Terapia nel paziente diabetico anziano: cosa dicono le linee guida nazionali e internazionali

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Potenziali conflitti di interesse

Il Prof Giorgio Sesti dichiara di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

Novo Nordisk, MSD, Boehringer-Ingelheim, Lilly, Janssen, AstraZeneca, Novartis e Takeda per attività di Relatore ad eventi.

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Ringrazio caldamente la SID per lo straordinario contributo alla mia formazione culturale, scientifica e clinica.

Senza il fondamentale sostegno della SID non sarei oggi qui a presentare questa mia relazione.

SID
Società Italiana
di Diabetologia

Standards of Medical Care in Diabetes — 2016

American Diabetes Association

American Diabetes Association Standards of Medical Care in Diabetes. Older adults. Diabetes Care 2016; 39 (Suppl. 1): S81-S85

Older Adults

- **26% of patients aged >65 have diabetes.**
- **Older adults have higher rates of premature death, functional disability & coexisting illnesses.**
- **At greater risk for polypharmacy, cognitive impairment, urinary incontinence, injurious falls & persistent pain.**
- **Screening for complications should be individualized and periodically revisited.**
- **At higher risk for depression.**

American Diabetes Association

American Diabetes Association Standards of Medical Care in Diabetes. Older adults. Diabetes Care 2016; 39 (Suppl. 1): S81-S85

Recommendations: Older Adults

- Consider the **assessment of medical, functional, mental, and social geriatric domains f**or diabetes management in older adults to provide a framework to **determine targets and therapeutic approaches**.
- Screening for geriatric syndromes may be appropriate in older adults experiencing limitations in their basic and instrumental activities of daily living, as they may affect diabetes self-management.
- **Older adults** who are **functional and cognitively intact** and have **significant life expectancy** may receive diabetes care with **goals similar** to those developed for **younger adults.**

American Diabetes Association

American Diabetes Association Standards of Medical Care in Diabetes. Older adults. Diabetes Care 2016; 39 (Suppl. 1): S81-S85

Recommendations: Older Adults

- **Glycemic goals for some older adults might be relaxed but hyperglycemia leading to symptoms or risk of acute hyperglycemic complications should be avoided in all patients.**

- **Hypoglycemia should be avoided in older adults with diabetes. It should be screened for and managed by adjusting glycemic targets and pharmacologic interventions.**

- **Screening for diabetes complications should be individualized in older adults, but particular attention should be paid to complications that would lead to functional impairment.**

American Diabetes Association

American Diabetes Association Standards of Medical Care in Diabetes. Older adults. Diabetes Care 2016; 39 (Suppl. 1): S81-S85

Framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes

Patient characteristics/ health status	Rationale	Reasonable A1C goal‡	Fasting or preprandial glucose	Bedtime glucose	Blood pressure	Lipids
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)	<140/80 mmHg	Statin unless contraindicated or not tolerated

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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)	<140/90 mmHg	Statin unless contraindicated or not tolerated

***Coexisting chronic illnesses are conditions serious enough to require medications or lifestyle management and may include arthritis, cancer, congestive heart failure, depression, emphysema, falls, hypertension, incontinence, stage 3 or worse chronic kidney disease, myocardial infarction, and stroke. By "multiple," we mean at least three, but many patients may have five or more.**

ADL: Activities of daily living

American Diabetes Association

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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)	<150/90 mmHg	Consider likelihood of benefit with statin (secondary prevention more so than primary)

****The presence of a single end-stage chronic illness, such as stage 3–4 congestive heart failure or oxygen-dependent lung disease, chronic kidney disease requiring dialysis, or uncontrolled metastatic cancer, may cause significant symptoms or impairment of functional status and significantly reduce life expectancy. ADL: Activities of daily living**

American Diabetes Association

American Diabetes Association Standards of Medical Care in Diabetes. Older adults. Diabetes Care 2016; 39 (Suppl. 1): S81-S85

INTERNATIONAL DIABETES FEDERATION

MANAGING OLDER PEOPLE WITH TYPE 2 DIABETES

GLOBAL GUIDELINE

International Diabetes Federation

- Glycaemic control targets should be **individualized taking into account functional status, comorbidities,** especially the presence of **established CVD, history and risk of hypoglycaemia, and presence of microvascular complications**.
- Begin **oral glucose lowering** therapy when **lifestyle** interventions alone are **unable** to maintain **target** blood glucose levels.
- Maintain support for lifestyle measures throughout the use of these medicines.
- Discuss with the **individual and principal caregiver care** goals and medicine dose, regimen, and tablet burden before choosing glucose lowering agents.

- Use the “start low and go slow” principle in initiating and increasing medication and monitor response to each initiation or dose increase for up to a 3 month trial period.

- Consider discontinuing ineffective and unnecessary therapies.

- Consider the cost and the risk-to-benefit ratio when choosing a medicine: risk includes adverse event, hypoglycaemia, weight gain or weight loss, need for caregiver involvement, impact of worsening renal or hepatic function, gastro-intestinal symptoms.

CATEGORY 1:

FUNCTIONALLY INDEPENDENT

This category is characterized by people who are living independently, have no important impairments of activities of daily living (ADL), and who are receiving none or minimal caregiver support. Although diabetes may be the main medical problem, this category includes those who have other medical comorbidities which may influence diabetes care.

CATEGORY 2:

FUNCTIONALLY DEPENDENT

This category represents those individuals who, due to loss of function, have impairments of ADL such as bathing, dressing, or personal care. This increases the likelihood of requiring additional medical and social care. Such individuals living in the community are at particular risk of admission to a care (nursing) home. This category includes a range of functionally dependent older people with diabetes.

Two groups require special consideration:

1. **Subcategory A: Frail**
2. **Subcategory B: Dementia**

CATEGORY 2:

Subcategory A: Frail

These individuals are characterized by a combination of significant fatigue, recent weight loss, severe restriction in mobility and strength, increased propensity to falls, and increased risk of institutionalization. Frailty is a recognized condition and accounts for up to 25% of older people with diabetes. A Clinical Frailty Scale is recommended to assist the clinician in identifying individuals in this sub-category. There is a small proportion of frail older people with diabetes who may be relatively independent but in time dependency develops.

