Pilot 4T cohort and 7.11% in the 4T Study 1 cohort. In 4T Study 1, the mean and s.d. of GMI were the same in participants with and without HbA1c values at 12 months. HbA1c was available at 12 months ± 6 weeks in 45.9% ($n = 61$) of young people in the 4T Study and 30.4% ($n = 41$) in the Pilot 4T. We examined the differences between participants with and without HbA1c at 12 months and found that young people from minoritized groups and those who were non-English-speaking were overrepresented in the groups having HbA1c values. Cohen's d was below 0.5 for all characteristics suggesting at most moderate differences (Supplementary Table 3).

We calculated the GMI at 2-week intervals throughout the study period in the 4T Study 1 and the Pilot 4T cohorts. CGM data, defined as having any CGM data available during the study period, was available in 100% of those in the 4T Study 1 cohort and 97.0% of the Pilot 4T cohort. The median CGM wear time, calculated as the percentage of time the CGM was worn out of eligible hours of wear over 12 months, was 96.4% (IQR = 89.3–97.9) in the 4T Study 1 and 90.7% (IQR = 55.8–96.0) in the Pilot 4T cohort. The GMI and average CGM glucose followed a similar trajectory as the HbA1c, with the lowest GMI occurring between 10 and 20 weeks after diabetes diagnosis and increasing slowly throughout the remainder of the study period (Fig. 3a,b). Throughout the study period, the GMI and average CGM glucose were lower in the 4T Study 1 cohort compared to the Pilot 4T cohort.

In both cohorts, the TIR (70–180 mg dl^{-1}) and the time in tighter range (TITR) (70–140 mg dl^{-1}) were highest 3–4 months after diabetes diagnosis, when HbA1c was at the nadir. The TIR and TITR remained higher in the 4T Study 1 cohort compared to the Pilot 4T cohort (Fig. 3c,d). At 12 months after diagnosis, the time below range (TBR) (<70 mg dl^{-1}; Fig. 3e) was comparable in the 4T Study 1 and Pilot 4T (2.5% versus 2.4%). Similarly, time in clinically significant hypoglycemia (<54 mg dl^{-1}; Fig. 3f) was similar in the 4T Study 1 versus Pilot 4T (0.4% versus 0.5%). At 12 months after diagnosis, the TIR in the Pilot 4T cohort (Fig. 4a) was 63% compared to 68% in the 4T Study 1 cohort (Fig. 4b).

More young people met the HbA1c targets with 4T and tight targets

During the Pilot 4T study, the HbA1c target was set at <7.5%, which was consistent with the ADA HbA1c target in 2018 when the study was initiated. In 2020, the HbA1c target was lowered to <7%, which was used as the HbA1c target for the 4T Study 1. At 6 months after diabetes diagnosis, 88% of participants in the 4T Study 1, 83% in the Pilot 4T and 69% in the historical cohort achieved an HbA1c < 7.5% (Fig. 5a). By 12 months after diagnosis, 77% in the 4T Study 1, 62% in the Pilot 4T and 44% in the historical control still met an HbA1c target of <7.5% (Fig. 5a).

Using a lowered HbA1c target of <7%, 71% of participants in the 4T Study 1 met this target at 6 months after diagnosis compared to 70% in the Pilot 4T cohort and 51% in the historical cohort (Fig. 5b). By 12 months after diagnosis, 64% in 4T Study 1 still met an HbA1c target of <7%, but 50% in the Pilot 4T and 28% in the historical control met this target (Fig. 5b).

When GMI was used in addition to HbA1c, 86% met the HbA1c target of <7.5% (Fig. 5c) and 64% met the target of <7% (Fig. 5d) in the 4T Study 1 cohort compared to 81% and 67% in the Pilot 4T cohort at 6 months. By 12 months, 57% in the 4T Study 1 and 46% in the Pilot 4T cohort still met an HbA1c target of <7% (Fig. 5d).

There were two episodes of severe hypoglycemia, which was an expected severe adverse event. One episode was due to unexpected activity and the second episode was due to intentional administration of excess insulin.

Discussion

The 4T Study implemented a team-based program to initiate CGM within the first month of diabetes diagnosis combined with weekly population health dashboard-facilitated RPM to all young people with new-onset T1D to significantly improve glycemia. Participants received consistent guidance, at both clinic visits and during weekly RPM asynchronous review, from members of the care team regarding glucose targets consistent with an HbA1c goal of <7%. At 12 months after diabetes diagnosis, young people in this study had a mean HbA1c of 6.58% and mean GMI of 7.11%. An HbA1c < 7%, the ADA[17] and ISPAD target[10], was reached by 64% of participants by A1c and 57% by GMI. Participants had a mean TIR of 68% with minimal hypoglycemia. Young people in 4T Study 1 had a lower HbA1c nadir at 6 months after diagnosis. We achieved these outcomes while providing equitable access to CGM and RPM.

