Innere Medizin fachübergreifend, München, 3.2.2023

Fachklinik Bad Heilbrunn
Diabetes- und Stoffwechselzentrum

Internationale Leitlinie (ADA/EASD) Typ 1 Diabetes mellitus, was ist neu?

Dr. med. Bernhard Gehr
Diabetes- und Stoffwechselzentrum, m&i Fachklinik Bad Heilbrunn

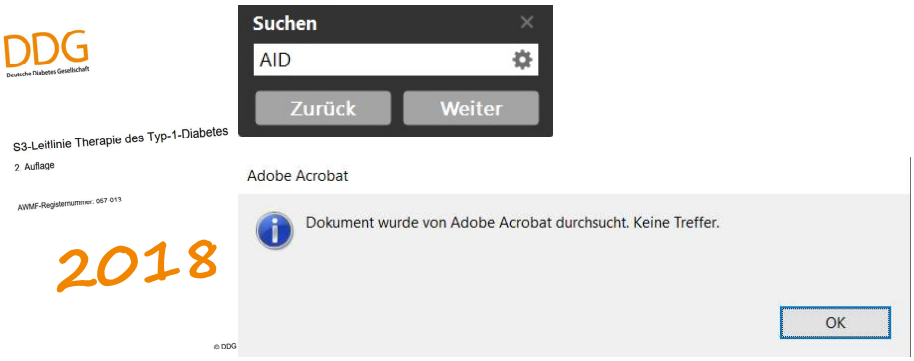
m&i Fachklinik Bad Heilbrunn
Diabetes- und Stoffwechselzentrum

Bild zur Verfügung gestellt von Dr. Gehr

Agenda

1. DDG S3-Leitlinie Therapie des Typ-1-Diabetes
2. ADA/EASD Consensus Report
3. Ausblick

Aktuelle DDG Leitlinie zur Therapie des Typ-1-Diabetes



DDG: S3-Leitlinie Therapie des Typ-1-Diabetes, 2. Auflage 2018

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Agenda

1. DDG S3-Leitlinie Therapie des Typ-1-Diabetes
2. ADA/EASD Consensus Report
3. Ausblick

The Management of Type 1 Diabetes in Adults: Consensus of…

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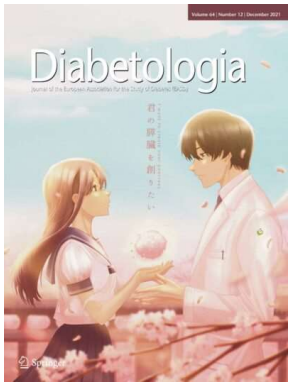
EASD European Association for the Study of Diabetes

Diabetes Care, Volume 44, Issue 11, November 2021



Diabetologia, Volume 64, Issue 12, December 2021

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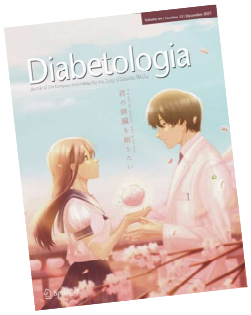
ADA/EASD Consensus: Management of T1D in adults



- Erste gemeinsame Leitlinie von ADA und EASD nur zur Therapie des Typ 1 Diabetes
- Klinisch orientiert
- 7 Autoren aus Europa, 7 aus den U.S.A.

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ADA/EASD Consensus: Management of T1D in adults

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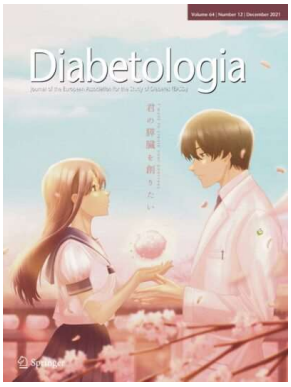

Diabetologia, Volume 64, Issue 12, December 2021

Diabetologia
https://doi.org/10.1007/s00125-021-05568-3

CONSENSUS REPORT

The management of type 1 diabetes in adults. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

Richard I. G. Holt[1,2] · J. Hans DeVries[3,4] · Amy Hess-Fischl[5] · Irl B. Hirsch[6] · M. Sue Kirkman[7] · Tomasz Klupa[8] · Barbara Ludwig[9] · Kirsten Nørgaard[10,11] · Jeremy Pettus[12] · Eric Renard[13,14] · Jay S. Skyler[15] · Frank J. Snoek[16] · Ruth S. Weinstock[17] · Anne L. Peters[18]

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Abstract

The American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) convened a writing group to develop a consensus statement on the management of type 1 diabetes in adults. The writing group has considered the rapid development of new treatments and technologies and addressed the following topics: diagnosis, aims of management, schedule of care, diabetes self-management education and support, glucose monitoring, insulin therapy, hypoglycaemia, behavioural considerations, psychosocial care, diabetic ketoacidosis, pancreas and islet transplantation, adjunctive therapies, special populations, inpatient management and future perspectives. Although we discuss the schedule for follow-up examinations and testing, we have not included the evaluation and treatment of the chronic microvascular and macrovascular complications of diabetes as these are well-reviewed and discussed elsewhere. The writing group was aware of both national and international guidance on type 1 diabetes and did not seek to replicate this but rather aimed to highlight the major areas that healthcare professionals should consider when managing adults with type 1 diabetes. Though evidence-based where possible, the recommendations in the report represent the consensus opinion of the authors.