CATEGORY 2:

Subcategory B: Dementia

Individuals in this sub-category have a degree of cognitive impairment that has led to significant memory problems, a degree of disorientation, or a change in personality, and who now are unable to self-care. Many will be relatively physically well. Several cognitive screening tests are available to assist the clinician in identifying individuals in this sub-category.

CATEGORY 3:

END OF LIFE CARE

These individuals are characterized by a significant medical illness or malignancy and have a life expectancy reduced to less than 1 year.

General glycaemic targets according to functional category

Functional category	General HbA1c target
Functionally Independent	7.0-7.5%
Functionally dependent	7.0-8.0%
• Frail	Up to 8.5%
• Dementia	Up to 8.5%
End of life	Avoid symptomatic hyperglycaemia

Glycaemic targets should be individualized taking into account functional status, comorbidities, especially the presence of established CVD, history and risk of hypoglycaemia, and presence of microvascular complications.

International Diabetes Federation

Category 1: Functionally Independent

First-line Therapy

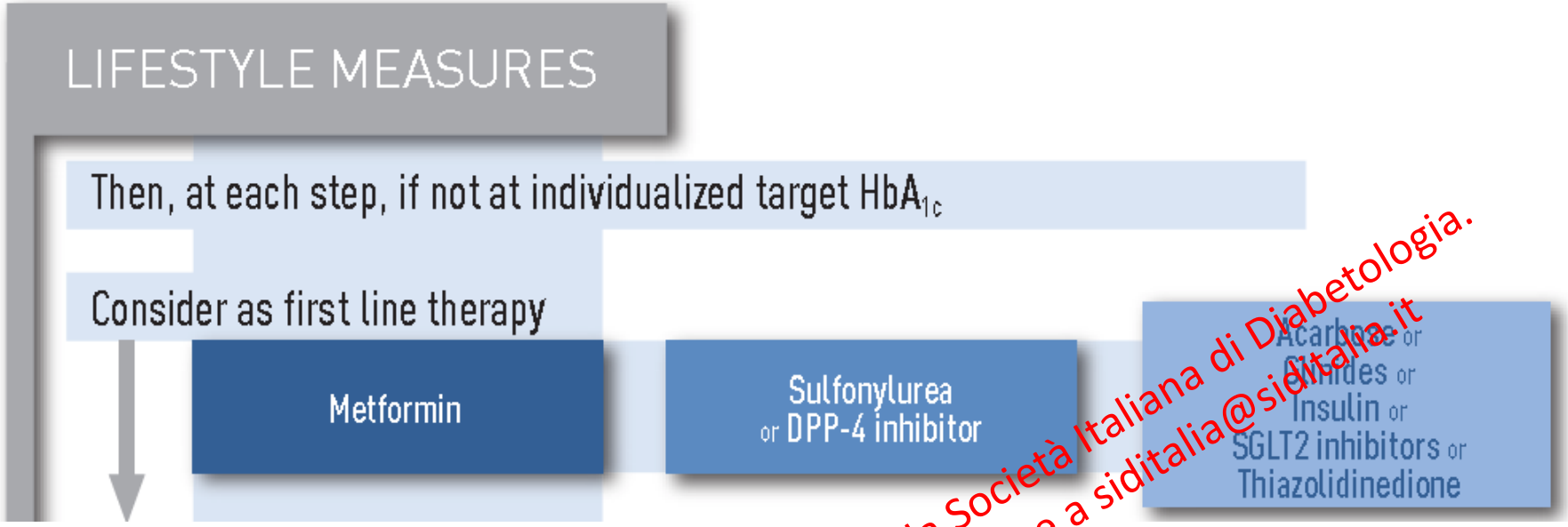
- Consider **metformin as first-line therapy** unless there is evidence of **renal impairment or other contraindications**. **Titrate** the dose over **initial** weeks to **minimize gastrointestinal** intolerance. Monitor renal function closely (eGFR is more accurate than serum creatinine in older people).

- Calculation of eGFR in older individuals using the **MDRD** and **CKD-EPI** formulae have a similar performance while the Cockroft Gault formula tends to underestimate eGFR.

- A **sulfonylurea** can be used if metformin is not tolerated or contraindicated. Use a sulfonylurea with a low risk of hypoglycaemia and avoid glibenclamide.

- A **dipeptidyl dipeptidase 4 (DPP-4) inhibitor** may also be considered if available and affordable.

- **Glinides** may be considered in older people with **postprandial hyperglycaemia** and **erratic eating** habits but can **interact** with certain **medications** in older people (e.g. non-selective beta-blockers, salicylates, non-steroidal anti-inflammatory medications, macrolides, ACE-inhibitors).