One of the key tenets of the 4T Study 1 is equity in the delivery of the intervention. We approached all young people with new-onset T1D who intended to follow in our clinic for enrollment. We eliminated

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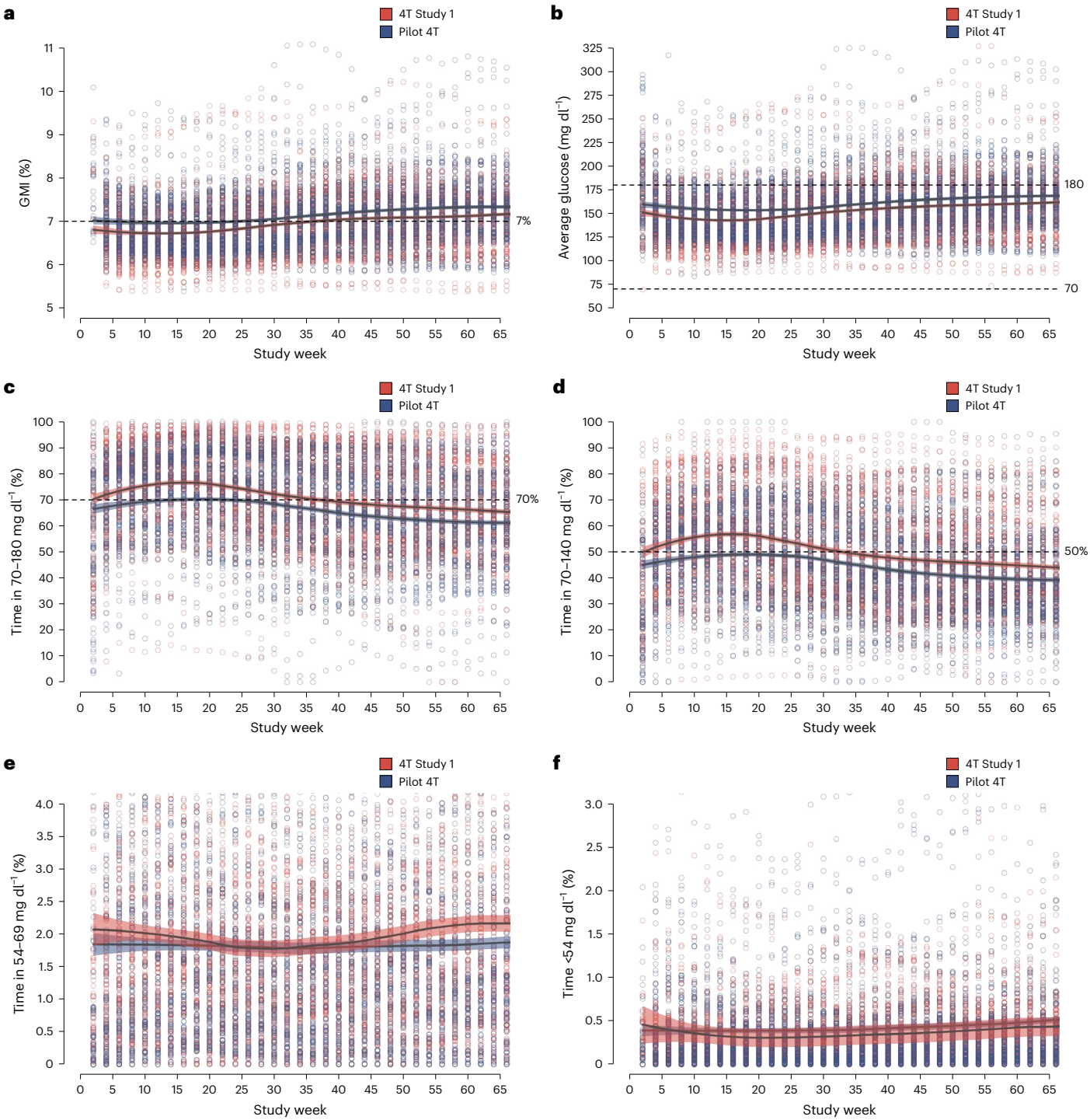

Fig. 3 | Participants in 4T Study 1 had improved CGM metrics in compared to those in the Pilot 4T Study. a–**f**, Scatter plots showing GMI (**a**), average CGM glucose (**b**), TIR (**c**), TITR (**d**), TBR (**e**), and time in clinically significant hypoglycemia (**f**). GMI, mean glucose, TIR and TITR were more favorable in the 4T Study 1 cohort compared to the Pilot 4T cohort. TBR and time in clinically significant hypoglycemia was low in both groups. Error bars represent 95% confidence bands.

exclusion criteria such as language and social stressors, which are normally barriers to enrollment. We had a multilingual, multicultural study staff to meet the needs of the diverse cohort, including recruitment, retention and logistical support for families (such as technology support for video visits, patient portal messaging and sensor issues). For young people who did not have CGM coverage, we obtained philanthropic then research funding to support the first year of CGM access. Accessing CGM data from the cloud was important for RPM. We used philanthropic then research funding to provide iPod Touch devices to young people who did not have compatible smartphones. Our team helped bridge connectivity issues by helping families advocate for access to the school Wi-Fi.