Keywords Adjunctive therapy · Diabetic ketoacidosis · Diagnosis · Exercise · Glucose monitoring · Hypoglycaemia · Insulin · Nutrition · Psychosocial care · Schedule of care · Transplantation · Type 1 diabetes

Abbreviations

App Application
BGAT Blood glucose awareness training
BGM Blood glucose monitoring
CGM Continuous glucose monitoring
COVID-19 Coronavirus disease-2019
DKA Diabetic ketoacidosis
DSMES Diabetes self-management education and support
EDIC Epidemiology of Diabetes Interventions and Complications
FDA US Food and Drug Administration
GLP-1 RA Glucagon like peptide-1 receptor agonists
GMI Glucose management indicator
IAH Impaired awareness of hypoglycaemia
is-CGM Intermittently scanned continuous glucose monitoring
MDI Multiple daily injections
PTA Pancreas transplants alone
rt-CGM Real-time continuous glucose monitoring
SGLT Sodium–glucose cotransporter
SPK Simultaneous pancreas and kidney
TBR Time below range
TIR Time in range

This Consensus Report is jointly published in Diabetologia, published by Springer Verlag, GmbH, on behalf of the European Association for the Study of Diabetes. https://doi.org/10.1007/s00125-021-05568-3, and Diabetes Care, published by the American Diabetes Association https://doi.org/10.2337/DC21-0043.

A consensus report of a particular topic contains a comprehensive examination and is authored by an expert panel and represents the panel's collective analysis, evaluation, and opinion. The article was reviewed for EASD by its Committee on Clinical Affairs and approved by its Executive Board and for ADA by its Professional Practice Committee.

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Extended author information available on the last page of the article

Published online: 30 September 2021

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ADA/EASD Consensus: Management of T1D in adults

Was ist neu?

- Konsens zur Diagnose des Typ 1 Diabetes
- Universelle Anwendung von CGM
- Psychosoziale Unterstützung
- Patientenschulung

Was fehlt?

- Keine Kapitel zur Therapie diabetesassoziierten Folgeerkrankungen

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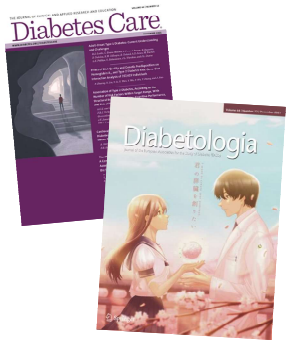

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Section 1: Introduction and Rationale for the Consensus Report
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Section 3: Aims and Goals of Management of Type 1 Diabetes
Section 4: Schedule of Care
Section 5: Diabetes Self-Management Education and Support
Section 6: Monitoring of Glucose Levels
Section 7: Insulin Therapy
Section 8: Hypoglycemia
Section 9: Additional Behavioral Considerations
Section 10: Psychosocial Care
Section 11: Diabetic Ketoacidosis
Section 12: Pancreas and Islet Transplantation
Section 13: Adjunctive Therapies
Section 14: Special Populations
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Section 16: Emergent and Future Perspectives

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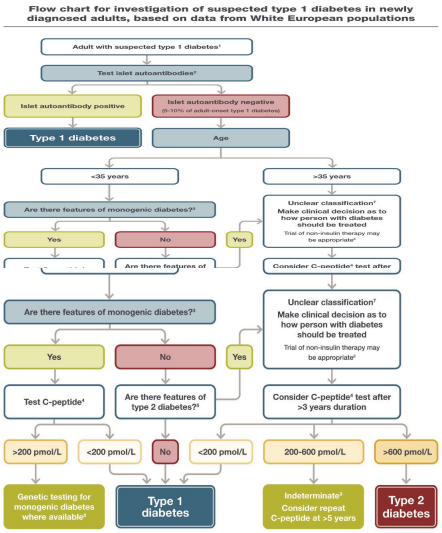
„Typologie“

„Mehr als 40% der Patient/innen, die im Alter von >30 Jahren einen T1D entwickeln, werden initial behandelt als hätten sie einen T2D.“



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Erwachsener mit Verdacht auf Typ 1 Diabetes

Anzeichen für Typ-1-Diabetes

- Es gibt kein einzelnes sicheres klinisches Anzeichen für T1D!
- Alter unter 35 Jahre bei Erstdiagnose
- BMI < 25 kg/m² bei Erstdiagnose
- Unabsichtlicher Gewichtsverlust
- Ketoazidose und BZ > 360 mg/dl bei Erstdiagnose

*Bei neu-diagnostizierten Erwachsenen, basierend auf Daten einer weißen europäischen Population. Version Juni 2021.