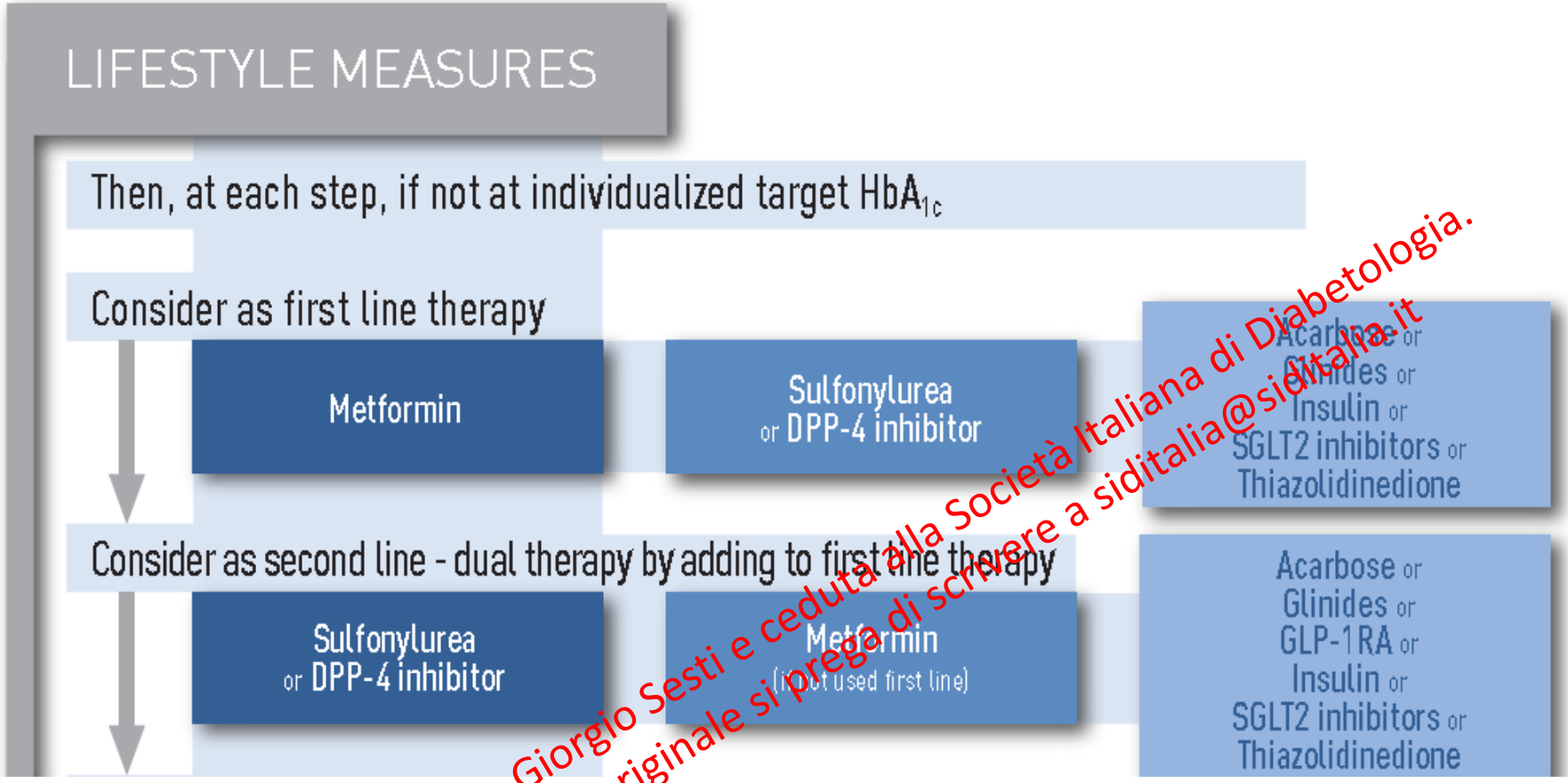


Second-line Therapy

- **Add a sulfonylurea (with low risk of hypoglycaemia) to metformin if glycaemic targets are not achieved.**

- **Alternatively add a DPP-4 inhibitor.**

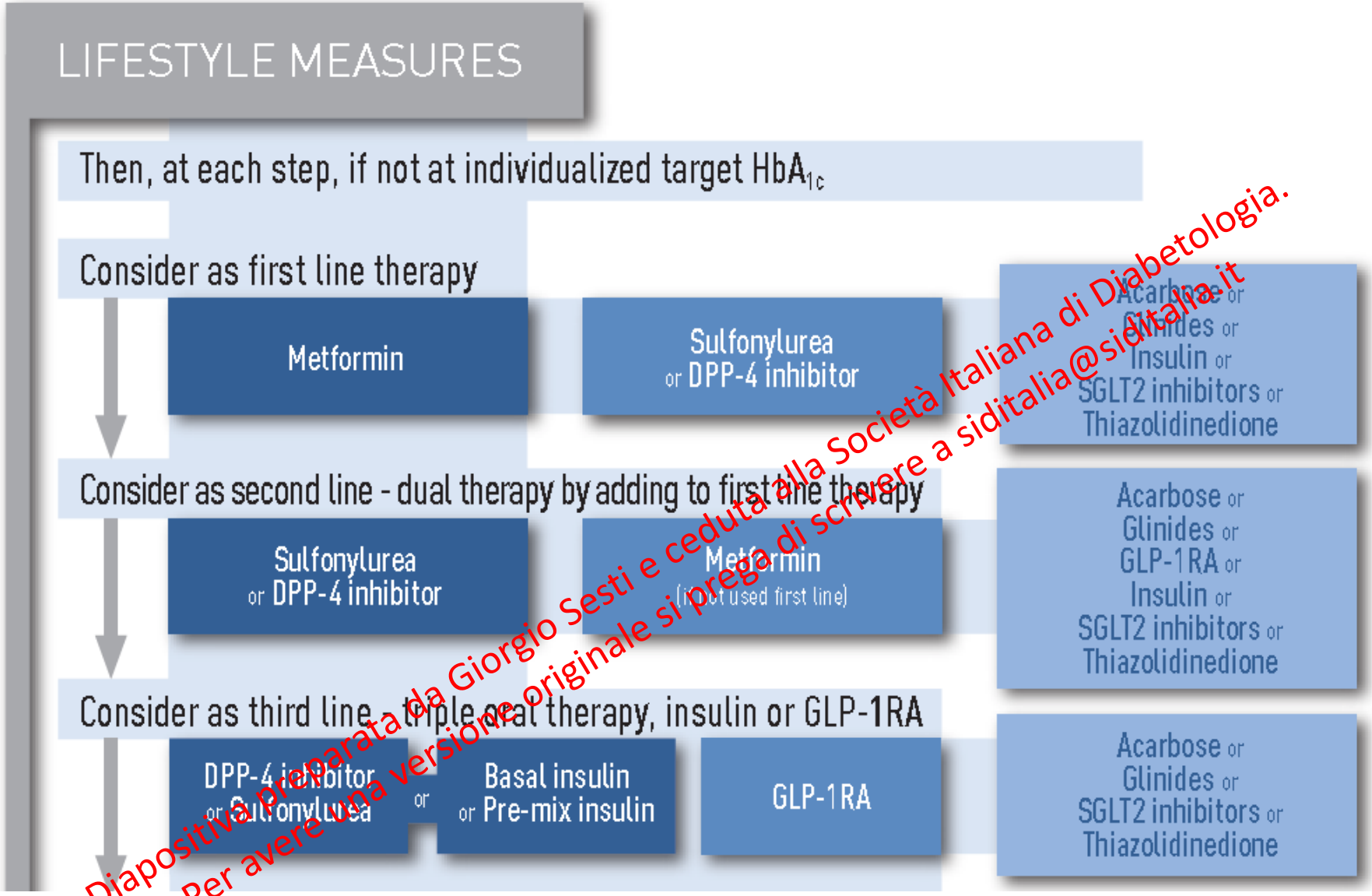
- **If oral glucose lowering agents are contraindicated or not tolerated, a long acting basal insulin is an alternate option.**