The 4T Study is a prospective pragmatic research study that did not include randomization and used a historical control group as a comparator, which is a limitation. While biases may account for some of the observed benefits, the results achieved by the 4T Study 1 are similar to those achieved in randomized controlled trials testing AID technologies[35,36], which have greatly advanced since a first out-of-hospital

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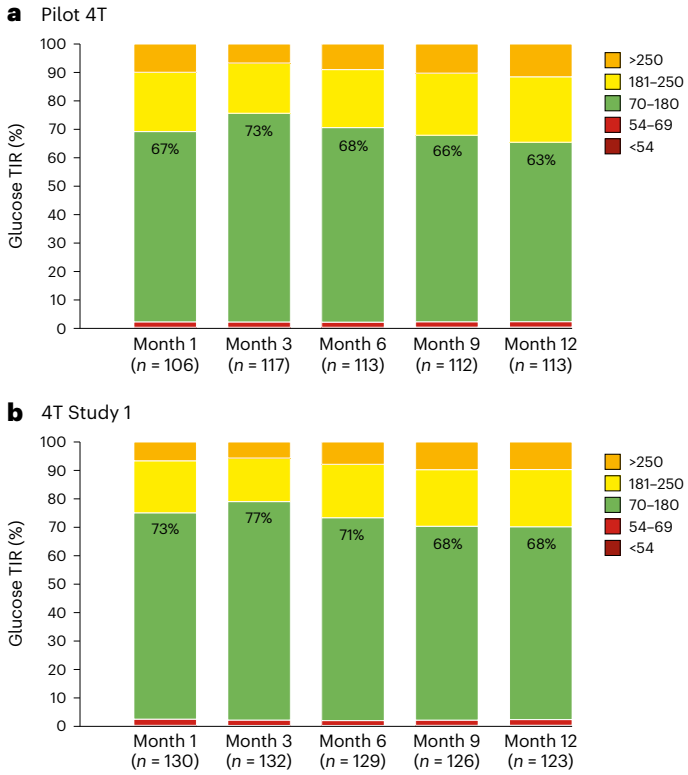

Fig. 4 | Participants in 4T Study 1 had improved TIR throughout the study period compared to those in Pilot 4T. a,**b**, Glucose distribution in the Pilot 4T cohort (**a**) compared to the 4T Study 1 cohort (**b**).

trial by Philip et al.[37]. These studies have been successful in improving glycemia, but often have less diverse cohorts[38]. In the Closed Loop from Onset in Type 1 Diabetes (CLOuD) trial, initiation of AID insulin therapy during the first 21 days of diabetes diagnosis was compared to standard insulin therapy for beta cell preservation[35]. At 12 months after diabetes diagnosis, the mean TIR from young people in the closed loop group was 64 ± 14%, which was lower than the TIR in the 4T Study 1 (68%); the TBR was higher in the CLOuD trial AID group (6.2 ± 3.8%) compared to the 4T Study 1 cohort (1.9 ± 1.7%). Similarly, in a double-blind, randomized clinical trial of young people with new-onset T1D randomized to oral verapamil (hypothesized to preserve beta cell function) or placebo and then randomized to intensive diabetes management (AID) or standard therapy (CLVer study), young people in the verapamil group had improved glycemic outcomes compared to those in the placebo group[36,39]. At 1 year after diagnosis, young people in the AID group had a TIR of 78% and young people in the standard care group (CGM with multiple daily injections or open loop pump systems) had a mean TIR of 64% (ref. 39). The 4T Study 1 study population included a greater proportion of minoritized young people, who historically have had more suboptimal glycemic outcomes[20,40–46], than the CLOuD trial and CLVer study. In the 4T Study 1, 60.9% of participants were from minoritized ethnic groups, 35.3% were on public insurance and 15.8% were non-English-speaking. In contrast, individuals from minoritized ethnic groups comprised only 19% of the study population in the CLOud trial and 10% of the study population in the CLVer study. In the CLVer study, only 10% were on public insurance. Both studies required participants to be English-speaking, as in many diabetes technology studies[38,47], while the 4T Study 1 enrolled non-English speakers.

While this study was conducted at a single academic institution, the intervention involves existing diabetes team members and can be scaled to other multidisciplinary diabetes clinics. Multidisciplinary team involvement was essential and there was a focus to develop RPM and the Timely Interventions for Diabetes Excellence (TIDE) platform collaboratively between Certified Diabetes Care and Education Specialists (CDCES), and endocrinology and engineering colleagues. Insulin dose adjustments are typically performed at quarterly diabetes clinic visits. However, more frequent insulin dose adjustments can prevent the deterioration of glucose control[48]. While modern diabetes technologies can share glucose data remotely, RPM is not routinely performed because of data sharing challenges and limitations on staff capacity. As part of the 4T study we developed TIDE, a population health dashboard for precision health to facilitate RPM, and increase clinic capacity for CGM data review and insulin dose adjustments by prioritizing patients who would benefit from CGM data review and RPM messaging by a CDCES[48–50]. In addition, use of RPM allowed us to identify individuals who were not using CGM and provided additional education or device support to help with persistence of CGM use. This technology-enabled intervention improved HbA1c throughout the first year of diagnosis. This is important because HbA1c trajectories after T1D diagnosis predict future glycemia[51,52]. Our RPM platform is open source and can be implemented at other institutions with an information technology infrastructure. We did not prospectively track messaging in the 4T Study 1; however, we plan to prospectively track messaging with the goal of personalizing messages to improve outcomes. In our study, because of the cadence of visits and increased usage of telehealth, not all young people had HbA1c measured at 12 months from diagnosis. While this is a limitation, young people with HbA1c values at 12 months after diagnosis were older and there was an overrepresentation of young people from minoritized communities and non-English-speaking families, all of which are typically associated with higher HbA1c[53], potentially introducing bias to the null effect of the 4T intervention. Also, there was a difference in mean HbA1c and GMI. However, this could also be explained by GMI calculations overestimating HbA1c at the lower end of the range[54,55]. The GMI was the same for those who had 12-month HbA1c values and those who did not.

