

How does diabetes affect my patient's heart?


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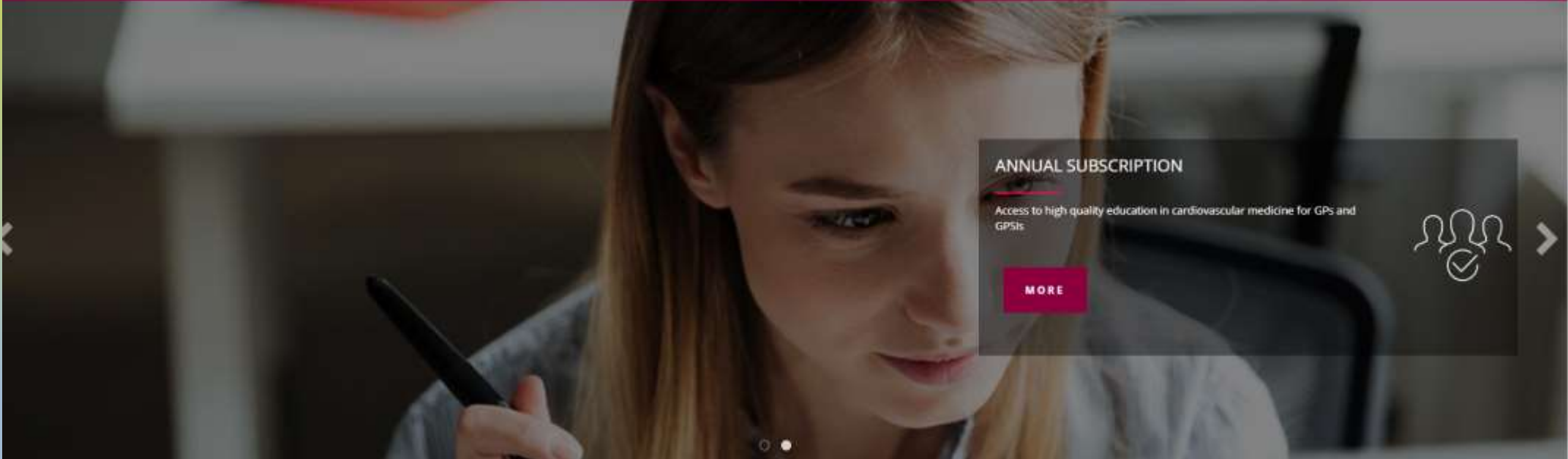


Primary Care
Cardiovascular
Society

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REGISTER/LOGIN


Driving primary care to deliver the best in cardiovascular health



ANNUAL SUBSCRIPTION

Access to high quality education in cardiovascular medicine for GPs and GPsIs

MORE



ANNUAL SUBSCRIPTION

GPs - £50
Pharmacists, GP Registrars and Nurses - £25

PCCS OBJECTIVES

- » Represent primary care cardiovascular health needs at policy level
- » Promote best practice in primary care cardiovascular health through education, training and service development
- » Support the development of primary health care professionals in cardiovascular medicine
- » Facilitate and lead primary care cardiovascular research
- » Influence commissioners for the next decade (or longer)