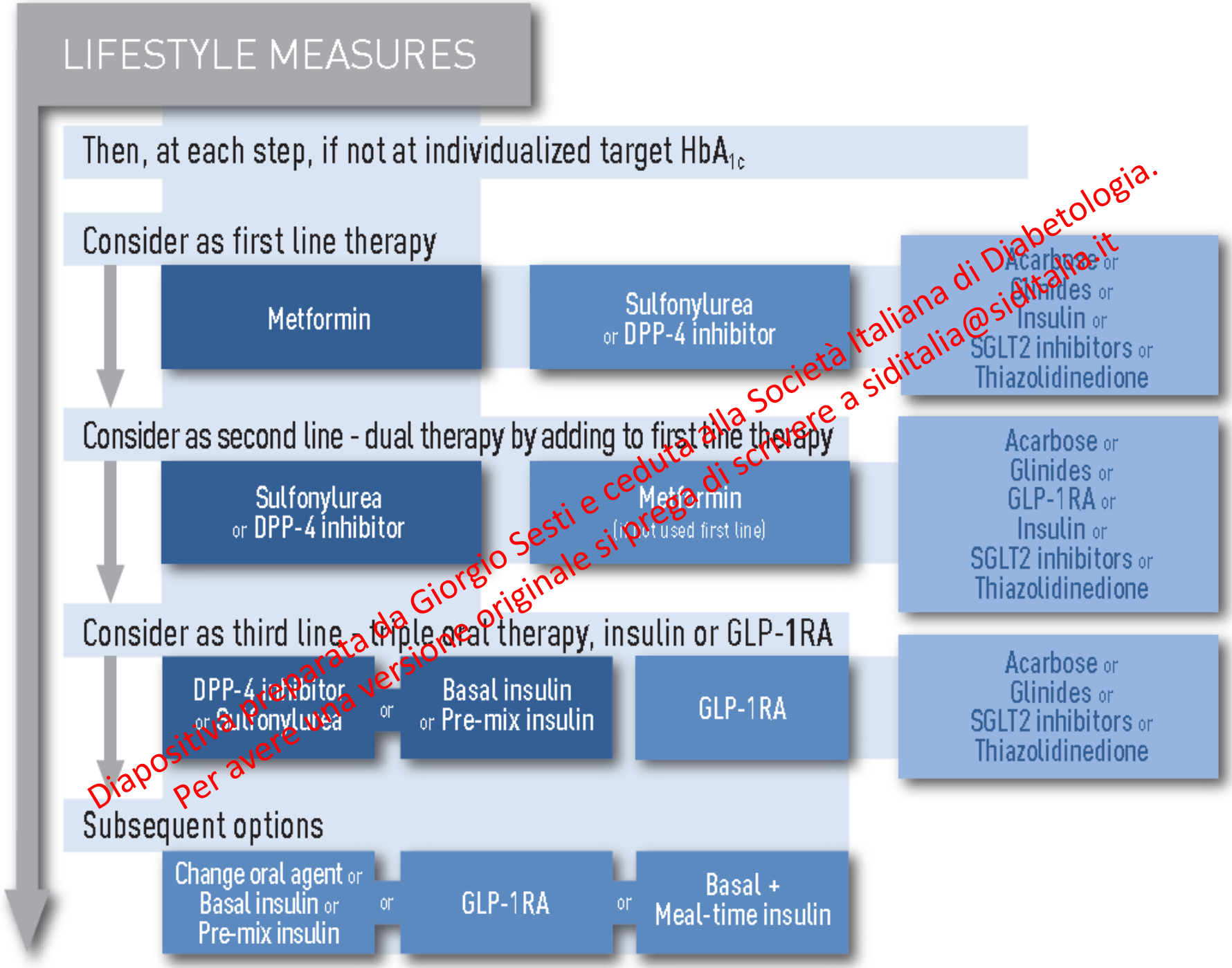


Third-line Therapy

Options include:

- **Triple oral therapy.**
- **Basal or pre-mixed insulin.**
- **Glucagon-like peptide-1 receptor agonist (GLP-1 RA) - gastrointestinal side-effects may be problematic and weight loss can be detrimental in the frail, underweight older person.**





Category 2: Functionally Dependent

- **The principles are as for Category 1 - Functionally Independent but additional precautions are required.**
- **When prescribing an oral glucose lowering agent, choose one with a low potential for hypoglycaemia.**
- **Use simplified insulin regimens with a low hypoglycaemic risk.**
- **Avoid complex regimens and higher treatment burden to reduce the risk of medication errors.**

Sub-category A: Frail

- **Avoid** or discontinue agents that might **cause nausea or gastrointestinal** disturbance or excess weight loss (e.g. **metformin or a GLP-1 RA**).
- **Insulin** may provide **anabolic** benefits.

Sub-category B: Dementia

- **Caregivers** and/or family should be educated to recognize the subtle indicators of **hypoglycaemia**.

Category 3: End of Life Care

- The glycaemic target is to avoid symptomatic hyperglycaemia.
- The same precautions as indicated for people in Category 2: Functionally Dependent apply.
- Minimize hypoglycaemia and symptomatic hyperglycaemia by appropriate individualized management.
- Consider appropriate withdrawal of therapy, including insulin, during the terminal stage.

Canadian Diabetes Association Clinical Practice Guidelines

Diabetes in the Elderly

Chapter 37

(Updated March 2016)

Graydon S. Meneilly, Daniel Tessier, Aileen Knip

2016

Canadian Diabetes Association

Recommendation 1

1. **Healthy**, elderly people with diabetes should be treated to achieve the **same** glycemic, blood pressure, and lipid targets **as younger** people with diabetes [Grade D, Consensus].

Consider A1C 7.1-8.5% if …

- Limited life expectancy
- High level of functional dependency
- Extensive coronary artery disease at high risk of ischemic events
- Multiple co-morbidities
- History of recurrents severe hypoglycemia
- Hypoglycemia unawareness
- Longstanding diabetes for whom is it difficult to achieve an A1C ≤7%, despite effective doses of multiple antihyperglycemic agents, including intensified basal-bolus insulin therapy

Canadian Diabetes Association

Recommendation 2

2. In the **frail elderly**, while avoiding symptomatic hyperglycemia, glycemic targets should be an **A1C of ≤8.5% and FPG or pre-prandial PG of 5.0-12.0** mmol/L, depending on the level of frailty.