When designing the 4T program, we wanted to build a program that can be implemented at other pediatric academic centers in the United States. The program used existing clinical CDCES staffing for RPM. While we did not bill for RPM during the course of the study, creating billing workflows will be part of future work. Previous health economic analyses by our group described a path toward financial sustainability[56]. There may be a need for advocacy efforts to ensure that RPM billing codes are reimbursed by public insurers in different states in the United States. Now that we have shown the benefits to glycemic outcomes, we will further investigate sustainability and scalability as we transition to the 4T sustainability cohort. Additionally, when translating this program to other clinics, it is important to ensure that the program is implemented equitably. While we had access to philanthropic support for young people who did not receive insurance coverage for CGM, this may not be possible everywhere. Thus, it is important to advocate for equitable coverage of diabetes technology, as has been achieved for CGM in Australia[57]. In addition, participation in RPM requires a Wi-Fi-enabled device and Internet access. Given the growth of connected technologies, Wi-Fi integration into devices themselves can help bridge this gap. Until then, there should be advocacy for Wi-Fi-enabled devices (cell phones, tablets) to be part of medical technology. We bridged gaps in Internet access by partnering with schools for data transfer; this approach may be available for most young people with diabetes.

The use of this digital health, team-based approach to new-onset diabetes management can be translated to other clinics to improve outcomes for young people with T1D. The underlying principles of the approach enable flexibility in its implementation, where newer technologies, such as AID systems, can be incorporated, as well as recently approved therapeutics. It is also important to understand the psychosocial impact of these interventions on young people and their caregivers. Finally, the incorporation of exercise education and

