GUIDELINES FOR THE MANAGEMENT OF THE DIABETIC PATIENTS:AN OVERVIEW

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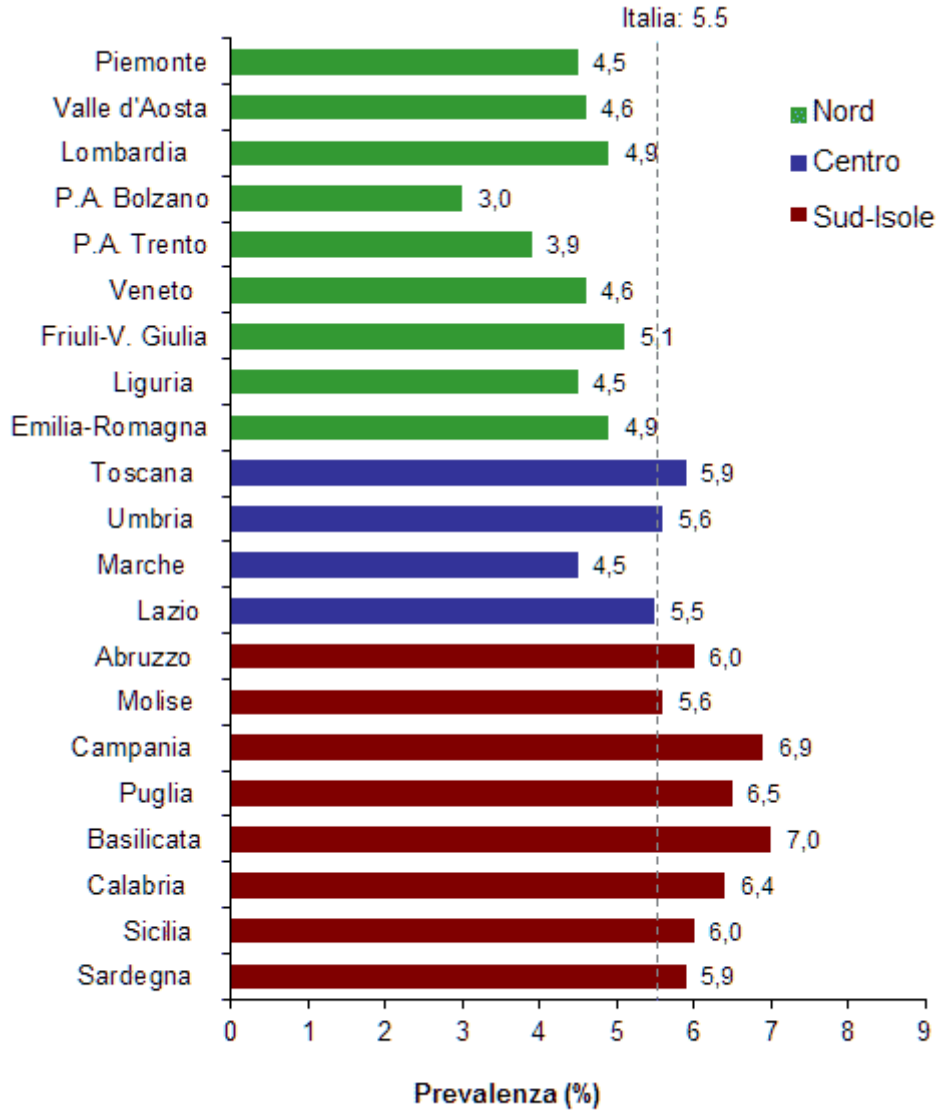
Tassi di prevalenza del diabete in Italia