   Avoidance of hypoglycemia should take priority over attainment of glycemic targets because the risks of hypoglycemia are magnified in this patient population [Grade D; Consensus].

Recommendations 3 and 4

3. In elderly people with **cognitive impairment**, strategies should be employed to **strictly avoid hypoglycemia**, which include the **choice of antihyperglycemic** therapy and **less stringent A1C** target [Grade D, Consensus].

4. Elderly people with type 2 diabetes should perform **aerobic exercise and/or resistance training**, if not contraindicated, to improve glycemic control [Grade B, Level 2].

Recommendation 5

5. In elderly people with T2DM, **sulfonylureas** should be used with **caution** because the risk of **hypoglycemia** increases exponentially with age [Grade D, Level 4].
   - In general, **initial doses** of sulfonylureas in the elderly should be **half** of those used for younger people, and doses should be increased more slowly [Grade D, Consensus].
   - **Gliclazide and gliclazide MR** [Grade B, Level 2] and **glimepiride** [Grade C, Level 3] should be used **instead of glyburide**, as they are associated with a reduced frequency of hypoglycemic events.
   - **Meglitinides** may be used **instead of glyburide** to reduce the risk of hypoglycemia [Grade C Level 2 for repaglinide; Grade C, Level 3 for nateglinide], particularly in patients with irregular eating habits [Grade D, Consensus].

Recommendation 6

6. In elderly people, **thiazolidinediones** should be used with caution due to the increased risk of **fractures and heart failure** [Grade D, Consensus].

Canadian Diabetes Association

Recommendations 7 and 8

7. **Detemir** and **glargine** may be used instead of NPH or human 30/70 insulin to lower the frequency of hypoglycemic events [Grade B, Level 2].

2013

8. In elderly people, if insulin mixture is required, **premixed insulins and prefilled insulin pens** should be used **instead of mixing insulins** to reduce dosing errors, and to potentially improve glycemic control [Grade B, Level 2].

2013

Canadian Diabetes Association

Diabetes Mellitus in Older People: Position Statement on behalf of the International Association of Gerontology and Geriatrics (IAGG), the European Diabetes Working Party for Older People (EDWPOP), and the International Task Force of Experts in Diabetes

JAMDA 13: 497-502, 2012

Glucose Targets

Consensus statements

1. The clinician must consider individual comorbidities, and cognitive and functional status when determining what glucose goals should be agreed with the patient and/or carer.
2. In general, on treatment, an HbA1c target range of HbA1c 7.0%-7.5 % should be aimed for.
3. To reduce the risk of hypoglycemia, no patient should have a fasting glucose on treatment of less than 108 mg/dL (6 mmol/L): "Not below 6."
4. No patient should commence glucose-lowering therapy with drugs until the fasting glucose level is consistently 126 mg/dL (7 mmol/L) or higher: "Not before 7."
5. Low blood glucose states (levels of glucose of <90 mg/dL) should be strictly avoided.
6. A random glucose level higher than 198 mg/dL (11 mmol/L) should be avoided to minimize symptoms and reduce the risk of other diabetes-related complications.

Therapy

Consensus statements

1. **All patients should participate as actively as possible in a tailored physical activity program involving resistance training, balance exercises, and cardiovascular fitness training.**
2. **In view of their limited benefits, restrictive diets should be avoided in those patients 70 years and older, and in those with undernutrition.**
3. **Metformin can be considered as first-line glucose-lowering therapy in older people with type 2 diabetes, and as an adjunct to insulin therapy in those recommended for combination therapy.**
4. **In those patients at higher risk of hypoglycemia, sulphonylurea therapy should be avoided.**

JAMDA 13: 497-502, 2012

Therapy

Consensus statements

5. In selected patients, a **basal insulin** regimen may be **safer** in terms of **hypoglycemia** risk than a **basal/bolus or premixed insulin** regimen.
6. In selected **older patients not in target** or where there is **poor tolerance** to the glucose-lowering agents, the use of a dipeptidyl peptidase 4 **(DPP4) inhibitor** can be considered as **second-line** therapy.
7. In subjects who are **obese** (body mass index [BMI] >35), or where there is poor tolerance or lack of response to other agents, a **glucagon-like peptide 1 agonist** can be considered as both **second-line and third-line** therapy.
8. In selected patients **not at high risk of heart failure or of bone loss** or a previous diagnosis of osteoporosis, who have no history of bladder cancer, treatment with **pioglitazone** can be considered as **second-line therapy** after metformin.

JAMDA 13: 497-502, 2012

Standard italiani per la cura del diabete mellito 2016

Cura del diabete nelle persone anziane

RACCOMANDAZIONI

Il compenso glicemico e il trattamento ipoglicemizzante

- **Nei diabetici anziani gli obiettivi glicemici dovrebbero essere individualizzati. Gli obiettivi di emoglobina glicata potranno essere ambiziosi (<7%-7,5%; 53-58 mmol/mol) per pazienti autosufficienti, in condizioni generali buone e aspettativa di vita di almeno 8-10 anni (Livello della prova VI, Forza della raccomandazione B).**

- **Negli anziani fragili (con complicanze, affetti da demenza, con pluripatologie, nei quali il rischio di ipoglicemia è alto e nei quali i rischi di un controllo glicemico intensivo superino i benefici attesi) è appropriato un obiettivo meno restrittivo (<8,0-8,5%; 64-69 mmol/mol) (Livello della prova VI, Forza della raccomandazione B).**

Cura del diabete nelle persone anziane

RACCOMANDAZIONI

Il compenso glicemico e il trattamento ipoglicemizzante

- **Gli obiettivi metabolici vanno perseguiti in sicurezza, evitando o cercando di ridurre al minimo il rischio di ipoglicemia. Non è raccomandato il perseguimento di una glicemia a digiuno <108 mg/dl e si sconsiglia di iniziare un trattamento ipoglicemizzante se la glicemia a digiuno non è stabilmente >126 mg/dl (Livello della prova VI, Forza della raccomandazione B).**

