S.I.Te.C.S.

SOCIETÀ ITALIANA DI TERAPIA CLINICA E SPERIMENTALE

XIII CONGRESSO NAZIONALE

Milano 25-26 Ottobre 2019

Four Points by Sheraton Milan Center

PRESENTE E FUTURO NELLA PREVENZIONE CARDIOVASCOLARE

Linee guida diabete

Antonio C. Bossi
Treviglio (Bg)

PRESIDENTE DEL CONGRESSO
Alberico L. Catapano

DISCLOSURES

Nell'arco degli ultimi tre anni dichiaro di aver ricevuto onorari per conferenze, collaborazioni scientifiche, lavori di ricerca clinica e documentale dalle seguenti Aziende:

- ***Lilly Italia Spa***
- ***Novo Nordisk Italia SpA***
- ***Johnson & Johnson SpA***
- ***Boehringer Ingelheim SpA***
- ***Artsana SpA***
- ***Takeda SpA***
- ***Bayer SA***
- ***Sanofi SpA***
- ***Astra Zeneca SpA***
- ***MSD Italia SpA***

Se oggi sono qui in qualità di relatore è perché la SID ha contribuito alla mia formazione culturale, scientifica, clinica.

Linee guida diabete

Agenda

L'impatto socio-sanitario del diabete mellito

Come stanno cambiando le Linee Guida

Un confronto con il mondo reale

Conclusioni

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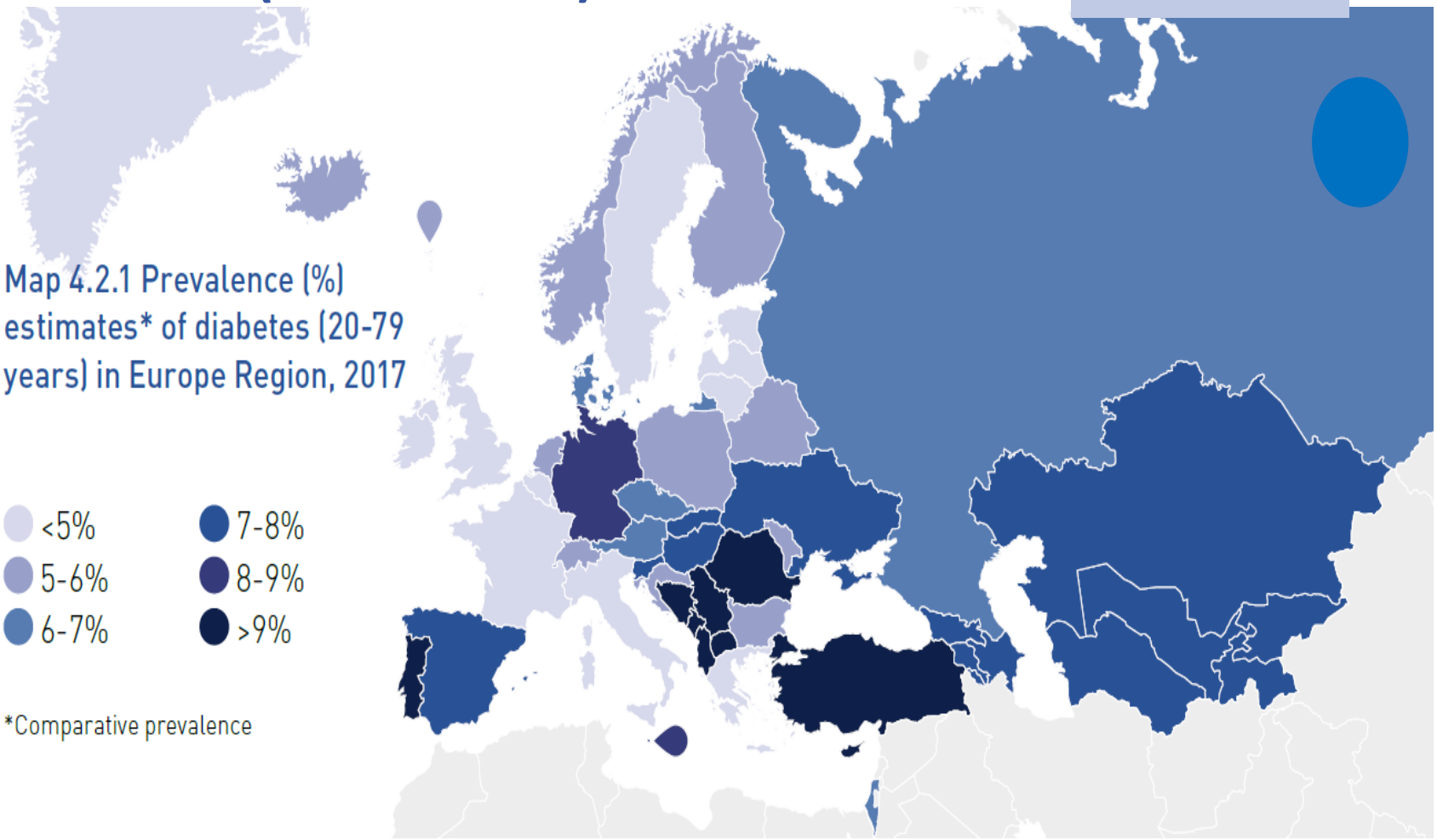
Linee guida diabete

Agenda

L'impatto socio-sanitario del diabete mellito

FREQUENZA DEL DIABETE IN EUROPA (20-79 ANNI) NEL 2017

International Diabetes Federation



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IDF DIABETES ATLAS
Eighth edition 2017

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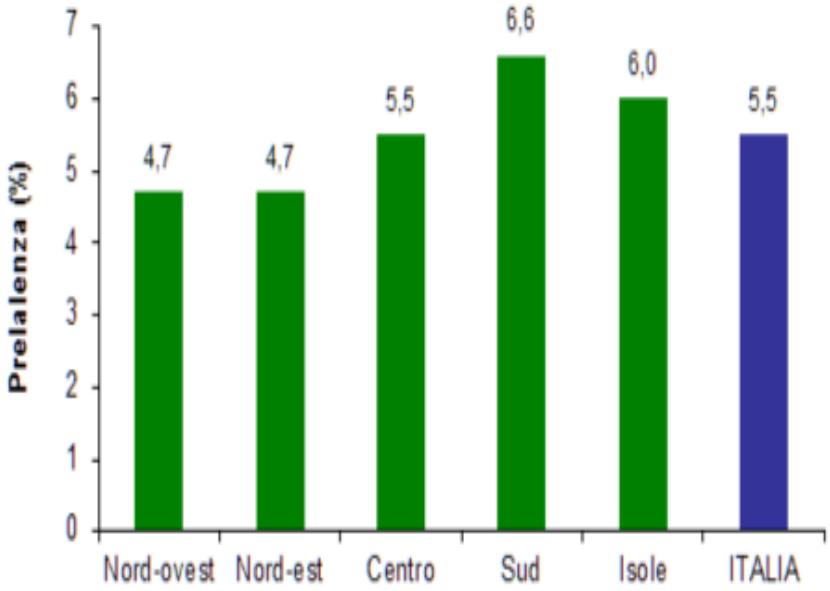
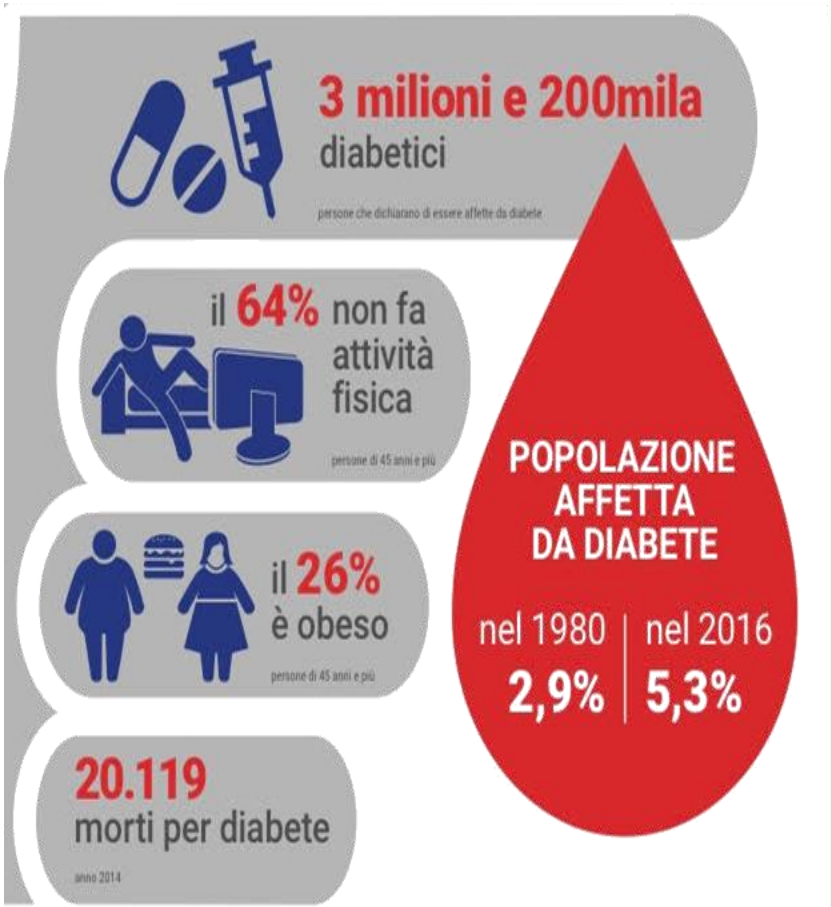
IL DIABETE IN ITALIA

