# Ny (og mere) medicin til type 2 diabetes – hvem skal have hvad og hvem skal ikke?

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# Interessekonflikter

- **Foredrag for** AstraZeneca, Boehringer Ingelheim, MSD, Novo Nordisk, Sanofi
- **Advisory board** AstraZeneca, Amgen, Novartis, Novo Nordisk, Mundipharma, Boehringer Ingelheim
- **Støtte til forskning fra** Amgen, AstraZeneca, Novo Nordisk

Ny medicin til type 2 diabetes

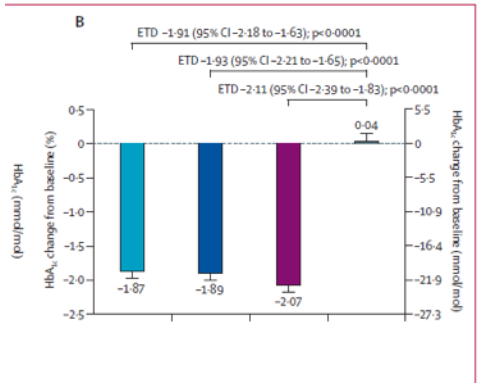
- men ikke nødvendigvis mere……

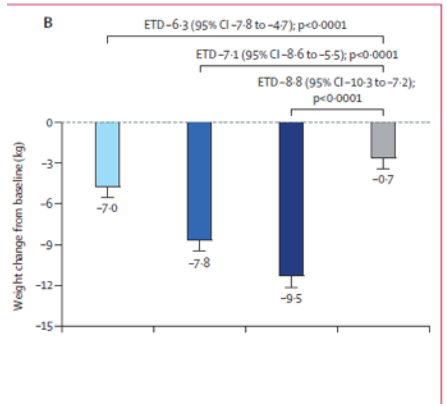
# Nye behandlinger – eller lige om hjørnet

- Tirzepatid (Mountjaro)
- Finerenon (Kerendia)
- Ugentlig insulin m.m

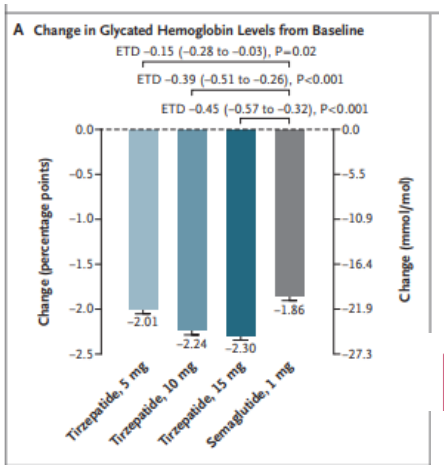
# Glucose-dependent insulinotropic polypeptide (GIP) receptor and GLP-1 receptor agonist (tirzepatide)

## SURPASS-1




## SURPASS-2

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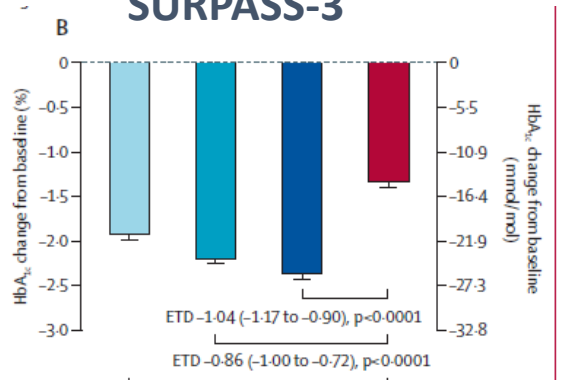
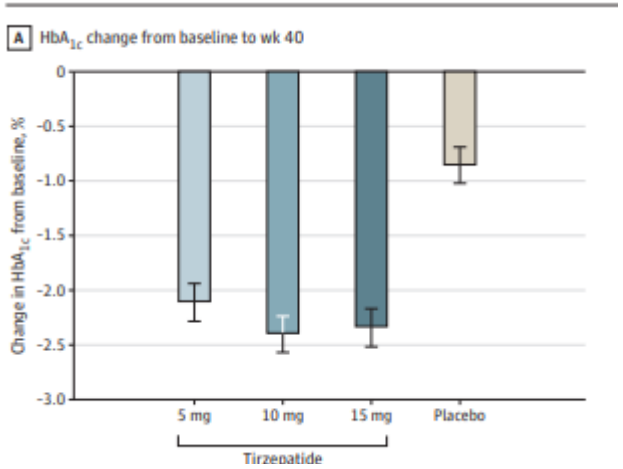




