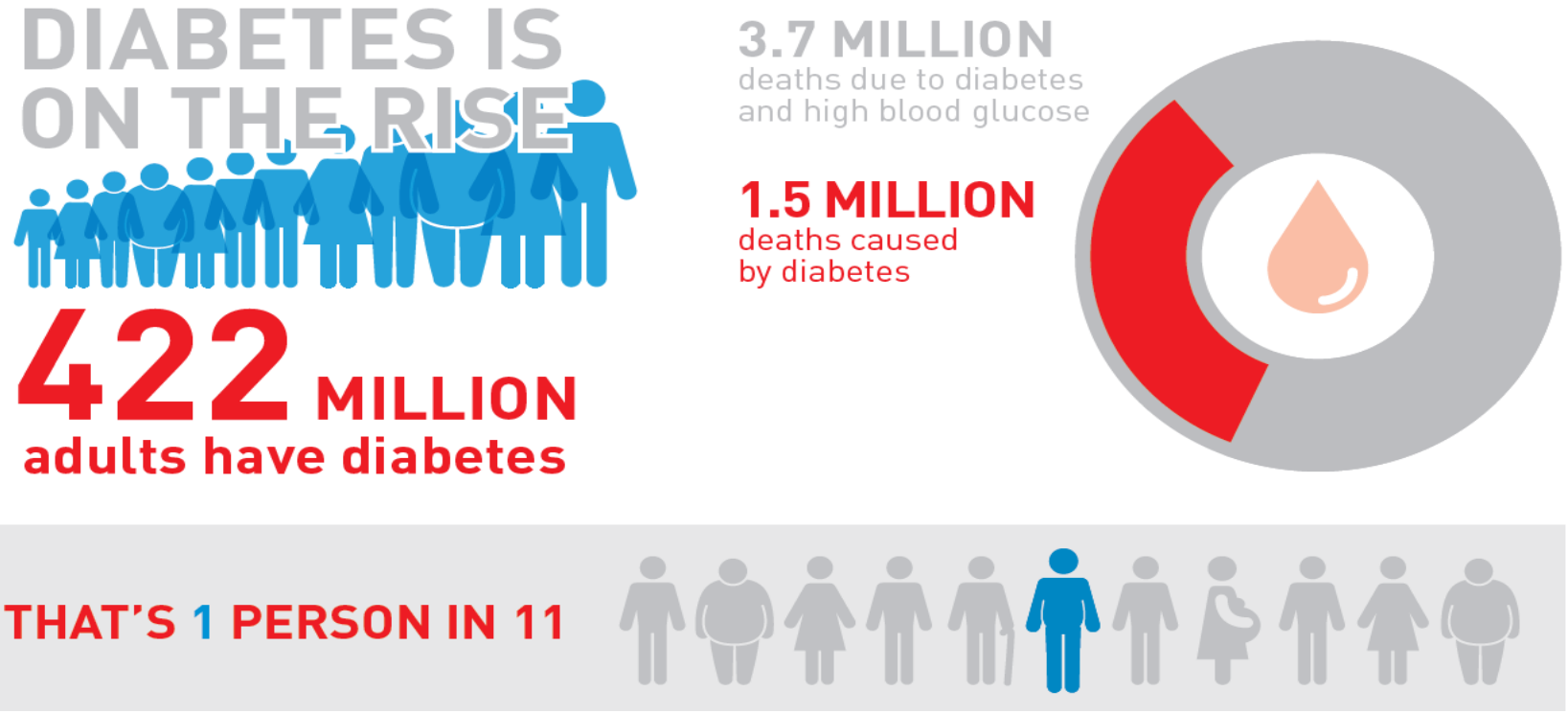
Type 2 Diabetes Management and focus on Multifactorial Intervention

Introduction

- The burden of Type 2 diabetes (T2D) is increasing exponentially in the world with an alarming rise in developing countries.



Available at http://www.who.int/mediacentre/factsheets/fs312/en/ accessed on 20-08-2019

Introduction

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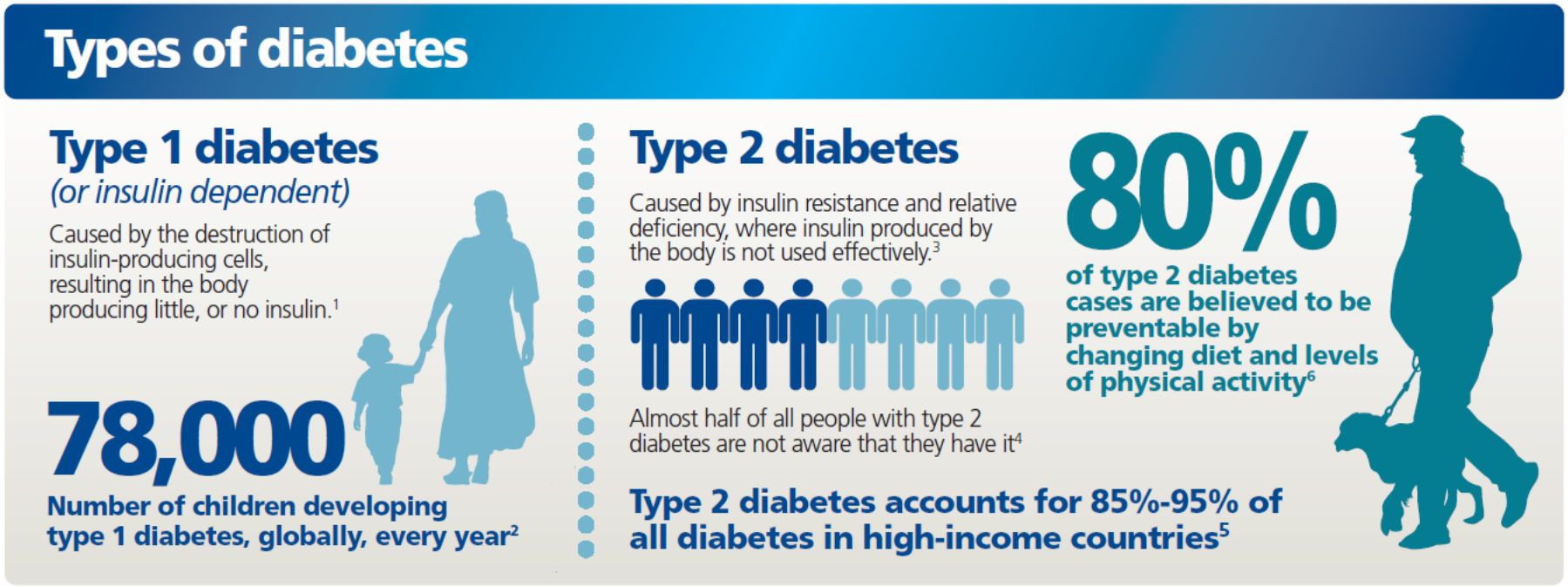
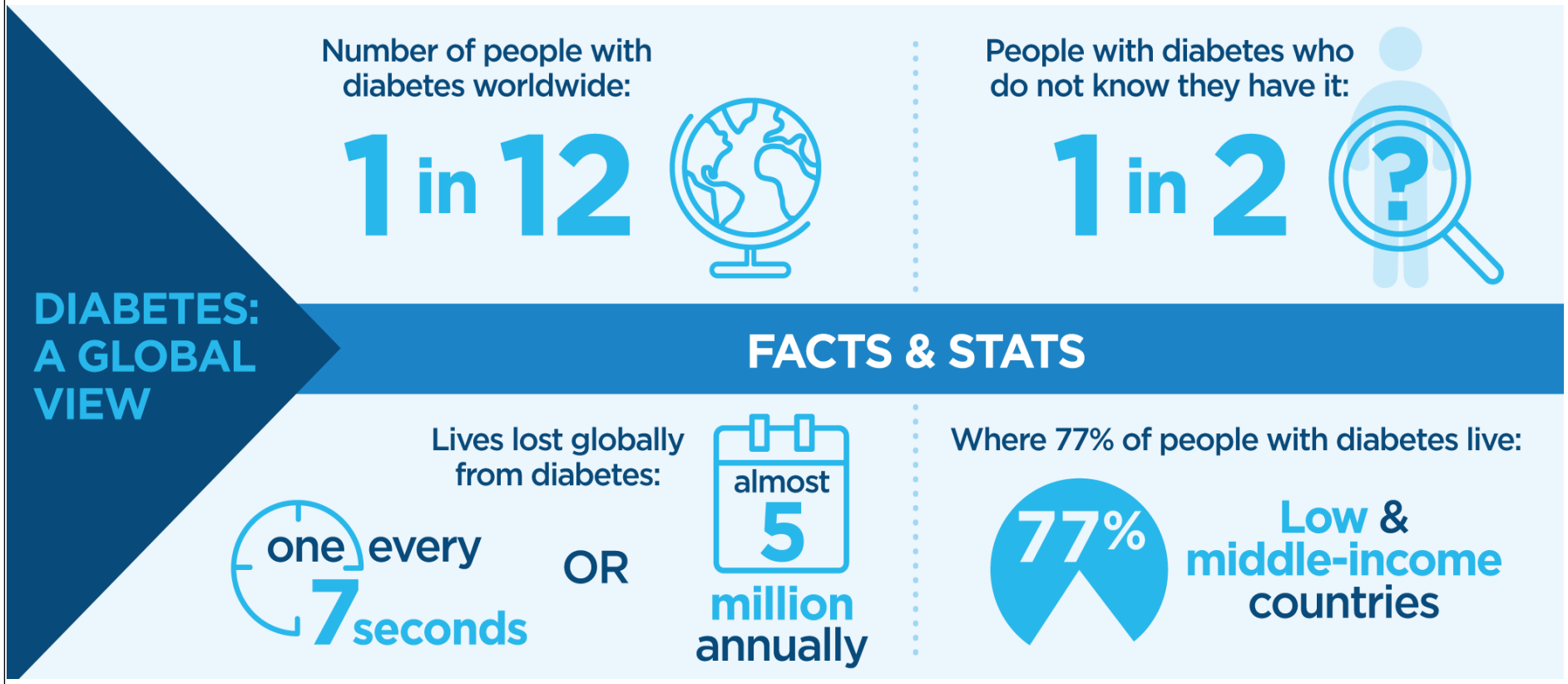