Prevalenza del diabete per area geografica



Fonte ISTAT 2014, elaborazione ISS



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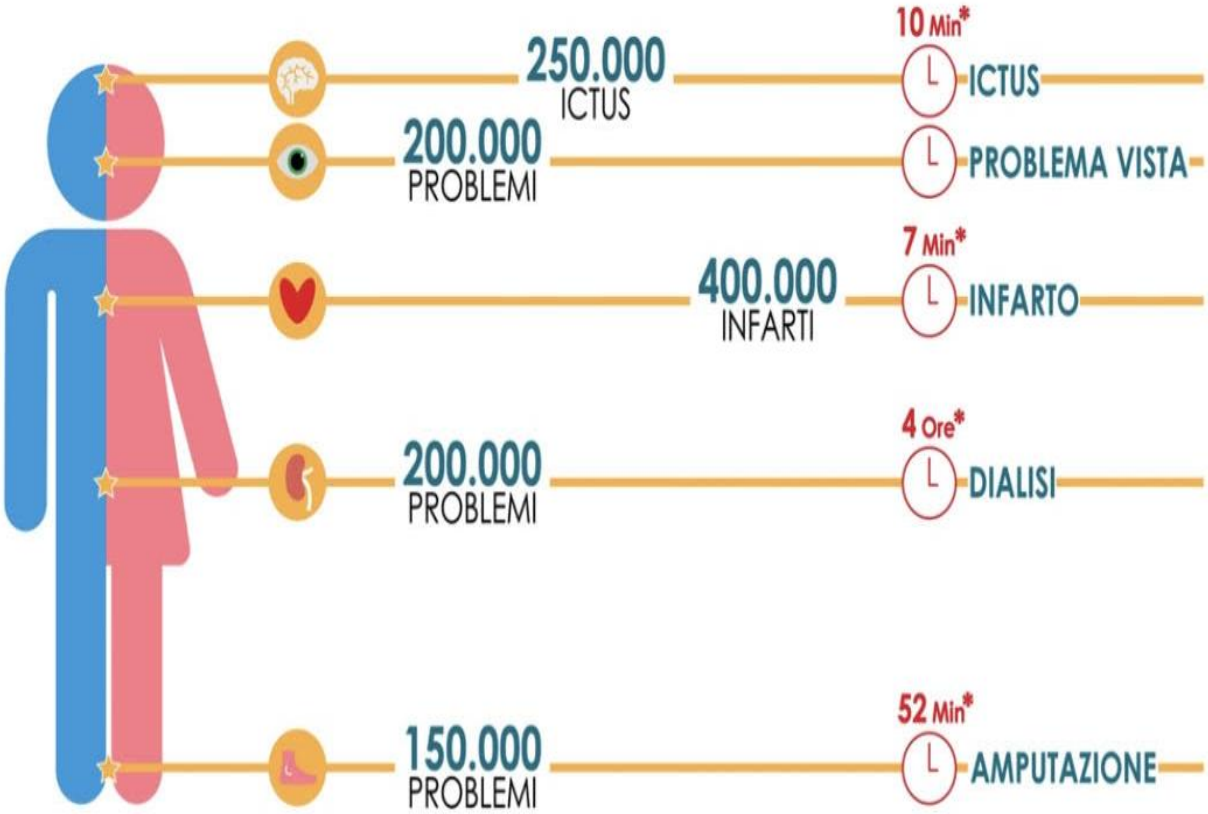
IL DIABETE E LE SUE COMORBIDITA'



Fonte: ISTAT 2015, Associazione Ricerca & Diabete SID, Italian Diabetes & Obesity Barometer Report 2017

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Linee guida diabete

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L'impatto socio-sanitario del diabete mellito

Come stanno cambiando le Linee Guida

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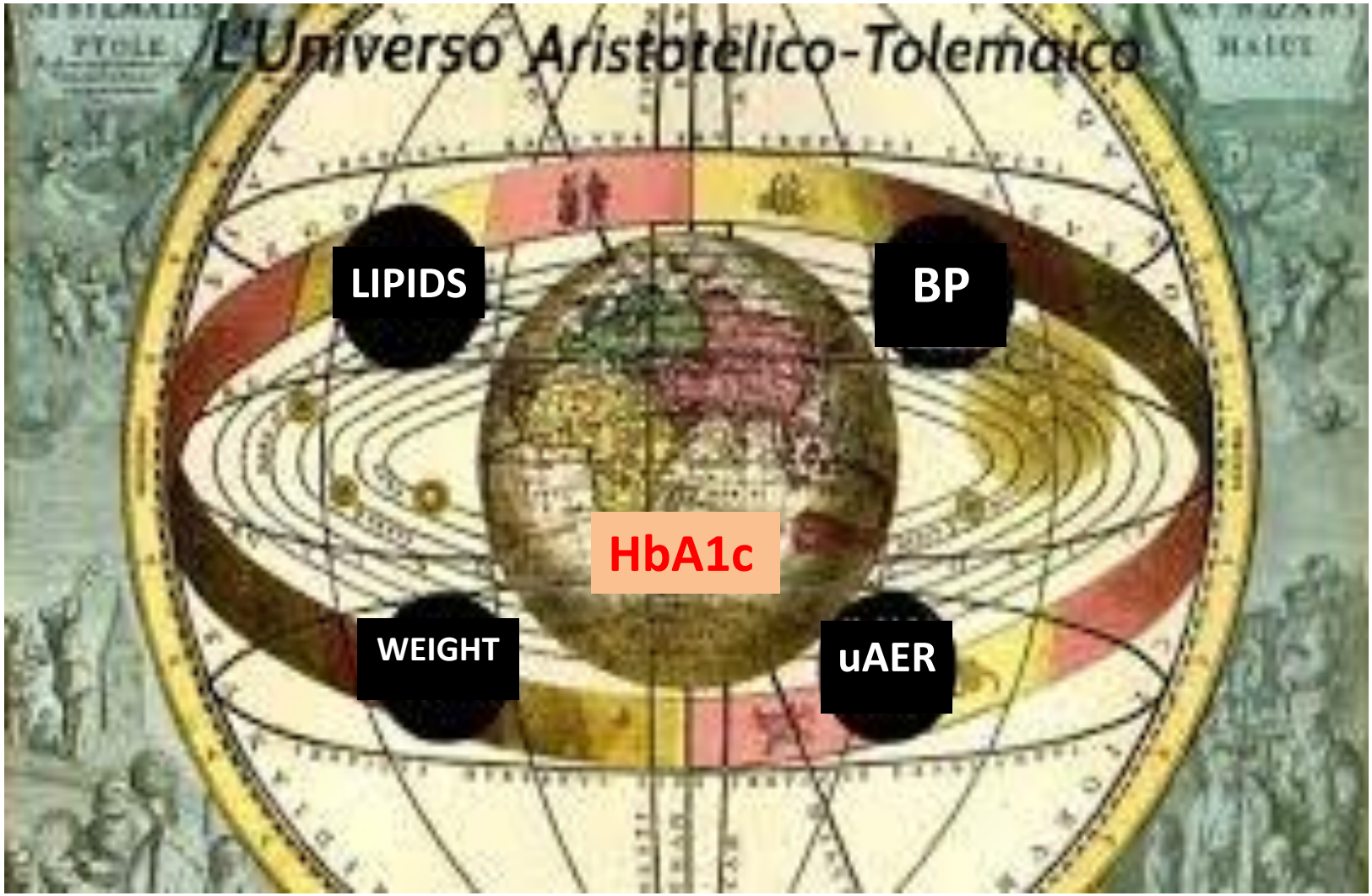

