Type 1 Diabetes

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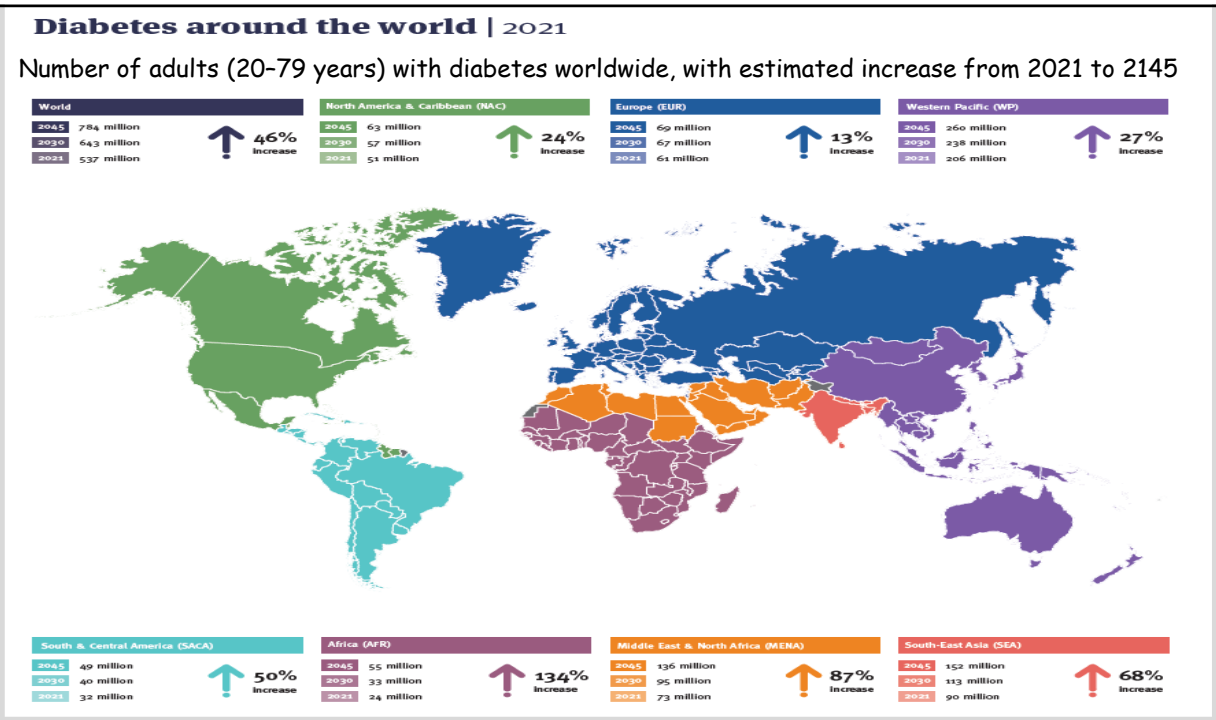
Objectives

- Review epidemiology of T1D
- Understand diagnosis of T1D
- Describe management of T1D
- Discuss special populations with T1D