https://doi.org/10.1038/s41591-024-02975-y

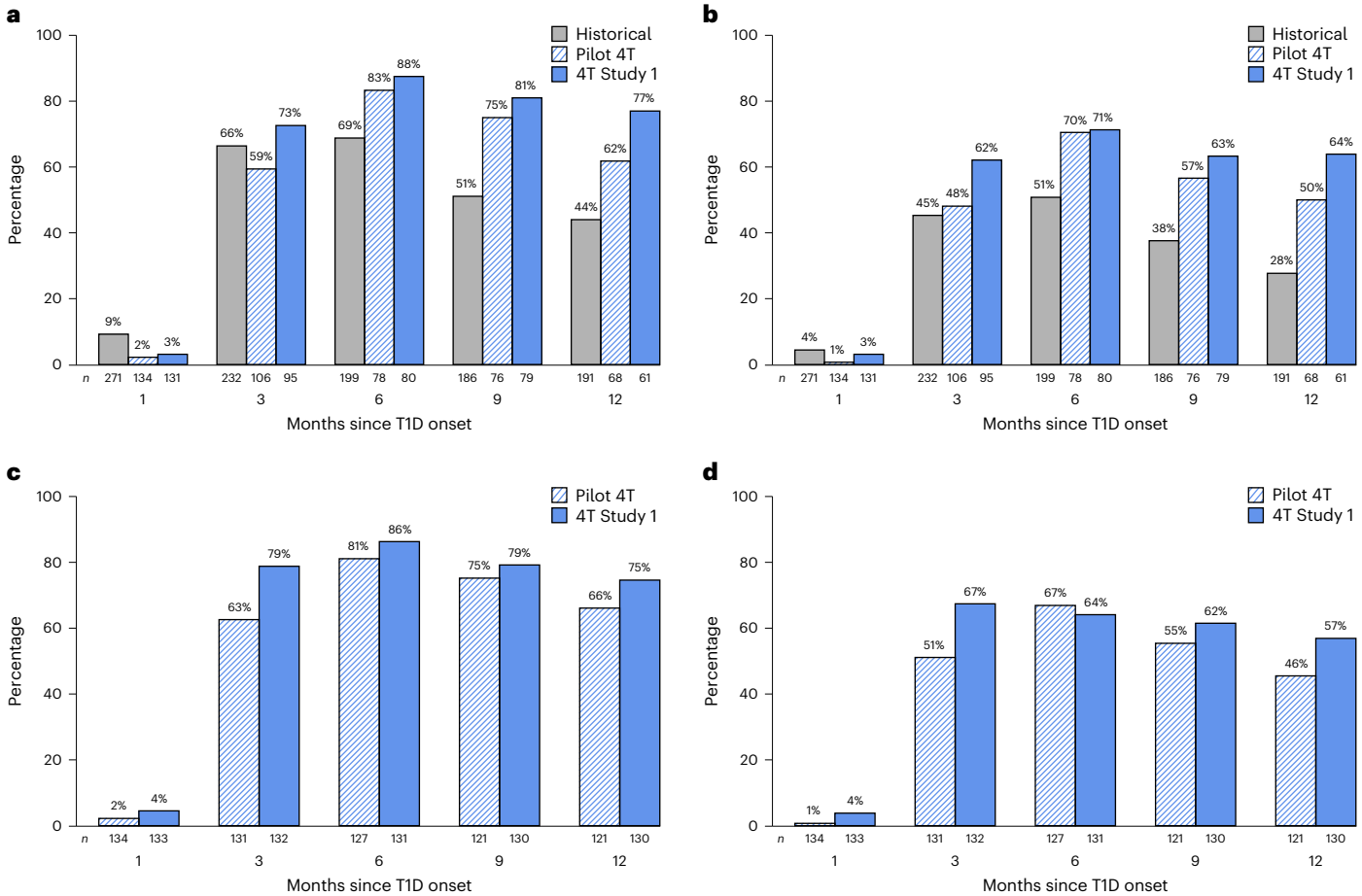

Fig. 5 | More youth in 4T Study 1 met HbA1c and GMI targets compared to those in the Pilot 4T Study. a–d, More young people in the 4T Study 1 achieved HbA1c targets of <7.5% (**a**) and <7% (**b**) compared to the Pilot 4T and historical cohorts; this was corroborated in the 4T Study 1 (**c**) and Pilot 4T (**d**) cohorts when HbA1c was supplemented with GMI. The number of young people with HbA1c or GMI available at each time point is shown below each bar.

physical activity tracking may also contribute to improved outcomes[29]. Future directions being tested in the current 4T Study 2 cohort include the benefit and safety of aiming for an HbA1c of <6.5% (refs. 10,17) plus systematically including an insulin pump education class between 1 and 3 months to initiate AID therapy earlier. Additionally, data on quality of life will be reported separately and may be a focus of future emphasis in pediatric diabetes practice. To ease adoption, we have made the code for TIDE open source. We are planning on a future dissemination research study to evaluate the scalability of the 4T program outside of Stanford University. The CDCES team members participating in RPM were part of our existing clinical staff. We implemented this program without hiring additional CDCES team members. We added a pharmacy technician who supported multiple activities that allowed CDCES to work at the top of their license. Initiation of the 4T program may require initial investment to activate the program. This is the topic of future work.

In conclusion, for an inclusive, general clinic population, the 4T Study 1 was able to implement learnings from the DCCT and achieve similar outcomes to randomized controlled trials using AID systems with stringent inclusion criteria. Through a combination of teamwork and universal CGM use, the 4T Study group implemented tight glucose targets (HbA1c < 7%) and reduce deterioration in glycemia. This program is adaptable and can incorporate newer technologies and treatments. The 4T Study 1 offers a great example of a change in clinical approaches within the spirit of the Chronic Care Model to produce robust positive outcomes. Such a team-based approach, including a technology-assisted RPM program, can be scaled to other multidisciplinary diabetes centers to improve outcomes in young people with diabetes. Furthermore, the concepts of the 4T approach can be more broadly applicable to improving the management of individuals with other chronic diseases and incorporating population-level RPM into clinical practice.

Online content

Any methods, additional references, Nature Portfolio reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41591-024-02975-y.

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Methods

Participants

The protocol for the 4T Program has been described previously[27,28]. Briefly, the 4T Study is a prospective, pragmatic, open-label research study that did not include randomization. The Pilot 4T study recruited all young people with new-onset T1D diagnosed between July 2018 and June 2020. Inclusion criteria included a diagnosis of T1D within the preceding 30 days, willingness to share CGM data with the clinic and plan to follow up in the clinic. Young people were excluded from the study if they did not consent to sharing CGM data or plan on following up in our clinic. Young people in this cohort were started on a CGM in the first month of diabetes diagnosis. Young people diagnosed starting in May 2019 also received RPM, which consisted of weekly CGM data review. The ADA target HbA1c at this time was <7.5%, which was also the target for this study. In Study 1, we recruited young people diagnosed between 13 June 2020 and 5 March 2022. Young people in this cohort were also offered the opportunity to start CGM in the first month of diagnosis. Given the benefits of RPM we saw in the Pilot 4T study, we offered RPM to all young people in Study 1. The HbA1c target was lowered to <7% because this was the new ADA target and in line with the ISPAD target. Learning from the Pilot 4T was used to refine the 4T Study 1 (Supplementary Table 4). Briefly, all young people (aged 1–21 years) with new-onset T1D were offered the opportunity to start on CGM in the first 30 days of diabetes diagnosis (ClinicalTrials.gov registration NCT04336969; Supplementary Fig. 1). There was no randomization. Consent was obtained from parents of children younger than 18 years. Children aged 7 years and older were asked to provide assent. A CGM starter pack (one transmitter and three sensors; Dexcom G6, Dexcom) was provided to participants; ongoing CGM coverage was applied for through the participant's insurance. To promote equitable access to the 4T program, participants who did not receive insurance approval for CGM, received CGM through the study. Participants were asked to share their CGM data through the manufacturer's cloud-based platform. If a participant did not have a compatible smartphone, an iPod Touch was provided so that all young people could participate. For those without Internet access, our team worked with schools to allow for data transfer during the school day. Participants received weekly CGM-based RPM by a CDCES facilitated by the TIDE platform, developed at Stanford, and hosted on a hospital server. The TIDE platform processes CGM data and prioritizes participants who would benefit from CGM data review and contact based on clinical metrics (>1% of the time with level 2 hypoglycemia (<55 mg dl^{-1}), >4% of the time with level 1 hypoglycemia (<70 mg dl^{-1}), week-over-week decrease in TIR >15%, TIR <65% and wear time <50%, meeting targets) adapted from consensus guidelines[58]. Participants received education and insulin dose adjustments through secure EHR portal messaging. The target HbA1c was <7% with associated glycemia targets[50,59]. This study was approved by the Stanford institutional review board; informed consent (and assent for participants aged 7–18 years) was obtained from all participants.