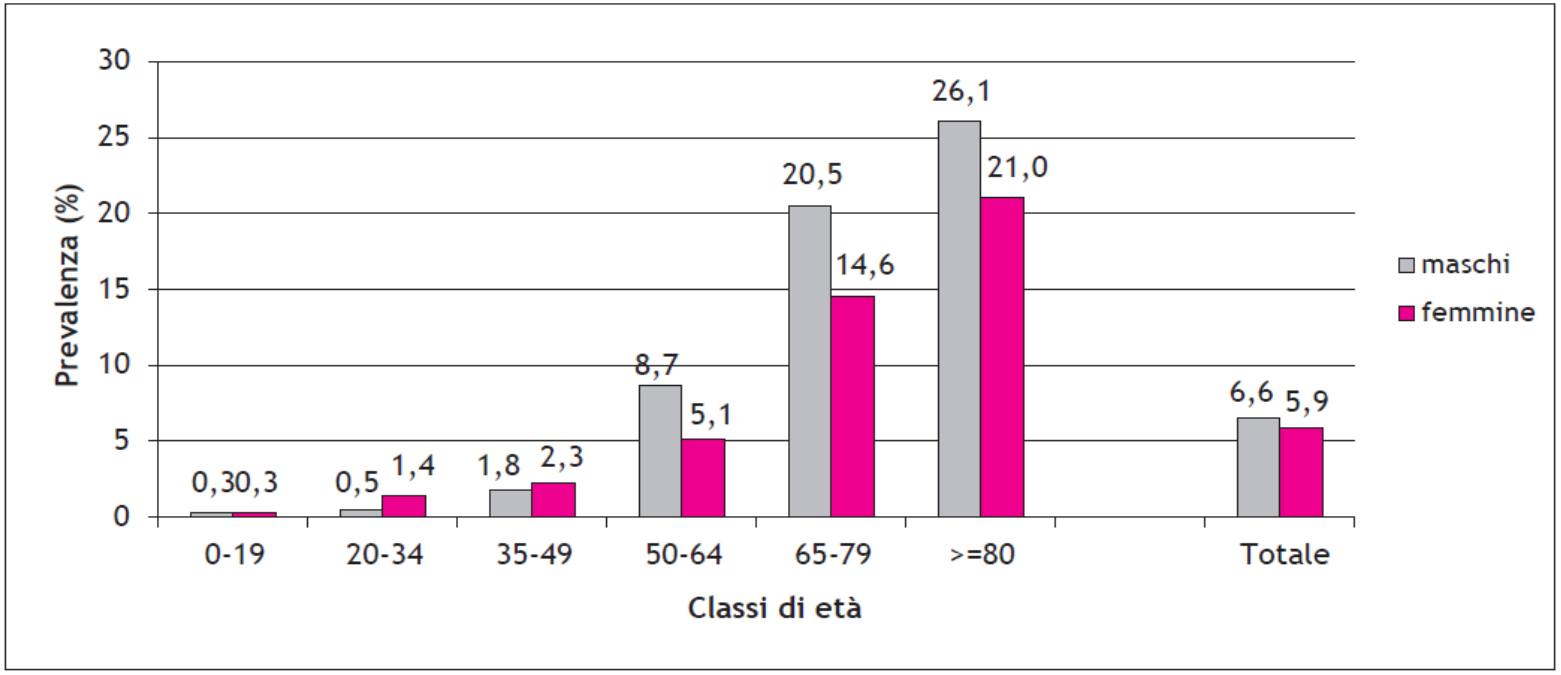
Fonte ISTAT 2014, elaborazione ISS

Prevalenza del diabete in funzione di sesso ed età

Osservatorio ARNO Diabete 2015

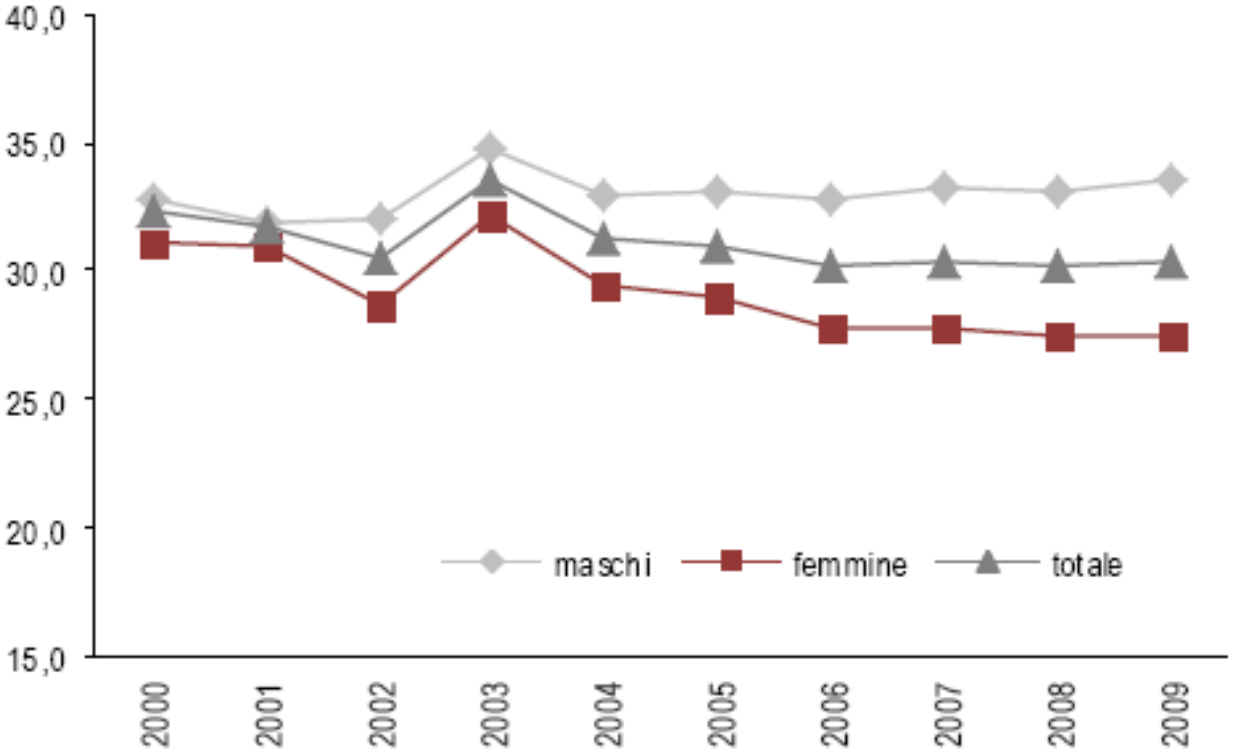
Grafico 3

Prevalenza del diabete in funzione del sesso e dell'età[1]



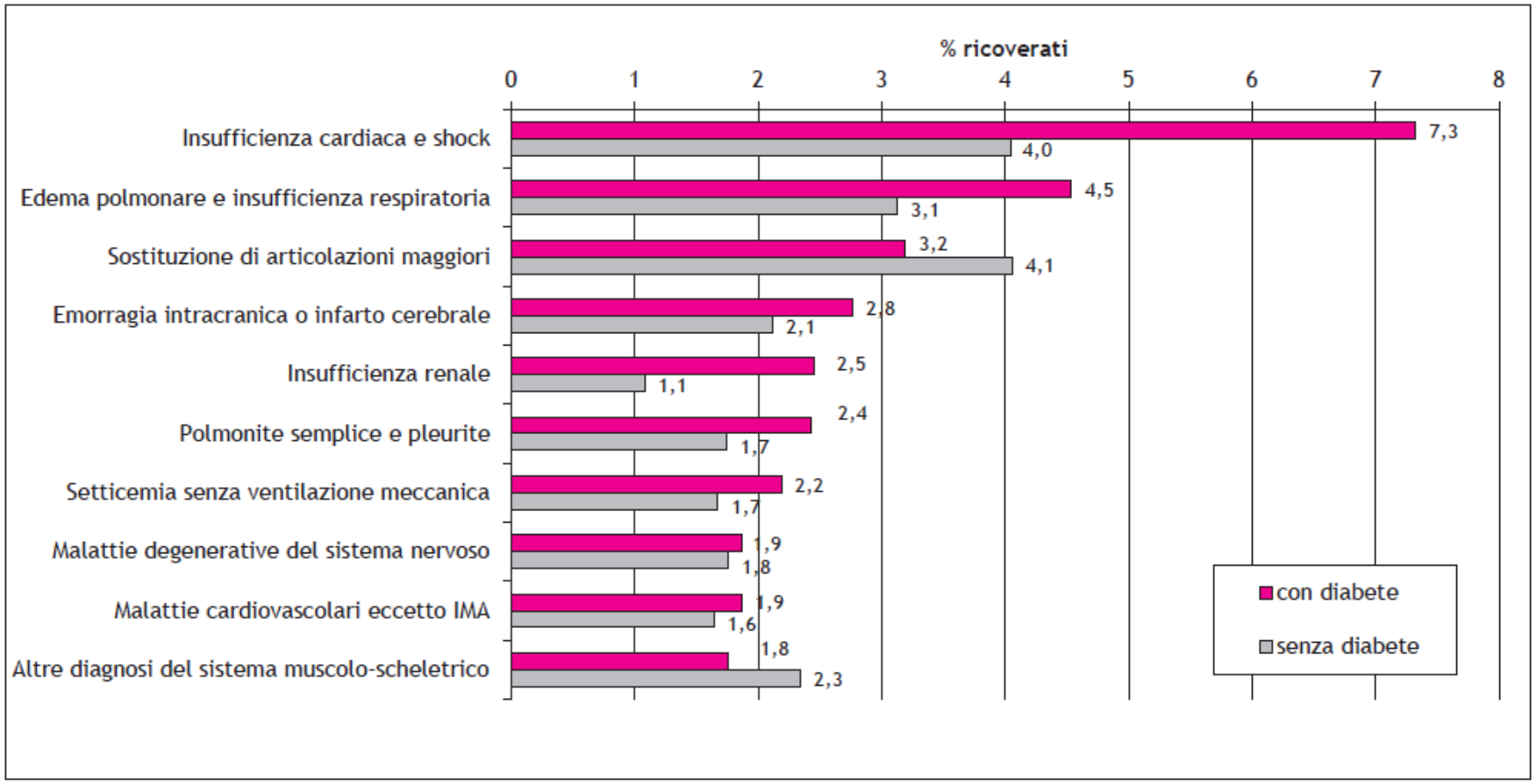
FOCUS ISTAT: diabetes in Italy

FIGURA 2. TASSO STANDARDIZZATO DI MORTALITÀ PER DIABETE IN ITALIA. Anni 2000-2009, valori per 100.000 mila abitanti