## SURPASS-5




| | Tirzepatide 5 mg (n=326) | Tirzepatide 10 mg (n=321) | Tirzepatide 15 mg (n=334) | Insulin glargine (n=978) |
|---|---|---|---|---|
| **HbA$_{1c}$, %** | | | | |
| Baseline | 8·52 (0·049) | 8·60 (0·049) | 8·52 (0·048) | 8·51 (0·028) |
| At week 52 | 6·29 (0·054) | 6·09 (0·054) | 5·95 (0·054) | 7·09 (0·031) |
| Change from baseline at week 52*† | −2·24 (0·053) | −2·43 (0·053) | −2·58 (0·053) | −1·44 (0·030) |
| ETD *vs* insulin glargine | −0·80 (−0·92 to −0·68), p<0·0001‡ | −0·99 (−1·11 to −0·87), p<0·0001‡ | −1·14 (−1·26 to −1·02), p<0·0001‡ | .. |

## SURPASS-4


Rosenstock J *et al*; *Lancet* 2021; 398: 143-55
Frias JP *et* al; NEJM 2021;385:503-
Ludvik B *et* al; *Lancet* 2021; 398: 583–98
Del Prato S Kahn SE *et al*; *Lancet* 2021; 398:1811-1824
Dahl D et al; JAMA. 2022;327(6):534-545

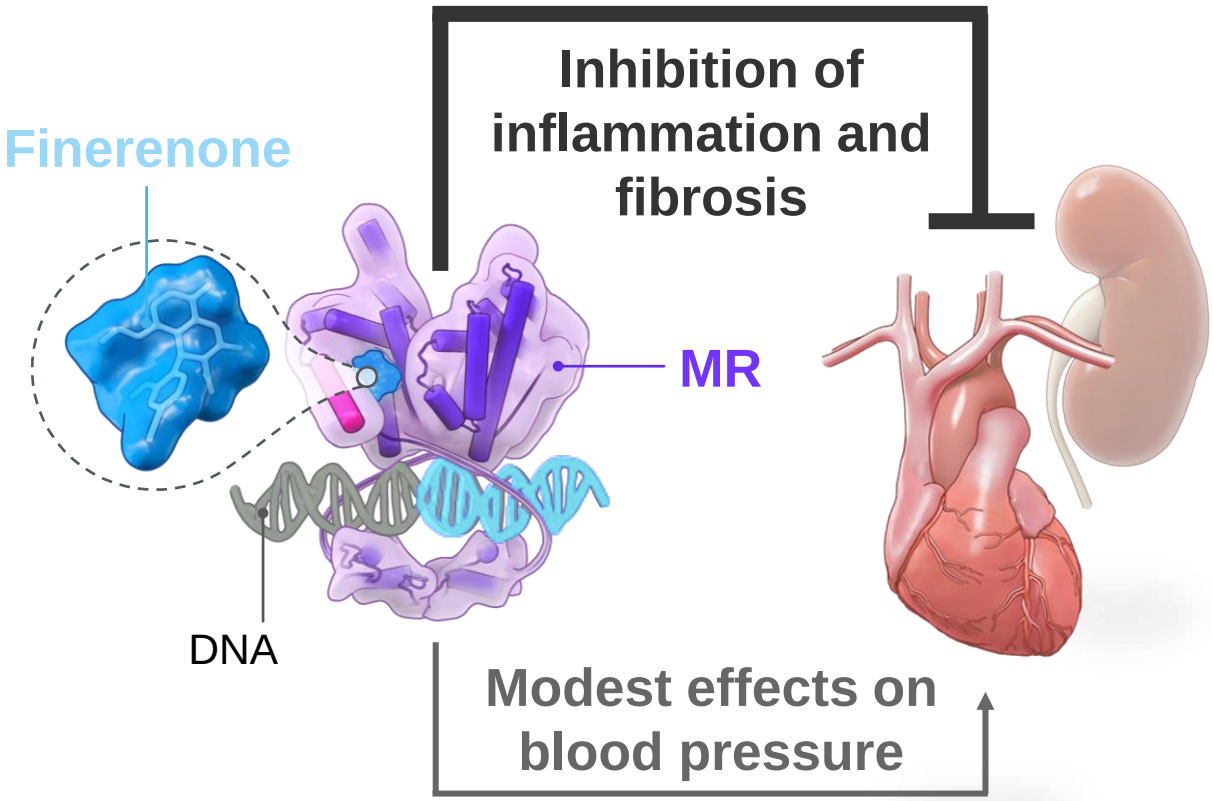

American Diabetes Association®



EASD European Association for the Study of Diabetes

# Finerenone is a selective nonsteroidal MRA that interacts with the MR in a different way to steroidal MRAs

- Finerenone blocks MR overactivation, which contributes to inflammation and fibrosis, leading to kidney and CV damage[1,2]
- Finerenone has a unique binding mechanism and distribution vs steroidal MRAs, which results in high potency, selectivity and a differential effect on MR cofactor binding[1,2]
- In FIDELIO-DKD, finerenone slowed CKD progression and improved CV outcomes in patients with CKD and T2D[3]
  - The incidence of hyperkalaemia leading to permanent discontinuation was low