How to register for Membership

Annual Subscription

GPs £40

Pharmacists, GP Registrars and Nurses £20

How to Register

To register for membership please follow this link

<http://pccs.lcwmed.co.uk>

Or call 01444 414264

Or email registrations@LCWmed.co.uk

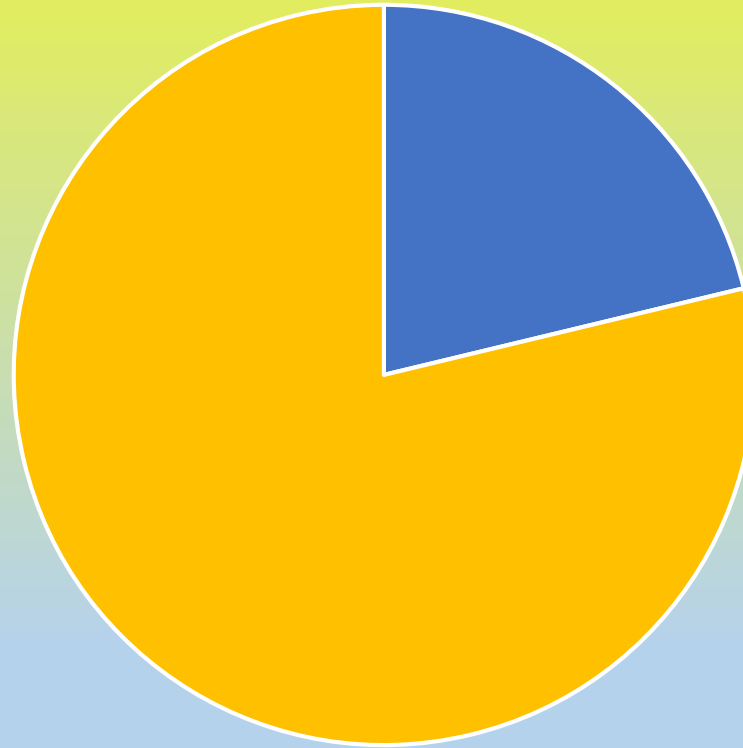
Aims



By the end of this session you will be able to

- i) evaluate the impact of diabetes and heart health
- ii) recognise lifestyle interventions which can improve cardiovascular outcomes and
- iii) consider the impact that drug therapies can have on heart health, beyond glycaemic control.

The real of the cost of diabetes



†

‡

Excess mortality in Type 2 Diabetes is largely related to Cardiovascular Disease¹



Around **one third** of people with T2D also have CV disease²



CV disease is responsible for approximately **half of all deaths** in people with T2D², with many of these deaths premature³



CV disease can occur **10–15 years earlier** in patients with diabetes compared with those without diabetes^{4,5}



Diabetes accelerates the time to the first CV event^{6*}

*Time to first myocardial infarction event or first heart failure hospitalisation. CV = cardiovascular; T2D = type 2 diabetes.

1. Tancredi M, et al. *N Engl J Med* 2015;373:1720–1732; 2. Einarson TR, et al. *Cardiovasc Diabetol* 2018;17:83; 3. Fisher M, Shaw KM. *Pract Diab Int* 2001;18:183–184; 4. Malmberg K, et al. *Circulation* 2000;102:1014–1019; 5. Booth GL, et al. *Lancet* 2006;368:29–36; 6. McMurray JJV, et al. *Lancet Diabetes Endocrinol* 2014;2:843–851.

What happens?