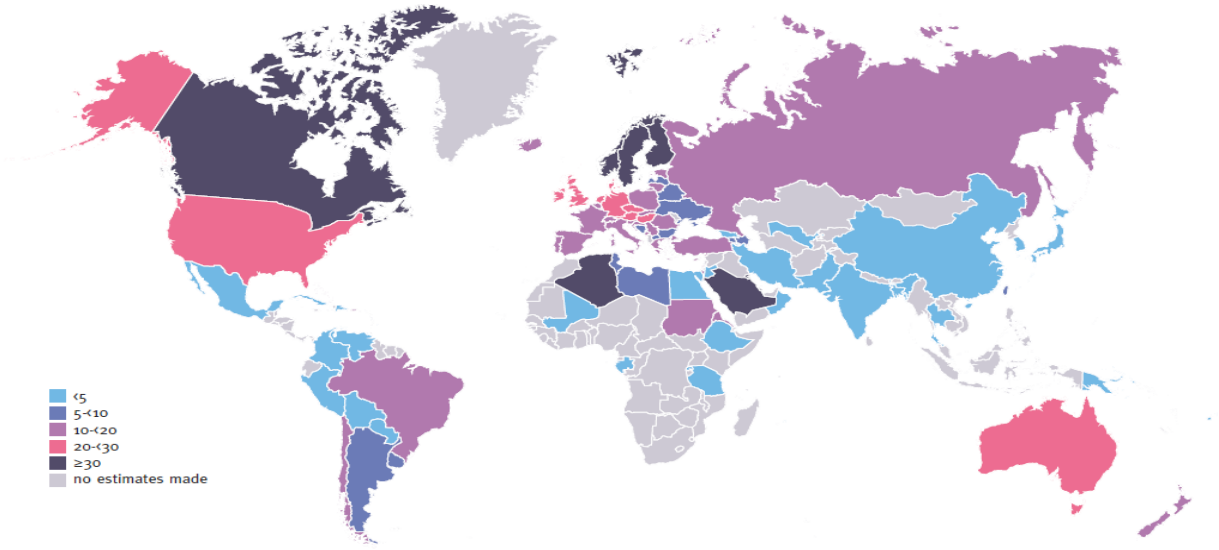


IDF Data for T1D

- Of the 215 countries and territories covered by the IDF Diabetes Atlas, only 97 have their own incidence data for T1D.
  - For most, this is limited to children and adolescents under 15 years of age
  - Among the countries without data for age <20 are some very populous nations, such as Nigeria, Indonesia, the Philippines, Vietnam, and South Africa. For these countries data are extrapolated from a nearby country with similar characteristics. However there are various reasons why such data may not be accurate.

www.diabetesatlas.org

Map 3.4 Age-sex standardised incidence rates (per 100,000 population per annum) of type 1 diabetes in children and adolescents aged 0–14 years



The IDF Europe Region has the highest number of children and adolescents (0–19 years) with T1D – 295,000 in total

www.diabetesatlas.org

Table 3.10 Top 10 countries or territories for estimated number of incident (new) cases of type 1 diabetes in children and adolescents (0–19 years) per annum

Rank	Country or territory	Number of incident (new) cases (0–19 years) in thousands
1	India	24.0
2	United States of America	18.2
3	Brazil	8.9
4	Algeria	6.5
5	China	6.1
6	Morocco[i]	5.1
7	Russian Federation	4.0
8	Nigeria	3.8
9	Saudi Arabia	3.8
10	Germany	3.6

i The figure for Morocco uses incidence rates extrapolated from Algeria

Table 3.12 Top 10 countries or territories for incidence rates (per 100,000 population per annum) of type 1 diabetes in children (0–14 years)

Rank	Country or territory	Incidence rates (per 100,000 population per year) 0–14 years
1	Finland	52.2
2	Sweden	44.1
3	Kuwait	41.7
4	Qatar	38.1
5	Canada	37.9
6	Algeria	34.8
7	Norway	33.6
8	Saudi Arabia	31.4
9	United Kingdom	28.1
10	Ireland	27.5

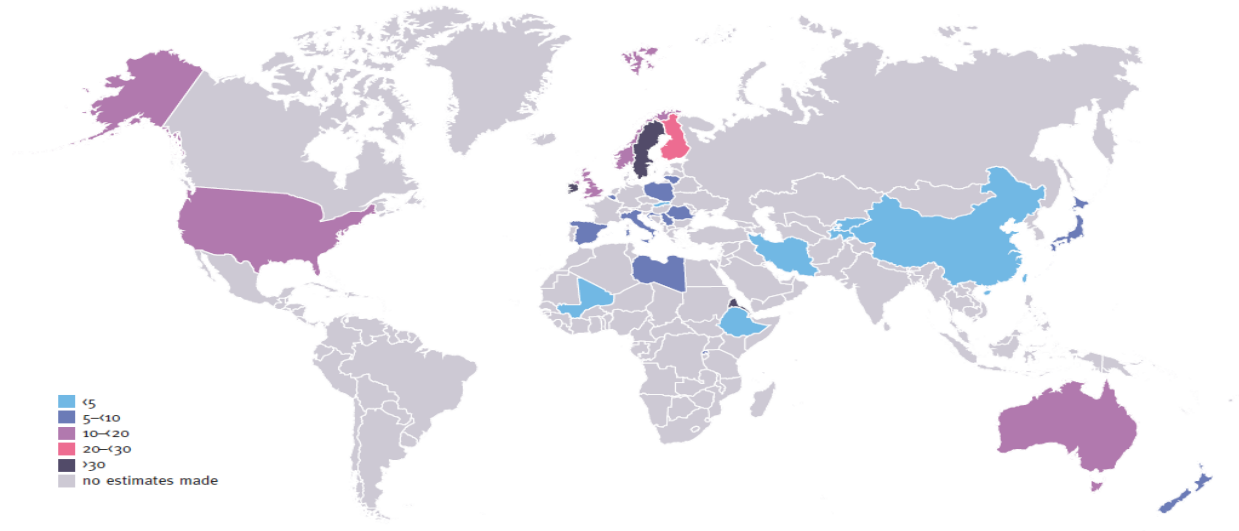
Table 3.11 Top 10 countries or territories for estimated number of prevalent (existing) cases of type 1 diabetes in children and adolescents (0–19 years) per annum