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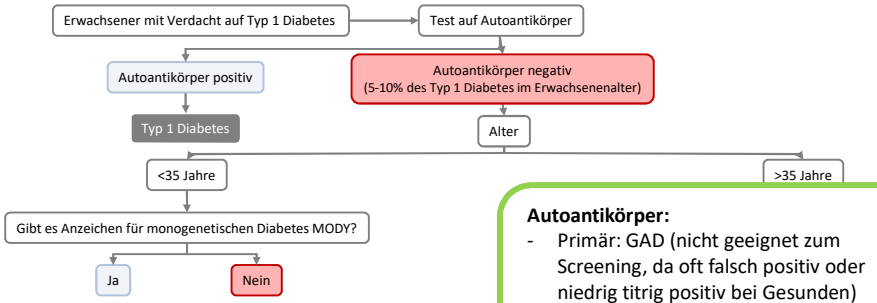

Autoantikörper:
- Primär: GAD (nicht geeignet zum Screening, da oft falsch positiv oder niedrig titrig positiv bei Gesunden)
- Falls GAD negativ: IA2, ZNT8
- Nicht mehr empfohlen: Inselzellantikörper

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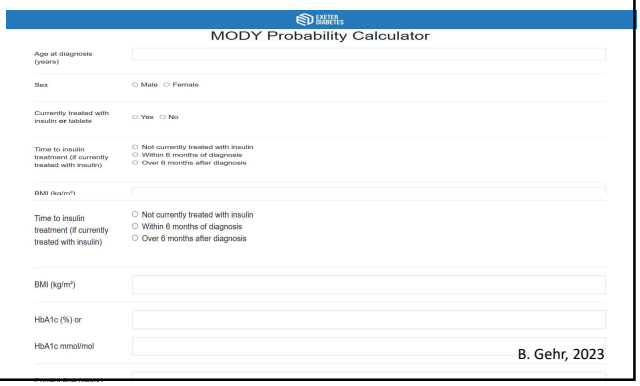
Anzeichen von MODY
- Alter bei Erstdiagnose < 35 Jahre
- HbA1c bei Erstdiagnose < 7,5 %
- Ein Elternteil mit Diabetes
- Kennzeichen anderer monogenetischer Erkrankungen, z. B. Nierenzysten oder Taubheit

Wahrscheinlichkeit für MODY
- Bei Erstdiagnose < 30 Jahre ⇒ 4% MODY
- Zusätzlich Ak negativ und erhaltenes C-Peptid ⇒ 20 % MODY

https://www.diabetesgenes.org/exeter-diabetes-app/ModyCalculator



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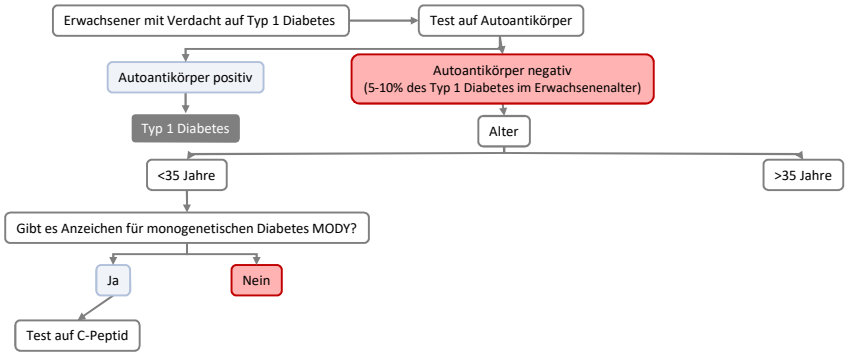

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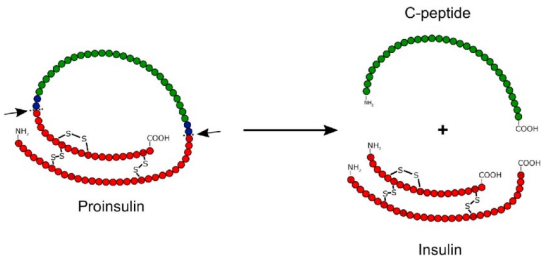

Bestimmung von C-Peptid

- Nur indiziert bei insulinbehandeltem Diabetes
- Immer C-Peptid + Laborglukose
- Abnahme **innerhalb 5 Std. nach einer Mahlzeit** kann einen formalen Stimulationstest ersetzen

Interpretation

- ≥ 600 pmol/l: Klares Ergebnis, relevante Insulinrestsekretion
- < 600 pmol/l bei Laborglukose <72 mg/dl oder im Fastenzustand ⇒ Test wiederholen
- < 80 pmol/l ⇒ klares Ergebnis, keine ausreichende Insulinrestsekretion

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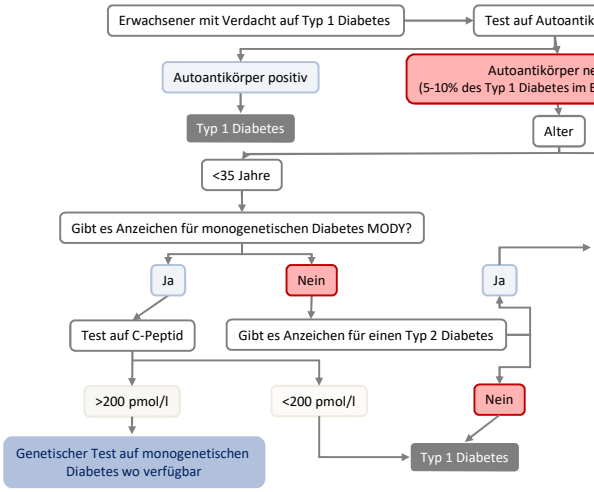