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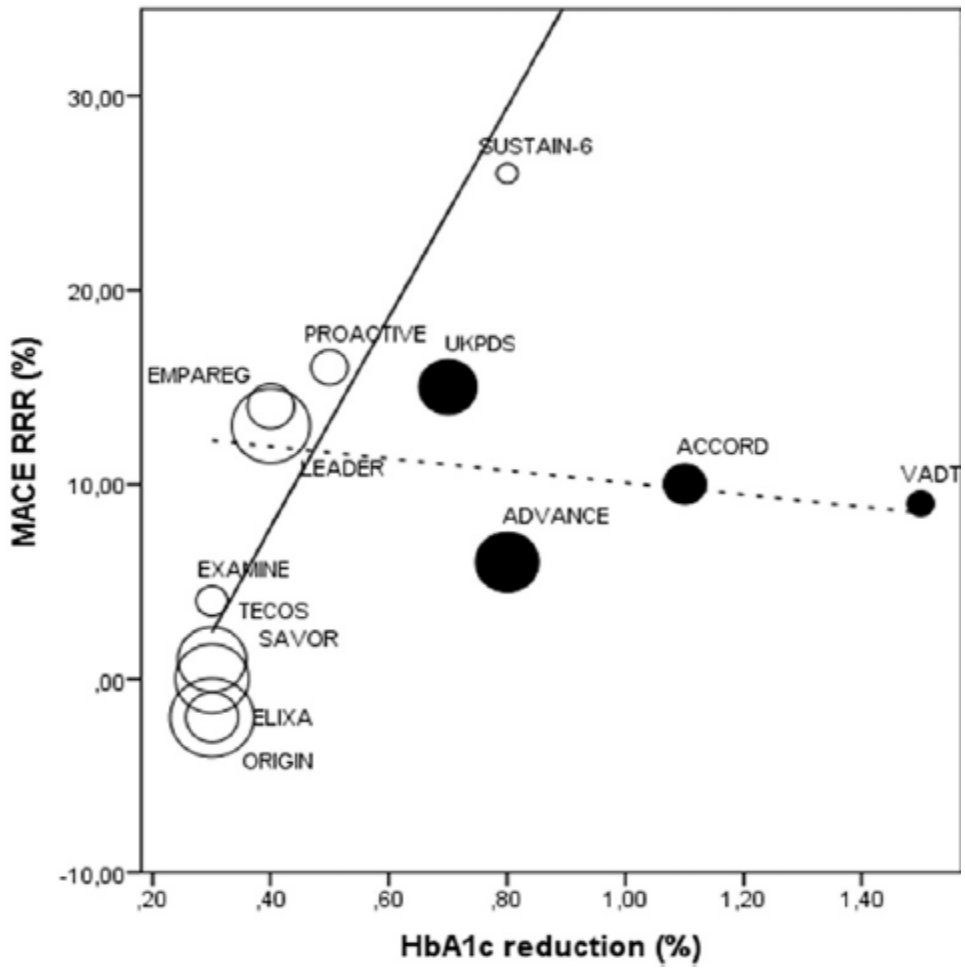
Back to glycemic control: An alternative look at the results of cardiovascular outcome trials in type 2 diabetes



CVOT ———

IT trial------

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Monami M et Al. NMCD 2018
http://dx.doi.org/10.1016/j.numecd.2017.01.003

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GOALS OF CARE

- Prevent complications
- Optimize quality of life

ASSESS KEY PATIENT CHARACTERISTICS

- Current lifestyle
- Comorbidities, i.e., ASCVD, CKD, HF
- Clinical characteristics, i.e., age, HbA_{1c}, weight
- Issues such as motivation and depression
- Cultural and socioeconomic context

CONSIDER SPECIFIC FACTORS THAT IMPACT CHOICE OF TREATMENT

- Individualized HbA_{1c} target
- Impact on weight and hypoglycemia
- Side effect profile of medication
- Complexity of regimen, i.e., frequency, mode of administration
- Choose regimen to optimize adherence and persistence
- Access, cost, and availability of medication

SHARED DECISION MAKING TO CREATE A MANAGEMENT PLAN

- Involves an educated and informed patient (and their family/caregiver)
- Seeks patient preferences
- Effective consultation includes motivational interviewing, goal setting, and shared decision making
- Empowers the patient
- Ensures access to DSMES

AGREE ON MANAGEMENT PLAN

- Specify SMART goals:
  - **S**pecific
  - **M**easurable
  - **A**chievable
  - **R**ealistic
  - **T**ime limited

IMPLEMENT MANAGEMENT PLAN

- Patients not meeting goals generally should be seen at least every 3 months as long as progress is being made, more frequent contact initially is often desirable for DSMES

ONGOING MONITORING AND SUPPORT INCLUDING:

- Emotional well-being
- Check tolerability of medication
- Monitor glycemic status
- Biofeedback including SMBG, weight, step count, HbA_{1c}, blood pressure, lipids

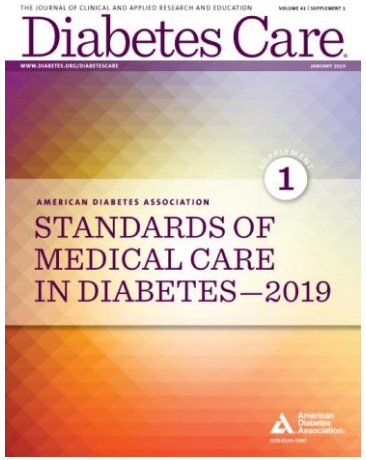
REVIEW AND AGREE ON MANAGEMENT PLAN

- Review management plan
- Mutual agreement on changes
- Ensure agreed modification of therapy is implemented in a timely fashion to avoid clinical inertia
- Decision cycle undertaken regularly (at least once/twice a year)

ASCVD = Atherosclerotic Cardiovascular Disease
CKD = Chronic Kidney Disease
HF = Heart Failure
DSMES = Diabetes Self-Management Education and Support
SMBG = Self-Monitored Blood Glucose

Diabetes Care 2019;42(Suppl. 1):S34–S45 | https://doi.org/10.2337/dc19-S004

STANDARDS OF MEDICAL CARE IN DIABETES 2019



RECOMMENDATIONS

➢ A reasonable **A1C goal** for many non-pregnant adults is **<7%** (53 mmol/mol). **A**

➢ Providers might reasonably suggest **more stringent A1C goals** (such as **<6.5%** [48 mmol/mol]) for **selected individual patients** if this can be achieved **without significant hypoglycemia or other adverse effects** of treatment (i.e., polypharmacy).
Appropriate patients might include those with

- ***short duration of diabetes***,
- ***T2D treated with lifestyle or metformin only***,
- ***long life expectancy***, or
- ***no significant cardiovascular disease***. **C**

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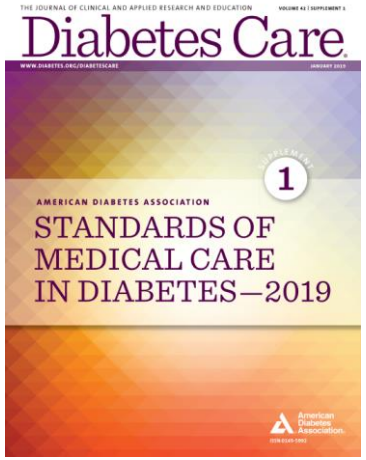
STANDARDS OF MEDICAL CARE IN DIABETES 2019



RECOMMENDATIONS

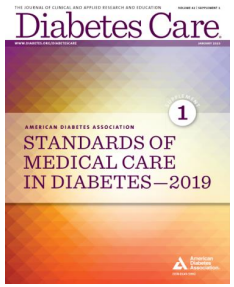
- Less stringent **A1C goals** (such as **<8%** [64 mmol/mol]) may be appropriate for patients
  - with a history of severe **hypoglycemia**,
  - **limited life expectancy**,
  - advanced **micro- or macrovascular complications**,
  - extensive **comorbid conditions**,
  - **long-standing diabetes**

in whom the goal is difficult to achieve despite
- diabetes self-management education,
- appropriate glucose monitoring, and
- effective doses of multiple glucose-lowering agents including insulin. **B**