Unnikrishnan R et al. Nat Rev Endocrinol. 2016 Jun;12(6):357-70

Diabetes Burden



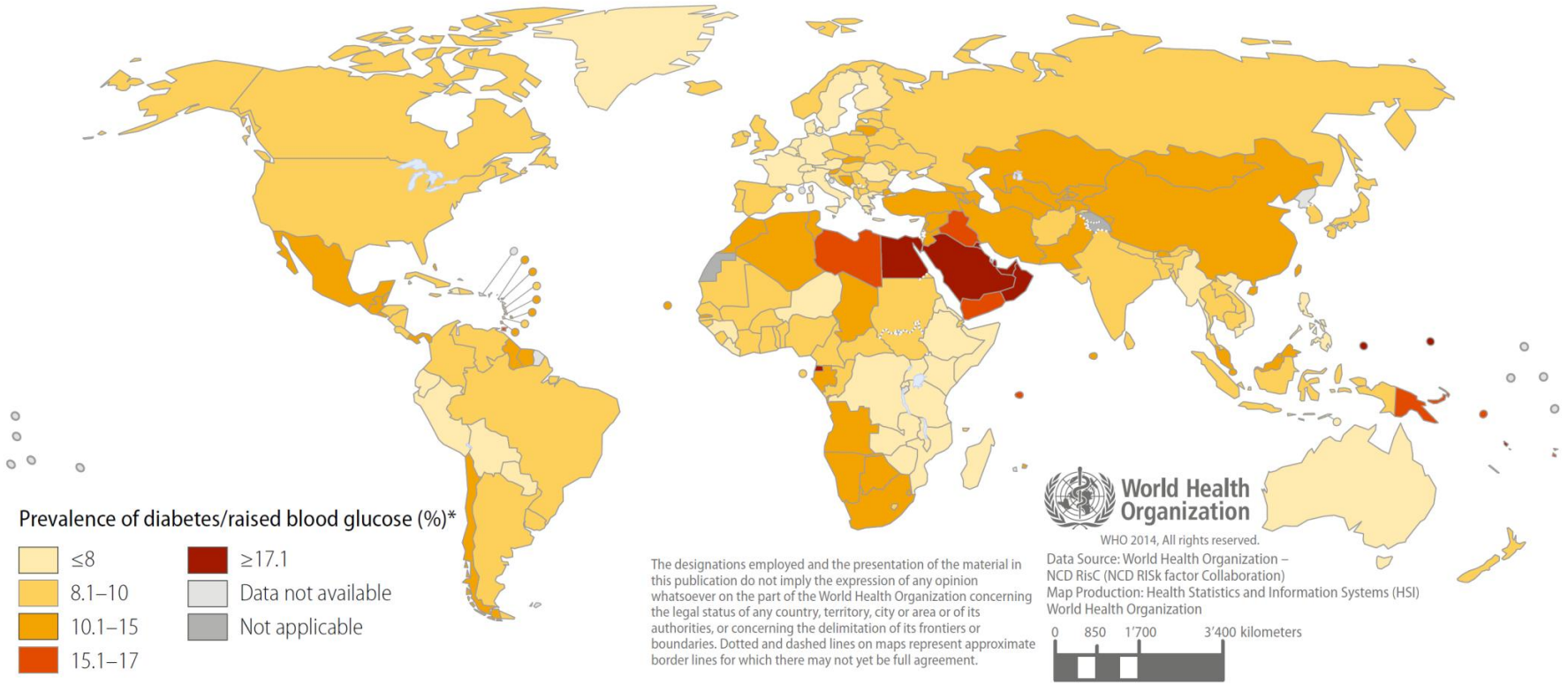
Unnikrishnan R et al. Nat Rev Endocrinol. 2016 Jun;12(6):357-70

Diabetes in India

- India is one of the epicentres of the global diabetes mellitus pandemic.
- India has about 90 million diabetic patients, and the disease leads to the enormous burden on the health care systems of the country
- In 2000, India (31.7 million) topped the world with the highest number of people with diabetes mellitus followed by China (20.8 million) with the United States (17.7 million) in second and third place respectively.

Kumar KH et al. Med J DY Patil Univ 2016;9:195-9

Diabetes in India

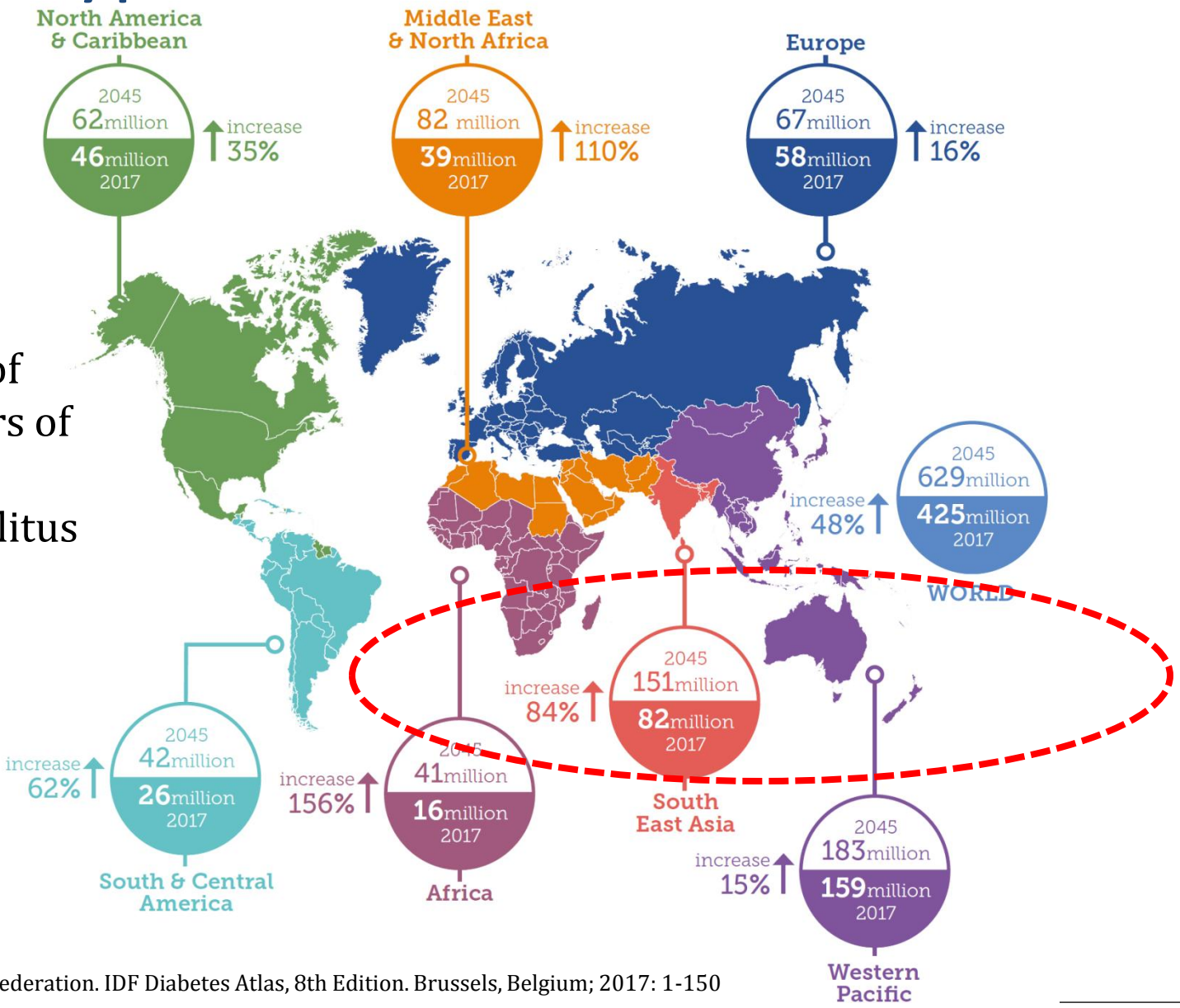


* Defined as fasting blood glucose ≥ 7 mmol/l or on medication for raised blood glucose or with a history of diagnosis of diabetes.

Unnikrishnan R et al. Nat Rev Endocrinol. 2016 Jun;12(6):357-70

Type II Diabetes Mellitus

- India is one of the epicenters of the global diabetes mellitus pandemic.



International Diabetes Federation. IDF Diabetes Atlas, 8th Edition. Brussels, Belgium; 2017: 1-150

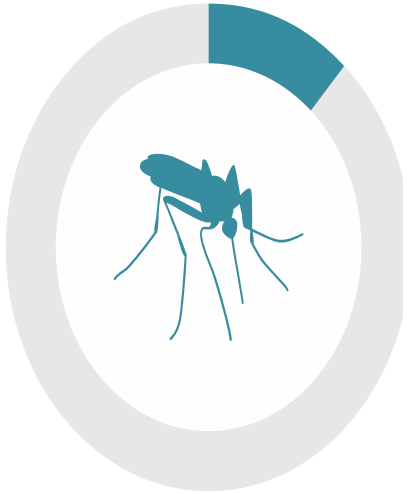
Mortality due to diabetes

Adults who died from diabetes, HIV/AIDS, tuberculosis, and malaria

5.0 million
from diabetes
2015
IDF

1.5 million
from HIV/AIDS
2013
WHO Global Health Observatory Data Repository 2013