Anzeichen von Typ 2 Diabetes

- BMI > 25 kg/m²
- Kein Gewichtsverlust bei Erstdiagnose
- Keine Ketoazidose, nur milde Hypoglykämien
- Weniger sichere Anzeichen: Nichtweiße Ethnizität, Familienanamnese für T2D, Symptomatik bei Erstdiagnose milder und länger anhaltend, weitere Faktoren des metabolischen Syndroms, Familienanamnese leer für Autoimmunerkrankungen

*Bei neu-diagnostizierten Erwachsenen, basierend auf Daten einer weißen europäischen Population. Version Juni 2021.

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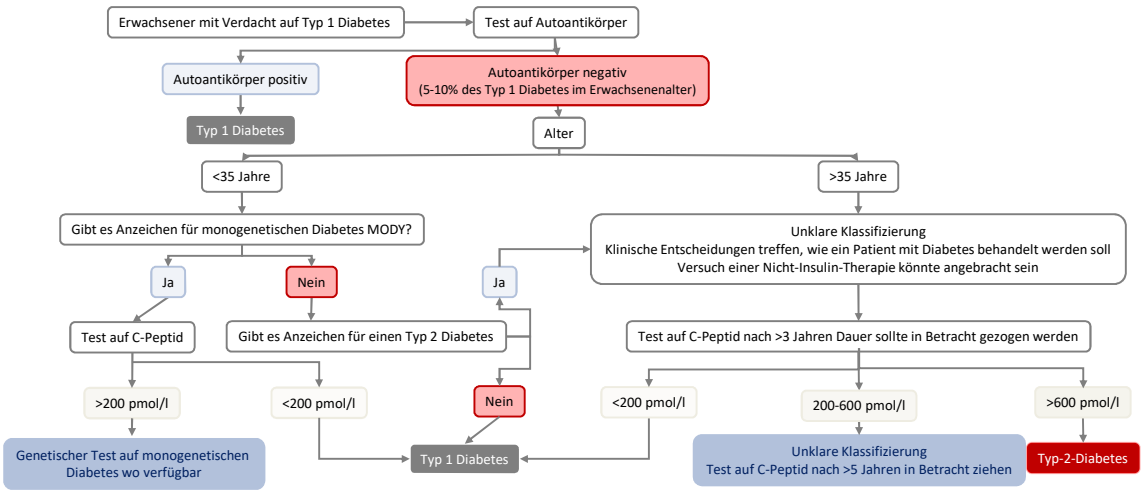

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Flow chart for investigation of suspected type 1 diabetes in newly diagnosed adults, based on data from White European populations

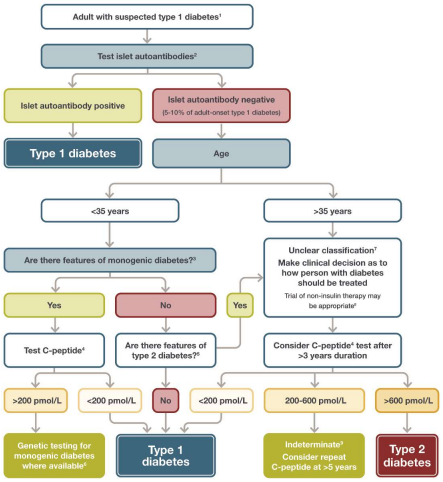

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Table 4—Nonglycemic factors that alter HbA_{1c} levels (70)

Effect on HbA_{1c}	Factor
Apparent increase	• Age • Ethnicity: HbA_{1c} is slightly higher in African Americans than in people of White Northern-European ancestry[a] • Anemias with decreased erythrocyte turnover: iron, • Renal failure • Advanced liver disease drugs: dapsone; trimethoprim/sulfamethoxazole • Vitamin E ingestion • Ribavirin and interferon α • Erythrocyte transfusion
Apparent increase or decrease	• Hemoglobin variants • Vitamin C ingestion

[a]Variability within races is greater than variability between races (293).

Continuous Glucose Monitoring

CGM is the standard for glucose monitoring for most adults with type 1 diabetes.