STANDARDS OF MEDICAL CARE IN DIABETES 2019

Table 12.1—Framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes (2)

Patient characteristics/ health status	Rationale	Reasonable A1C goal‡	Fasting or preprandial glucose	Bedtime glucose
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.5% (58 mmol/mol)	90–130 mg/dL (5.0–7.2 mmol/L)	90–150 mg/dL (5.0–8.3 mmol/L)
Complex/intermediate (multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild-to-moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0% (64 mmol/mol)	90–150 mg/dL (5.0–8.3 mmol/L)	100–180 mg/dL (5.6–10.0 mmol/L)
Very complex/poor health (LTC or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or 2+ ADL dependencies)	Limited remaining life expectancy makes benefit uncertain	<8.5%† (69 mmol/mol)	100–180 mg/dL (5.6–10.0 mmol/L)	110–200 mg/dL (6.1–11.1 mmol/L)



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FIRST-LINE therapy is metformin and comprehensive lifestyle (including weight management and physical activity)
if HbA_{1c} above target proceed as below

TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)

ESTABLISHED ASCVD OR CKD

ASCVD PREDOMINATES

EITHER/OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1], if eGFR adequate[2]

If HbA_{1c} above target

If further intensification is required or patient is now unable to tolerate GLP-1 RA and/or SGLT2i, choose agents demonstrating CV safety:

- Consider adding the other class (GLP-1 RA or SGLT2i) with proven CVD benefit
- DPP-4i if not on GLP-1 RA
- Basal insulin[4]
- TZD[5]
- SU[6]

HF OR CKD PREDOMINATES

PREFERABLY

SGLT2i with evidence of reducing HF and/or CKD progression in CVOTs if eGFR adequate[3]

OR

If SGLT2i not tolerated or contraindicated or if eGFR less than adequate[2] add GLP-1 RA with proven CVD benefit[1]

If HbA_{1c} above target

- Avoid TZD in the setting of HF

Choose agents demonstrating CV safety:

- Consider adding the other class with proven CVD benefit[1]
- DPP-4i (not saxagliptin) in the setting of HF (if not on GLP-1 RA)
- Basal insulin[4]
- SU[6]

WITHOUT ESTABLISHED ASCVD OR CKD

COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA

DPP-4i	GLP-1 RA	SGLT2i[2]	TZD
If HbA_{1c} above target			
SGLT2i[2] **OR** TZD	SGLT2i[2] **OR** TZD	GLP-1 RA **OR** DPP-4i **OR** TZD	SGLT2i[2] **OR** DPP-4i **OR** GLP-1 RA

If HbA_{1c} above target

Continue with addition of other agents as outlined above

If HbA_{1c} above target

Consider the addition of SU[6] **OR** basal insulin:

- Choose later generation SU with lower risk of hypoglycemia
- Consider basal insulin with lower risk of hypoglycemia[7]

COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

EITHER/OR

- GLP-1 RA with good efficacy for weight loss[8]
- SGLT2i[2]

If HbA_{1c} above target

- SGLT2i[2]
- GLP-1 RA with good efficacy for weight loss[8]

If HbA_{1c} above target

If triple therapy required or SGLT2i and/or GLP-1 RA not tolerated or contraindicated use regimen with lowest risk of weight gain

PREFERABLY

DPP-4i (if not on GLP-1 RA) based on weight neutrality

If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:

• SU[6] • TZD[5] • Basal insulin

COST IS A MAJOR ISSUE[9-10]

SU[6]	TZD[10]
If HbA_{1c} above target	
TZD[10]	SU[6]

If HbA_{1c} above target

- **Insulin therapy** basal insulin with lowest acquisition cost

OR

- Consider DPP-4i **OR** SGLT2i with lowest acquisition cost[10]

1. Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 RA strongest evidence for liraglutide > semaglutide > exenatide extended release. For SGLT2i evidence modestly stronger for empagliflozin > canagliflozin.
2. Be aware that SGLT2i vary by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Both empagliflozin and canagliflozin have shown reduction in HF and reduction in CKD progression in CVOTs
4. Degludec or U100 glargine have demonstrated CVD safety
5. Low dose may be better tolerated though less well studied for CVD effects
6. Choose later generation SU with lower risk of hypoglycemia
7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin
8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
9. If no specific comorbidities (i.e., no established CVD, low risk of hypoglycemia, and lower priority to avoid weight gain or no weight-related comorbidities)
10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper

Diabetes Care 2019;42(Suppl.1):S90–S102
https://doi.org/10.2337/dc19-S009

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS
AMERICAN COLLEGE OF ENDOCRINOLOGY

AACE/ACE COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM

2019

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COMPLICATIONS-CENTRIC MODEL FOR CARE OF THE PATIENT WITH OVERWEIGHT/OBESITY

STEP 1 — EVALUATION FOR COMPLICATIONS AND STAGING

CARDIOMETABOLIC DISEASE | BIOMECHANICAL COMPLICATIONS

BMI <25	NO COMPLICATIONS	COMPLICATIONS	
NO OVERWEIGHT OR OBESITY	BMI ≥25	BMI ≥25	
	OVERWEIGHT OR OBESITY	MILD TO MODERATE	SEVERE
	STAGE 0	STAGE 1	STAGE 2

STEP 2 — SELECT: Therapeutic targets for improvement in complications + Treatment modality + Treatment intensity based on staging

Lifestyle Therapy:	Physician/RD counseling, web/remote program, structured multidisciplinary program
Medical Therapy (BMI ≥27):	Individualize care by selecting one of the following based on efficacy, safety, and patients' clinical profile: phentermine, orlistat, lorcaserin, phentermine/topiramate ER, naltrexone/bupropion, liraglutide 3 mg
Surgical Therapy (BMI ≥35):	Gastric banding, sleeve, or bypass

STEP 3 — If therapeutic targets for complications not met, intensify lifestyle, medical, and/or surgical treatment modalities for greater weight loss. Obesity is a chronic progressive disease and requires commitment to long-term therapy and follow-up.

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ASCVD RISK FACTOR MODIFICATIONS ALGORITHM

DYSLIPIDEMIA

LIFESTYLE THERAPY (Including Medically Assisted Weight Loss)

LIPID PANEL: Assess ASCVD Risk

STATIN THERAPY
If TG >500 mg/dL, fibrates, Rx-grade omega-3 fatty acids, niacin

If statin-intolerant

Try alternate statin, lower statin dose or frequency, or add nonstatin LDL-C- lowering therapies

Repeat lipid panel; assess adequacy, tolerance of therapy

Intensify therapies to attain goals according to risk levels

RISK LEVELS	HIGH	VERY HIGH	EXTREME
	DESIRABLE LEVELS	DESIRABLE LEVELS	DESIRABLE LEVELS
LDL-C (mg/dL)	<100	<70	<55
Non-HDL-C (mg/dL)	<130	<100	<80
TG (mg/dL)	<150	<150	<150
Apo B (mg/dL)	<90	<80	<70

RISK LEVELS:
- **HIGH:** DM but no other major risk and/or age <40
- **VERY HIGH:** DM + major ASCVD risk(s) (HTN, Fam Hx, low HDL-C, smoking, CKD3,4)*
- **EXTREME:** DM plus established clinical CVD

If not at desirable levels: Intensify lifestyle therapy (weight loss, physical activity, dietary changes) and glycemic control; consider additional therapy

To lower LDL-C: Intensify statin, add ezetimibe, PCSK9i, colesevelam, or niacin
To lower Non-HDL-C, TG: Intensify statin and/or add Rx-grade OM3 fatty acid, fibrate, and/or niacin
To lower Apo B, LDL-P: Intensify statin and/or add ezetimibe, PCSK9i, colesevelam, and/or niacin
To lower LDL-C in FH:** Statin + PCSK9i

Assess adequacy & tolerance of therapy with focused laboratory evaluations and patient follow-up

HYPERTENSION

GOAL: SYSTOLIC <130, DIASTOLIC <80 mm Hg

ACEi or ARB

For initial blood pressure >150/100 mm Hg:
DUAL THERAPY
ACEi or ARB + Calcium Channel Blocker ✓ / ß-blocker ✓ / Thiazide ✓

If not at goal (2–3 months)

Add calcium channel blocker, ß-blocker or thiazide diuretic

If not at goal (2–3 months)

Add next agent from the above group, repeat

If not at goal (2–3 months)

Additional choices (α-blockers, central agents, vasodilators, aldosterone antagonist)