DNA, deoxyribonucleic acid; MR, mineralocorticoid receptor; MRA, mineralocorticoid receptor antagonist

1. Agarwal R, *et al. Eur Heart J* 2021;42:152–161; 2. Agarwal R, *et al. Nephrol Dial Transplant* 2020; doi: 10.1093/ndt/gfaa294; 3. Bakris GB, *et al. N Engl J Med* 2020;383:2219–2229

# FIDELITY is a large individual patient data meta-analysis of FIDELIO-DKD[1] and FIGARO-DKD[2]

**13,171 patients randomised**

**48 countries**

**3 years' median follow-up**

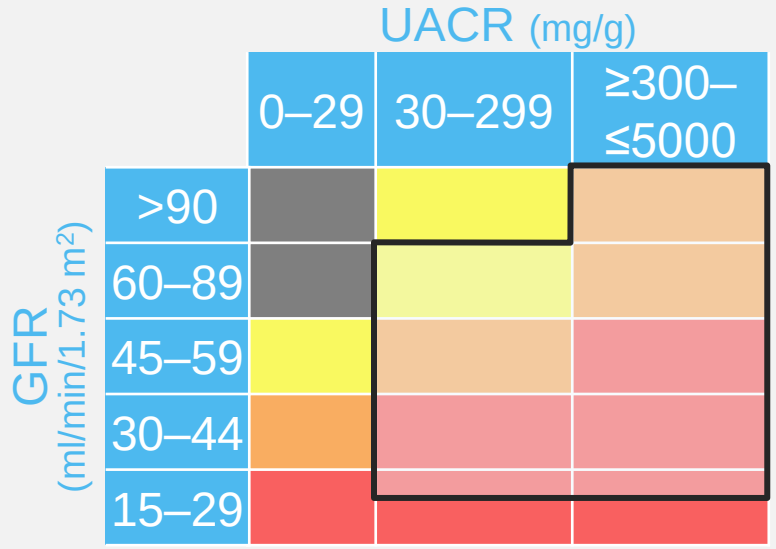
R

**Finerenone 10 or 20 mg od***

**Placebo**

## Key eligibility criteria

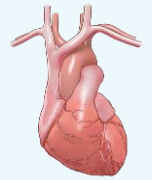
- ✓ **T2D**
- ✓ **CKD**
- ✓ On single RASi
- ✓ Serum [$K^+$] ≤4.8 mmol
- ✗ Symptomatic HFrEF




## Key outcomes

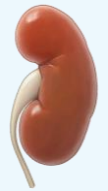
**CV composite**

Time to CV death, non-fatal MI, non-fatal stroke, or HHF



**57% eGFR kidney composite**

Time to kidney failure,[#] sustained ≥57% decrease in eGFR from baseline, or renal death