Rank	Country or territory	Number of children and adolescents with type 1 diabetes (0–19 years) in thousands
1	India	229.4
2	United States of America	157.9
3	Brazil	92.3
4	China	56.0
5	Algeria	50.8
6	Morocco[i]	43.3
7	Russian Federation	38.1
8	Germany	35.1
9	United Kingdom	31.6
10	Saudi Arabia	28.9

i The figure for Morocco uses incidence rates extrapolated from Algeria

www.diabetesatlas.org

Map 3.5 Incidence of adult-onset type 1 diabetes in adults 20–40 years



Annual incidence of type 1 diabetes (per 100,000 per year) among adults aged 20–40 years (men and women) per country/region (estimated from studies between 1973 and 2020)

Among the 46 studies identified, incidence of adult-onset (≥20 years) T1D was available for 32 countries and regions reporting estimates between 1973 and 2019.

www.diabetesatlas.org

Table 3.13 Countries with the highest incidence of adult-onset type 1 diabetes

Rank	Country	Study year	Incidence (per 100,000)
1	Eritrea	2019	46.2
2	Sweden	2009	30.6
3	Ireland	2011–2016	30.6
4	Finland	2017	24.0
5	United Kingdom	2009–2013	17.8
6	Norway	1978–1982	16.7
7	United States	2017	16.5
8	Australia	2020	16.4
9	Libya	1981–1990	9.9
10	Spain	1987–1990	9.9

www.diabetesatlas.org

The majority of available studies are limited by the use of clinical diagnosis or diagnostic codes for ascertainment of T1D in adults and, therefore, likely underestimate the true burden.

Limitations of the Data

- ICD10 Coding
  - Youth and Adolescents are often coded as T1D even when documentation is clear that diagnosis is T2DM
    - This has minimal impact on the data as T2DM is a very small percent of the diabetes diagnosed in youth and adolescence
  - Most adults with documented T1D are still coded as T2DM
    - EHR defaults "diabetes mellitus" to E11.9
  - Many adults are not tested for T1D but are merely presumed to be T2DM
- Clinical Diagnosis typically uses initiation of insulin within 6 or 12 months of diagnosis as indication of T1D

Sources of Data

- International Diabetes Federation
  - IDF Diabetes Atlas, 10th Edition, Dec 2021
  - www.diabetesatlas.org
- American Diabetes Association
- UK General Practice Research Database
- CDC National Diabetes Statistics Report, 2020

CDC National Diabetes Statistics Report, 2020

US Data, 2018-2020

- 64,000 new diagnoses of T1D annually
  - 27,000 cases in youth (0-19 years)
  - 37,000 cases in adults (20-64 years)
- 1.6 million American are living with T1D
  - 200,000 of these are < age 20
  - 1.4 million are age 20+
- This number is projected to rise to 5 million people (3X increase) in the U.S. by 2050, including nearly 600,000 youth

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Diagnosis of T1D in Adults

- Most studies reporting the incidence of adult-onset T1D rely on a clinical diagnosis, usually defined as physician-diagnosed T1D, plus the need for insulin therapy within 12 months of diagnosis.
  - incidence is generally higher in studies that defined T1D using biomarkers, compared to those using algorithms based on administrative data
    - However, most studies do not report diagnosis based on biomarkers

Diagnosis of T1D in Adults

- Adult onset T1D often does not present with classical symptoms such as DKA, typically has slower disease progression, and has delayed initiation of insulin treatment.
  - insulin initiation is often delayed by > 1 year in adults
  - This leads to cases being misdiagnosed and mismanaged as T2DM and underestimations of the true incidence of adult-onset T1D
- Adult Onset T1D
  - Consider T1D for all BMI ranges, but especially in the overweight range
  - Do not assume T2DM because age > 18 years