Macrovascular disease

Transient ischaemic attack
Stroke

Angina
Myocardial infarction
Cardiac failure

Peripheral
vascular
disease

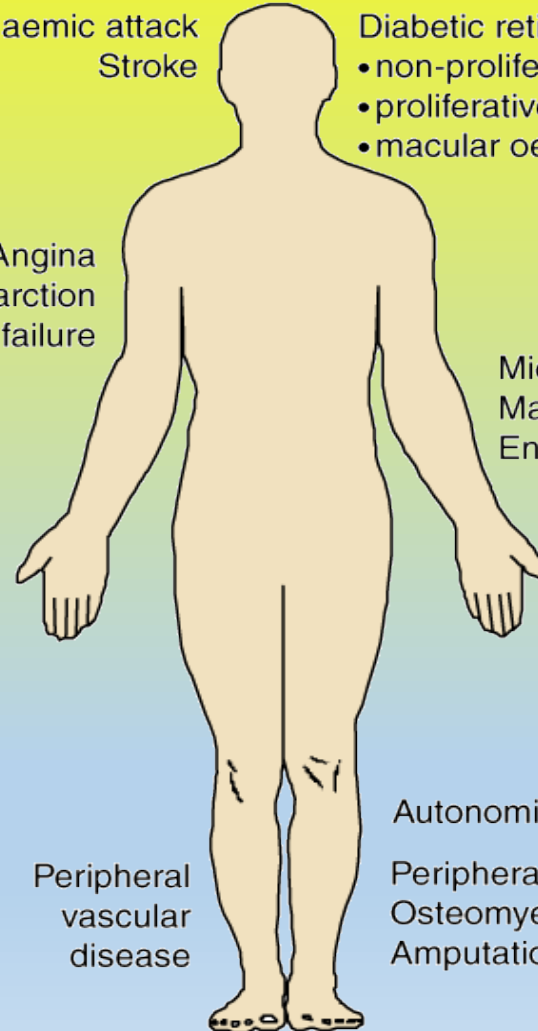
Microvascular disease

Diabetic retinopathy
• non-proliferative
• proliferative
• macular oedema

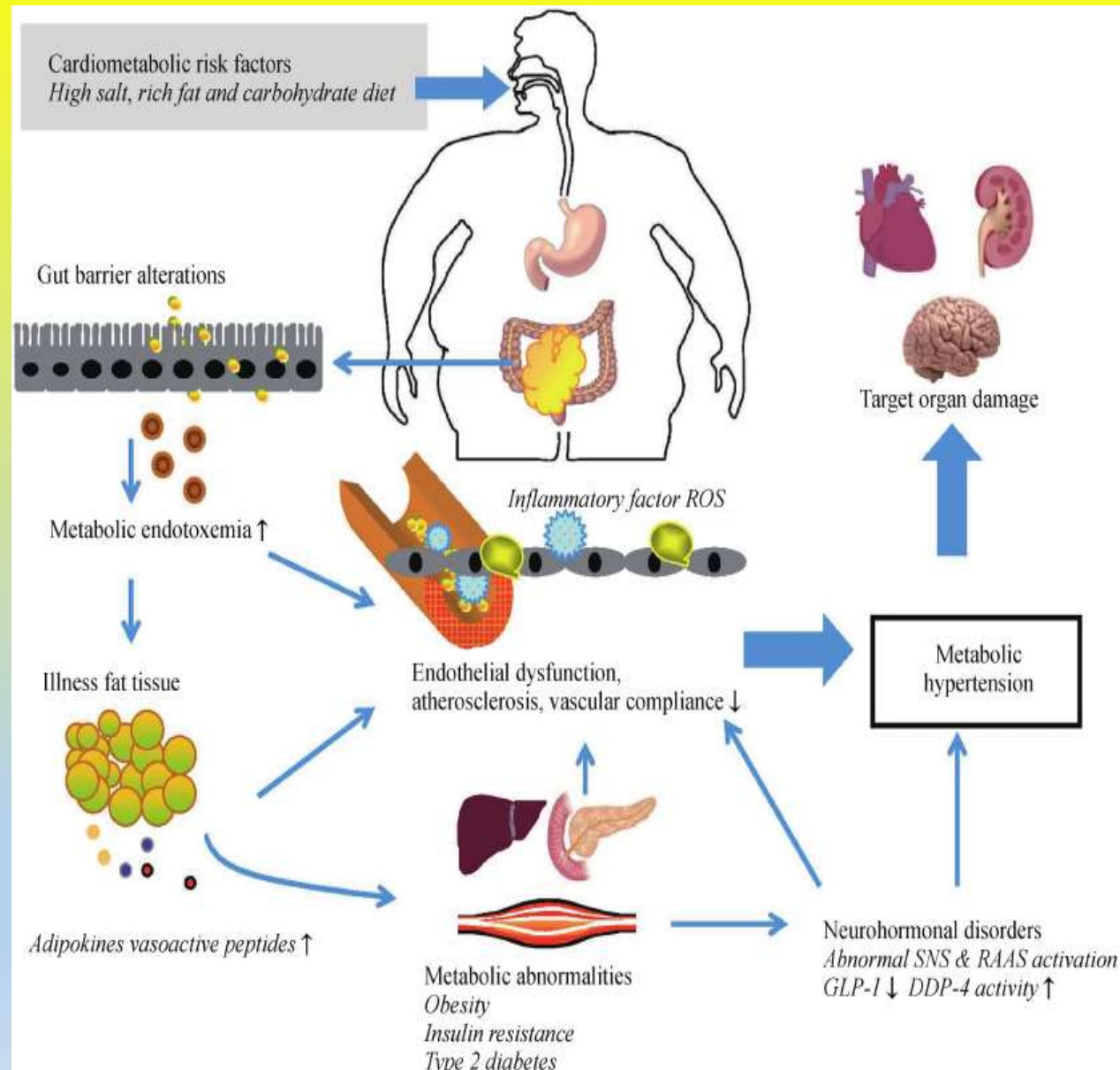
Microalbuminuria
Macroalbuminuria
End-stage renal disease