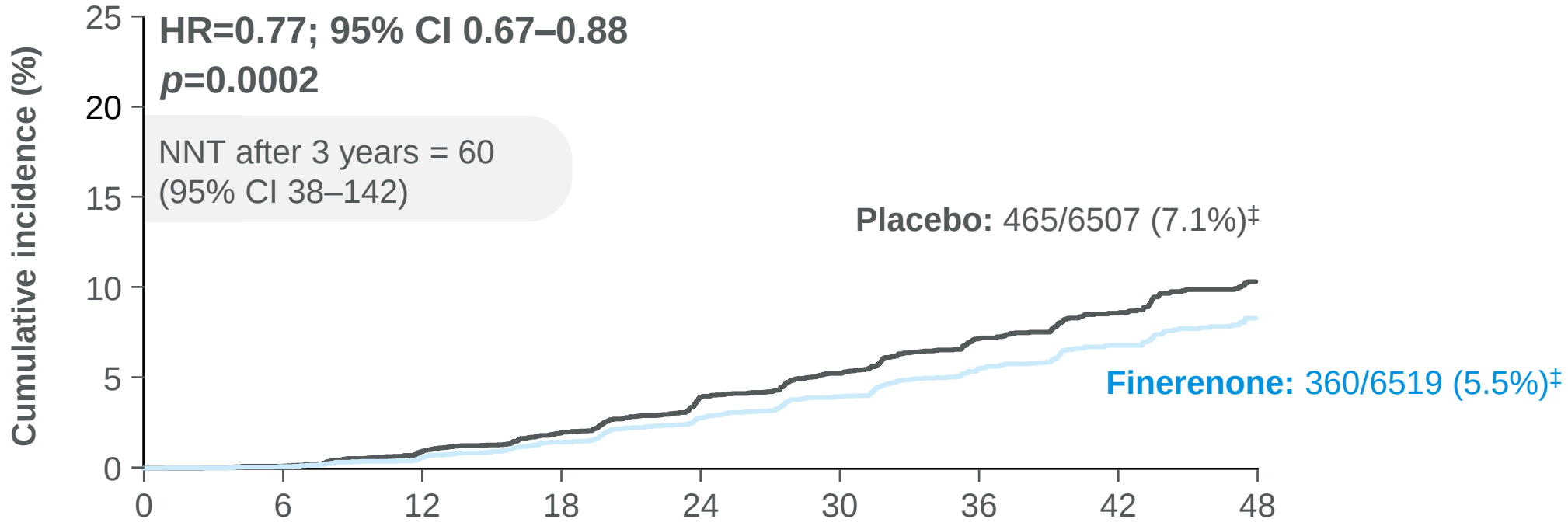
*10 mg if screening eGFR 25–<60 ml/min/1.73 m$^2$; 20 mg if ≥60 ml/min/1.73 m$^2$, up-titration encouraged from month 1 if serum [$K^+$] ≤4.8 mEq/l and eGFR stable; [#]kidney failure defined as either ESKD (initiation of chronic dialysis for ≥90 days or kidney transplant) or sustained decrease in eGFR <15 ml/min/1.73 m$^2$

CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; GFR, glomerular filtration rate; HHF, hospitalisation for heart failure; HFrEF, heart failure with reduced ejection fraction; $[K^+]_s$, potassium concentration; MI, myocardial infarction; od, once daily; RASi, renin–angiotensin system inhibitor; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio

1. Bakris GB, *et al. N Engl J Med* 2020;383:2219–2229; 2. Pitt B *et al. N Engl J Med* 2021;doi:10.1056/NEJMoa2110956

# Finerenone significantly reduced the risk of the ≥57% eGFR kidney composite outcome by 23%

## Time to kidney failure,* sustained ≥57% decrease in eGFR from baseline, or renal death#

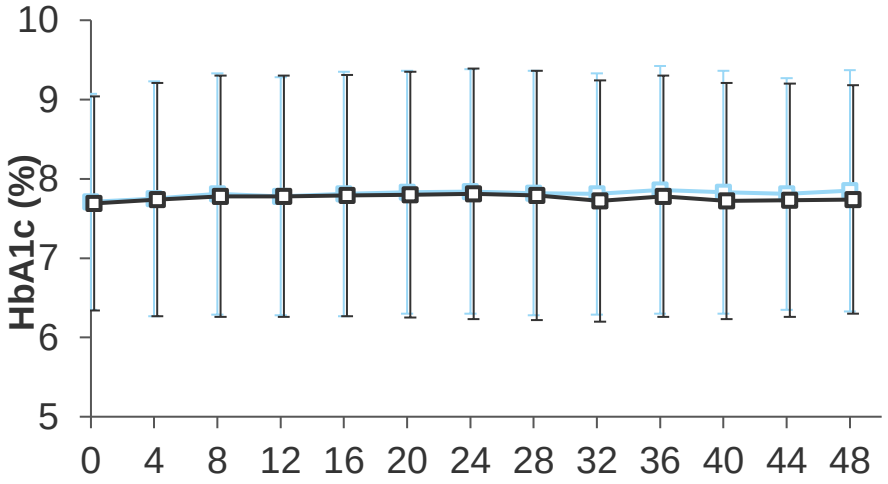



| No. at risk | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Finerenone | 6519 | 6291 | 6107 | 5848 | 5027 | 3973 | 2815 | 2024 | 959 |
| Placebo | 6507 | 6292 | 6071 | 5815 | 4949 | 3932 | 2798 | 1988 | 962 |