Participants in the 4T Study 1 were compared to our clinic's historical cohort who received standard new-onset education (diagnosed June 2014 to December 2016, $n = 272$)[31] and the Pilot 4T cohort with a target HbA1c of <7.5% (diagnosed July 2018 to June 2020, $n = 135$)[27]. In addition, only a subset of participants in the Pilot 4T cohort received RPM.

Data management

Prospective data collection for the Pilot 4T and 4T Study 1 studies was conducted in REDCap[60], a secure, web-based software platform designed to support data capture for research studies. Databases for all study cohorts were linked to Stanford Health Care's Epic EHR system via Fast Healthcare Interoperability Resources to enable automated data pull. The Stanford REDCap platform (redcap.stanford.edu) is developed and operated by the Stanford Medicine Research team, with services subsidized by (1) the Stanford School of Medicine Research Office, and (2) the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health (NIH), through grant no. UL1 TR001085.

Study outcomes

Our primary outcome was change in HbA1c from 4 months (nadir of HbA1c in our historical cohort) to 12 months after diagnosis. Our secondary outcome was achievement of the ADA's recommended HbA1c targets of <7.5% (at Pilot 4T study initiation in 2018) and <7% (as of 2020 for the 4T Study 1). Exploratory outcomes assessed in the Pilot 4T and 4T Study 1 cohorts included GMI[54] and average CGM sensor glucose (mg dl^{-1}), as well as sensor glucose TIR (70–180 mg dl^{-1}, goal >70%), TITR (70–140 mg dl^{-1}), TBR (<70 mg dl^{-1}, goal <4%) and time with clinically significant hypoglycemia (<54 mg dl^{-1}, goal <1%)[58].

Point-of-care HbA1c was performed using a DCA Vantage Analyzer (Siemens). Because of the coronavirus disease 2019 pandemic, care beginning in March 2020 was transitioned primarily to telehealth with a gradual return to in-person visits. For clinical care, GMI was used as a substitute for point-of-care HbA1c. Despite clinics reopening, many patients continued to receive care via telehealth. In November 2020, we incorporated home HbA1c measurements (University of Minnesota Advanced Research and Diagnostic Laboratory) for Pilot 4T and 4T Study 1 participants who did not have an HbA1c in the last 3 months[27,61].

Statistical analysis

Participants were followed from their T1D diagnosis date (baseline) to study completion or until the participant withdrew from the study. The baseline and follow-up characteristics of the historical, Pilot 4T and 4T Study 1 cohorts were summarized as counts with percentages, quartiles or means with s.d.

All participants who started on CGM in the first year were included in this analysis under the intention-to-treat principle. The GMI, an established estimator of HbA1c, was computed at 2-week intervals by applying the formula developed by Bergenstal et al.[54] to CGM glucose readings, averaged across a lookback window of up to 90 days. Although other equations to estimate HbA1c are available, we chose GMI because it is the most widely used and the basis for the GMI calculation in the Dexcom Clarity report. CGM-based metrics (GMI, TIR, TITR and TBR) were visualized using LOESS over the first 12 months since diabetes onset. The level of smoothing in LOESS is determined by the span parameter; we selected the value that minimized the mean squared error via tenfold cross-validation. TIR was also visualized as stacked bar plots over time, with month 1 spanning the first 30 days after diagnosis and later time points spanning approximately 3-month intervals.

The HbA1c trajectories of the three cohorts were visualized using LOESS. A linear mixed-effects regression model that allows for piecewise linear slopes of HbA1c values to be estimated from diagnosis to 4 months after diagnosis (historical nadir in HbA1c) and from 4 months to 12 months after diagnosis was used to estimate cohort-specific changes in HbA1c since month 4, with cohort differences with respect to Study 1 assessed via an interaction term. This model was implemented via the nlme R package, adjusted for characteristics at diagnosis (age, sex, Hispanic ethnicity and public insurance); we modeled within-participant correlation of HbA1c values over time through the inclusion of a participant-specific random effect. Changes in HbA1c since month 4, as well as monthly differences with respect to the 4T Study 1 cohort, were visualized as forest plots. Hypotheses were tested with a significance level of 0.05. Given the observed volume of patients seen at our institution before 2019, we anticipated enrolling 125 patients per year who would provide at least 1 year of follow-up observations. Under this constraint, we performed power calculations under three sample size scenarios (80, 100, 120) and four s.d. values for the rate of change (0.25, 0.3, 0.35, 0.4) using a one-sample t-test for between-group differences and the historical mean change considered as a fixed value. Assuming an s.d. of 0.35, our study design provided

93% power to detect a meaningful difference in HbA1c of 0.11%. Note that effect size determination was based on empirical findings from our historical data. Therefore, with a final cohort of 133 patients, the study was designed with sufficient power to detect clinically meaningful effect sizes of >0.5% change in HbA1c.