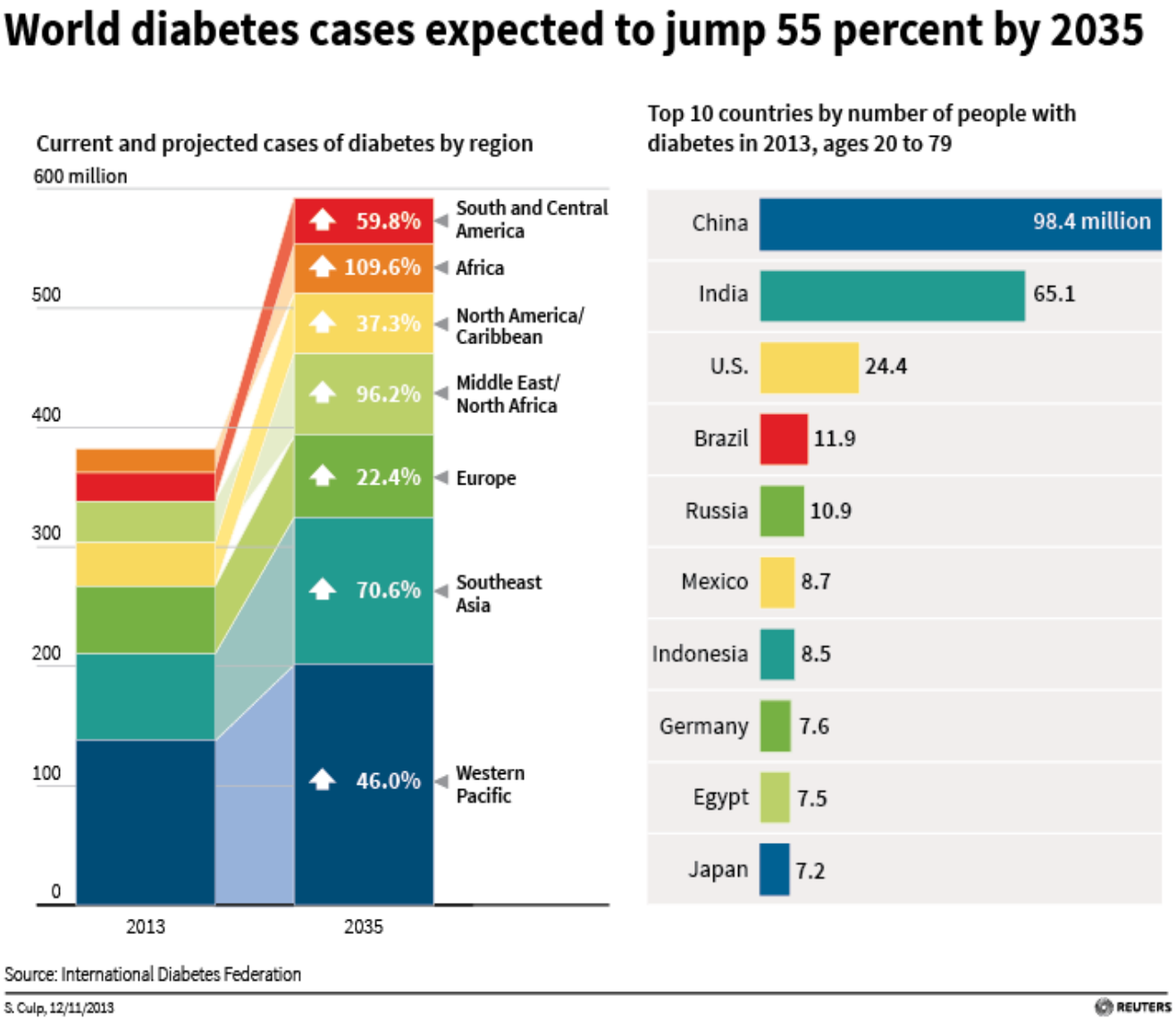
1.5 million
from tuberculosis
2013
WHO Global Health Observatory Data Repository 2013



0.6 million
from malaria
2013
WHO Global Health Observatory Data Repository 2013

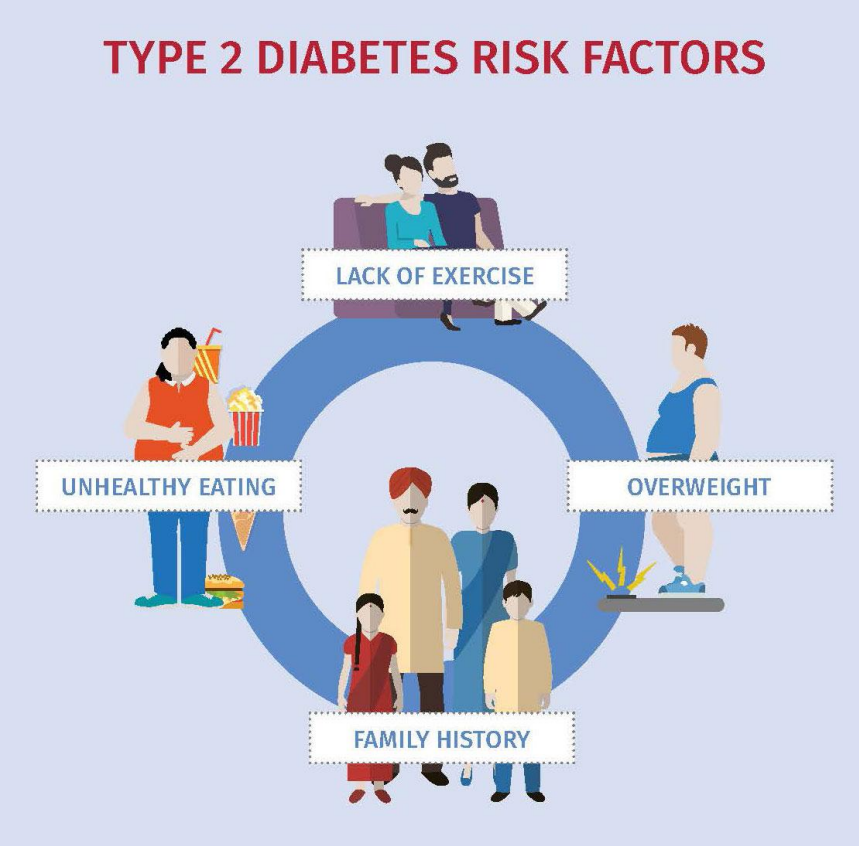
IDF Diabetes Atlas, 2015

Trends in diabetes burden



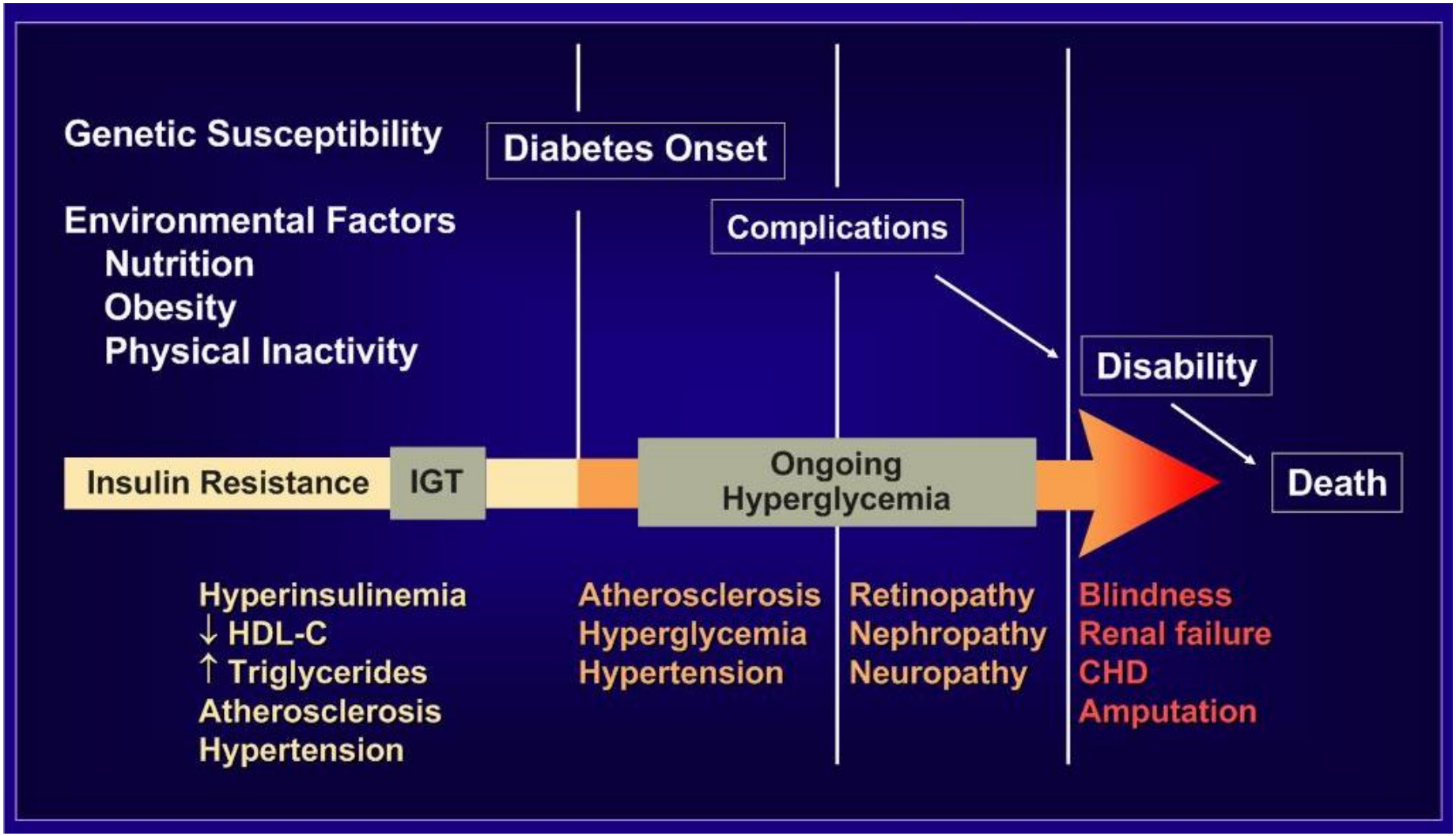
Diabetes: Risk Factors

- Family history of diabetes
- Overweight
- Unhealthy diet
- Physical inactivity
- Increasing age
- High blood pressure
- Ethnicity
- Impaired glucose tolerance
- History of gestational diabetes
- Poor nutrition during pregnancy