- **Se in un soggetto anziano è indicata una terapia con antidiabetici orali, non è opportuno l'utilizzo di glibenclamide (Livello della prova IV, Forza della raccomandazione A).**

- **La gliclazide è la sulfonilurea da preferire, in quanto associata a un rischio minore di ipoglicemia (Livello della prova II, Forza della raccomandazione B).**

Cura del diabete nelle persone anziane

RACCOMANDAZIONI

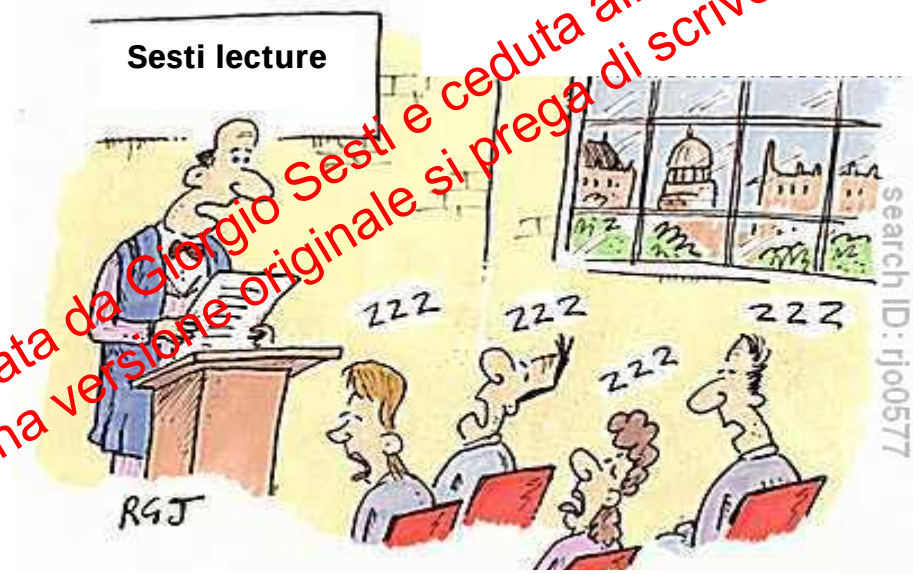
Il compenso glicemico e il trattamento ipoglicemizzante

- In diabetici anziani la **metformina** è utilizzabile con cautela **fino a un VFG stimato di 30 ml/min/1,73 m²**, purché siano attentamente considerati i fattori di rischio di peggioramento della funzione renale; al di sotto di tali valori non è opportuno l'uso di metformina (**Livello della prova IV, Forza della raccomandazione B**).

- In diabetici anziani trattati con metformina il **controllo del filtrato glomerulare** stimato dovrebbe essere effettuato **almeno una volta all'anno** e in occasione di ogni incremento posologico (**Livello della prova VI, Forza della raccomandazione B**).

THANK YOU !

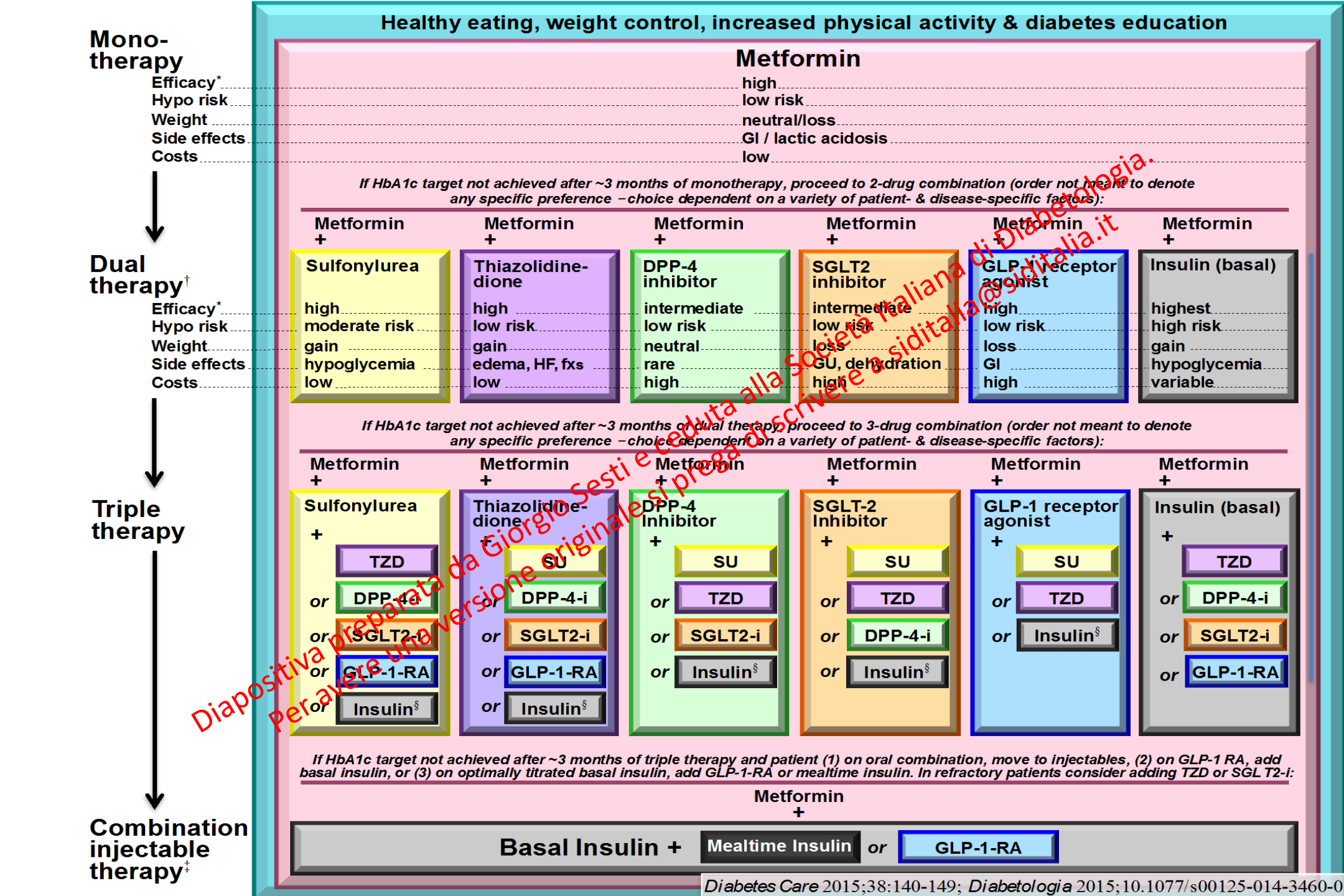
Now it’s time for discussion.