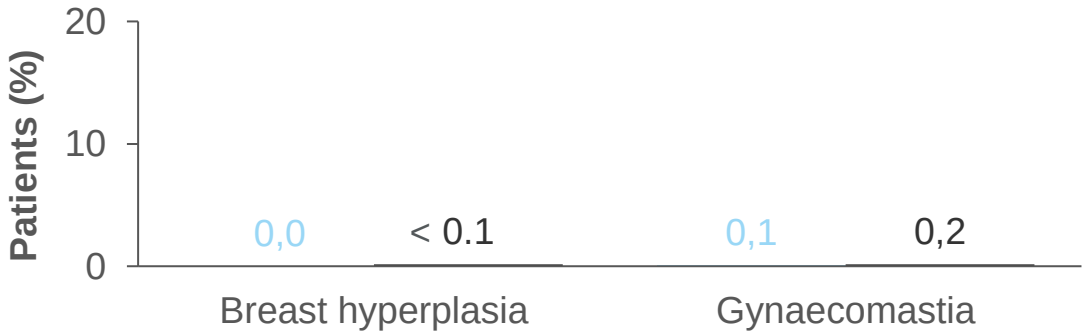
*ESKD or an eGFR <15 ml/min/1.73 m²; #events were classified as renal death if: (1) the patient died; (2) kidney replacement therapy had not been initiated despite being clinically indicated; and (3) there was no other likely cause of death; ‡cumulative incidence calculated by Aalen–Johansen estimator using deaths due to other causes as competing risk; ¶number of patients with an event over a median of 3.0 years of follow-up
CI, confidence interval; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HR, hazard ratio; NNT, number needed to treat
Filippatos G. Abstract 7161 presented at the European Society of Cardiology 2021 (ESC 2021)

# Finerenone showed no effect on HbA1c, no imbalance in sexual side effects and a modest effects on blood pressure

## No clinically meaningful effect on HbA1c




## No imbalance in sexual side-effects




**Finerenone (n=6510)**

**Placebo (n=6489)**

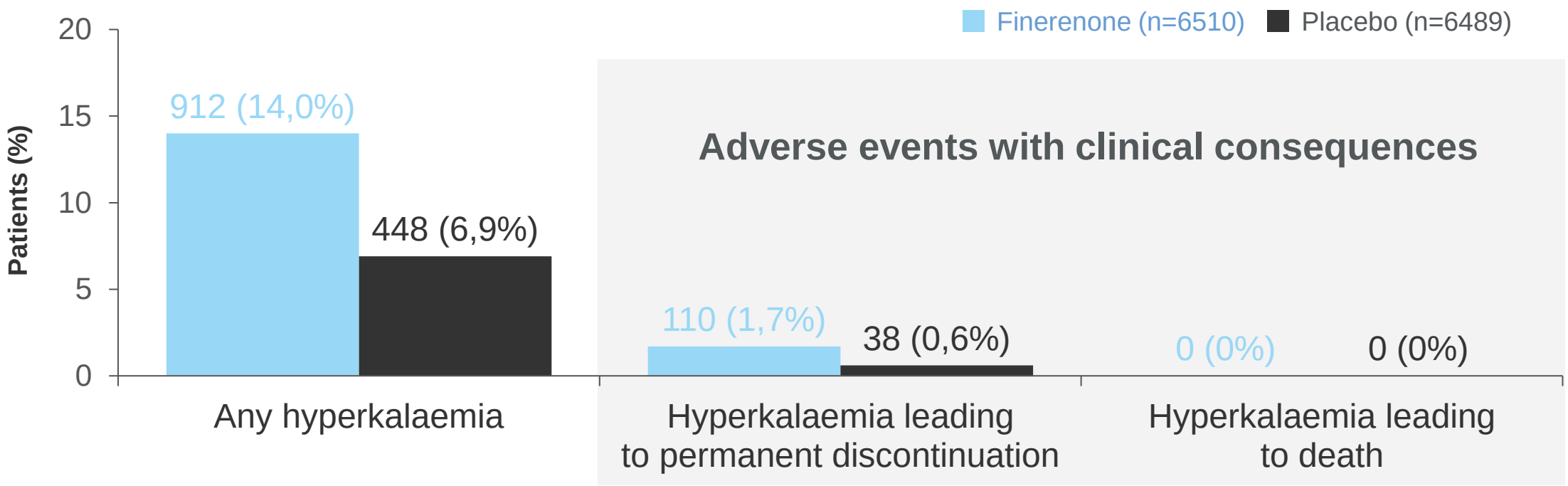
## Modest effect on systolic blood pressure

Maximum placebo-corrected change in mean SBP of **-3.0 mmHg** at 12 months

Agarwal et al. Eur Heart J 2021; doi:10.1093/eurheartj/ehab777

# In FIDELITY, finerenone increased hyperkalaemia, but the clinical impact of hyperkalaemia was minimal

## Investigator-reported hyperkalaemia adverse events*[1]




**With a robust [$K^+$] management strategy guided by regular serum [$K^+$] monitoring, there were no hyperkalaemia-related deaths in over 13,000 patients over 3 years median follow-up[1–4]**