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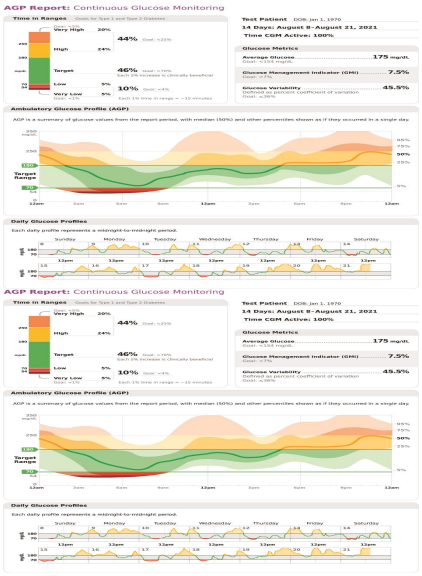
Sensoren sollen ausgelesen werden

Empfehlung AGP-Report



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Glykämische Therapieziele

Table 1 Glycaemic targets for most adults with type 1 diabetes

Variable	Target value
HbA_{1c}	<53 mmol/mol (<7.0%)
GMI	<53 mmol/mol (<7.0%)
Preprandial glucose	4.4–7.2 mmol/l (80–130 mg/dl)
1–2 h postprandial glucose[a]	<10.0 mmol/l (<180 mg/dl)
TIR	>70%
TBR	
Readings and time <3.9 mmol/l (<70 mg/dl; Level 1 and Level 2 hypoglycaemia)[b]	<4%
Readings and time <3.0 mmol/l (<54 mg/dl; Level 2 hypoglycaemia)[b]	<1%
Time above range	
Readings and time >10.0 mmol/l (>180 mg/dl; Level 1 and Level 2 hyperglycaemia)[c]	<25%
Readings and time >13.9 mmol/l (>250 mg/dl; Level 2 hyperglycaemia)[c]	<5%
Glycaemic variability (%CV)[d]	≤36%

All glycaemic targets should be individualised and agreed with the person with diabetes. Lower or higher targets may be appropriate according to individual characteristics

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Keton-Messung

„***Blutketonmessung*** *ist die Methode der Wahl.*

Daher sollte Erwachsenen mit Typ-1-Diabetes ein Blutketonmessgerät und -teststreifen angeboten werden.“

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Schematic for management of new-onset type 1 diabetes in an adult

Treatment depends on individual preferences, capabilities, and circumstances
Goal: to replace insulin as physiologically as possible, avoiding hypo- and hyperglycemia, reaching HbA_{1c} and/or TIR targets

Type 1 diabetes self-management education and support Fundamentals of nutrition, carbohydrate counting, and physical activity	Start glucose monitoring	Start insulin therapy	Prepare for hyperglycemia	Prepare for hypoglycemia
Consider referral to mental health provider/counseling if: • Person with diabetes requests it • Difficulty adjusting to diagnosis • Evidence for depression, eating disorder, high level of diabetes distress, or other psychological issues.	CGM is preferred, however, all should learn BGM for backup and monitoring if CGM not available and/or desired. Set testing frequency and HbA_{1c}, TIR, and TBR targets.	Preferably MDI but other regimens, including pump or hybrid closed-loop technology, can be started based on individual circumstances[1] (see Table 5)	Provide education on recognition, management, and prevention of hyperglycemia. Discuss when and how to measure ketones and provide method for ketone testing[2].	Teach principles for prevention and management of hypoglycemia. Provide glucagon and education on how it should be used.

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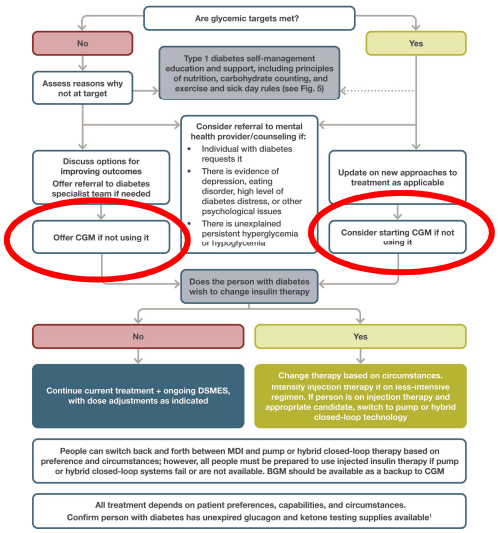
General principles for management of blood glucose in existing type 1 diabetes in an adult



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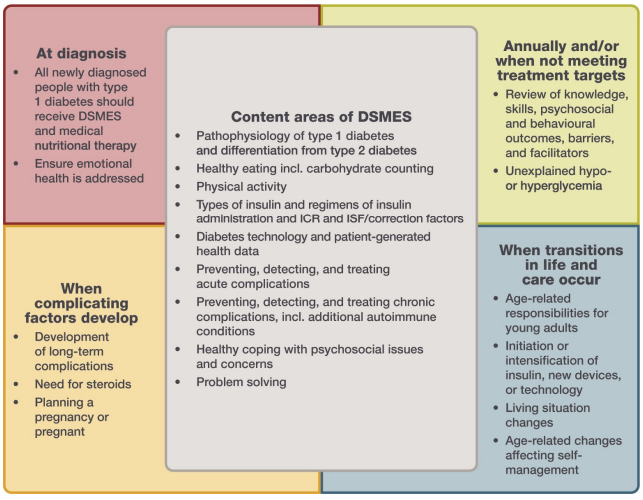
Patientenschulung