Our primary analysis under the mixed-effects framework assumes that HbA1c values are missing at random, conditional on baseline characteristics. As a sensitivity analysis, we performed multiple imputation by chained equations using the mice R package[62,63]. The imputation model included all baseline characteristics, as well as GMI calculated at 4, 12, 26, 40 and 52 weeks. The analysis model was applied to ten imputed datasets, and the results were combined using Rubin's rules. To further understand patterns of missingness, we tabulated patient characteristics according to whether HbA1c was available at 12 months, with differences between groups assessed using Cohen's *d*, a measure of the difference between the distribution of a characteristic in two groups expressed in units of s.d. A larger *d* corresponds to a larger difference and may be interpreted using Cohen's guidelines (0.2 = small effect; 0.5 = medium effect; 0.8 = large effect). The secondary outcome of achieving the ADA's HbA1c targets was presented descriptively using bar plots over time. For the Pilot 4T and 4T Study 1 cohorts, HbA1c, where unavailable, was supplemented with GMI calculated at 4, 12, 26, 40 and 52 weeks in a separate visualization of achieving HbA1c targets. All analyses were conducted in the R v.4.2.3.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

The datasets include information that is protected health information; as it currently sits, it can lead to the identification of potential participants. Thus, the current institutional review board coverage for this study does not allow data sharing. However, the authors are willing to share non-privileged data on a case by case bases as appropriate and indicated. Per the NIH guidelines, de-identified datasets will be made available on completion of all phases of the study, which we anticipate to occur in mid-2025. Please address any data requests to prahalad@stanford.edu and data requests will be reviewed per National Institute of Diabetes and Digestive and Kidney Diseases guidelines and timelines.

Code availability

To ease adoption at other institutions, our RPM platform is open source (github.com/jferstad/SURF-TIDE). The custom code used to perform the analyses is available at github.com/qsuProjects/4T-Study1.

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Acknowledgements

We thank all the young people who participated in the 4T Study. We thank the other members of the research team, including the research coordinators, clinical staff, students in the Systems Utilization for Stanford Medicine group, the Quantitative Sciences Unit and the T1D Working Group in Statistics and Informatics at Stanford Medicine Children's Health. We especially thank all staff and team members who are involved in the 4T Study including: D. Naranjo, C. Guestrin, M. Tannenbaum, E. Fox, A. Cortes, E. Pang, R. Tam, I. Balistreri, A. Loyola, N. Alramahi, E. Frank, J. Leverenz, P. Sagan, A. Martinez-Singh, B. Conrad, A. Chmielewski, S. Lin, K. Clash,J. Senaldi, E. Hodgeson, K. Seeley, G. Keoung, G. Kim MS, P. Dupenloup, J. Kurtzig, R. Sesanayake, M. Petel, P.-A. Laforcade, V. Ritter, B. Shaw, B. Bunning, B. J. Zou, A. Wang, Y. Jeong, N. Pageler, S. Ghuman, C. Brown, B. Watkins and G. Loving. This work was supported in part by the NIH via the Stanford Diabetes Research Center (1P30DK11607401) and grant no. R18DK122422 to D.M.M. Funding support was also received from the Helmsley Charitable Trust (grant no. G-2002-04251-2 to D.P.Z.), the National Science Foundation (NSF) (grant no. 2205084 to R.J.), Stanford Human-Centered Artificial Intelligence (HAI) to D.M.M., D.S., P.P. and R.J. and Stanford Maternal & Child Health Research Institute (MCHRI) grants to P.P., R.J. and M.Y.L. Clinical and Translational Science Award, including Biostatistics, Epidemiology, and Research Design Program (UL1 TR003142) and the Stanford REDCap Platform (UL1 T001085) provided additional support. A.A. received support from grant no. K23 DK131342. M.Y.L. received support from grant no. T32DK007217. J.F. has received support from the Stanford Data Science Scholars Program. This manuscript was partially supported by the Biostatistics Shared Resource of the National Cancer Institute-sponsored Stanford Cancer Institute (P30CA124435). Funding for the iOS devices and some CGM supplies was provided by a grant through the Lucile Packard Children's Hospital Auxiliaries Endowment to P.P. The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

Author contributions

D.M.M., P.P., M.D., D.S. and K.H. designed the interventions. V.Y.D. and M.D. performed the data analyses. M.Y.L. and J.F. performed the analysis of RPM messaging. P.P. and V.Y.D. wrote the manuscript. D.M.M., M.D., K.H., D.S., D.P.Z., A.A., F.K.B. and R.J. contributed to the discussion and reviewed and edited the manuscript.