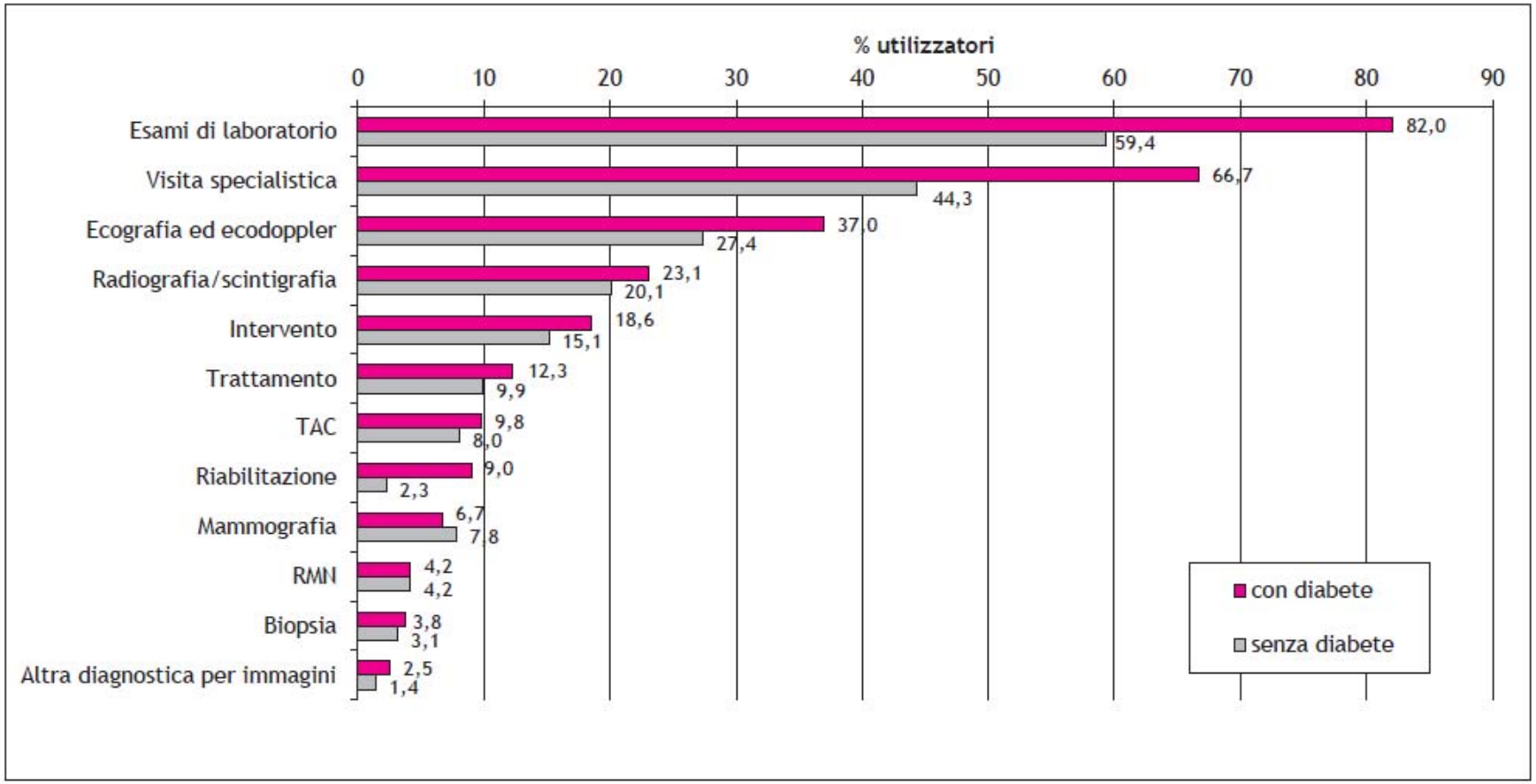
DRG più frequenti(%) e diabete

Osservatorio ARNO Diabete 2015



Prestazioni specialistiche e diabete

Osservatorio ARNO Diabete 2015



Diagnostic criteria

- HbA1c ≥6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay

or

- Fasting plasma glucose (FPG) ≥ 126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.

or

- Two-hour plasma glucose ≥200 mg/ dL (11.1 mmol/L) during an oral glucose tolerance test (OGTT). The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.

or

- In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose≥200 mg/dL (11.1 mmol/L).

In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.

Standards of Medical Care in Diabetes, ADA 2018 and Italian Standards of Care for Diabetes SID-AMD 2018

Diagnostic criteria

To diagnose diabetes the measurements of

post-prandial plasma glucose,

basal insulin and/or under OGTT,
C-peptide,

Autoantibodies (IA2, ICA, GAD)

are not necessary (IIIE)

Italian Standards of Care for Diabetes SID-AMD 2018

Diagnostic criteria for prediabetes

Impaired fasting glucose (IFG) : fasting plasma glucose 100-125 mg/dl

Impaired glucose tolerance (IGT): plasma glucose after 2 h OGTT 140-199 mg/dl

Impaired HbA1c: HbA1c 42-48 mmol/mol (6.0-6.49 %) (IFCC aligned)

evidence level (IIIB)

Italian Standards of Care for Diabetes SID-AMD 2018

Prevalence of prediabetes

Prevalence of IGT

Wordl 6.7%

Italy 6.%

Conversion rate at 10 year

Risk 11 time greater in IGT

Risk 3.9 time greater in IFG

Risk 20 time greater in IFG+IGT

IDF 2015

Ten years incidence and ORs for diabetes according to the category of glucose homeostasis at baseline

Baseline	Person -years	Diabetes cases	Incidence rate/1,000 person-years (95%CI)	OR (95%CI)	p
NFG/NGT	6704	29	4.3 (2.7-5.9)	1.0	
NFG/IGT	471	8	17.0 (5.3-28.7)	3.9 (1.6-9.3	0.002
IFG/NGT	486	18	37.0 (20.2-53.8)	11.0 (5.6-21.9)	<0.001
IFG/IGT	183	9	49.2 (17.9-80.5)	20.5 (7.6-55.3)	<0.001

Bonora E:Diabetes,2004

Glucose monitoring: HbA1c

1) Perform the A1C test at least two times a year in patients who are meeting treatment goals (and who have stable glycemic control) (**E**)

2) Perform the A1C test quarterly in patients whose therapy has changed or who are not meeting glycemic goals. (**E**)

3) HbA1c should be measured with methods calibrated to the IFCC reference system. The result should be reported in units mmol / mol (**A**)

Standards of Medical Care in Diabetes, ADA 2018 and Italian Standards of Care for Diabetes SID-AMD 2018

Glucose monitoring: glycemia

1) Patients affected by type 1 diabetes and those using intensive insulin regimen should perform self-monitoring of blood glucose (SMBG) prior to meals, at bedtime, occasionally post-prandial prior to exercise, when they suspect low blood glucose, after treating low blood glucose, prior to critical tasks (**B**)

2)When prescrived as a part of an educational programm SMBG may help to guide treatment decision and/or self-management for patients taking less frequent insulin injection (**B**) or non insulin therapies (**E**)

3) When prescribing SMBG ensure that patients receive ongoing instruction and regular evaluation of SMBG technique and their ability to use SMBG data to adjust therapy (**A**)

Standards of Medical Care in Diabetes, ADA 2018 and Italian Standards of Care for Diabetes SID-AMD 2018

Glicemic goals

1) Lowering A1C to below or around 7% has been shown to reduce microvascular complications of diabetes and, if implemented soon after the diagnosis of diabetes, is associated with long-term reduction in macrovascular disease. Therefore, a reasonable A1C goal for many nonpregnant adults is 7% (**B**).