DSMES = Diabetes Self-Management Education and Support

„Patientenschulung ist ein essentieller Bestandteil der Therapie des T1D und ist eine Grundvoraussetzung dafür, dass die anderen Therapiebestandteile gut funktionieren können.“

Four critical times for DSMES in type 1 diabetes



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Representative relative attributes of insulin delivery approaches in people with type 1 diabetes[1]

Injected insulin regimens	Flexibility	Lower risk of hypoglycemia	Higher costs
MDI with LAA + RAA or URAA	+++	+++	+++
Less-preferred, alternative injected insulin regimens			
MDI with NPH + RAA or URAA	++	++	++
MDI with NPH + short-acting (regular) insulin	++	+	+
Two daily injections with NPH + short-acting (regular) insulin or premixed	+	+	+

Continuous insulin infusion regimens	Flexibility	Lower risk of hypoglycemia	Higher costs
Hybrid closed-loop technology	+++++	+++++	++++++
Insulin pump with threshold/ predictive low-glucose suspend	++++	++++	+++++
Insulin pump therapy without automation	+++	+++	++++

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From: **The Management of Type 1 Diabetes in Adults. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)**

Diabetes Care. 2021;44(11):2589-2625. doi:10.2337/dci21-0043

Table 5—Examples of subcutaneous insulin regimens

Regimen	Timing and distribution	Advantages	Disadvantages	Adjusting doses
Regimens that more closely mimic normal insulin secretion				
Insulin pump therapy (hybrid closed-loop, low-glucose suspend, CGM-augmented open-loop, BGM-augmented open-loop)	Basal delivery of URAA or RAA; generally 40–60% of TDD. Mealtime and correction: URAA or RAA by bolus based on ICR and/or ISF and target glucose, with pre-meal insulin ~15 min before eating.	Can adjust basal rates for varying insulin sensitivity by time of day, for exercise and for sick days. Flexibility in meal timing and content. Pump can deliver insulin in increments of fractions of units. Potential for integration with CGM for low-glucose suspend or hybrid closed-loop. TIR % highest and TBR % lowest with: hybrid closed-loop > low-glucose suspend > CGM-augmented open-loop > BGM-augmented open-loop.	Most expensive regimen. Must continuously wear one or more devices. Risk of rapid development of ketosis or DKA with interruption of insulin delivery. Potential reactions to adhesives and site infections. Most technically complex approach (harder for people with lower numeracy or literacy skills).	Mealtime insulin: if carbohydrate counting is accurate, change ICR if glucose after meal consistently out of target. Correction insulin: adjust ISF and/or target glucose if correction does not consistently bring glucose into range. Basal rates: adjust based on overnight, fasting or daytime glucose outside of activity of URAA/RAA bolus.

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Table 5—Continued

Regimen	Timing and distribution	Advantages	Disadvantages	Adjusting doses
MDI regimens with less flexibility				
Four injections daily with fixed doses of N and RAA	Pre-breakfast: RAA ~20% of TDD. Pre-lunch: RAA ~10% of TDD. Pre-dinner: RAA ~10% of TDD. Bedtime: N ~50% of TDD.	May be feasible if unable to carbohydrate count. All meals have RAA coverage. N less expensive than LAAs.	Shorter duration RAA may lead to basal deficit during day; may need twice-daily N. Greater risk of nocturnal hypoglycemia with N. Requires relatively consistent mealtimes and carbohydrate intake.	Pre-breakfast RAA: based on BGM after breakfast or before lunch. Pre-lunch RAA: based on BGM after lunch or before dinner. Pre-dinner RAA: based on BGM after dinner or at bedtime. Evening N: based on fasting or overnight BGM.
Four injections daily with fixed doses of N and R	Pre-breakfast: R ~20% of TDD. Pre-lunch: R ~10% of TDD. Pre-dinner: R ~10% of TDD. Bedtime: N ~50% of TDD.	May be feasible if unable to carbohydrate count. R can be dosed based on ICR and correction. All meals have R coverage. Least expensive insulins.	Greater risk of nocturnal hypoglycemia with N. Greater risk of delayed post-meal hypoglycemia with R. Requires relatively consistent mealtimes and carbohydrate intake. R must be injected at least 30 min before meal for better effect.	Pre-breakfast R: based on BGM after breakfast or before lunch. Pre-lunch R: based on BGM after lunch or before dinner. Pre-dinner R: based on BGM after dinner or at bedtime. Evening N: based on fasting or overnight BGM.
Regimens with fewer daily injections				
Three injections daily: N+R or N+RAA	Pre-breakfast: ~40% N + ~15% R or RAA. Pre-dinner: ~15% R or RAA. Bedtime: 30% N.	Morning insulins can be mixed in one syringe. May be appropriate for those who cannot take injection in middle of day. Morning N covers lunch to some extent. Same advantages of RAAs over R. Least (N + R) or less expensive insulins than MDI with analogs.	Greater risk of nocturnal hypoglycemia with N than LAAs. Greater risk of delayed post-meal hypoglycemia with R than RAAs. Requires relatively consistent mealtimes and carbohydrate intake. Coverage of post-lunch glucose often suboptimal. R must be injected at least 30 min before meal for better effect.	Morning N: based on pre-dinner BGM. Morning R: based on pre-lunch BGM. Morning RAA: based on post-breakfast or pre-lunch BGM. Pre-dinner R: based on bedtime BGM. Pre-dinner RAA: based on post-dinner or bedtime BGM. Evening N: based on fasting BGM.