*Investigator-reported AEs using the MedDRA preferred terms 'hyperkalaemia' and 'blood potassium increased'
[$K^+$], potassium concentration, MedDRA, Medical Dictionary for Regulatory Activities
1. Agarwal R, et al. Eur Heart J 2021; doi:10.1093/eurheartj/ehab777; 2. Bakris GL, et al. N Engl J Med 2020;383:2219–2229; 3. Pitt B, et al. N Engl J Med 2021; doi: 10.1056/NEJMoa2110956; 4. Agarwal R, et al. JASN 2022, 33 (1) 225-237 doi: 10.1681/ASN.2021070942

10

# Finerenon (Kerendia) – nu med tilskud

- *Til behandling af voksne med type 2-diabetes og diabetisk nyresygdom med eGFR ≥25 - <60 og vedvarende albuminuri (urin-albumin/kreatinin-ratio på >30mg/g) trods behandling med de for patienten maksimalt tolerable doser af ACE-hæmmer/ARB og SGLT2-hæmmer.*

- *Behandlingen skal være iværksat af eller konfereret med en speciallæge i nefrologi eller endokrinologi*

# Putting the Person with Diabetes at the Centre of Care

American Diabetes Association®

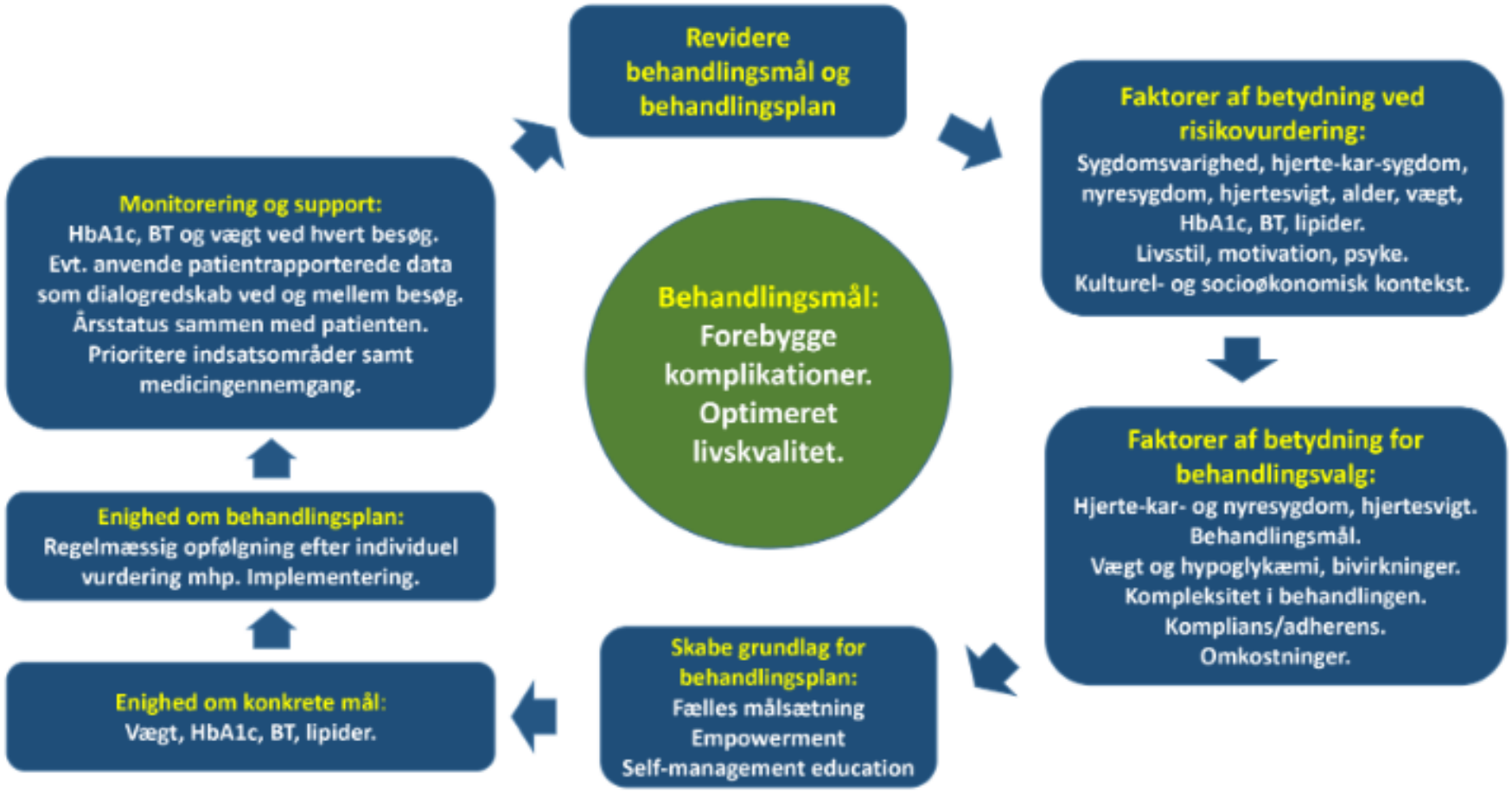
Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

*Diabetes Care* 2022; https://doi.org/10.2337/dci22-0034. *Diabetologia* 2022; https://doi.org/10.1007/s00125-022-05787-2.