Erectile dysfunction

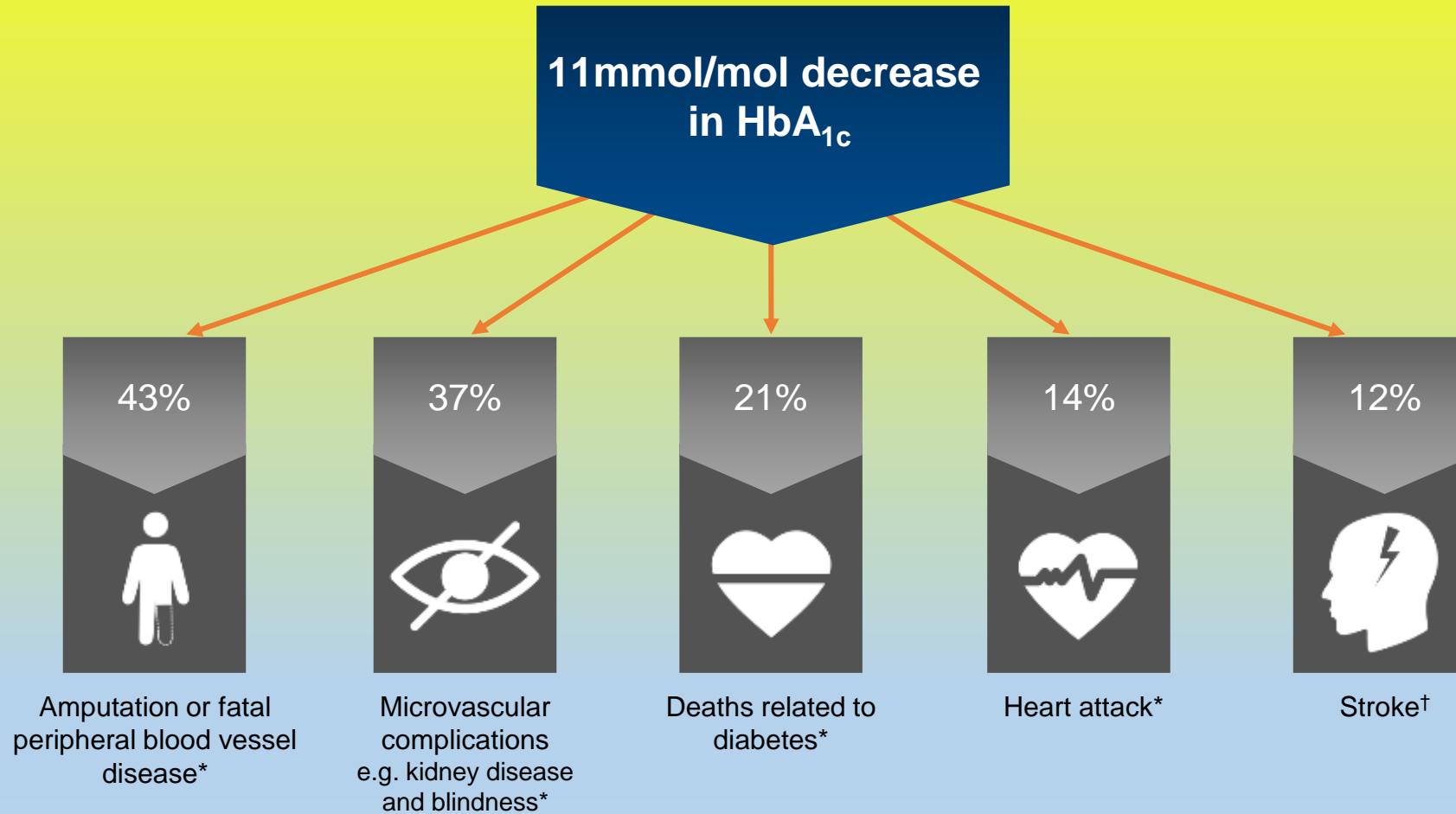
Autonomic neuropathy
Peripheral neuropathy
Osteomyelitis
Amputation



Why?



UKPDS: HbA_{1c} lowering and complication risk



*P<0.0001; †P=0.035.
UKPDS=UK Prospective Diabetes Study.

Stratton IM et al (2000) BMJ 321: 405–12

Lifestyle – underpins all



Clinical practice in the UK: NICE Guideline 28 does not currently include Cardiovascular Outcome Trial Data



Dec 2015

May 2017

2020

NG28
published

NG28
updated

NG28: review due
(new guidance TBC)

BMI = body mass index; DPP-4i = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1; SGLT2i = sodium-glucose co-transporter-2 inhibitor; SU = sulphonylurea.

National Institute for Health and Care Excellence (December 2015, last updated April 2017) Algorithm for blood glucose lowering therapy in adults with type 2 diabetes.

Available from: <http://www.nice.org.uk/guidance/ng28/resources/algorithm-for-blood-glucose-lowering-therapy-in-adults-with-type-2-diabetes-2185604173> (accessed January 2019).