IDF Diabetes Atlas, 2015

Complications of Diabetes

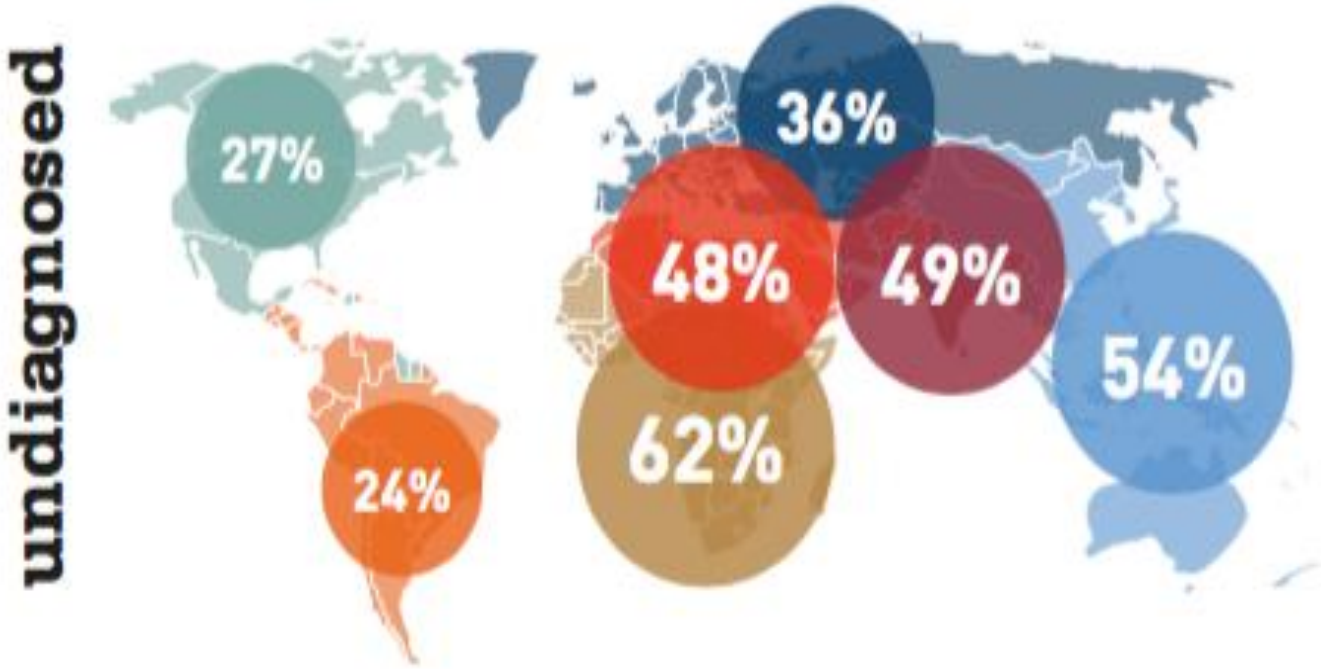


1. http://www.idf.org/membership/sea/india
2. http://www.searo.who.int/india/mediacentre/events/world_health_day/brief_note_on_diabetes_in_india-6april.pdf

Managing Diabetes

The human and economic costs of diabetes could be significantly reduced by investing in prevention, particularly early detection, in order to avoid the onset of diabetic complications

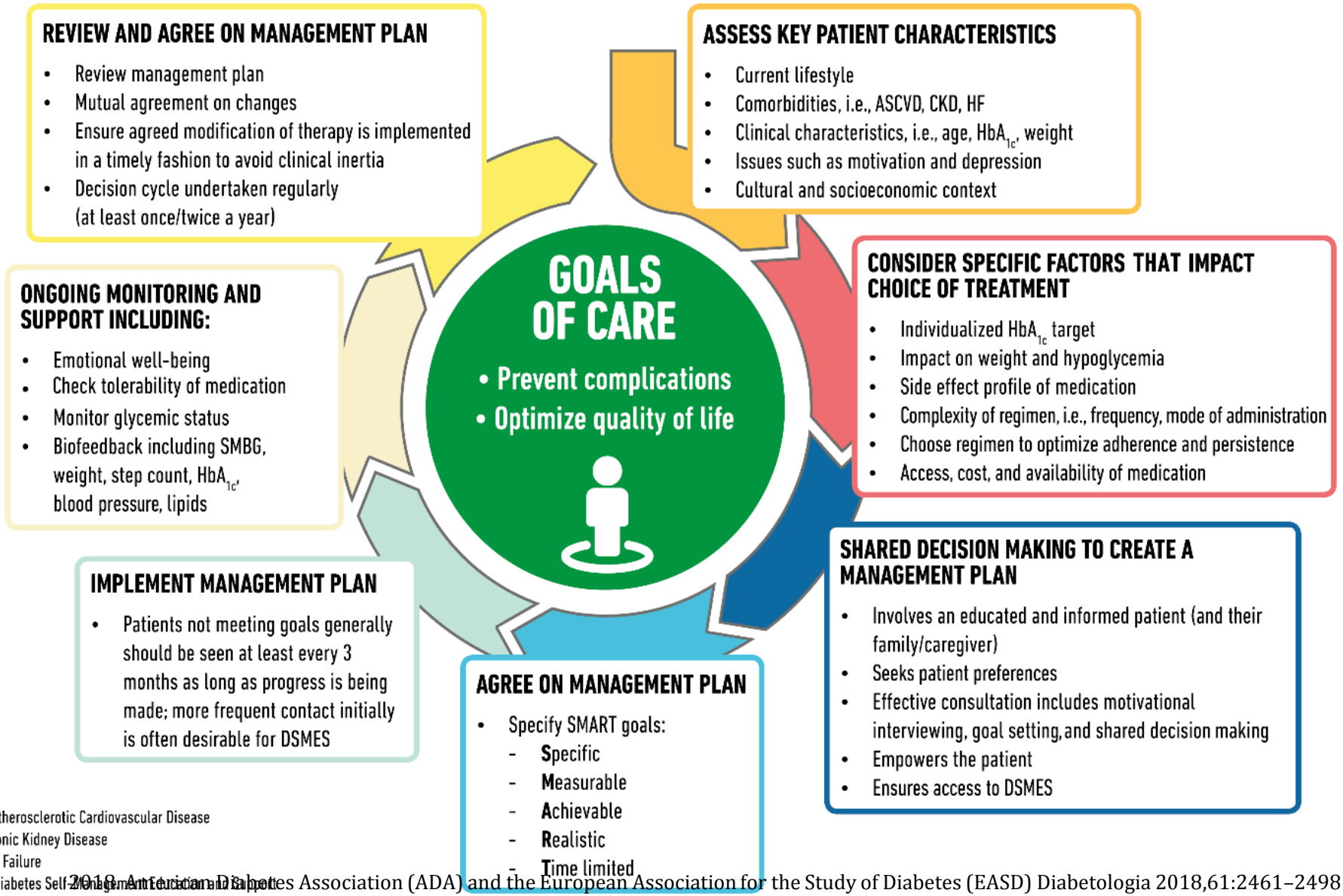
At least 50% of all people with diabetes are unaware of their condition



IDF Diabetes Atlas, 2015

Diabetes Management

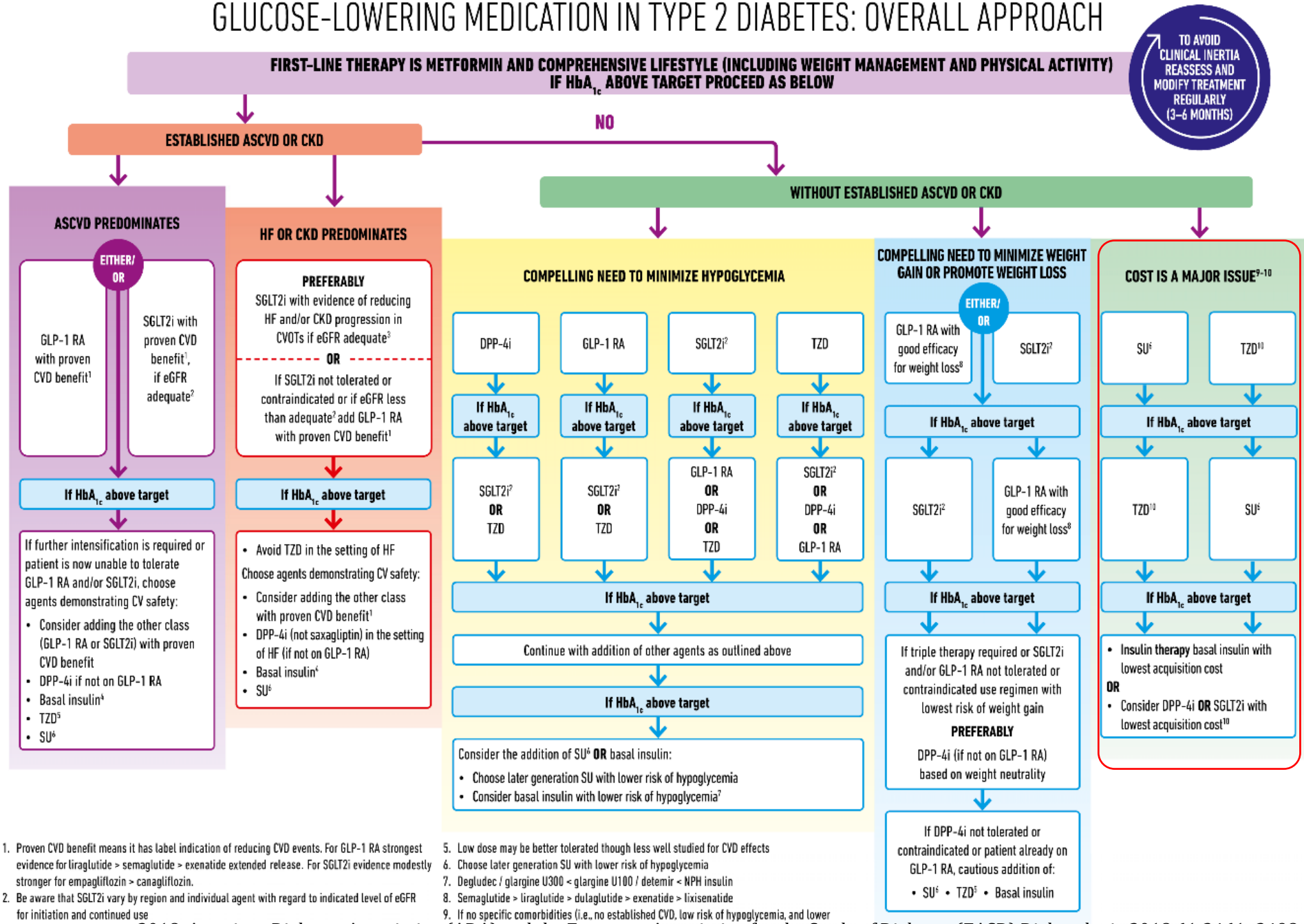
Decision cycle for patient-centered glycemic management in type 2 diabetes



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

2018 American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) Diabetologia 2018,61:2461–2498
Standards Of Medical Care In Diabetes—2019 Diabetes Care. 2019 Jan;42(Suppl 1):S1-S205.