EASD European Association for the Study of Diabetes

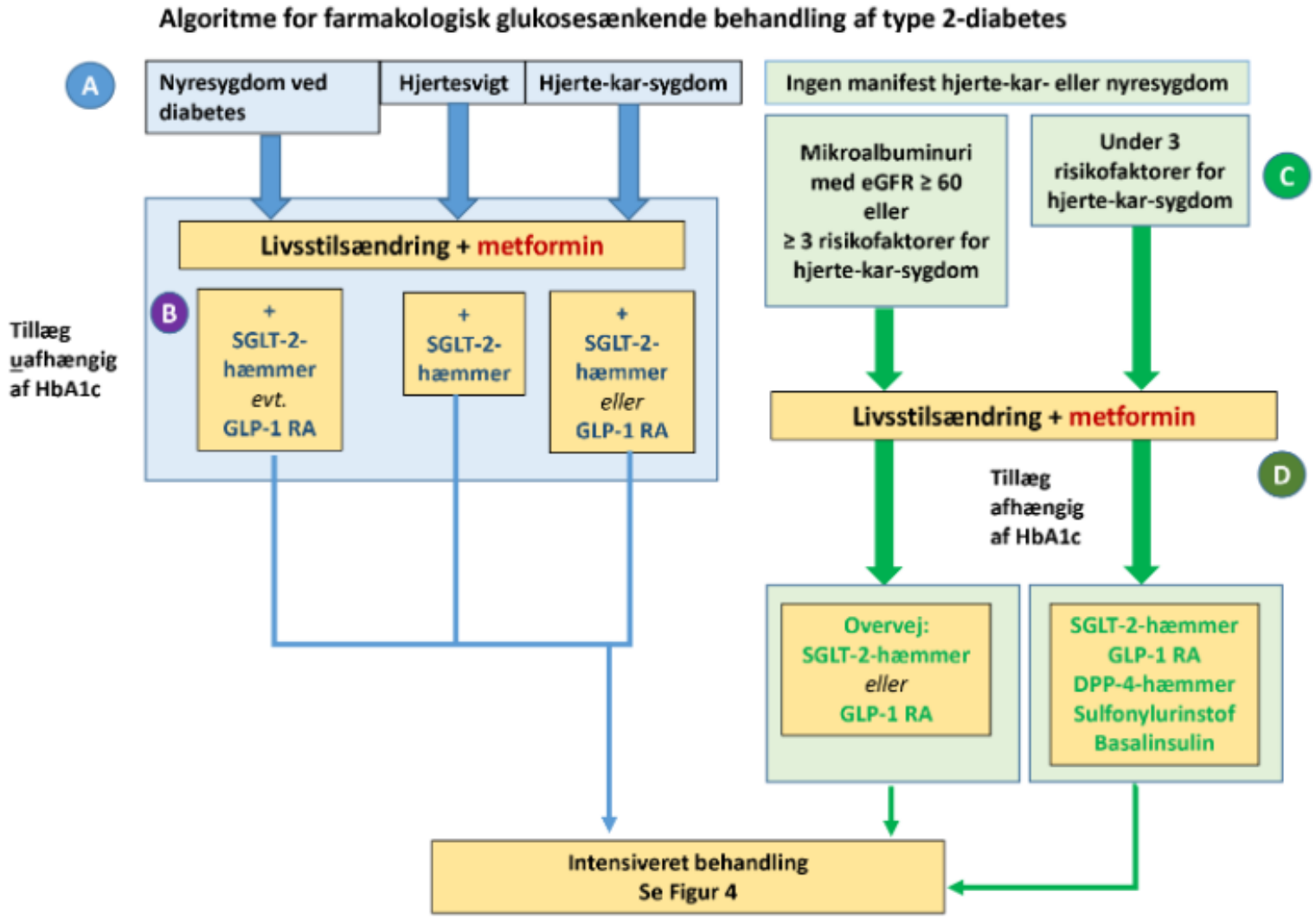
# Personcentreret behandling af type 2-diabetes