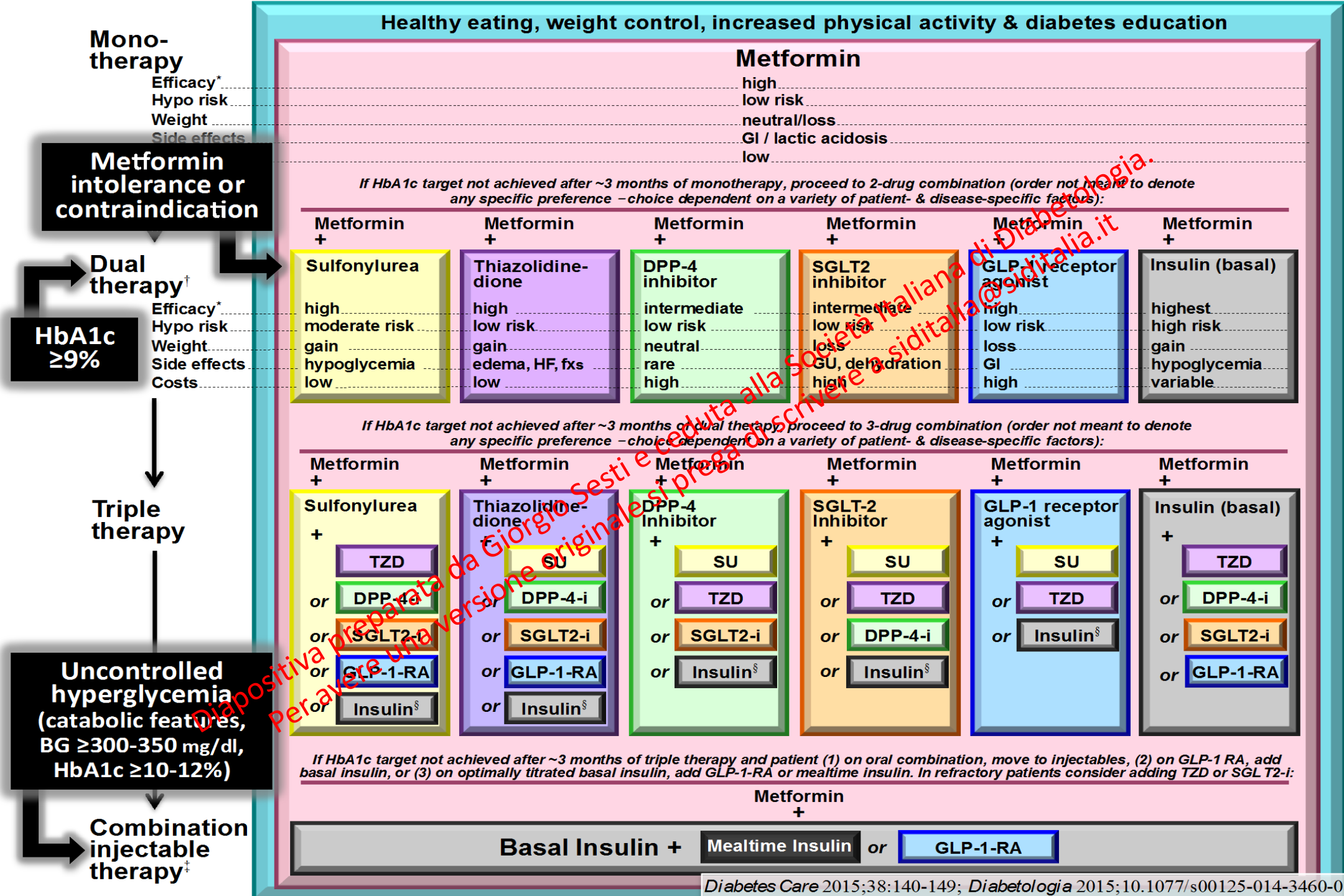


Management of Hyperglycemia in Type 2 Diabetes, 2015: A Patient-Centered Approach