Diagnosis of T1D in Adults

- Biomarkers
  - Autoantibodies
    - GAD65
    - ICA
    - IAA
    - IA2A
    - ZnT8
    - Tetraspanin 7 (emerging marker)
  - Beta-cell function
    - c-peptide with simultaneous glucose level
      - Consider insulin & proinsulin levels if not on insulin therapy

Diagnosis of T1D in Adults

- Biomarkers
  - Autoantibodies
    - GAD65 **70% will have the GAD antibody**
    - ICA
    - IAA
    - IA2A
    - ZnT8
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Diagnosis of T1D in Adults

- This combination of biomarkers will give an estimate of possible duration of "honeymoon phase"
  - Autoantibodies
    - GAD65 **70% will have the GAD antibody**
      - very low titer GAD ***tends*** to have slower progression and more features of metabolic syndrome
  - Beta-cell function
    - c-peptide with simultaneous glucose level

Issues in the Treatment of Adult Onset T1D

- Metformin
  - Many patients are misdiagnosed as T2DM leading to initial therapy with metformin
    - although there is little evidence for the use of metformin, there is no evidence against its use
- Sulfonylureas
  - there is limited evidence to suggest the efficacy of SU in subjects with adult onset T1D
  - Data is emerging show that the use of SUs in adult onset T1D is associated with worse metabolic control and a more rapid decline in c-peptide level compared with treatment with insulin

Type 1 Diabetes

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Type 1 diabetes management

- Insulin
- Glucose monitoring
- Nutrition
- Exercise

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Pharmacokinetics of available short-acting insulin

	Insulin type	Onset	Effective peak	Duration of action
Prandial insulin	Lispro, aspart, glulisine	30 minutes	1-3 hours	5-7 hours
	lispro-aabc, rapid aspart	15-20 minutes	2-2.9 hours	4-6
	Regular	30 minutes	1.5-3.5 hours	8 hours

Pharmacokinetics of basal insulin

	Insulin type	Onset	Half-life	Effective peak	Duration of action
Basal insulin	NPH	1-2 hours	4.4 hours	6-10 hours	14-24 hours
	Glargine U-100	3-4 hours	12 hours	None	20->24 hours
	Glargine U-300	6 hours	19 hours	None	20-34 hours
	Detemir	3-4 hours	5-7 hours	3-9 hours	6-24 hours
	Degludec (U-100, U-200)	1 hour	25 hours	None (9 hours)	>24 hours

Insulin administration

- Multiple daily injections: basal insulin 1-2 times per day, prandial insulin with meals
- Continuous subcutaneous insulin infusion pump (CSII)

Insulin Pumps

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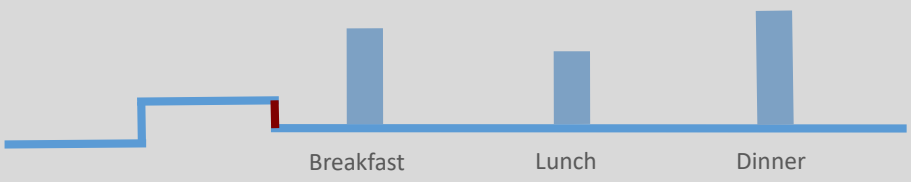
Insulin Pump Basics

- A small mechanical device that continuously delivers insulin through a catheter placed under the skin
- Delivers fast acting insulin two ways
  - Bolus (meal coverage and/or correction)
  - Basal (background coverage)



Insulin Pump Supplies

1. Insulin Pump / PDM
2. Reservoir / Cartridge / Pod (3 days of insulin)
3. Infusion Set / Tubing (carries insulin to the body)
4. Blood Glucose Meter

Author:Guus Herbschleb (CC BY 3.0)

Author: MailariX (CC BY-SA 4.0)

Insulin pump

- Can be used alone or with a continuous glucose monitor (CGM)
  - Sensor-augmented pump therapy: uses CGM and pump without any automation
  - Hybrid-closed loop therapy: automated insulin delivery based on CGM glucose readings

Pump Advantages

- Precise insulin delivery (0.5 to 0.001 unit)
- No injections
- Bolus calculator
- Temporary basal rate
- Free software for data collection
- Flexibility with insulin delivery
- Eliminates unpredictable effects of long-acting insulin