Achievement of target blood pressure is critical

* EVEN MORE INTENSIVE THERAPY MIGHT BE WARRANTED ** FAMILIAL HYPERCHOLESTEROLEMIA

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GLYCEMIC CONTROL ALGORITHM

INDIVIDUALIZE GOALS

A1C ≤6.5% For patients without concurrent serious illness and at low hypoglycemic risk

A1C >6.5% For patients with concurrent serious illness and at risk for hypoglycemia

LIFESTYLE THERAPY (Including Medically Assisted Weight Loss)

Entry A1C <7.5%

MONOTHERAPY[1]

- ✓ Metformin
- ✓ GLP1-RA [2,3]
- ✓ SGLT2i [2,3]
- ✓ DPP4i
- ⚠ TZD
- ✓ AGi
- ⚠ SU/GLN

If not at goal in 3 months proceed to Dual Therapy

Entry A1C ≥7.5%

DUAL THERAPY[1]

MET or other 1st-line agent +

- ✓ GLP1-RA [2,3]
- ✓ SGLT2i [2,3]
- ✓ DPP4i
- ⚠ TZD
- ⚠ Basal Insulin
- ✓ Colesevelam
- ✓ Bromocriptine QR
- ✓ AGi
- ⚠ SU/GLN

If not at goal in 3 months proceed to Triple Therapy

TRIPLE THERAPY[1]

MET or other 1st-line agent + 2nd-line agent +

- ✓ GLP1-RA [2,3]
- ✓ SGLT2i [2,3]
- ⚠ TZD
- ⚠ Basal Insulin
- ✓ DPP4i
- ✓ Colesevelam
- ✓ Bromocriptine QR
- ✓ AGi
- ⚠ SU/GLN

If not at goal in 3 months proceed to or intensify insulin therapy

Entry A1C >9.0%

SYMPTOMS

NO

DUAL Therapy

OR

TRIPLE Therapy

YES

INSULIN ± Other Agents

ADD OR INTENSIFY INSULIN

Refer to Insulin Algorithm

LEGEND

- ✓ Few adverse events and/or possible benefits
- ⚠ Use with caution

1. Order of medications represents a suggested hierarchy of usage; length of line reflects strength of recommendation
2. Certain GLP1-RAs and SGLT2is have shown CVD and CKD benefits—preferred in patients with those complications
3. Include one of these medications if CHD present

PROGRESSION OF DISEASE

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2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

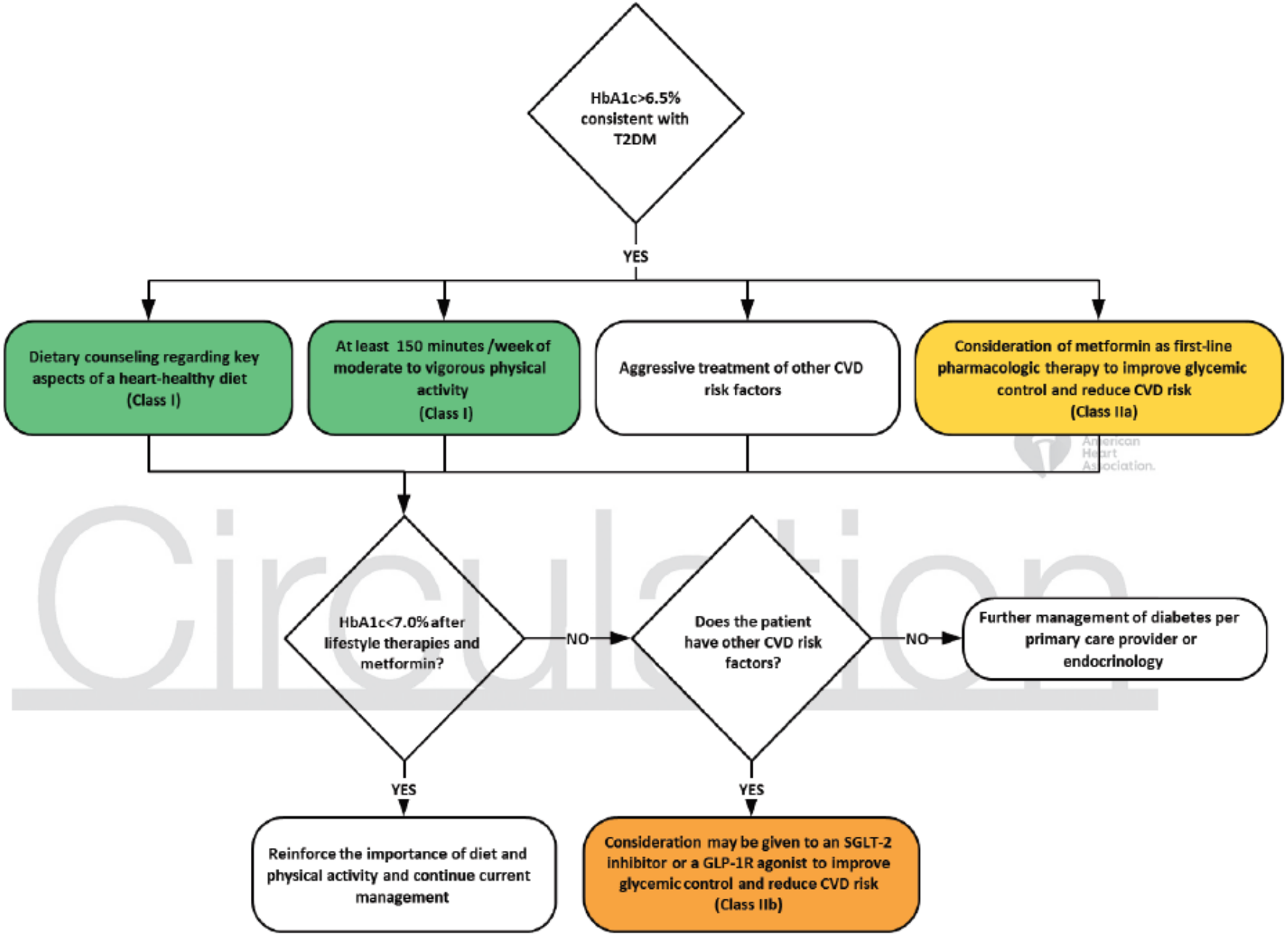
Recommendations for Adults With Type 2 Diabetes Mellitus

Referenced studies that support recommendations are summarized in Online Data Supplement 10.

COR	LOE	Recommendations
I	A	1. **NUTRITIONAL PLAN**
I	A	2. **PHYSICAL ACTIVITY**
IIa	B-R	3. **METFORMIN (1st line)**
IIb	B-R	4. **IF ASCVD: ADD SGLT2-i or GLP1-RA**

Arnett DK et al. Circulation 2019

Treatment of T2DM for Primary Prevention of CVD

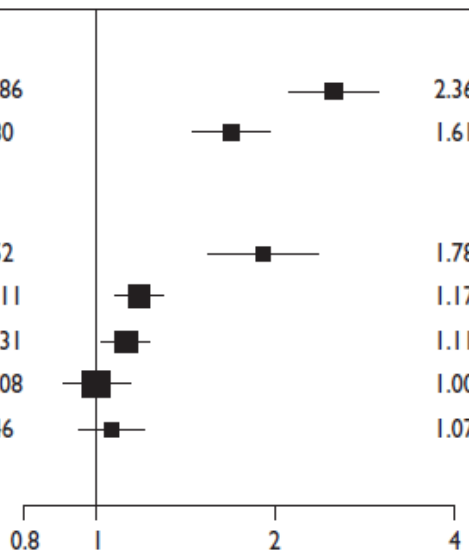


Circulation

2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD

The Task Force for diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD)

Fasting blood glucose concentration	Number of participants (%)	Number of cases	HR (95% CI)
Known diabetes at baseline			
≥7 mmol/L	13 122 (4.7%)	1 186	2.36 (2.02–2.76)
<7 mmol/L	5 807 (2.1%)	380	1.61 (1.42–1.82)
No known diabetes at baseline			
≥7 mmol/L	7 240 (2.6%)	452	1.78 (1.56–2.03)
6.1 to <7 mmol/L 110-125 mg/dL	19 607 (7.0%)	1 011	1.17 (1.08–1.26)
5.6 to <6.1 mmol/L 101-110 mg/dL	32 008 (11.5%)	1 631	1.11 (1.04–1.18)
3.9 to <5.6 mmol/L[a]	185 590 (66.5%)	9 508	1.00 (0.95–1.06)
<3.9 mmol/L	15 916 (5.7%)	646	1.07 (0.97–1.18)