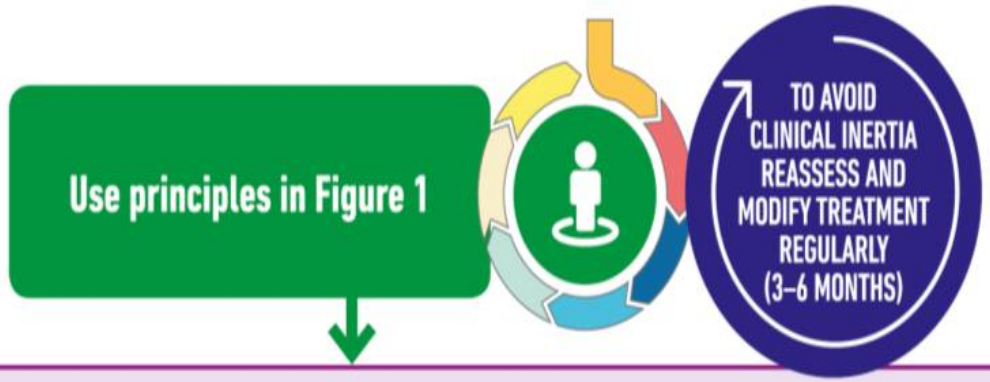
GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH



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 demonstrated reduction in hard CV outcomes and HF 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 body weight are important considerations)
10. Consider country- and region-specific cost of drugs. In some countries, TZDs relatively more expensive and DPP-4i relatively cheaper

2018 American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) Diabetologia 2018,61:2461–2498
Standards Of Medical Care In Diabetes—2019 Diabetes Care. 2019 Jan;42(Suppl 1):S1-S205.

CHOOSING GLUCOSE-LOWERING MEDICATION IN THOSE WITH ESTABLISHED ATHEROSCLEROTIC CARDIOVASCULAR DISEASE (ASCVD) OR CHRONIC KIDNEY DISEASE (CKD)



Use metformin unless contraindicated or not tolerated

If not at HbA_{1c} target:

- Continue metformin unless contraindicated (remember to adjust dose/stop metformin with declining eGFR)
- Add SGLT2i or GLP-1 RA with proven cardiovascular benefit[1] (see below)

If at HbA_{1c} target:

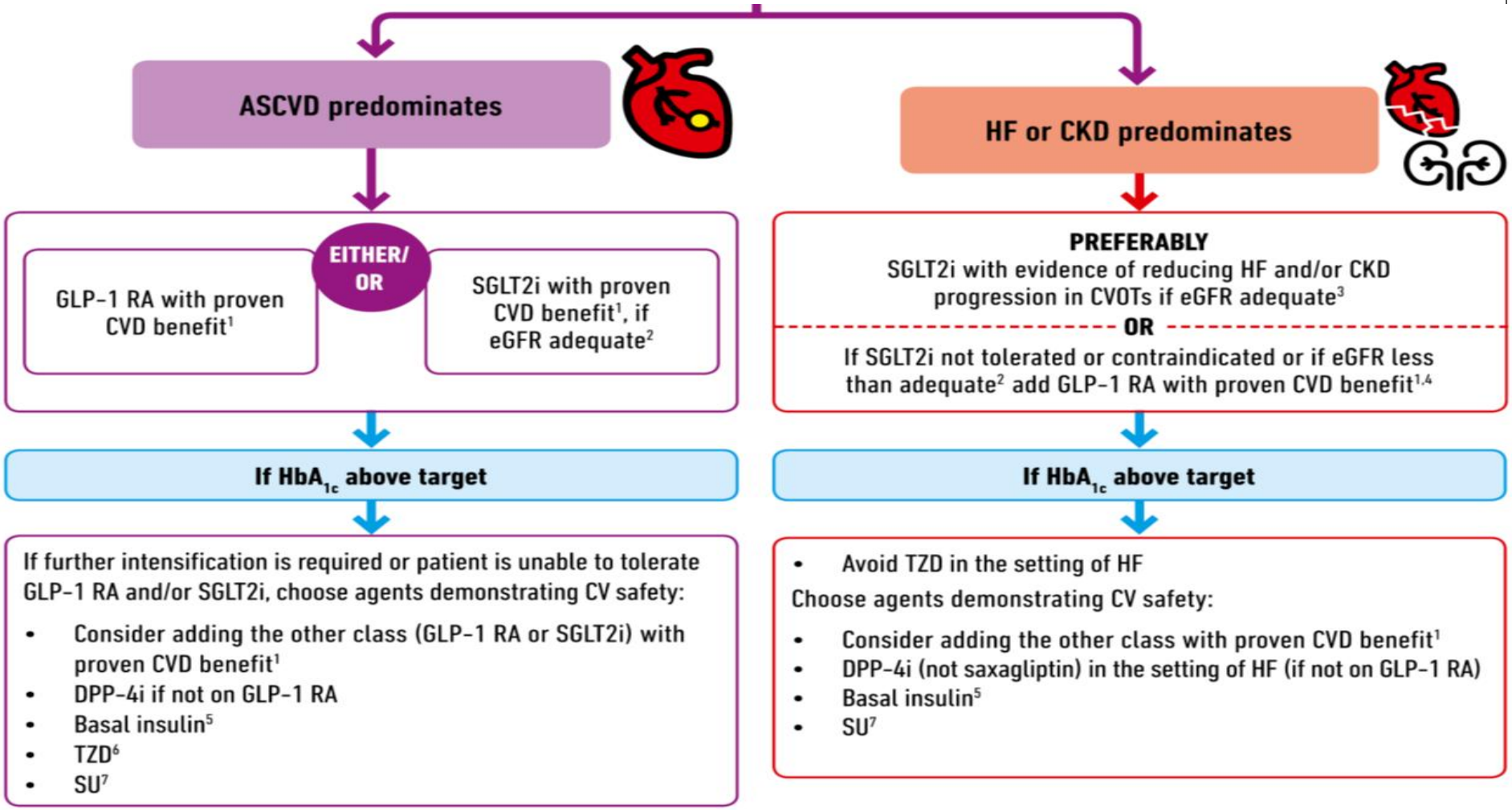
- If already on dual therapy, or multiple glucose-lowering therapies and not on an SGLT2i or GLP-1 RA, consider switching to one of these agents with proven cardiovascular benefit[1] (see below)

OR reconsider/lower individualized target and introduce SGLT2i or GLP-1 RA

OR reassess HbA_{1c} at 3-month intervals and add SGLT2i or GLP-1 RA if HbA_{1c} goes above target

2018. American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) Diabetologia 2018,61:2461–2498
Standards Of Medical Care In Diabetes—2019 Diabetes Care. 2019 Jan;42(Suppl 1):S1-S205.

Choosing glucose-lowering medication in those with established ASCVD, HF, and CKD



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4. Caution with GLP-1 RA in ESRD
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CHOOSING GLUCOSE-LOWERING MEDICATION IF COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

In those WITHOUT established ASCVD OR CKD

Use principles in Figure 1

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

First-line therapy is metformin

If HbA_{1c} is ≥17 mmol/mol (1.5%) above individualized HbA_{1c} target consider early combination therapy

If HbA_{1c} above target

EITHER/ OR

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

SGLT2i if eGFR adequate[2]

If HbA_{1c} above target

SGLT2i if eGFR adequate[2]

GLP-1 RA with good efficacy for weight loss

Implement strategies for maximizing weight loss

General lifestyle advice
- Medical nutritional therapy
- Eating patterns
- Physical activity

Non-surgical energy restriction for weight loss

Weight loss of 15 kg can lead to remission of T2DM in patient <6 years' duration, **consider evidence-based weight loss programs**