2) Providers might reasonably suggest more stringent A1C goals (such as 6.5%) for selected individual patients, if this can be achieved without significant hypoglycemia orother adverse effects of treatment. Appropriate patients might include those with short duration of diabetes, long life expectancy, and no significant CVD (**C**)

3) Less stringent A1C goals (such as 8%) may be appropriate for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, and extensive comorbid conditions and inthose with long-standing diabetes in whom the general goal is difficult to attain despite diabetes selfmanagement education (DSME), appropriate glucose monitoring, and effective doses of multiple glucoselowering agents including insulin.(**B**)

Standards of Medical Care in Diabetes, ADA 2018, Italian Standard of Care for Diabetes SID-AMD 2018

Summary of glycemic reccomandations for adults with diabetes

Table 6.2—Summary of glycemic recommendations for many nonpregnant adults with diabetes

A1C	<7.0% (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* (10.0 mmol/L)

*More or less stringent glycemic goals may be appropriate for individual patients. Goals should be individualized based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations. †Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals. Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.

ADA standard Care 2018

Management of diabetes in older adults

DIAGNOSIS OF TYPE 2 DIABETES IN OLDER ADULTS

↓

Nutritional evaluation → promote **appropriate diet**
Plan adequate and balanced **physical activity**

↓

Personalization of glycemic targets → avoid hypoglycemia
Also consider: degree of hyperglycemia, overweight or obesity, CV disease, other risk factors, comorbidities (renal, heart, hepatic, pulmonary failure; cancer, dementia), patient preferences and needs

HbA1c < 7.0%	7.0% < HbA1c < 7.5%	7.5% < HbA1c < 8.0%
When treated with drugs with no hypoglycemia risk	*When treated with drugs with hypoglycemia risk*	*In presence of frailty condition* – *severe complications* – *cognitive impairment* – *dementia* – *comorbidities*

Sesti G: NMCD ,2018

Continuos glucose monitoring: reccommendations

- When used properly, continuous glucose monitoring (CGM) in conjunction with intensive insulin regimen is an useful tool to lower HbA1c in patients with type 1 diabetes who are not meeting glycemic targets (A);
- CGM may be an useful tool in those with hypoglycemia unawareness and/or frequent hypoglycemic episodes; (**C**)
- Given the variable adherence to CGM, assess individual readiness for continuing CGM use prior to prescribing. (**E**)

- Standard of Medical Care in Diabetes ADA 2018, Italian Standard of Care for Diabetes SID-AMD 2018

HbA1c : some hot-points

Recommendations for the implementation of the international standardization of glycated hemoglobin

recommendation 2

1) Reporting average glucose estimates (eAG) based on HbA_{1c} measurements using the equation proposed by the ADAG study has many limitations, so do not recommend the systematic use of the eAG.

2) The HbA1c values do not provide a measure of glucose variability or the presence of hypoglycemia. In these cases, glycemic control is evaluated more effectively through a combination of self- monitoring and measurement of HbA1c.

3) Any discrepancies between the measured value of HbA1c and glucose profiles home should be further explored by ensuring that the patient can perform all the measurements home, trying to identify and correct any errors and taking into account the conditions that affect erythrocyte turnover, such as hemolysis and bleeding, as well as hemoglobin variants that may be responsible for HbA1c unusually high or lowered

Effectiveness of HbA1c in screening: an Italian experience

ORIGINAL ARTICLE

Screening with HbA1c identifies only one in two individuals with diagnosis of prediabetes at oral glucose tolerance test: findings in a real-world Caucasian population

Nino Cristiano Chilelli · Chiara Cosma · Eugenio Ragazzi · Silvia Burlina · Martina Zaninotto · Mario Plebani · Annunziata Lapolla

1) Evaluate the effectiveness of HbA1c (according to the new IFCC * standard) compared to the 'gold standard' OGTT, as a screening test for identifying pre-diabetic alterations, in a large population of asymptomatic Caucasian subjects .

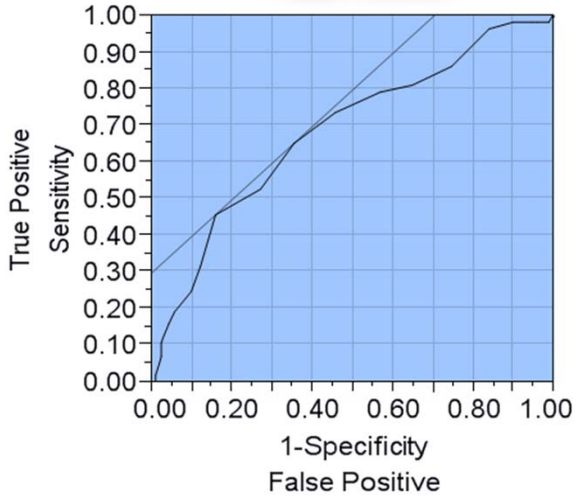
2) Check whether the use of different diagnostic tests, particularly adding HbA1c in the algorithm of screening, select different individuals with insulin resistance, assessed through the use of surrogate markers (HOMA-IR and QUICKI).

*International Federation of Clinical Chemistry and Laboratory Medicine

Effectiveness of HbA1c in screening: an Italian experience

ROC curve for the performance of HbA1c in predicting new cases of **IFG**

AUC	HbA1c cut-off	Sensitivity	Specificity	PPV	NPV
0.76	37.7 mmol/mol (5.6%)	79 %	63 %	59 %	81 %



ROC curve for the performance of HbA1c in predicting new cases of **IGT**

AUC	HbA1c cut-off	Sensitivity	Specificity	PPV	NPV
0.69	41 mmol/mol (5.9%)	46 %	84 %	31 %	91 %

Chilelli NC, Lapolla A et al. *Acta Diabetologica*, 2014

Effectiveness of HbA1c in screening: an Italian experience

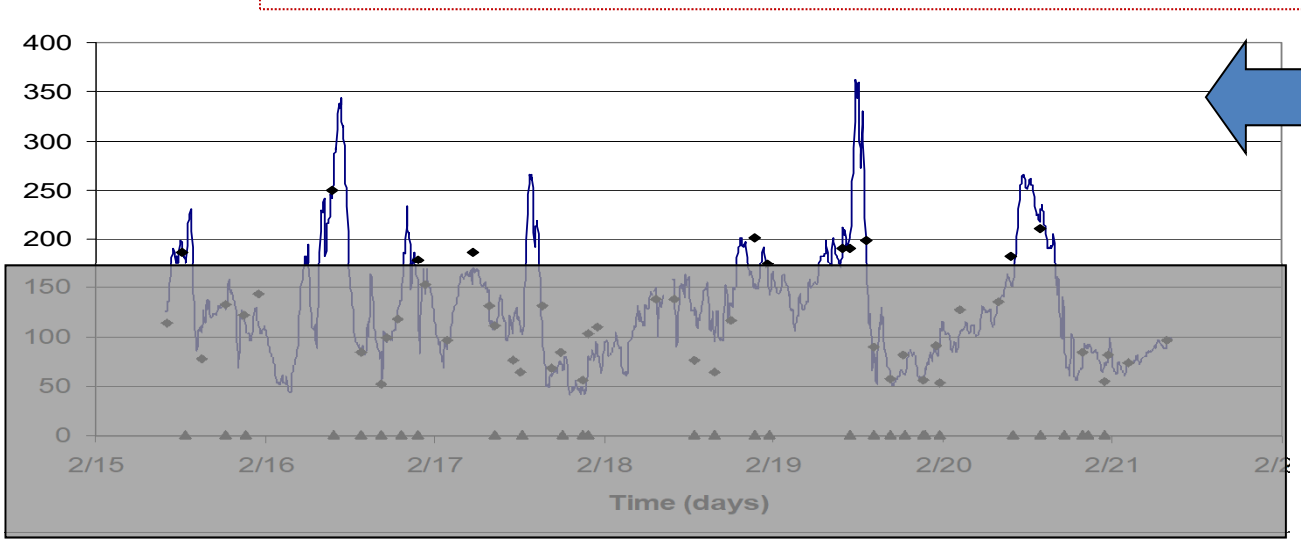
1) In the population considered, only 53.4% of patients with HbA1c 38.8-46,4 mmol / mol (5.7% -6.4%) were confirmed IFG and / or IGT; 19% had a normal glucose tolerance; 27.6% had fasting values and / or post-load compatible with a diagnosis of diabetes;
2) Effect on the prevalence of pre-diabetes adding HbA1c screening with OGTT has increased the prevalence of IFG / IGT of 12.2% (cost / benefit ratio?)