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Table 5—Continued

Regimen	Timing and distribution	Advantages	Disadvantages	Adjusting doses
Twice-daily "split-mixed": N+R or N+RAA	Pre-breakfast: ~40% N + ~15% R or RAA. Pre-dinner: ~30% N + ~15% R or RAA.	Least number of injections for people with strong preference for this. Insulins can be mixed in one syringe. Least (N+R) or less (N+RAA) expensive insulins vs analogs. Eliminates need for doses during the day.	Risk of hypoglycemia in afternoon or middle of night from N. Fixed mealtimes and meal content. Coverage of post-lunch glucose often suboptimal. Difficult to reach targets for blood glucose without hypoglycemia.	Morning N: based on pre-dinner BGM. Morning R: based on pre-lunch BGM. Morning RAA: based on post-breakfast or pre-lunch BGM. Evening R: based on bedtime BGM. Evening RAA: based on post-dinner or bedtime BGM. Evening N: based on fasting BGM.

ICR, insulin:carbohydrate ratio; ISF, insulin sensitivity factor; LAA, long-acting analog; N, NPH insulin; R, short-acting (regular) insulin; RAA: rapid-acting analog; TDD, total daily insulin dose; URAA, ultra-rapid-acting analog.

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Psychosocial Problems

Diabetes-specific emotional distress affects 20–40% of people with type 1 diabetes and can be experienced at any point in time from early adulthood to [illegible]. Two "critical" times, how[illegible]ing the diagnosis [illegible] develop [illegible]ss and ove[illegible]daily self-care [illegible]poglycemia, and wor[illegible]omplications are among the [illegible]ited sources of distress by people with type 1 diabetes. Prolonged significant diabetes distress is associated with depressed mood and elevated HbA_{1c} levels (169).

Diabetes distress!

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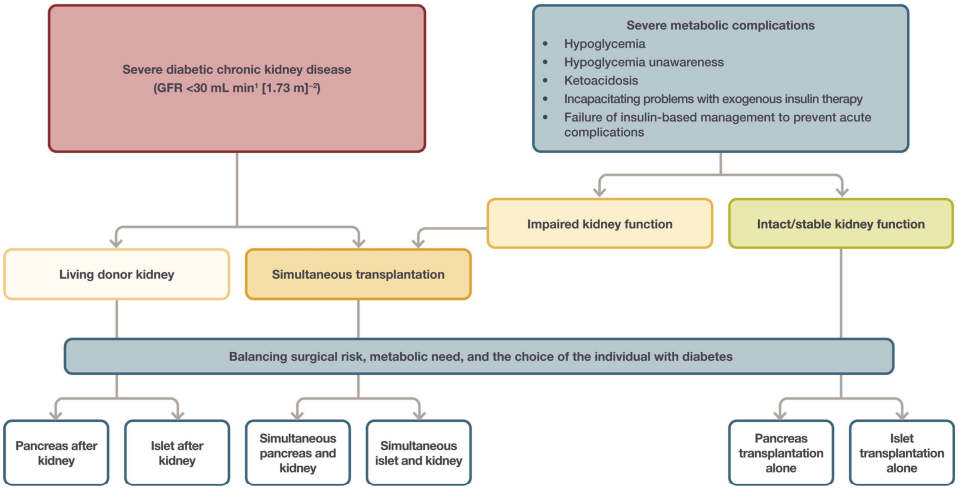
Simplified overview of indications for β-cell replacement therapy in people with type 1 diabetes



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Orale Antidiabetika & Inkretine bei T1D

Table 6—Adjunctive therapies for type 1 diabetes

Variable	Metformin	Pramlintide	GLP-1 RA	SGLT-2 or SGLT-1/2 inhibitors
HbA_{1c} reduction	~1 mmol/mol (~0.1%)	3–4 mmol/mol (0.3–0.4%)	2–4 mmol/mol (0.2–0.4%)	2–4 mmol/mol (0.2–0.4%)
Fasting glucose	Minimal effect	No effect	Minimal effect	Modest decrease (0.8 mmol/L [15 mg/dL])
Postprandial glucose	Minimal effect	Significant decrease	Modest decrease	Modest decrease
TIR	No data	No data	No data	Increased (~12% at higher doses)
Insulin dose	Unchanged	Mealtime reductions	Predominantly mealtime reductions	Mealtime and basal reductions (~10% total reduction)
Body weight	Modest (~1 kg)	Modest (~1 kg)	Significant (~5 kg)	Moderate (2–3 kg)
Systolic blood pressure	No change	No change	4 mmHg decrease (with increase in heart rate)	3–4 mmHg decrease
Hypoglycemia	Low risk	Potential increase in level 3 hypoglycemia if prandial insulin doses are not decreased	Increase in hypoglycemia	Low risk
Side effects	GI side effects	GI side effects	GI side effects; increase in ketosis	Genital mycotic infections; increased risk of DKA
Approval status for type 1 diabetes in EU/U.S.	Not currently approved	U.S. approved	Not currently approved	EU approved low dose when BMI ≥27 kg/m^2
Specific groups for whom treatment may be of benefit	Women with polycystic ovary syndrome	No specific groups	Overweight and obese; high insulin dose; risk of cardiovascular and renal disease	Risk of cardiovascular and renal disease

EU, European Union; GI, gastrointestinal.