Consider medication for weight loss

Consider metabolic surgery

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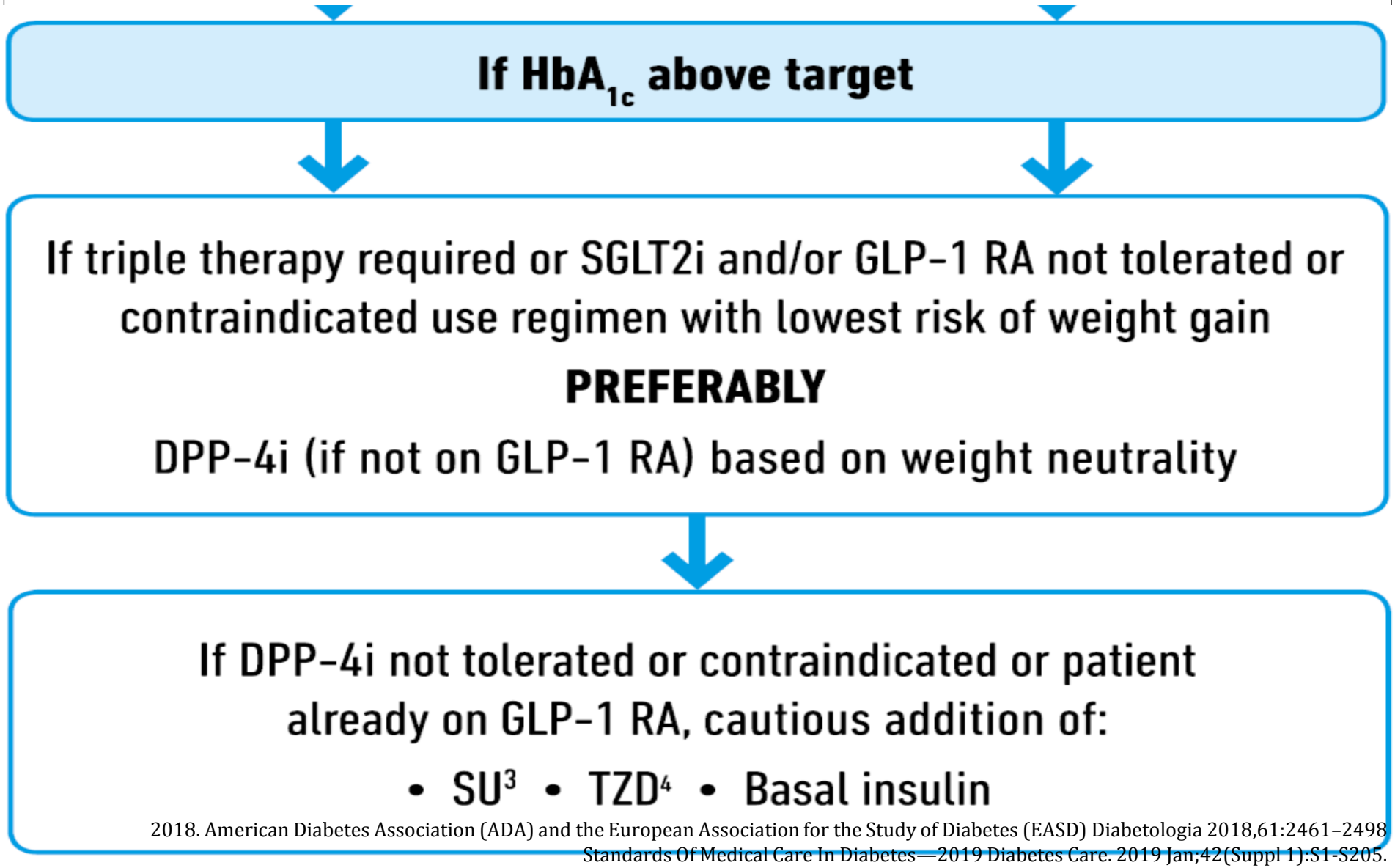
Choosing glucose-lowering medication if compelling need to minimize weight gain or promote weight loss



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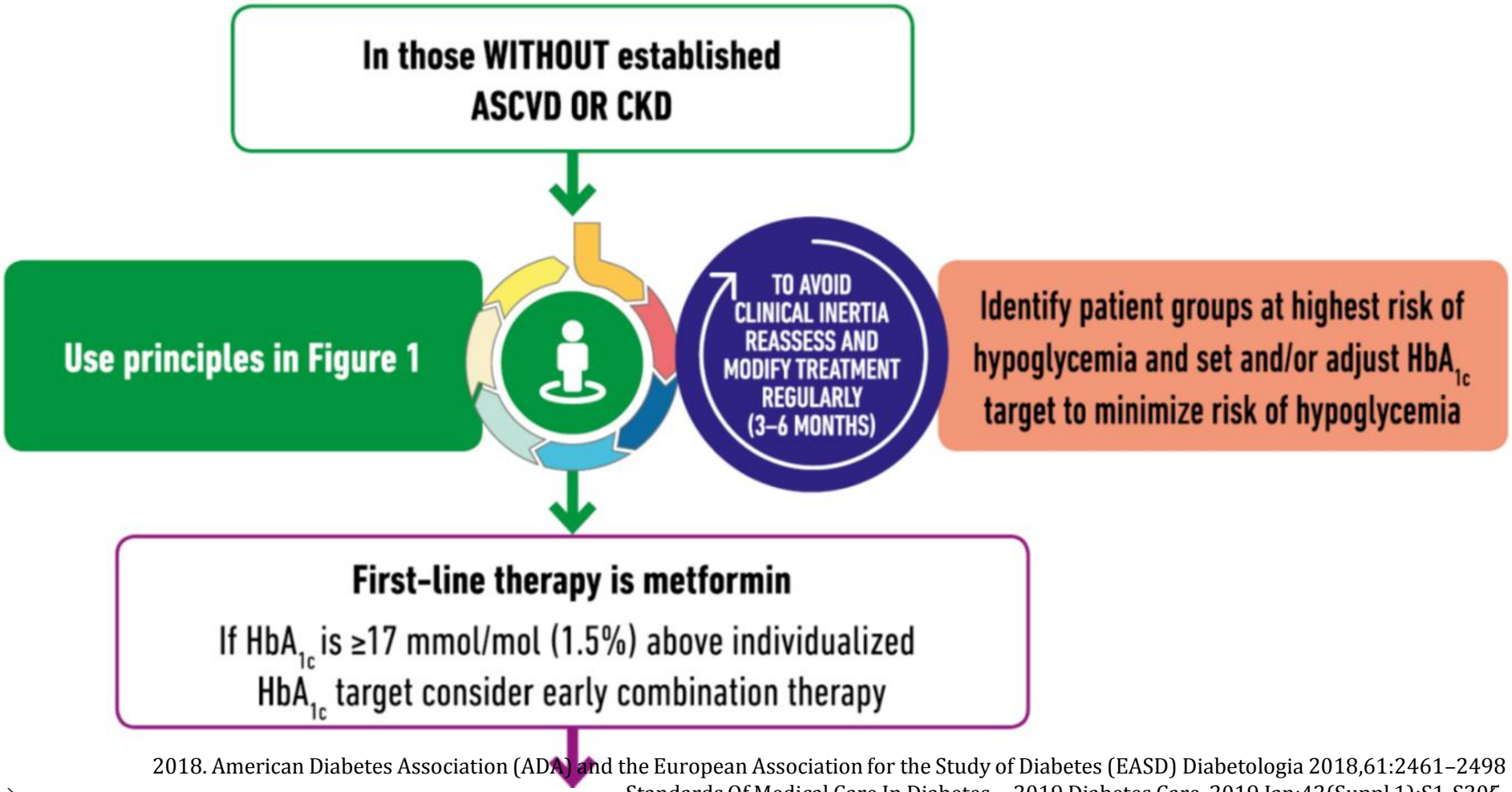
CHOOSING GLUCOSE-LOWERING MEDICATION IF COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA



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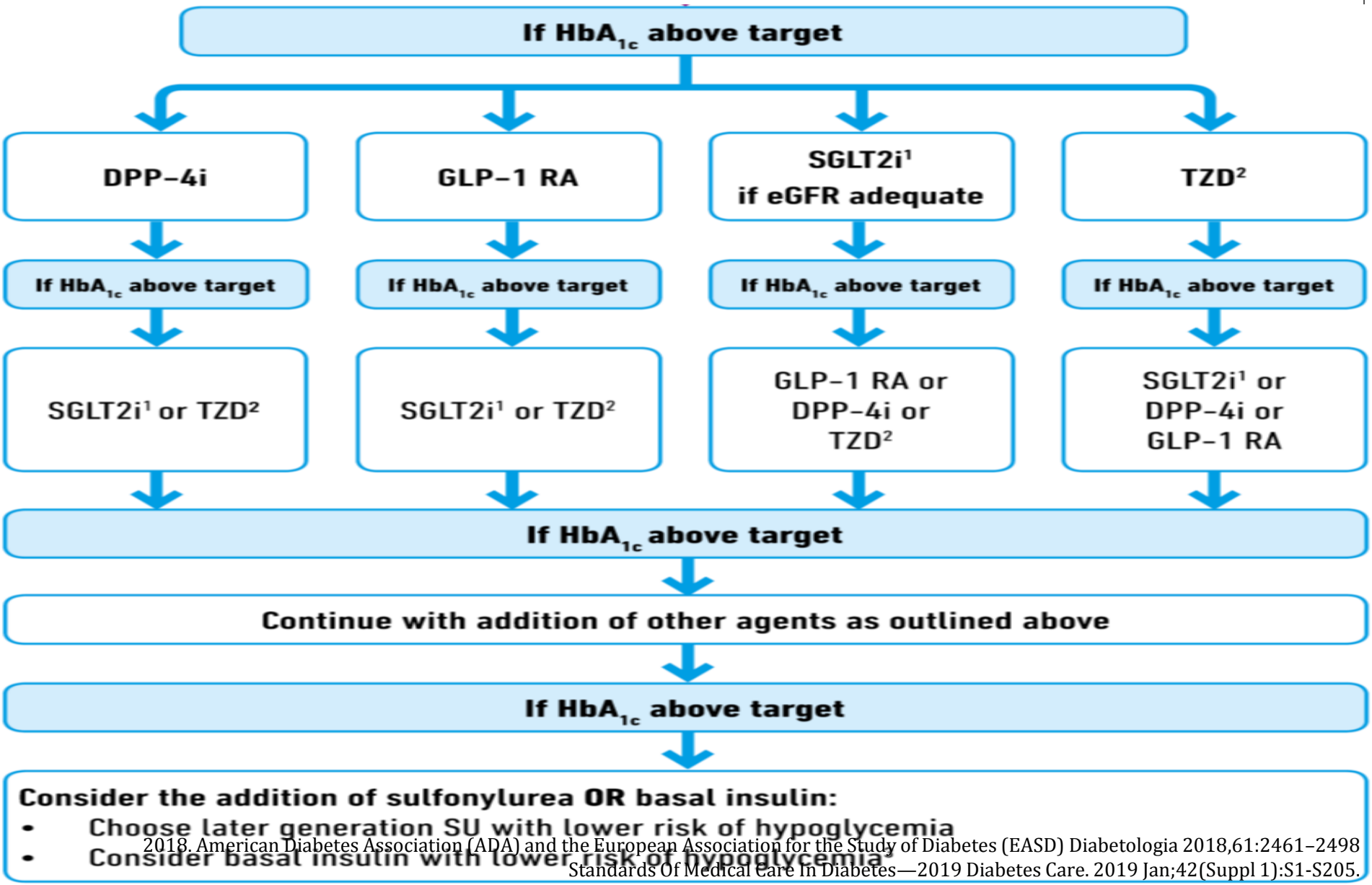