NICE guidance is prepared for the National Health Service in England and is subject to regular review and may be updated or withdrawn.

NICE has not checked the use of its content in this module to confirm that it accurately reflects the NICE publication from which it is taken.

The 2018 EASD/ADA consensus report has incorporated Cardiovascular Outcome Trial Data

GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH

**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

NO

WITHOUT ESTABLISHED ASCVD OR CKD

ASCVD PREDOMINATES

**EITHER/
OR**

GLP-1 RA
with proven
CVD benefit¹

SGLT2i with
proven CVD
benefit¹,
if eGFR
adequate²

HF OR CKD PREDOMINATES

PREFERABLY

SGLT2i with evidence of reducing
HF and/or CKD progression in
CVOTs if eGFR adequate²

OR

If SGLT2i not tolerated or
contraindicated or if eGFR less
than adequate² add GLP-1 RA
with proven CVD benefit¹

COMPELLING NEED TO MINIMISE HYPOGLYCAEMIA

DPP-4i

GLP-1 RA

SGLT2i³

TZD

If HbA_{1c}
above target

If HbA_{1c}
above target

If HbA_{1c}
above target

If HbA_{1c}
above target

**COMPELLING NEED TO MINIMISE WEIGHT
GAIN OR PROMOTE WEIGHT LOSS**

**EITHER/
OR**

GLP-1 RA with
good efficacy
for weight loss⁴

SGLT2i³

If HbA_{1c} above target

COST IS A MAJOR ISSUE⁷⁻¹⁰

SU⁶

TZD¹⁰

If HbA_{1c} above target

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

* Consider basal insulin with lower risk of hypoglycaemia

5. Low dose may be better tolerated though less well studied for CVD effects

6. Choose later generation SU with lower risk of hypoglycaemia

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 hypoglycaemia 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

If DPP-4i not tolerated or
contraindicated or patient already on
GLP-1 RA, cautious addition of:
• SU⁶ • TZD¹⁰ • Basal insulin

What about this?