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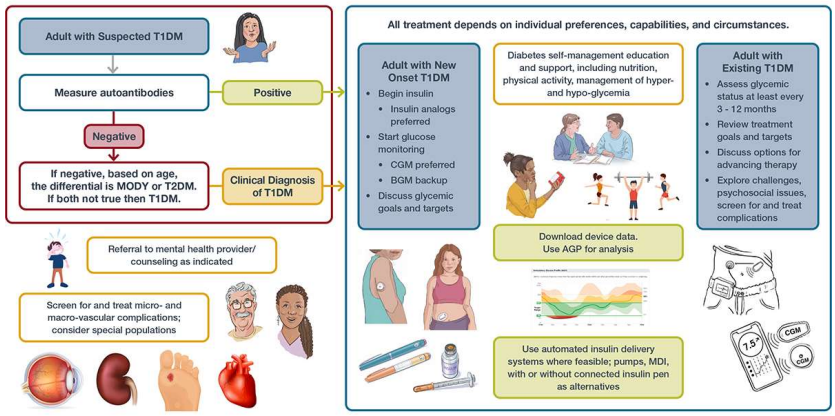
The Management of Type 1 Diabetes in Adults. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

„Graphical Abstract"

The management of type 1 diabetes in an adult



T1DM = type 1 diabetes mellitus, T2DM = type 2 diabetes mellitus, MODY = maturity onset diabetes of the young, CGM = continuous glucose monitoring, BGM = blood glucose monitoring, AGP = ambulatory glucose profile, MDI = multiple daily injections

We thank the Leona M. and Harry B. Helmsley Charitable Trust for their assistance with the images.

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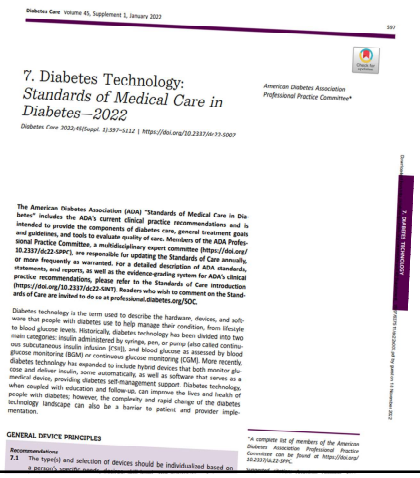
Agenda

1. DDG S3-Leitlinie Therapie des Typ-1-Diabetes
2. ADA/EASD Consensus Report
3. Ausblick

ADA Guidelines 2022: AID-Therapie ist erste Wahl zur Therapie des Typ-1-Diabetes

Insulin Pumps CSII, or insulin pumps, have been available in the U.S. for over 40 years. These devices deliver rapid-acting insulin throughout the day to help manage blood glucose levels. Most insulin pumps use tubing to deliver insulin through a cannula, while a few attach directly to the skin, without tubing. **AID systems**, discussed below, **are preferred over nonautomated pumps and MDI in people with type 1 diabetes.**


Diabetes Care Volume 45, Supplement 1, January 2022

7. Diabetes Technology: *Standards of Medical Care in Diabetes—2022*

American Diabetes Association Professional Practice Committee*

Diabetes Care 2022;45(Suppl. 1):S97–S112 | https://doi.org/10.2337/dc22-S007

7. DIABETES TECHNOLOGY

GENERAL DEVICE PRINCIPLES

Recommendations

ADA: Standards of Medical Care in Diabetes – 2022, Chapter 7. Diabetes Technology. Diabetes Care 2002;45(Suppl. 1): 597-5112

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ADA Guidelines 2022: Barrieren bzgl. AID-Therapie

Technology is rapidly changing, but there is **no "one-size-fits-all"** approach to technology use in people with diabetes. **Insurance coverage can lag behind device availability, patient interest in devices and willingness to change can vary, and providers may have trouble keeping up with newly released technology.**

ADA: Standards of Medical Care in Diabetes – 2022, Chapter 7. Diabetes Technology. Diabetes Care 2002;45(Suppl. 1): 597-5112

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Zusammenfassung: ADA/EASD Konsens

- Diagnosestellung: Vereinfachter Algorithmus; Inselzell-Ak sind „out"
- Öfter an MODY denken, ggf. Risikokalkulator online verwenden
- CGM ist erste Wahl bei Typ-1-Diabetes
- Bedeutung wiederholter Patientenschulung und von Psychologie

Link zum Paper:

Link zum MODY Risikokalkulator:

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Vielen Dank für Ihre Aufmerksamkeit!

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