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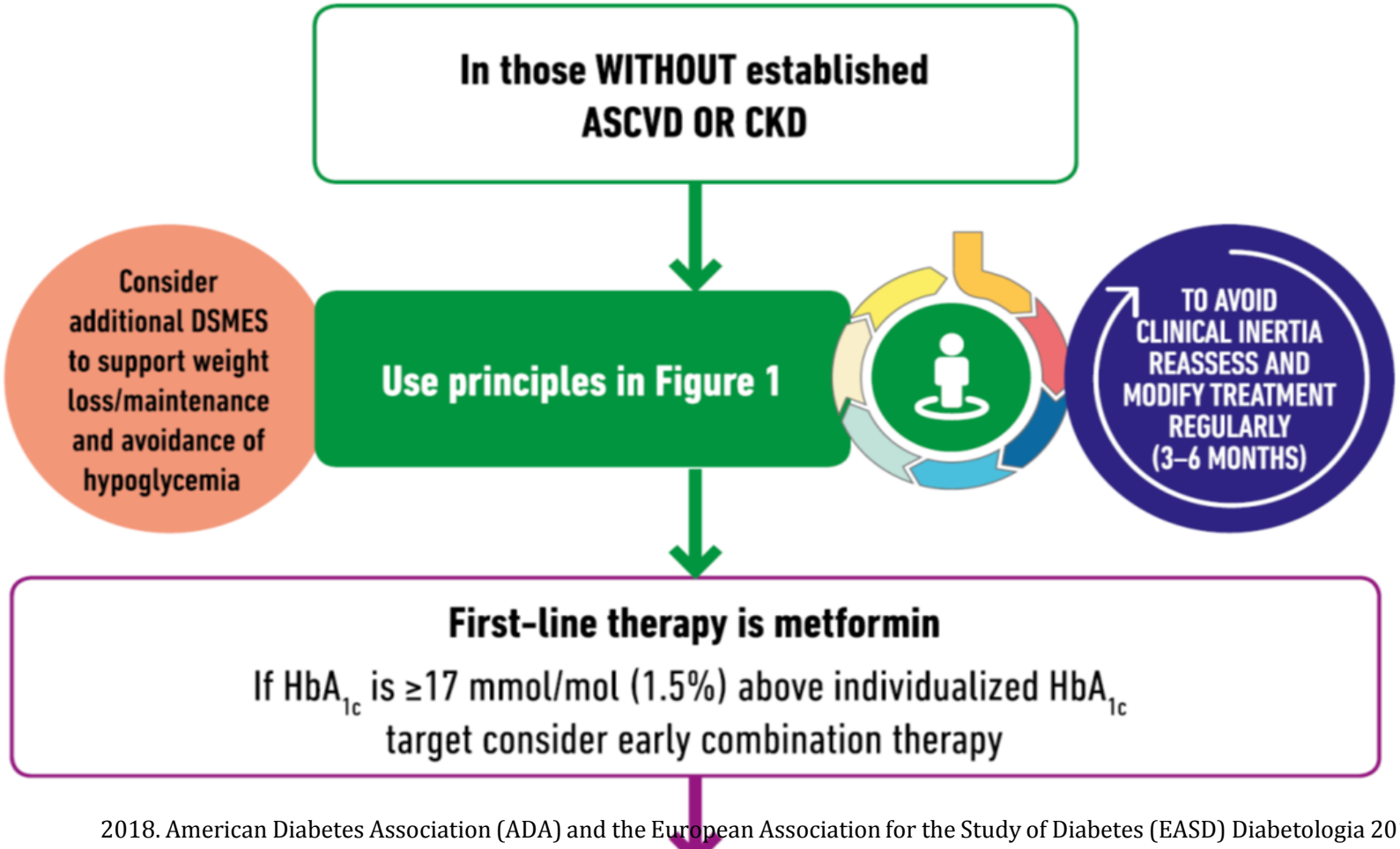
CHOOSING GLUCOSE-LOWERING MEDICATION IF COST IS A MAJOR ISSUE



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Multifactorial Intervention

- Type 2 diabetes mellitus is associated with a high rate of complications related to cardiovascular disease and diabetic nephropathy, retinopathy, and neuropathy

- The rate of death among patients with type 2 diabetes is approximately twice as high as that among persons without the disorder

- However, trials of interventions for single risk factors have shown efficacy in reducing the development and progression of complications

Gaede P et al. Diabetologia. 2016 Nov;59(11):2298-2307

Results from UKPDS Study

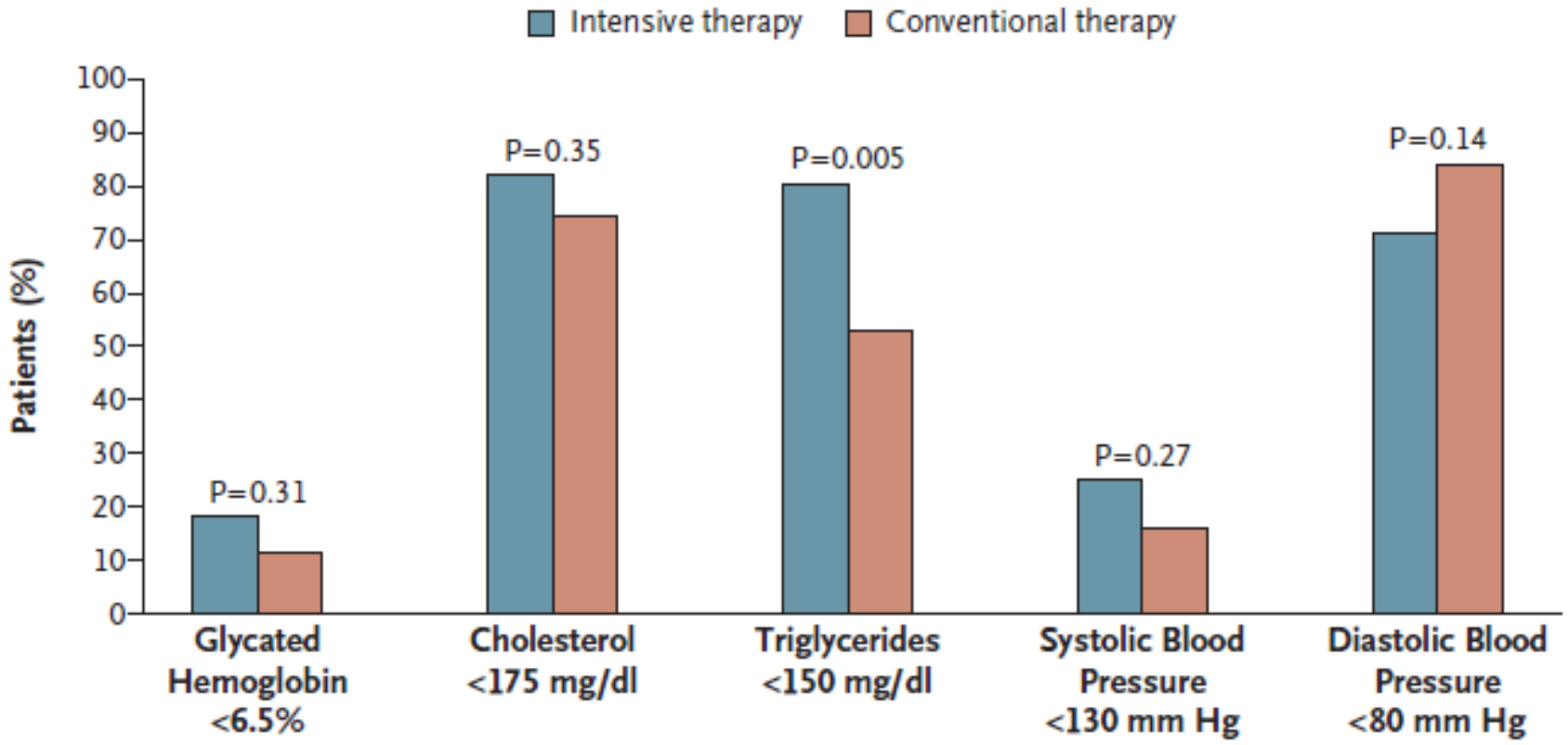
UK Prospective Diabetes Study assessed the association between micro and macro vascular complications and glycemia in 4585 white, Asian Indian, and Afro-Caribbean patients from 23 hospital based clinics

Each 1% decrease in updated mean HbA_{1c} causes

- 21% reduction in any end point related to diabetes ($p<0.0001$),
- 21% reduction in deaths related to diabetes ($p<0.0001$)
- 14% reduction in myocardial infarction ($p< 0.0001$)
- 37% reduction in microvascular complications ($p<0.0001$)

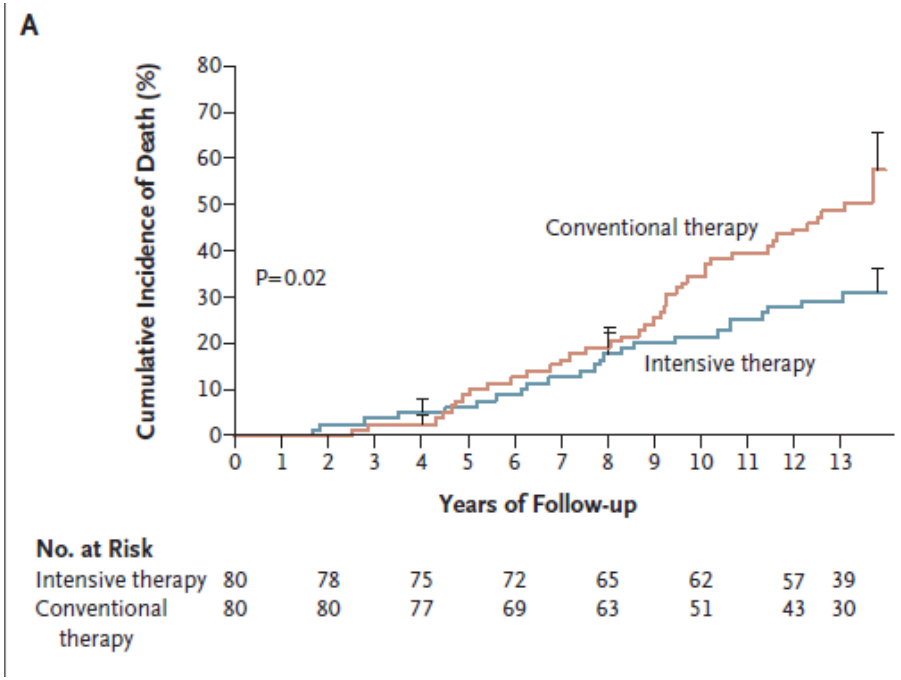
1. Stratton IM, *et al*. *BMJ.* 2000;321:405–12.