Competing interests

D.M.M., D.S., P.P., K.H. and R.J. have received support from Stanford MCHRI, Stanford HAI and the NSF. D.S., R.J., D.M.M., K.H., D.P.Z. and A.A. have received funding from the Helmsley Charitable Trust. J.F. has received support from an NSF grant. D.P.Z. has received speakers honoraria from Medtronic Diabetes, Ascensia Diabetes, and Insulet Canada and Dexcom Canada, as well as research support from the ISPAD-Juvenile Diabetes Research Foundation Research Fellowship. D.M.M. has had research support from the NIH and his institution has received research support from Dexcom. D.M.M. has consulted for Abbott, the Helmsley Charitable Trust, Lifescan, Sanofi, Medtronic, Provention Bio, Kriya, Biospex and Bayer. K.H. has received research support from Dexcom for investigator-initiated research, and consultant fees from the Lilly Innovation Center, LifeScan Diabetes Institute and MedIQ. He has also received consulting fees from Sanofi Health and Cecelia Health. D.S. is an adviser to Carta Health. A.A. has received research support from the NIH. The other authors declare no competing interests.

Additional information

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41591-024-02975-y.

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Peer review information *Nature Medicine* thanks Jennifer Sherr, Howard Wolpert and the other, anonymous, reviewer(s) for their contribution to the peer review of this work. Primary Handling Editor: Lorenzo Righetto, in collaboration with the *Nature Medicine* team.

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Last updated by author(s): March 19, 2024

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☐	☒ The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒ A description of all covariates tested
☐	☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Data was collected in REDCap. The data was automatically transferred from the Epic electronic health record to REDCap through an integration implemented at Stanford University. Some data were manually entered into the REDCap database.
Data analysis	All analyses were performed using R version 4.2.3. LOESS curves were fitted using the R base function loess.smooth. Linear mixed effects models were fitted using the 'nlme' package version 3.1-162 and multiple imputation performed using the 'mice' package version 3.16.0. Custom code is available at github.com/qsuProjects/4T-Study1.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

The datasets include information that are PHI as it currently sits can lead to the identification of the potential participants. Thus, the current IRB coverage for this study does not allow data sharing. However, the authors are willing to share non-privileged data on a case by case bases as appropriate/indicated. Per NIH guidelines, de-identified datasets will be made available upon completion of all phases of the study.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	The data for this study was pulled directly into our REDCap reporting database from the electronic health record. The sex reported in Epic was used for analysis in this study. Since the study recruited individuals as they were diagnosed with type 1 diabetes, we did not have pre-determined goals for recruitment of either sex.
Reporting on race, ethnicity, or other socially relevant groupings	We used self-identified race/ethnicity. The categories used were Non-Hispanic White, Non-Hispanic Black, Hispanic, Asian or Pacific Islander, American Indian or Alaska Native, Other, and Unknown/Declined to State. These groupings are standards that have established by the Office of Minority Health and HHS (https://minorityhealth.hhs.gov/data-collection-standards-race-ethnicity-sex-primary-language-and-disability-status).
Population characteristics	Age, sex, insurance type, primary language, race/ethnicity. Recruited from ethnically diverse general clinic population.
Recruitment	All youth with newly diagnosed type 1 diabetes were informed of this study during their initial appointment for diabetes education. Following this appointment, a research team member approached participants for enrollment. Enrollment was completed within 30 days of diabetes diagnosis. Participants were sequentially enrolled, decreasing the risk of biases.
Ethics oversight	The Stanford University IRB provided ethics oversight.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	The planned sample size of 120 participants provides 93% power to detect a difference of 0.11% in 4- to 12-month HbA1c change between the 4T Study 1 and Historical cohorts using a two-sided Wald test, assuming a type I error of 0.05 and standard deviation of 0.35 for the rate of change. Therefore, with a final cohort of 133 patients, the study is designed with sufficient power to detect clinically meaningful effect sizes of >0.5% change in HbA1c.
Data exclusions	All consented participants were included in this analysis under the intention-to-treat principle.
Replication	To ensure rigor and reproducibility, all statistical analyses were pre-specified and timestamped in the Statistical Analysis Plan document. A copy of the statistical analysis plan was sent to the associate editor. No experiments conducted.
Randomization	Participants were not randomized in this intervention. Potential or established confounders were accounted for in the regression model.
Blinding	Since there was no randomization, participants were not blinded. All participants received the same interventions.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	NCT04336969
Study protocol	Protocol is not publicly available. A copy of the protocol was sent to the associate editor.
Data collection	Clinical data was collected from the electronic health records, device data, and participant surveys. Participants were enrolled from from June 29, 2020 to March 18, 2022. For this study, participant data was collected through March 2023.
Outcomes	Primary outcome was change in HbA1c from 4 months (nadir of HbA1c in our Historical cohort) to 12 months post-diagnosis. Our secondary outcome was achievement of the ADA's recommended HbA1c targets of <7.5% (at Pilot 4T study initiation in 2018) and <7% (as of 2020 for 4T Study 1). Point-of-care HbA1c was performed using a DCA Vantage Analyzer (Siemens, Germany). Owing to the COVID-19 pandemic, care beginning in March 2020 was transitioned primarily to telehealth with a gradual return to in-person visits. For clinical care, GMI was used as a substitute for point-of-care HbA1c. Despite clinics re-opening, many patients continue to receive care via telehealth. In November 2020 we incorporated home HbA1c measurements (University of Minnesota Advanced Research and Diagnostic Laboratory) for Pilot 4T and 4T Study 1 participants who did not have a HbA1c in the last 3 months.

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A