Pump Disadvantages

- Cost
- DKA risk
- Being attached (1-2 devices)
- Skin sensitivities to tape
- User may feel overwhelmed

Classic PDM

DASH PDM

Omni-Pod

Other Tech Options

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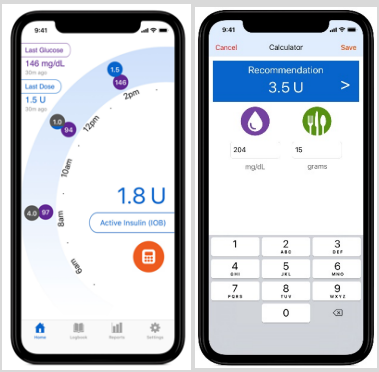
InPen by Companion Medical

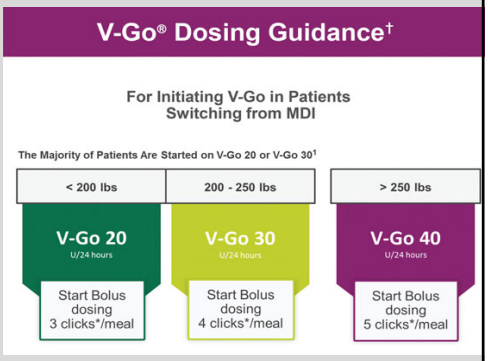


1. Bluetooth insulin pen with bolus calculator
   - Insulin-to-Carb Ratio
   - Sliding Scale / Sensitivity
   - Blood Sugar Target
   - Active Insulin Time
2. InPen costs no more than $35 per year
3. Delivers in half unit increments
4. Integrates with Dexcom through Apple Health

V-Go

- Disposable
- Change daily / applied like a patch
- On-demand dosing in 2 unit increments

- Does not alarm for empty reservoir
- Waterproof 3 feet, 3 inches up to 24 hours
- No history / memory



Self-monitored blood glucose

- Finger-stick glucose measurements or
- Continuous glucose monitoring

- HbA1c goal <7% without frequent hypoglycemia
- Customize target for those with limited life expectancy, hypoglycemia unawareness (<8%)
- Can be lower if able to achieve without significant hypoglycemia

ADA Standards of Care 2022, Volume 45, Suppl 1. Jan 2022.

Glycemic targets

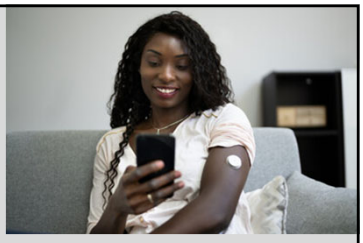
A1c	<7% (<53 mmol/mol)
Preprandial capillary plasma glucose	80-130 mg/dL (4.4-7.2 mmol/L)
Peak postprandial capillary plasma glucose	<180 mg/dL (10 mmol/L)

ADA Standards of Care 2022, Volume 45, Suppl 1. Jan 2022.

Continuous Glucose Monitors (CGM)

- CGMs measure interstitial glucose every 1-5 minutes
- An algorithm calibrates and interprets the data and sends to a receiver
  - Receivers can be stand-alone, smart phone or insulin pump
- Alerts user when glucose is out of range or trending quickly
- CGMs are a great tool but do not replace all finger stick monitoring

CGM Basics



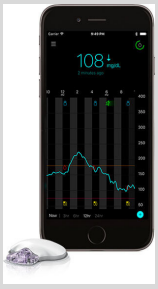
- Can be used alone or with an insulin pump
- Continuously monitors senor glucose 24 hours/day
  - Displays sensor glucose readings every 1 - 5 minutes
- Speed and direction of blood sugar ⬆ ⬇ ➡
- Optional Alert Features
  - High or low sensor glucose
  - Rising or falling sensor glucose
  - Temporarily suspends insulin (Medtronic & T-slim)

CGM Advantages

- ❑ Trend arrows
- ❑ Detects asymptomatic hypoglycemia
- ❑ Alerts when glucose is above/below target
- ❑ Alerts for rapid rise/fall in glucose
- ❑ Ability for user to share glucose alerts with a friend or family member
- ❑ Can be combined with some insulin pumps
- ❑ Record keeping right on the app