3) Individuals with diagnostic agreement (OGTT+/HbA1c+) have similar insulin resistance and insulin sensitivity, compared to subjects diagnosed with OGTT only (OGTT+/HbA1c-) → adding HbA1c screening with OGTT may be of limited use in identifying subjects with increased risk of progression to type 2 diabetes and / or increased cardiovascular risk

Chilelli NC, Lapolla A et al. *Acta Diabetologica*, 2014

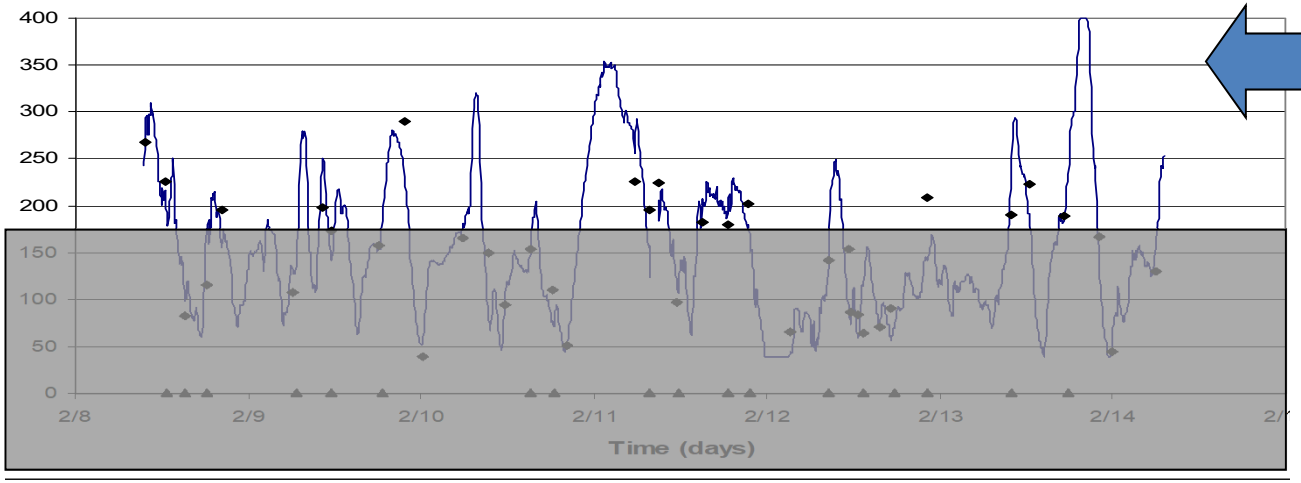
HbA1c and glycemic variability

7.3% vs 7.4 %: which is better?



Low variability

HbA1c 7.4%



High variability

HbA1c 7.3%

Dungan et al. Diabetes Care 2006; 29 (6): 1214-1219

The importance of HbA1c and glucose variability in patients with type 1 and type 2 diabetes: outcome of continuous glucose monitoring (CGM)

Giovanni Sartore · Nino Cristiano Chilelli · Silvia Burlina · Paola Di Stefano · Francesco Piarulli · Domenico Fedele · Andrea Mosca · Annunziata Lapolla

Acta Diabetol (2012) 49 (Suppl 1):S153–S160

Table 1 Comparisons between groups' demographic and clinical characteristics

Parameters	Group 1	Group 2	Group 3	*p* value
Age (years)	39 ± 11*†	58 ± 9	58 ± 9	<0.001
Gender (M/F)	17/18	6/11	10/6	n.s.
Duration of diabetes (years)	16.25 ± 8.97	16.9 ± 8.03	10.9 ± 8.73	n.s.
BMI (kg/m^2)	25.1 ± 2.6*	31.0 ± 5.7	27.0 ± 4.6	<0.001
HbA1c (%)	8.4 ± 1.6†	8.4 ± 1.5‡	7.0 ± 1.0	<0.05

All parameters are expressed as mean ± standard deviation. * group 1 versus group 2; † group 1 versus group 3; ‡ group 2 versus group 3

1) HbA1c is influenced by the spike hyperglycemic PP in patients with type 1 diabetes

2) HbA1c reflects the average blood glucose and chronic hyperglycemia, but does not represent the rapid fluctuations in blood glucose daily

Table 2. Correlations between HbA1c and indicators of metabolic control derived from CGM data in groups 1, 2 and 3.

	TIPO 1	TIPO 2 INS	TIPO 2 ADO
Indicators	**HbA1c Group 1**	**HbA1c Group 2**	**HbA1c Group 3**
AG_w			
Pearson's correlation coefficient	0.7369 *	0.7087	0.7069
p-value	0.0000	0.0021	0.0022
AUC PP			
Pearson's correlation coefficient	0.6857 *	0.3205	0.5271
p-value	0.0000	0.2097	0.0359
SD_w			
Pearson's correlation coefficient	0.3907	0.3527	0.6273
p-value	0.0203	0.1802	0.0093
CONGA2_day			
Pearson's correlation coefficient	0.2734	0.4331	0.3193
p-value	0.1121	0.0938	0.2280
CONGA2_night			
Pearson's correlation coefficient	0.4796	-0.0320	0.2823
p-value	0.0036	0.9064	0.2895
MAGE			
Pearson's correlation coefficient	0.3783	0.4460	0.6972
p-value	0.0250	0.0834	0.0270
MODD			
Pearson's correlation coefficient	-0.0307	0.0910	0.0012
p-value	0.8610	0.7374	0.9965
LBGI			
Pearson's correlation coefficient	-0.1890	-0.5273	-0.2163
p-value	0.2769	0.0358	0.4211
HBGI			
Pearson's correlation coefficient	0.7411 *	0.6886	0.6511
p-value	0.0000	0.0032	0.0063
BG ROC			
Pearson's correlation coefficient	0.1045	-0.5695	0.4251
p-value	0.5501	0.0213	0.1008

ORIGINAL ARTICLE

Association between glucose variability as assessed by continuous glucose monitoring (CGM) and diabetic retinopathy in type 1 and type 2 diabetes

Giovanni Sartore · Nino Cristiano Chilelli · Silvia Burlina · Annunziata Lapolla

Published online: 16 February 2013

Table 3. Risk of retinopathy in 35 type 1 and 33 type 2 diabetic patients, by logistic regression (cross-sectional analysis).