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ESC European Society of Cardiology

European Heart Journal (2019) **00**, 1–69
doi:10.1093/eurheartj/ehz486

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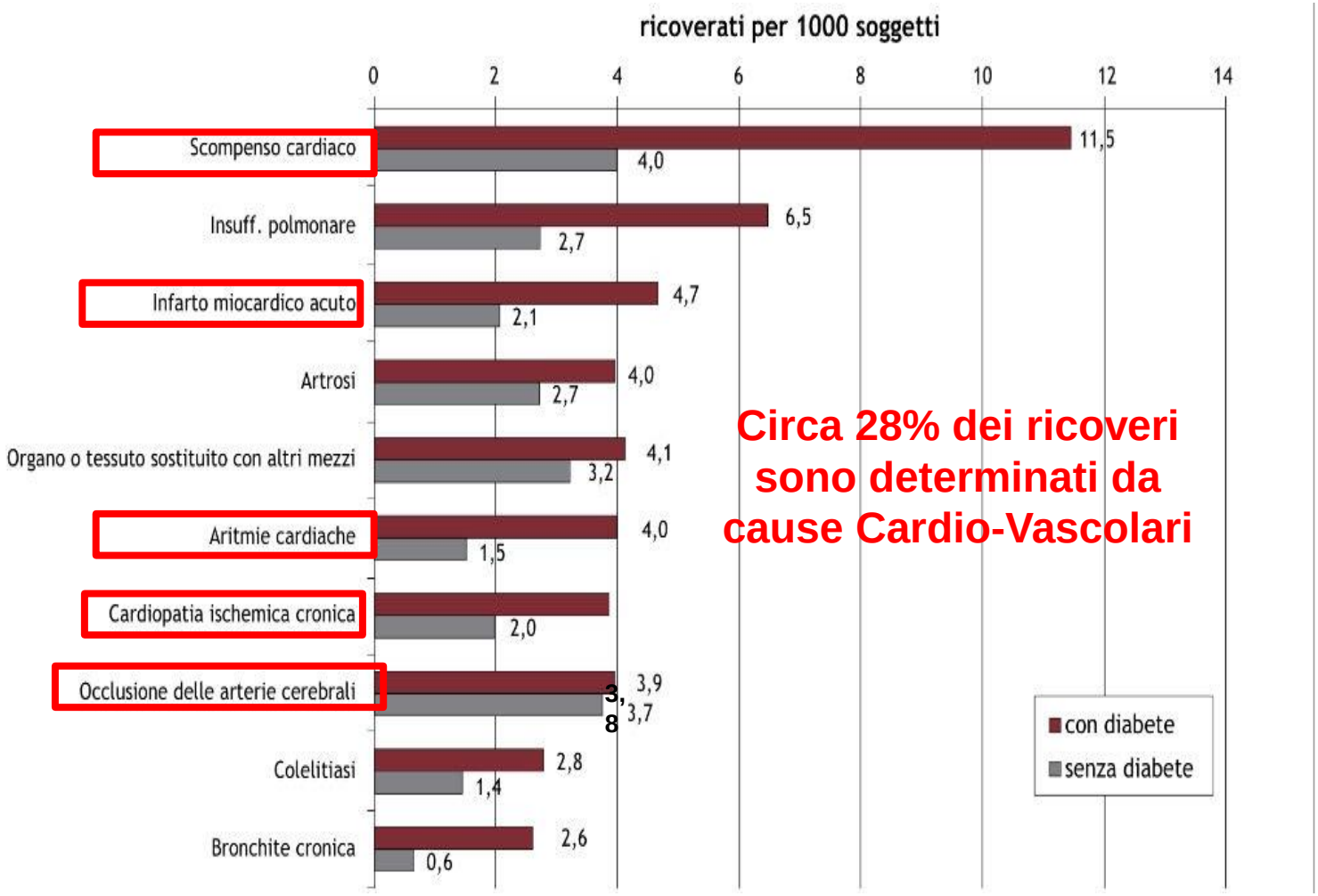
PRIME 10 CAUSE DI RICOVERO ORDINARIO NEI DIABETICI



Circa 28% dei ricoveri sono determinati da cause Cardio-Vascolari

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DATI ARNO 2017

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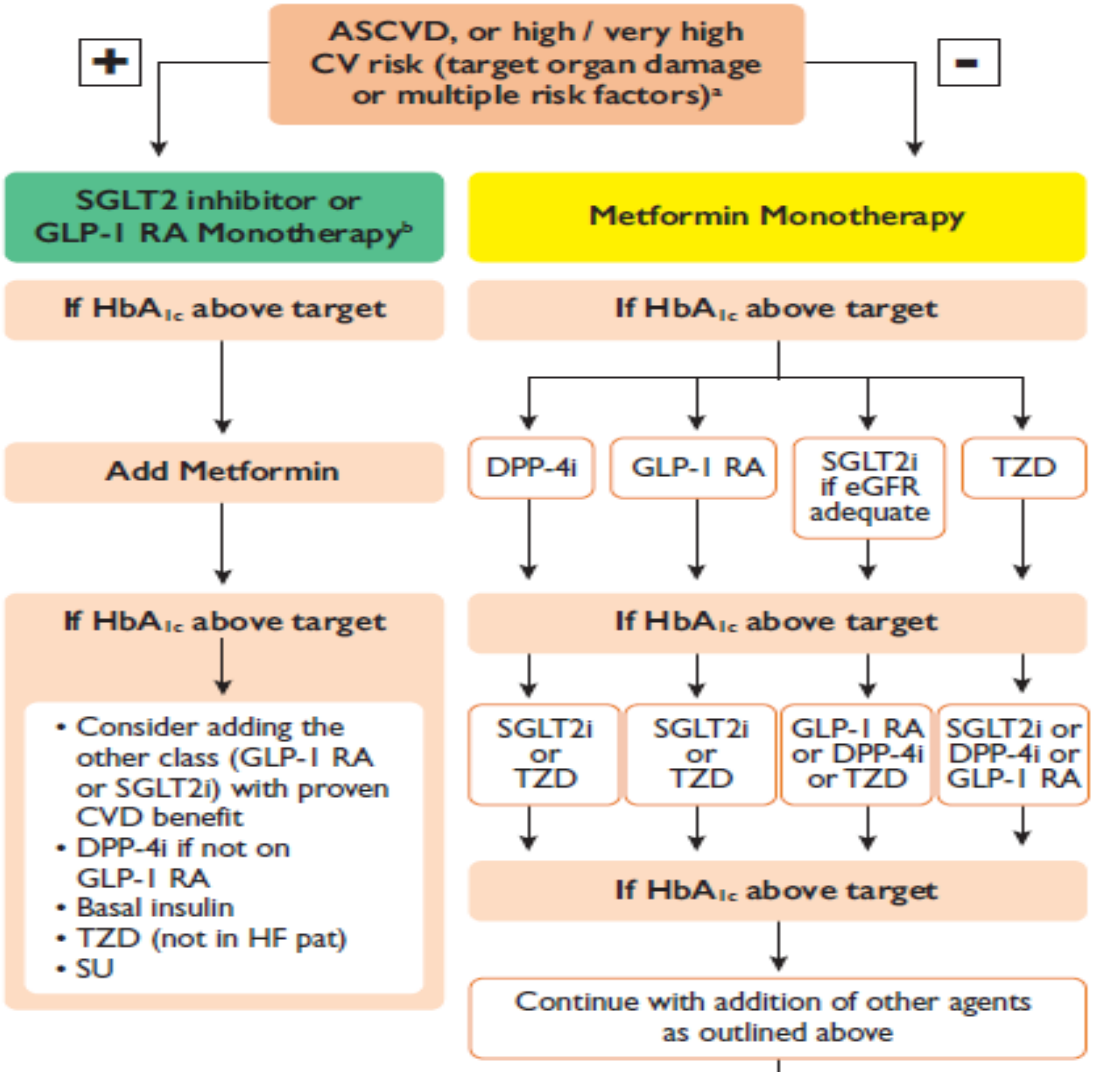
A Type 2 DM - Drug naïve patients