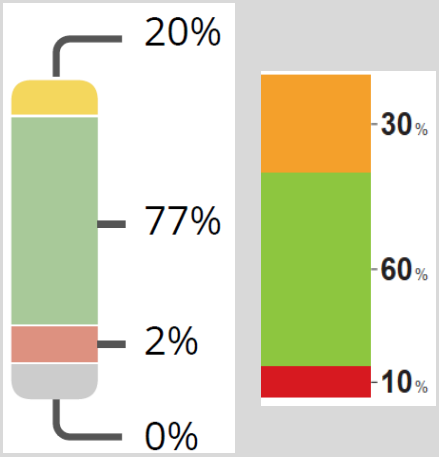
CGM Disadvantages

- ❑ Cost
- ❑ Does not replace all monitoring
- ❑ Skin sensitivities
- ❑ Two insertion sites if user is also wearing an insulin pump
- ❑ User may feel overwhelmed



Time-in-Range Matters MORE than HbA1c

- Time Above Range >180 mg/dL
- Time In Range 70-180 mg/dL
- Time Below Range <70 mg/dL



Time in Range goal

Diabetes group	Time in Range (TIR)		Time Below Range (TBR)		Time Above Range (TAR)	
	% of readings	Target range	% of readings	Below target level	% of readings	Above target level
Type 1	>70%	70-180 mg/dL (3.9-10 mmol/L)	<4% <1%	<70 mg/dL (<3.9 mmol/L) <54 mg/dL (<3 mmol/L)	<25% <5%	>180 mg/dL (>10 mmol/L) >250 mg/dL (>13.9 mmol/L)
Older/high risk type 1	>50%	70-180 mg/dl (3.9-10 mmol/L)	<1%	<70 mg/dL (<3.9 mmol/L)	<10%	>250 mg/dl (>13.9 mmol/L)

Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations from the International Consensus on Time in Range. Diabetes Care 2019;42:1593-1603.

Time in Range and Patient Goals

- For every 10% change in TIR, there is a corresponding 0.8% change in HbA1c

Vigersky RA, McMahon, C. The Relationship of Hemoglobin A1c to Time-in-Range in Patients with Diabetes. Diabetes Technology & Therapeutics 2019;21:81-85.

Hypoglycemia Management & Emergency

- Glucagon is a hormone that raises glucose in an emergency if patient with diabetes is unconscious or unable to take glucose by mouth
- A family member, roommate, or coworker should learn how to give glucagon
- Liquids and food should never be given to someone who is not alert or awake

Ketone Monitoring for those living with T1D

- Ketones are produced when the body is using fat for energy
  - When there is not enough insulin
- When should patients check?
  - BG > 300
  - BG > 200 during pregnancy
  - Any illness and with nausea, vomiting, diarrhea
- Large build up of ketones leads to **DKA**

Author: Caipira (CC BY-SA 3.0)

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- Review epidemiology of T1D
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Unique patient populations

- Teens and emerging adults
- Pregnancy
- Elderly

Transition of Care with Diabetes

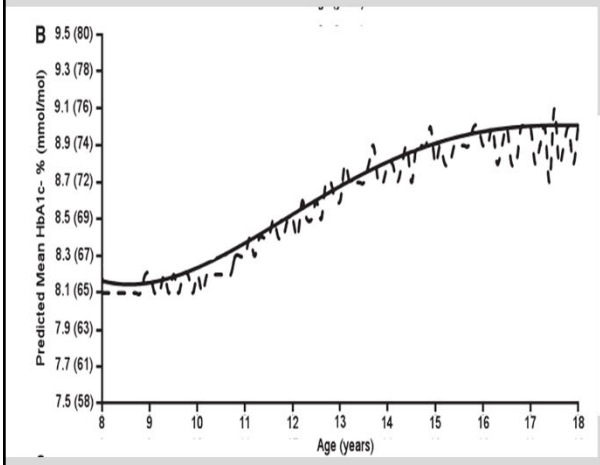
- Strong, practical transition plan
- Initiated early (early teenage years)
- Ongoing dialogue between family and youth
- Cover issues such as:
  - Finances, insurance, obtaining supplies
  - Psychosocial issues
  - Sexual and reproductive health issues
  - Alcohol, smoking, and drug use

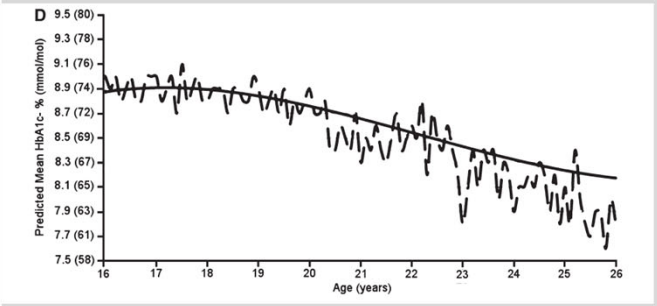
ADA Standards of Medical Care in Diabetes, Diabetes Care 2022;45,suppl 1. S208-231.