Parameters	Univariate analysis	*p*-value	Multivariate analysis	*p*-value
	OR (95%CI)		OR (95%CI)	
Duration of diabetes (years)	1.11 (1.04-1.19)	0.002*	1.05 (1.01-1.15)	0.010*
DM 1 (%)	0.68 (0.26-1.79)	0.434	---	---
Insulin treatment (%)	5.6 (1.14-27.30)	0.034*	2.76 (0.44-17.35)	0.279
SD-BG ROC (mg/dl)	1.03 (1.01-1.06)	0.012*	1.03 (0.98-1.08)	0.271
CONGA 2 (mg/dl)	1.02 (1.00-1.04)	0.035*	0.99 (0.95-1.03)	0.640
MAGE (mg/dl)	1.74 (0.69-4.40)	0.240	---	---
HBGI	1.10 (1.01-1.18)	0.034*	---	---
AG (mg/dl)	1.02 (1.00-1.03)	0.020*	---	---
HbA1c (%)	1.37 (0.98-1.90)	0.070	---	---

Table 1. Clinical features of DM1 and DM2 patients in relation to the baseline presence/absence of retinopathy (n=68).

	Retinopathy (n=28)	No retinopathy (n=40)	p-value
Age (years)	49.3 ± 12.6	48.1 ± 14.7	n.s.
Gender (% male)	53.6 %	55.1%	n.s.
Duration of diabetes (years)	19.1 ± 9.2	12.1 ± 7.7	0.02
BMI (kg/m^2)	27.9 ± 4.2	26.5 ± 4.9	n.s.
Insulin treatment (%)	75.0%	30.0%	0.05
Mean HbA1c (%)	8.3 ± 1.2	7.9 ± 1.8	0.06
Hypertension (%)	39.9%	30.0%	n.s.
Hypercholesterolemia (%)	44%	42%	n.s.

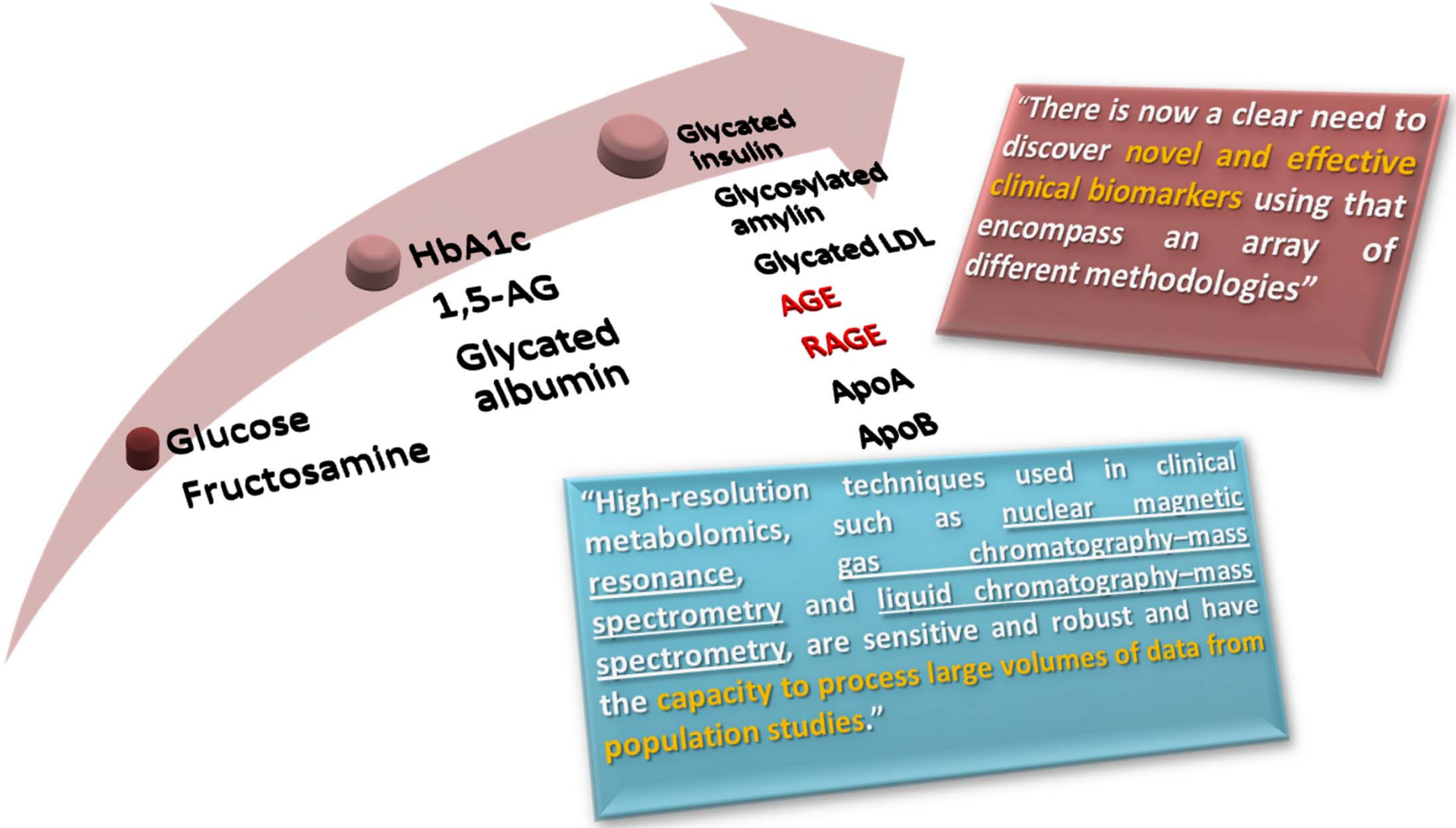
Glucose variability (expressed with indicators derived from CGM) is a factor related to the presence of retinopathy in both the DM 1 that in DM 2.

Old and new biochemical markers: clinical applications and recommendations

- Proteomic biomarkers: application in renal failure;
- C-peptide and insulin.

Emerging Applications of Metabolomic and Genomic Profiling in Diabetic Clinical Medicine

McKillop AM, Flatt PR Diabetes Care 34:2624–2630,2011



Proteomic biomarkers in diabetic CKD: an emerging issue

- Currently, eGFR and proteinuria are used as markers of CKD progression because of the widespread availability and ease of performing these tests.
  - **eGFR→** *pre-renal confunders* (dehydration, blood loss, altered vasomotor tone, age-related decreases in renal blood flow) or *post renal confunders* (obstruction or extravasation of urine to the peritoneal cavity); cannot be used to determine the *location of renal injury* (glomerular vs tubular).
  - **Microalbuminuria→** long *before the onset of microalbuminuria* in diabetic patients, hemodynamic changes occur in the glomeruli causing glomerular hyperfiltration and altered vascular endothelial tone.

Biomarkers

- ***Inflammatory b.→*** NGAL (high sensitivity and specificity in detecting AKI), IL 18
- ***Tubular proteins→*** KIM 1(high sensitivity and specificity in detecting acute tubular necrosis (ATN)
- ***Urinary peptides→*** qualitative differences in urine →candidate biomarkers to diagnose early CKD