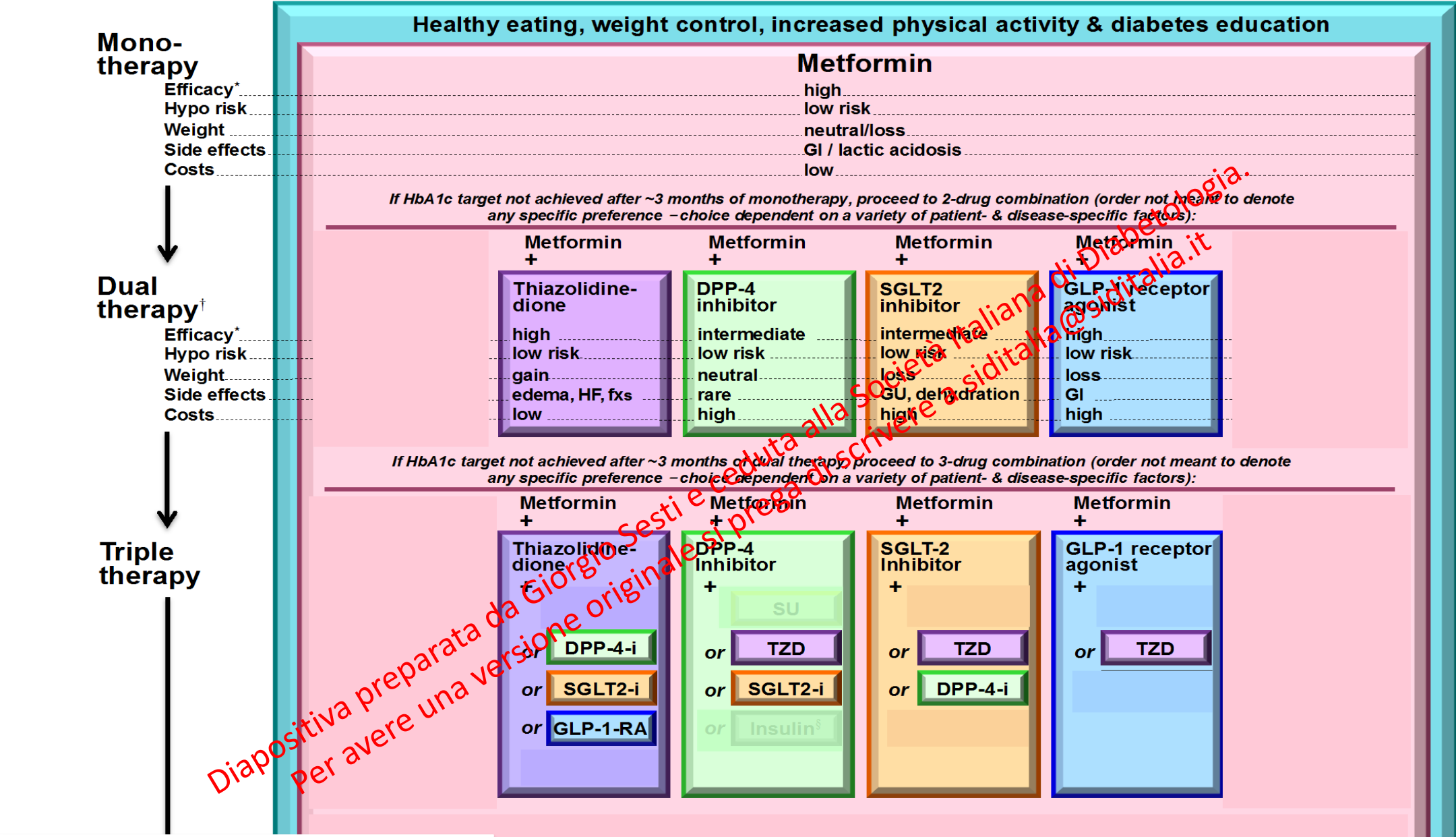
Update to a Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

Diabetes Care 2015;38:140–149
Diabetologia 2015;10.1077/s00125-014-3460-0





Diabetes Care 2015;38:140-149; *Diabetologia* 2015;10.1077/s00125-014-3460-0



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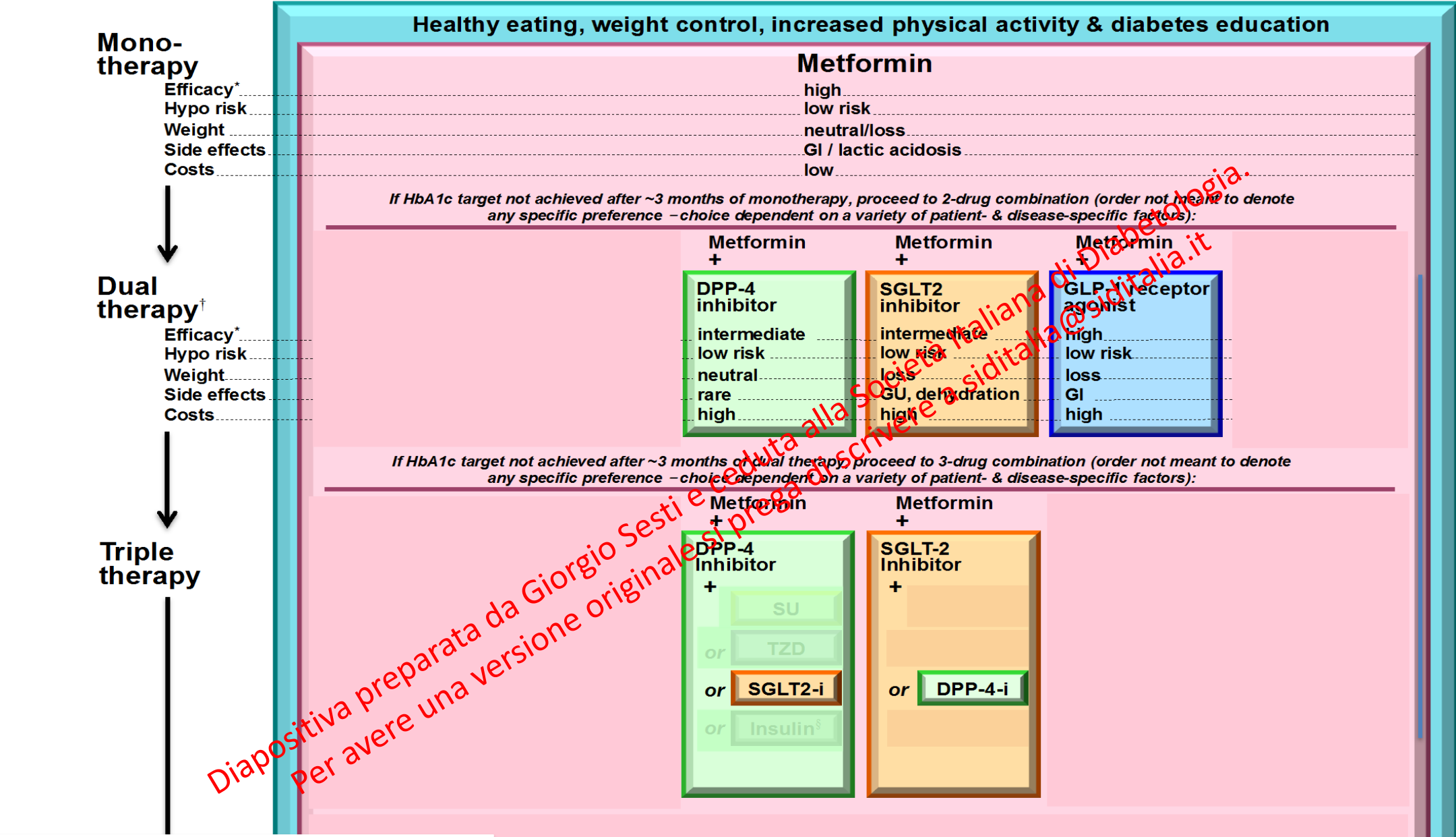

Diabetes Care 2015;38:140-149; *Diabetologia* 2015;10.1077/s00125-014-3460-0