Type 1 Diabetes Exchange Clinical Registry

- >25,000 individuals with T1D
- Aged 1 to 90 years of age
- 70 centers across the US

A1c changes over time: T1D exchange clinic registry





Clements, M.A., Foster, N.C., Maahs, D.M., Schatz, D.A., Olson, B.A., Tsalikian, E., Lee, J.M., Burt-Solorzano, C.M., Tamborlane, W.V., Chen, V., Miller, K.M., Beck, R.W. and (2016), Hemoglobin A1c (HbA1c) changes over time among adolescent and young adult participants in the T1D exchange clinic registry. Pediatr Diabetes, 17: 327-336. https://doi.org/10.1111/pedi.12295

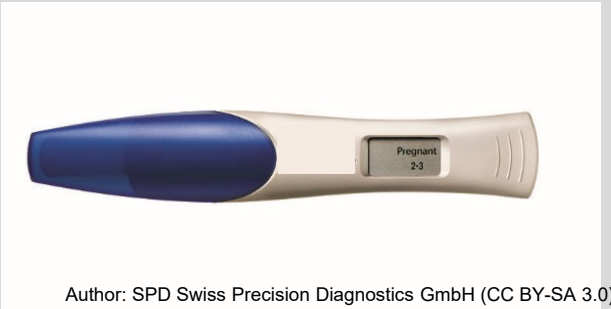
ADA recommendations for reproductive health

- Preconception counseling should be part of every visit starting at puberty
- If pregnancy desired:
  - A1c level as close to normal as possible (<6.5%) without hypoglycemia
  - Evaluate and treat complications
  - Evaluate medications' safety

ADA Standards of Medical Care in Diabetes, Diabetes Care 2022;45(Suppl 1),S232-243.

Are most pregnancies planned?

- 2/3 of pregnancies in women with diabetes are unplanned
- Leads to excess of malformations in infants of mothers with diabetes



Author: SPD Swiss Precision Diagnostics GmbH (CC BY-SA 3.0)

ADA Standards of Medical Care in Diabetes, Diabetes Care, 2022;44(Suppl 1)S232-243.

Congenital malformations

- Major congenital malformations are the leading cause of mortality and morbidity in infants of mothers with T1D and T2D
- Risk of malformations increases with higher maternal glycaemia during first 6-8 weeks

ADA Standards of Care 2021, Diabetes Care, Volume 44(Suppl 1), Jan 2021.

Elderly patients with T1D

- Screen for medical, psychological, functional, and social geriatric domains at initial visit
- Screen for mild cognitive impairment or dementia
- Greater risk of hypoglycemia
- Customize glycemic targets
- Screen for and treat other diabetes complications

ADA Standards of Medical Care in Diabetes, Diabetes Care 2022;45;suppl 1. S195-207.

Other autoimmune diseases

- Screen at diagnosis and with symptoms
- Thyroid disease (17-30%)
- Celiac disease (1.6-16.4%)
- Less common:
  - Addison's disease
  - Autoimmune hepatitis
  - Autoimmune gastritis
  - Dermatomyositis
  - Myasthenia gravis

ADA Standards of Medical Care in Diabetes, Diabetes Care 2022;45,suppl 1. S208-231.

Diabetes complications

- Blood pressure, pulse, weight
- Annual TSH, lipids, urine albumin-to-creatinine ratio
- Every 1-2 year dilated retinal exam (or retinal photography)
- Annual comprehensive foot exam
- Cardiovascular disease

Summary

- T1D
  - Age does not define the diagnosis
  - Consider measuring GAD Antibody on all new diagnoses of diabetes
  - Do not use SUs if Antibody positive, even if c-peptide is still present
- Patients can benefit from diabetes technology
- Customize diabetes care for unique populations