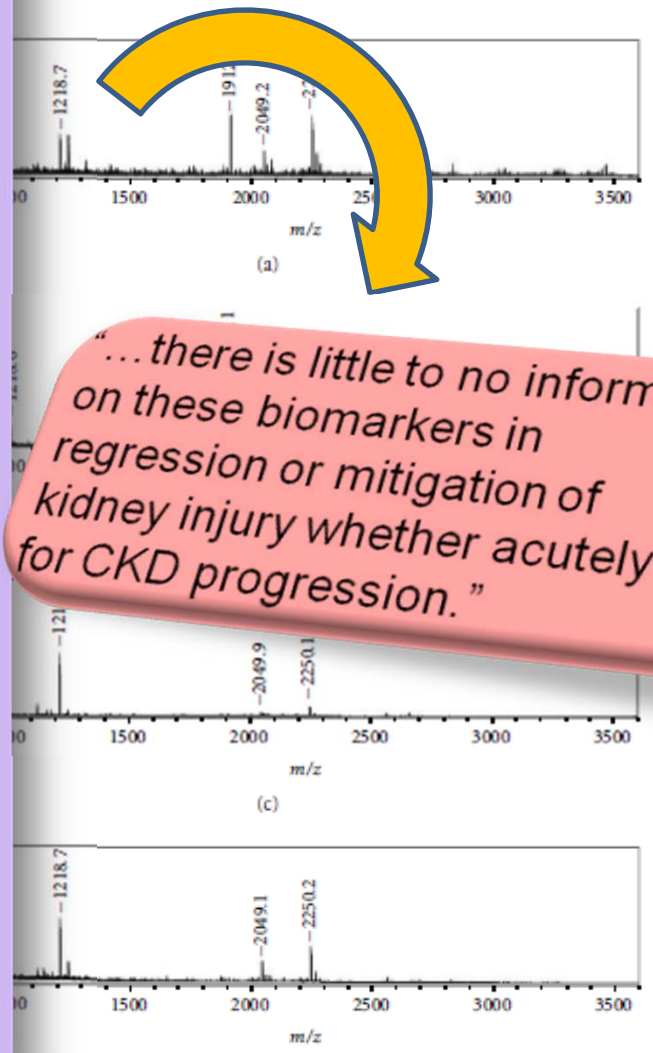
Chaudhary K, Curr Diab Rep (2010) 10:37–42

diabetic CKD: an

ue (2)

Table 1: Diabetes urinary protein biomarkers. [a]Accession number in National Center for Biotechnology Information databases. DM: Diabetic patients; DN: Diabetic nephropathy; DM-NP: Diabetic patients with macro- or microalbuminuria.

45.861	Haptoglobin precursor	P00738	Metabolism	Type 2 DM-NP	Downregulated	DIGE followed MALD1-TOF-MS	[29]
46,707	α1-antitrypsin	P01009	Defense response	Type 2 DM-NP	Upregulated	DIGE followed LC/MS/MS peptide analysis	[19]
51,643	α1-microglobulin/ bikunin precursor	P02790	Transport	Type 2 DM-NP	Downregulated	DIGE followed LC/MS/MS peptide analysis	[19]
51,643	Hemopexin	P02790	Defense response	Type 2 DM-NP	Upregulated	DIGE followed LC/MS/MS peptide analysis	[19]
52,964	Vitamin D-binding protein	P02774	Transport	Type 2 DM-NP	Upregulated	DIGE followed LC/MS/MS peptide analysis	[19]
54,239	α1B- Glycoprotein	P04217	Function not assigned	Type 2 DM-NP	Upregulated	DIGE followed LC/MS/MS peptide analysis	[19]
71,317	Albumin	P02768	Transport	Type 2 DM	Upregulated	Two-Dimensional Liquid Chromatography followed by MALDI	[20]
71,317	Serum albumin precursor	P02768	Transport	Type 2 DM-NP	Upregulated	DIGE followed MALDI-TOF-MS	[29]
72,451	Uromodulin precursor	P07911	Defense response	Type 2 DM-NP	Downregulated	DIGE followed MALDI-TOF-MS	[29]
72,984	Kininogen precursor	P01042	Defense response	Type 2 OM-NP	Upregulated	DIGE followed MALDI-TOF-MS	[29]
97.853	Epithelial-cadherin	P12830	Cell adhesion	Type 2 DM	Upregulated	Two-Dimensional Liquid Chromatography followed by MALDI	[20]
97,853	Epithelial-cadherin	P12830	Cell adhesion	Type 2 DM-NP	Upregulated	DIGE followed MALDI-TOF-MS	[29]
2,049	Collagen α-1 (I) chain precursor	P02452	Structural Component	Type 2 DM-NP and NP	Upregulated	MALDI/TOF/ TOF	[31]
2,063	Collagen alpha-1 (III) chain	P02461	Structural Component	Type 2 DM	Downregulated with respect to type i dm	CZE-MS	[28]
2,192	Collagen α-1(I) chain	P02452	Structural Component	Type 2 DM-NP	Downregulated	CZE coupled with ES1 mass spectrometry	[25]
2,192	Collagen alpha-1(I) chain	P02452	Structural Component	Type 2 DM	Downregulated with respect to type 1dm	CZE-MS	[28]
2,339	Collagen alpha-1(I) chain	P02452	Structural Component	Type 2 DM	Downregulated with respect to type 1 dm	CZE-MS	[28]
2,377	Collagen α-1(I) chain [227 to 250]	P02452	Structural Component	Type 2 DM-NP	Downregulated	CZE coupled with ESI mass spectrometry	[25]
2,430	Collagen alpha-1(I) chain	P02452	Structural Component	Type 2 DM	Downregulated with respect to type 1 dm	CZE-MS	[28]



"…there is little to no information on these biomarkers in regression or mitigation of kidney injury whether acutely or for CKD progression."

MicroRNAs associated with type 2 diabetes

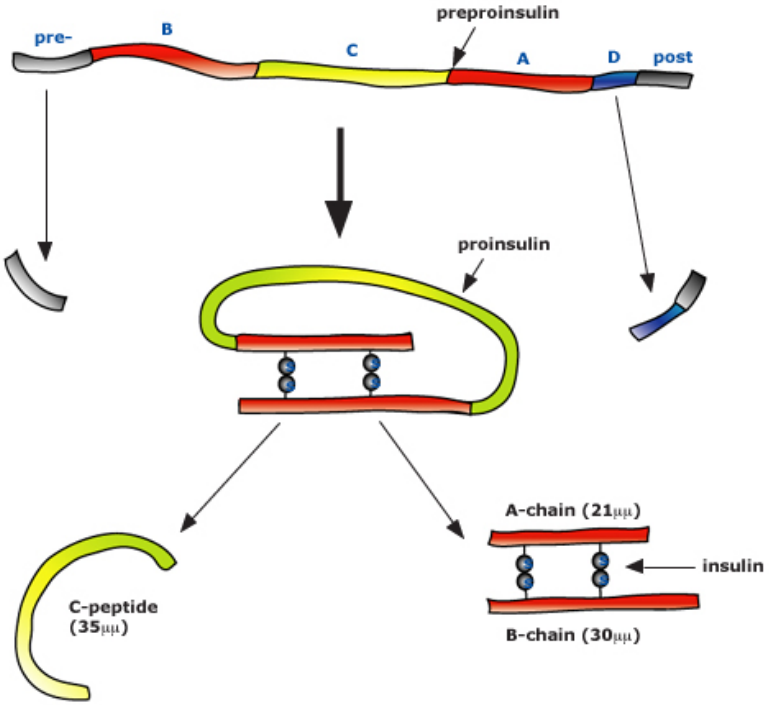
TABLE 1 | MicroRNAs (miRNAs) associated with type 2 diabetes mellitus (T2DM) and associated complications.