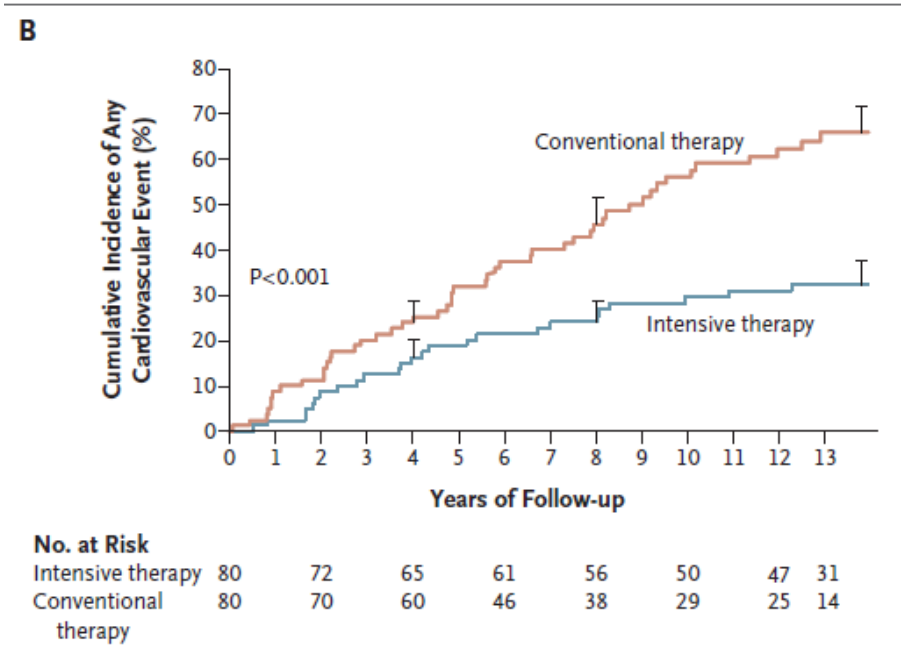
Multifactorial Intervention and Cardiovascular Disease in Patients with Type 2 Diabetes



Gaede P et al. N Engl J Med. 2003 Jan 30;348(5):383-93.

Multifactorial Intervention and Cardiovascular Disease in Patients with Type 2 Diabetes



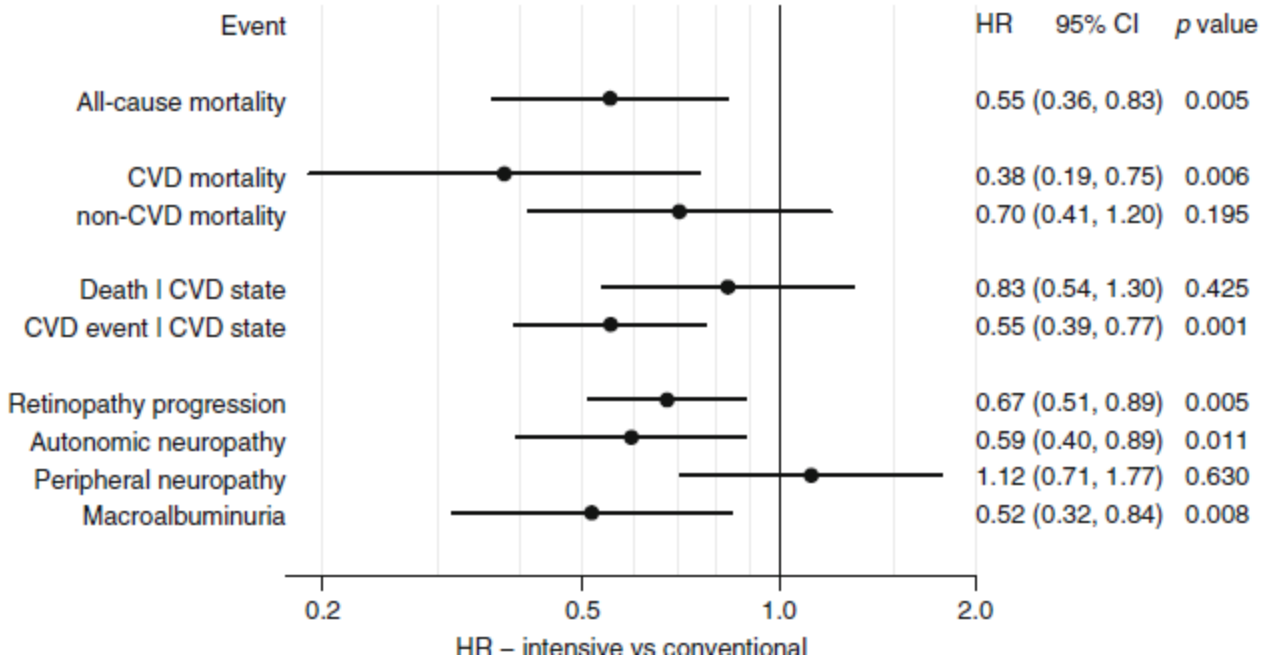


Kaplan–Meier Estimates of the Risk of Death from Any Cause and from Cardiovascular Causes and the Number of Cardiovascular Events, According to Treatment Group.

Gaede P et al. N Engl J Med. 2003 Jan 30;348(5):383-93.

21 years follow-up on the Steno-2 trial

- Forest plot of the HR (95% CI) for secondary and tertiary endpoints.
- Significant risk reductions for all-cause mortality, CVD mortality, CVD events and progression of retinopathy, autonomic neuropathy and macroalbuminuria in intensive group



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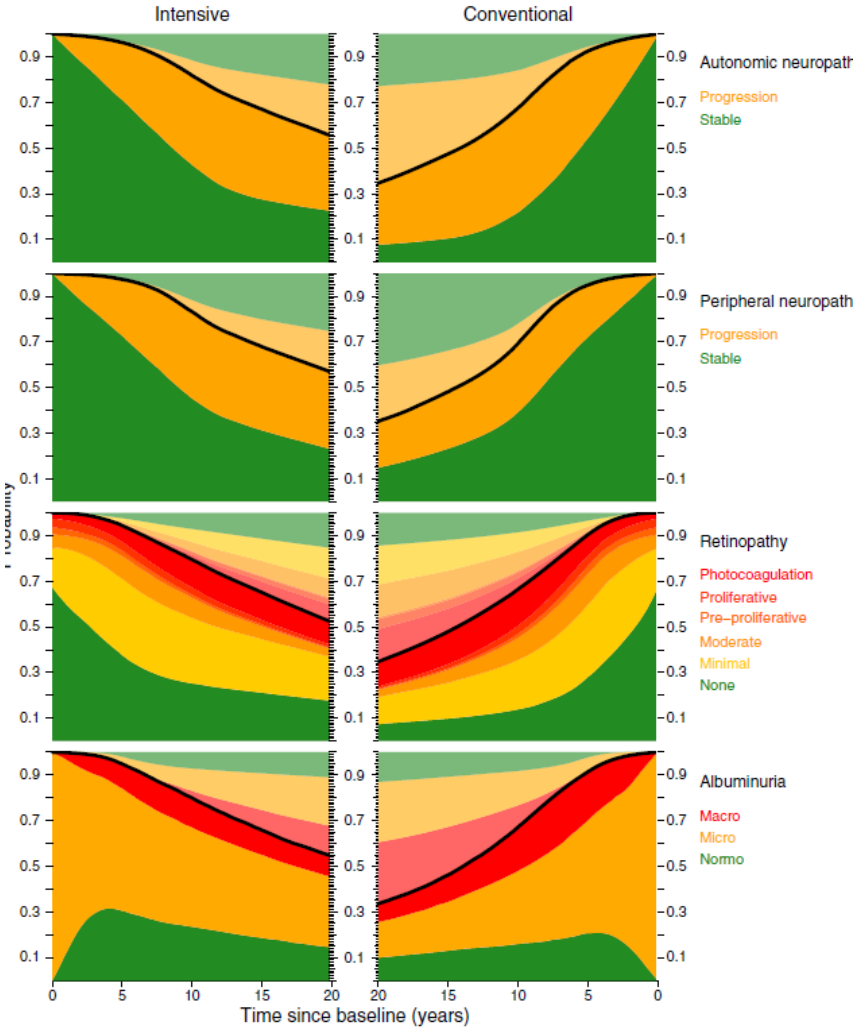
21 years follow-up on the Steno-2 trial

Progression of microvascular complications

- Progression of retinopathy was decreased by 33% in the intensive-therapy group.
- Blindness in at least one eye was reduced in the intensive-therapy group with an HR of 0.47 (95% CI 0.23, 0.98, p =0.044).
- Autonomic neuropathy was decreased by 41% in the intensive-therapy group.
- Progression to diabetic nephropathy (macroalbuminuria) was reduced by 48% in the intensive-therapy group



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Conclusion

- Preventing diabetes is of enormous value for any nation particularly in the developing world because of the high cost of treating diabetes and its complication.

- The need of the hour is to develop pragmatic, cost effective strategies for primary prevention to extend the benefits to the population at large.

- The significance of early, intensified risk factor control in patients with complicated type 2 diabetes to be emphasized.

Thank You