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B Type 2 DM - On metformin

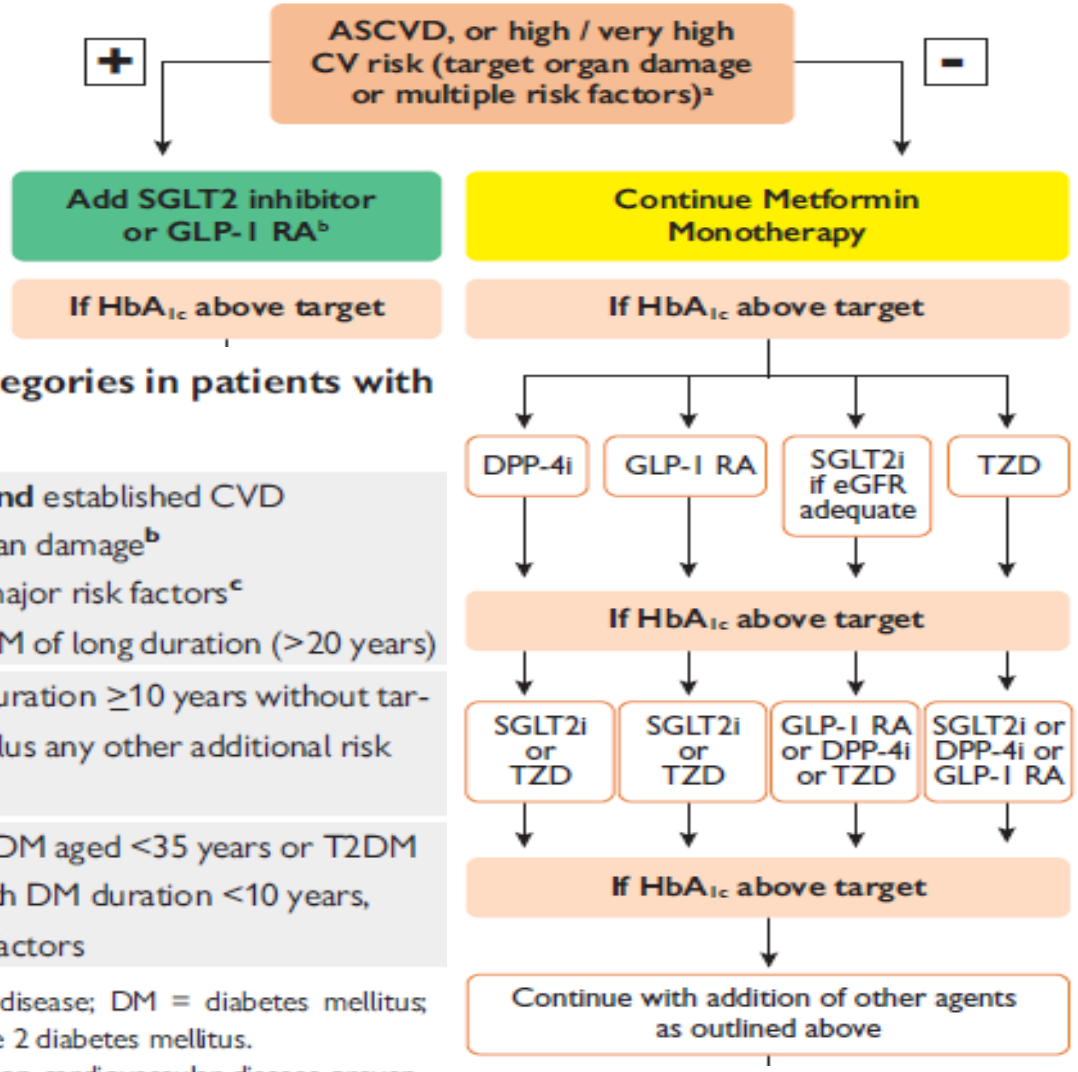


Table 7 Cardiovascular risk categories in patients with diabetes[a]

Very high risk	Patients with DM **and** established CVD **or** other target organ damage[b] **or** three or more major risk factors[c] **or** early onset T1DM of long duration (>20 years)
High risk	Patients with DM duration ≥10 years without target organ damage plus any other additional risk factor
Moderate risk	Young patients (T1DM aged <35 years or T2DM aged <50 years) with DM duration <10 years, without other risk factors

CV = cardiovascular; CVD = cardiovascular disease; DM = diabetes mellitus; T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus.

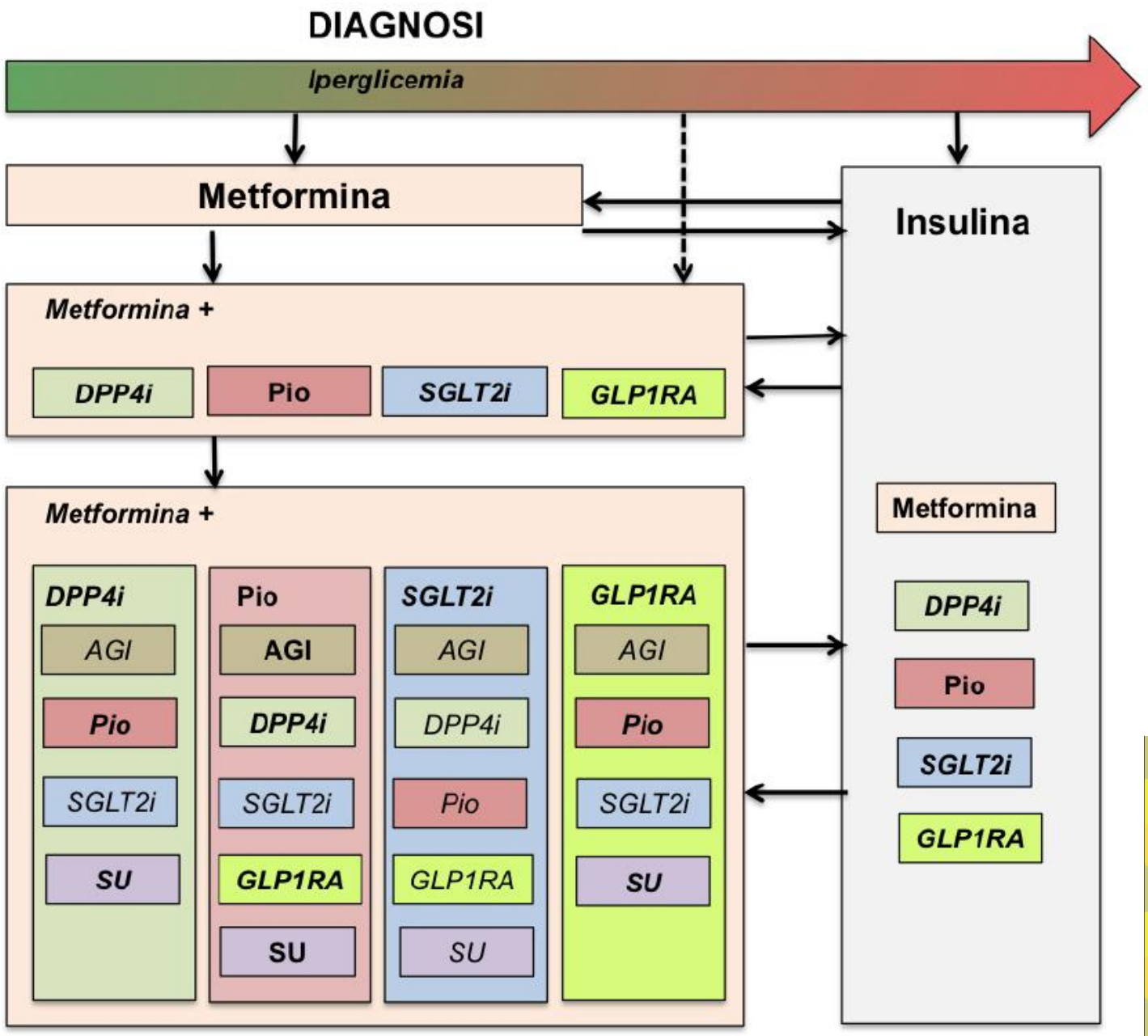
[a]Modified from the 2016 European Guidelines on cardiovascular disease prevention in clinical practice.[27]

[b]Proteinuria, renal impairment defined as eGFR ≥30 mL/min/1.73 m^2, left ventricular hypertrophy, or retinopathy.

[c]Age, hypertension, dyslipidemia, smoking, obesity.