S. No.		miRNA	Target	Expression level	Reference
1.	Obesity and T2DM	miR-124a	Mtpn, Foxa2, Flot2, Akt3, Sirt1, and NeuroD1	Up	(22)
2.		miR-101		Up	(44)
3.		miR-802		Up	(44)
4.		miR-96	Noc2	Down	(35)
5.		miR-103	SFRP4	Up	(45)
6.		miR-375	Mtpn, PDK1	Up/down	(44)
7.		miR-23a	SMAD4	Up	(21)
8.		miR-132	NF-kappa B	Down	(46)
9.		miR-34a	SIRT1	Down	(46)
10.		miR-145	ADAM17	Down	(21)
11.		miR-221	CAV-1	Up	(46)
12.		miR-144	IRS-1	Up	(21)
13.		miR-146a	TRAF6	Up	(21)
14.		miR-29	Spry1, AKT3	Up	(21)
15.		miR-34a	FGFR1, BetaKL	Up	(21)
16.		miR-15a	UP2	Down	(34)
17.		miR-126	IRS-1	Down	(34, 46)
18.		miR-29b	DNMT1	Down	(34)
19.		miR-223	Glut4, HDAC4, Pknox1, Nfat5	Down	(34)
20.		miR-335	Mest	Up	(47)
21.		miR-107	CAV-1	Up	(47)
22.		miR-223	STAT3	Up	(46)
23.		miR-143	ORP8, AKT	Up	(48)
24.		miR-935	CNR1, ESR1	Up	(46)

Vaishya S :Front Endocrinol, 2018

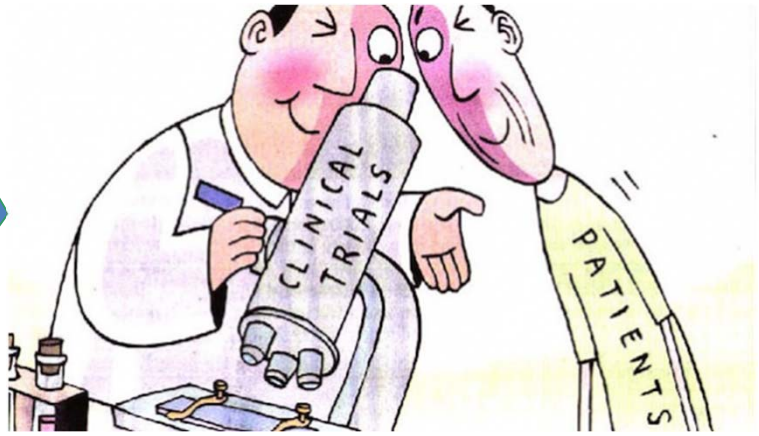
C-peptide and insulin: old dosages ... new recommendations?

Insulin is produced in the pancreatic b-cells by enzymatic cleavage of the prohormone precursor **proinsulin** to produce insulin and C-peptide in equimolar amounts.



Timing of dosage

- Fasting C-peptide;
- “Random”C-peptide;
- C-peptide after pharmacological stimulation.



Potential clinical/experimental applications of c-peptide and insulin dose

Etiological classification of diabetes: differentiation between type 1 diabetes and type 2, recognition of monogenic forms (MODY)

Determination of residual pancreatic reserve;

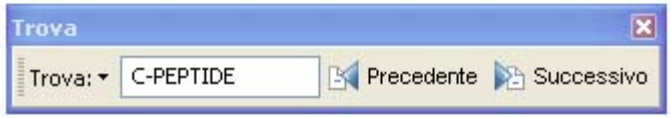
Therapeutic changes: indications for insulin therapy or a permanent shift to oral hypoglycemic agents; remission of diabetes after bariatric surgery;

Determination of peripheral insulin resistance: HOMA index

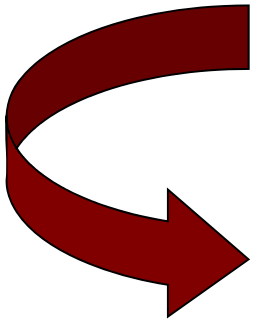
Selection and monitoring of patients undergoing transplantation of pancreatic islets

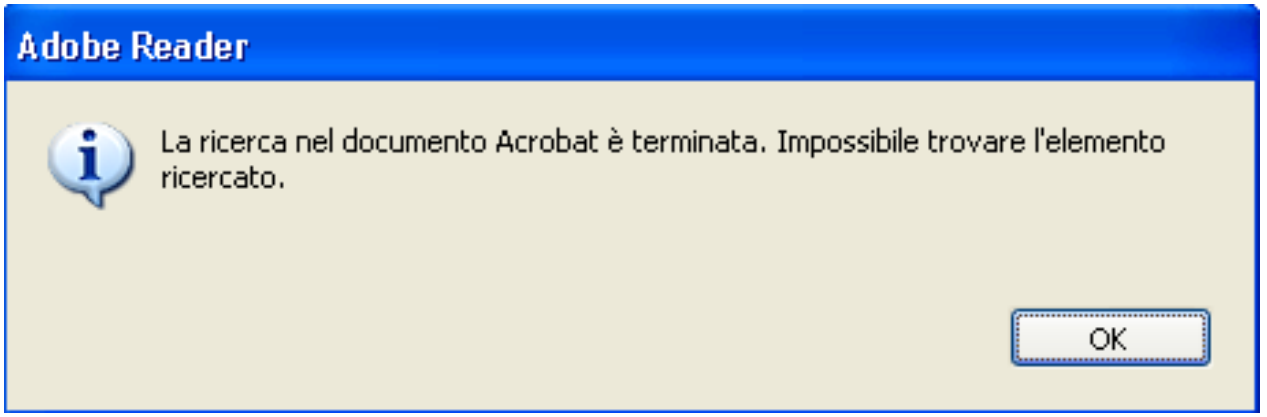
Clinical recommendations: state of the art

Diabetes Care Volume 37, Supplement 1, January 2014



Executive Summary: Standards of Medical Care in Diabetes—2014





Clinical recommendations: state of the art (2)

3.Q1.2. Classification of DM

R5. T1DM is usually characterized by absolute insulin deficiency and may be confirmed by the presence of autoantibodies to glutamic acid decarboxylase, pancreatic islet β cells (tyrosine phosphatase IA-2), and/or insulin (**Grade A; BEL 1**). Some forms of T1DM have no evidence of autoimmunity and have been termed idiopathic. T1DM or monogenic DM can also occur in obese children and adolescents. Therefore, documenting the levels of insulin and C-peptide and the presence or absence of immune markers and obtaining a careful family history in addition to the clinical presentation may be useful in establishing the correct diagnosis, determining treatment, and helping to distinguish between T1DM and T2DM in children (**Grade A; BEL 1**).

Clinical recommendations: state of the art (3)

Italian Standards of Care for Diabetes SID-AMD 2018

A. DIAGNOSTIC CRITERIA

Recommendations

For the diagnosis of diabetes mellitus, the following measurements are not useful:

- post-prandial glucose;
- C-peptide;
- Auto-antibodies

(**Level of Evidence III-E**)

Clinical recommendations: state of the art (4)

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David B. Sa

12. MISCELLANEOUS POTENTIALLY IMPORTANT ANALYTES

a. There is no role for routine testing for insulin, C-peptide, or proinsulin in most patients with diabetes. Differentiation between type 1 and type 2 diabetes may be made in most cases on the basis of the clinical presentation and the subsequent course. These assays are useful primarily for research purposes. Occasionally, C-peptide measurements may help distinguish type 1 from type 2 diabetes in ambiguous cases, such as patients who have a type 2 phenotype but present in ketoacidosis. **B (moderate)**

The guidelines *Medicine Committee of the* **AACC** *and the* ***National Academy of Clinical Biochemistry*** *and were accepted after* *approval by the Executive*

b. There is no role for measurement of insulin concentration in the assessment of cardiometabolic risk, because knowledge of this value does not alter the management of these patients. **B (moderate)**

THANK YOU
FOR YOUR ATTENTION !