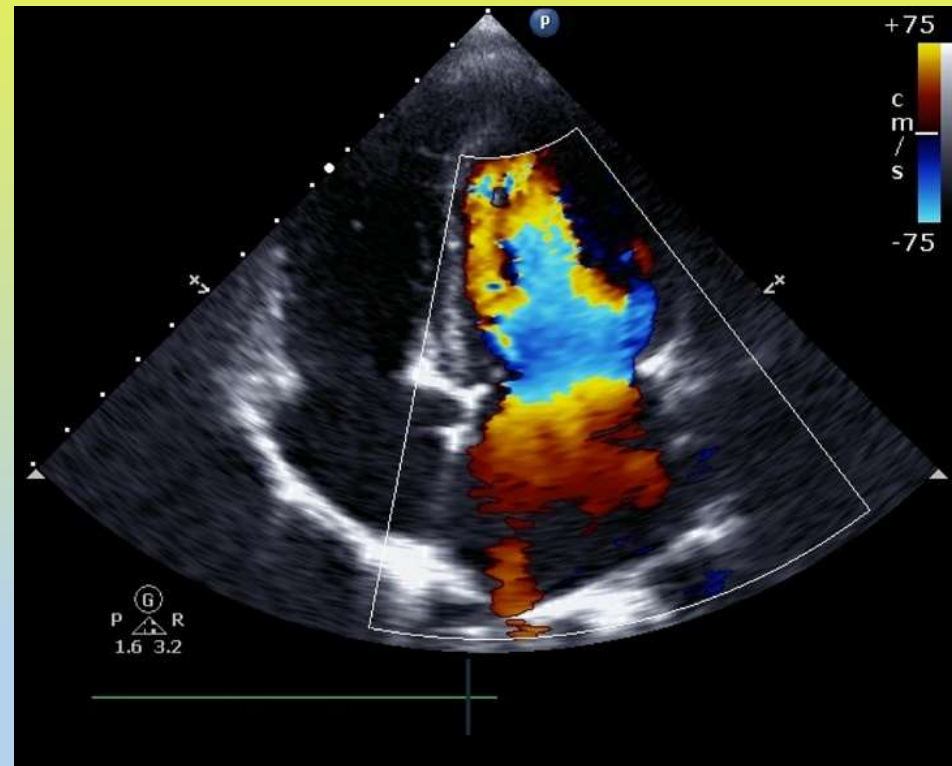
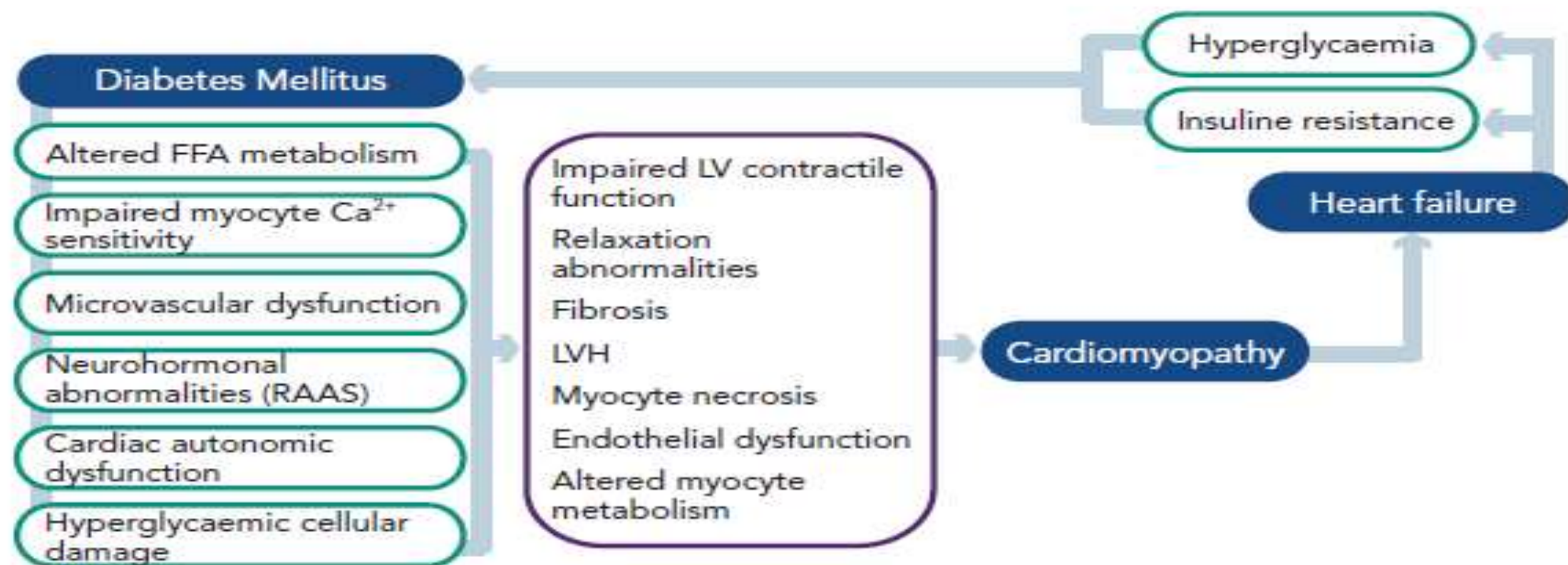


Figure 1: The Bi-directional Impact of Diabetes Mellitus and Heart Failure



FFA = free fatty acids; Ca^{2+} = Calcium; RAAS = Renin-angiotensin aldosterone system; LVH = Left ventricular hypertrophy.

Newer glycaemic agents – the great HOPE?

- SGLT2 inhibitors:
 - Lower plasma glucose & HbA1c
 - Induce moderate natriuresis
 - Reduce blood pressure
 - Reduce weight
 - Exert cardio-protective properties on the heart
- GLP1- RAs & CVD



Medication

- Triple whammy:
- Glycaemic control
- BP
- Lipids



In summary

- Diabetes impacts on vascular and heart health
- Cost is financial and in terms of quality of life/years of life lost
- Both lifestyle interventions and drug therapies can improve heart health, beyond glycaemic control, in those with established disease and those who are at increased risk
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Conclusion

- The management of CVD in diabetes remains a major priority
- We need to individualise treatment choices in CVD & with diabetes
- Individuals with diabetes and CVD may benefit most from SGLT2 inhibitors or certain GLP1 receptor agonists
- Individuals with diabetes and HF and/or CKD may benefit most from SGLT2 inhibitors
- Emerging evidence of SGLT2i beneficial in patients with heart failure without diabetes
- Guidelines are changing – most recently SIGN 2017 & ADA/EASD October 2018
- Watch this space!
 - DAPA-CKD, EMPA-KIDNEY, EMPEROR-Reduced, EMPEROR-Preserved, PRESERVED-HF