ESC European Society of Cardiology

European Heart Journal (2019) **00**, 1–69
doi:10.1093/eurheartj/ehz486


DIAGNOSI
Iperglicemia
Metformina
Insulina
Metformina +
DPP4i
Pio
SGLT2i
GLP1RA
Metformina +
DPP4i
AGI
Pio
SGLT2i
SU
Pio
AGI
DPP4i
SGLT2i
GLP1RA
SU
SGLT2i
AGI
DPP4i
Pio
GLP1RA
SU
GLP1RA
AGI
Pio
SGLT2i
SU
Metformina
DPP4i
Pio
SGLT2i
GLP1RA

AMD
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STANDARD ITALIANI
PER LA CURA DEL
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2018

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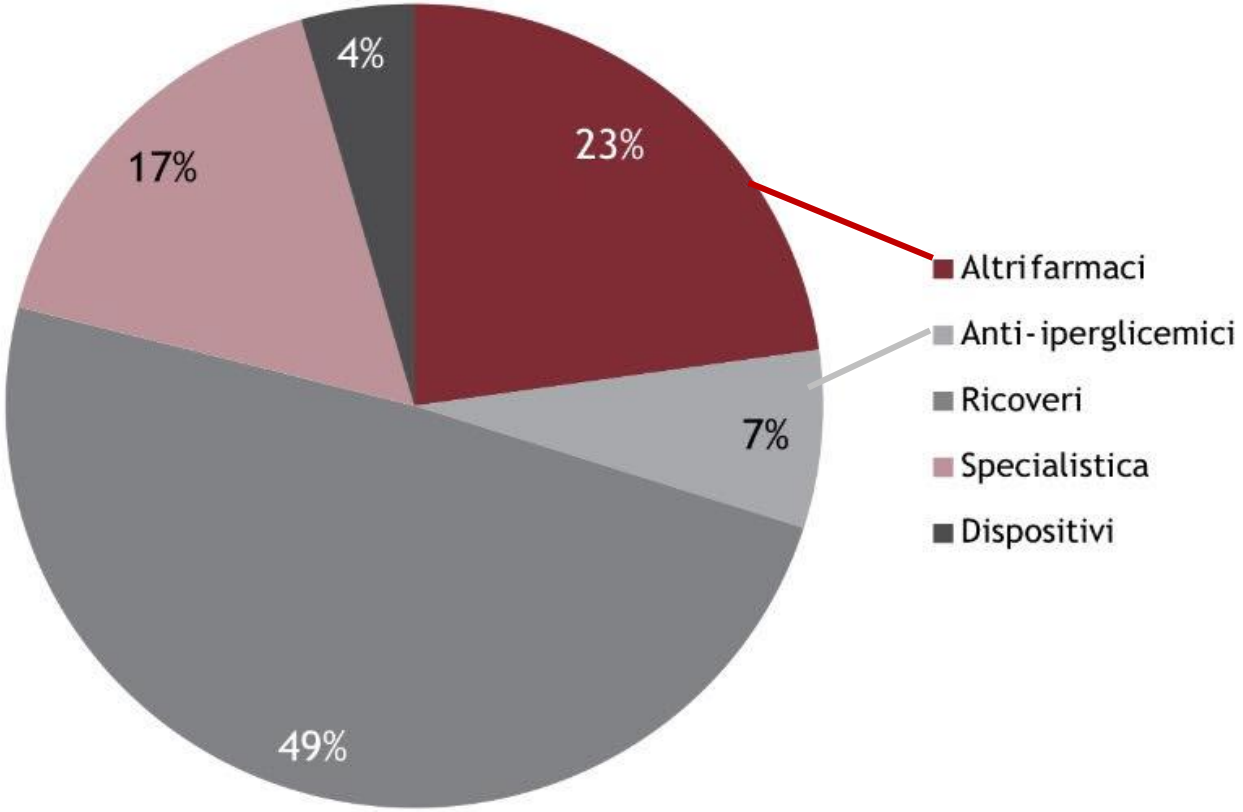
COMPOSIZIONE PERCENTUALE DELLA SPESA PER IL DIABETE



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SOGGETTI TRATTATI PER CLASSI DI FARMACI ANTIDIABETICI ITALIA (2017)

SULFANILUREE e METFORMINA+SULFANILUREE = 27,4%

SECRETAGOGHI=36,3%

GLINIDI= 8,9%

ANALOGHI INSULINA= 26%

DPP4 e METFORMINA+DPP4 = 12%

GLP1= 2,4%

SGLT2- METFORMINA + SGLT2 = 2,3%

Descrizione	Trattati (n=516.073)	% Trattati*	% spesa sul totale	Spesa media per trattato €	Spesa media pro capite € (n=640.846)
Iperglicemici orali o iniettabili	446.320	86,5	50	150	104,5
Metformina	321.009	62,2	9,4	39,3	19,7
Sulfoniluree	99.127	19,2	3,8	51,8	8
Glinidi (Repaglinide)	45.942	8,9	2,8	80,6	5,8
Metformina e sulfoniluree	42.527	8,2	1,9	59,2	3,9
Metformina e Inibitori DPP-4	35.942	7	10	371,5	20,8
Inibitori DDP-4	25.991	5	7	358,2	14,5
Inibitori alfa-glicosidasi (Acarbosio)	19.210	3,7	1,2	84,6	2,5
Metformina e pioglitazone	14.245	2,8	3	285,6	6,3
Analoghi GLP-1	12.447	2,4	7,2	778,5	15,1
Glitazoni (Pioglitazone)	9.582	1,9	1	141,9	2,1
Inibitori SGLT-2	7.236	1,4	1,4	257,1	2,9
Metformina e inibitori SGLT-2	4.425	0,9	0,8	230,8	1,6
Glimepiride e pioglitazone	1.361	0,3	0,3	310,2	0,7
Pioglitazone e alogliptin	1.009	0,2	0,2	270,9	0,4
Insuline umane	5.345	1	0,7	162,9	1,4
Insuline ad azione rapida	4.174	0,8	0,5	155,4	1
Insuline ad azione intermedia	1.314	0,3	0,1	105,6	0,2
Insuline ad azione intermedia e azione rapida miscelate	736	0,1	0,1	113,7	0,1
Analoghi dell'Insulina	134.409	26	49,4	491,8	103,2
Analoghi ad azione rapida	100.132	19,4	27,6	369,4	57,7
Analoghi ad azione intermedia e azione rapida miscelati	12.547	2,4	2,6	273,2	5,3
Analoghi ad azione intermedia	6.656	1,3	1	199,9	2,1
Analoghi ad azione lenta	105.998	20,5	18,2	229,8	38
Totale	516.073	-	100,0	259,5	209

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Precision medicine in the management of type 2 diabetes

Lancet Diabetes Endocrinol 2018
Published Online
April 23, 2018

Anna L Gloyn, Daniel J Drucker

Panel: Evolving clinical considerations underlying personalised medicine recommendations for intensification of therapy after metformin in people with type 2 diabetes*

Clinical characteristics influencing selection of glucose-lowering drugs

Older age, fragility
DPP-4 inhibitors, age-specific treatment goals

Severe or recurrent hypoglycaemia
DPP-4 inhibitors, SGLT2 inhibitors, GLP-1 receptor agonists, modern insulins

Poor, variable, or subotimal compliance
Once-weekly GLP-1 receptor agonists

Obesity
Bariatric surgery, GLP-1 receptor agonists, SGLT2 inhibitors

High HbA_{1c}, failure of oral antidiabetes drugs
Bariatric surgery, insulin, GLP-1 receptor agonists

Considerations based on non-glycaemic actions of glucose-lowering therapies and the reduction in rates of complications associated with diabetes

Non-alcoholic fatty liver disease, non-alcoholic steatohepatitis
Thiazolidinediones, GLP-1 receptor agonists

Heart failure
SGLT2 inhibitors

Coronary artery disease
GLP-1 receptor agonists

Stroke
Thiazolidinediones, GLP-1 receptor agonists

Chronic kidney disease
SGLT2 inhibitors

Catalog stats

Last data release on 2019-07-30

4085 publications
95875 SNPs
149855 associations

SNP-trait associations for "diabetes mellitus" on the diagram: 310

www.ebi.ac.uk/gwas

In a world that is increasingly stressful
and less predictable,
more economically challenging
and politically less governable,
Medicine is still about looking after the
individual who seeks care.

When health care is measured
by a "medical loss ratio",
and the percentage of spending on health care
is considered a "loss",
then we are really lost.

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Eric Manheimer, MD. Twelve patients.
Grand Central Publishing.
New York – Boston

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S.I.Te.C.S.

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Milano 25-26 Ottobre 2019

Four Points by Sheraton Milan Center

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Linee guida diabete

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