Frit efter ADA/EASD-konsensusrapport 2018

Karakterisér

Individualisér

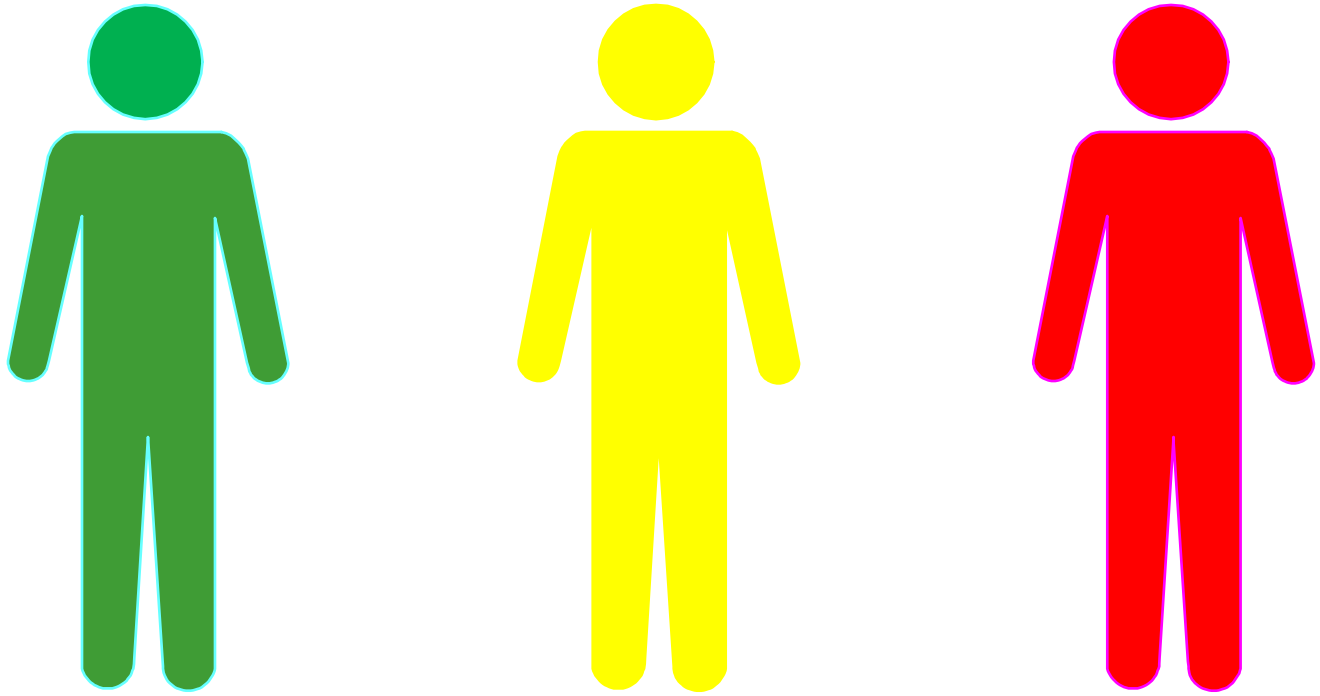

Algoritme for farmakologisk glukosesænkende behandling af type 2-diabetes
A
Nyresygdom ved diabetes
Hjertesvigt
Hjerte-kar-sygdom
Ingen manifest hjerte-kar- eller nyresygdom
Mikroalbuminuri med eGFR ≥ 60 eller ≥ 3 risikofaktorer for hjerte-kar-sygdom
Under 3 risikofaktorer for hjerte-kar-sygdom
C
Livsstilsændring + metformin
B
Tillæg uafhængig af HbA1c
+ SGLT-2-hæmmer evt. GLP-1 RA
+ SGLT-2-hæmmer
+ SGLT-2-hæmmer eller GLP-1 RA
Livsstilsændring + metformin
D
Tillæg afhængig af HbA1c
Overvej: SGLT-2-hæmmer eller GLP-1 RA
SGLT-2-hæmmer
GLP-1 RA
DPP-4-hæmmer
Sulfonylurinstof
Basalinsulin
Intensiveret behandling
Se Figur 4

# Stadier af kronisk nyresygdom (CKD)

| Stage | Description | GFR |
|---|---|---|
| **At increased risk** | *Risk factors* kidney disease (e.g. diabetes, high blood pressure, family history, older age, ethnic group) | >90 |
| **1** | Kidney damage (protein in the urine) and *normal* GFR | >90 |
| **2** | Kidney damage and *mild* decrease in GFR | 60 - 89 |
| **3** | *Moderate* decrease in GFR* | 30 - 59 |
| **4** | *Severe* decrease in GFR | 15 - 29 |
| **5** | *Kidney failure* | <15 |

For a diagnosis of stage 1 or 2, other evidence of kidney disease must be present, e.g. persistent proteinuria, hematuria or microalbuminuria, presence of structural or genetic kidney abnormality or biopsy-proven chronic glomerulonephritis.

# Urin albumin kreatinin ratio

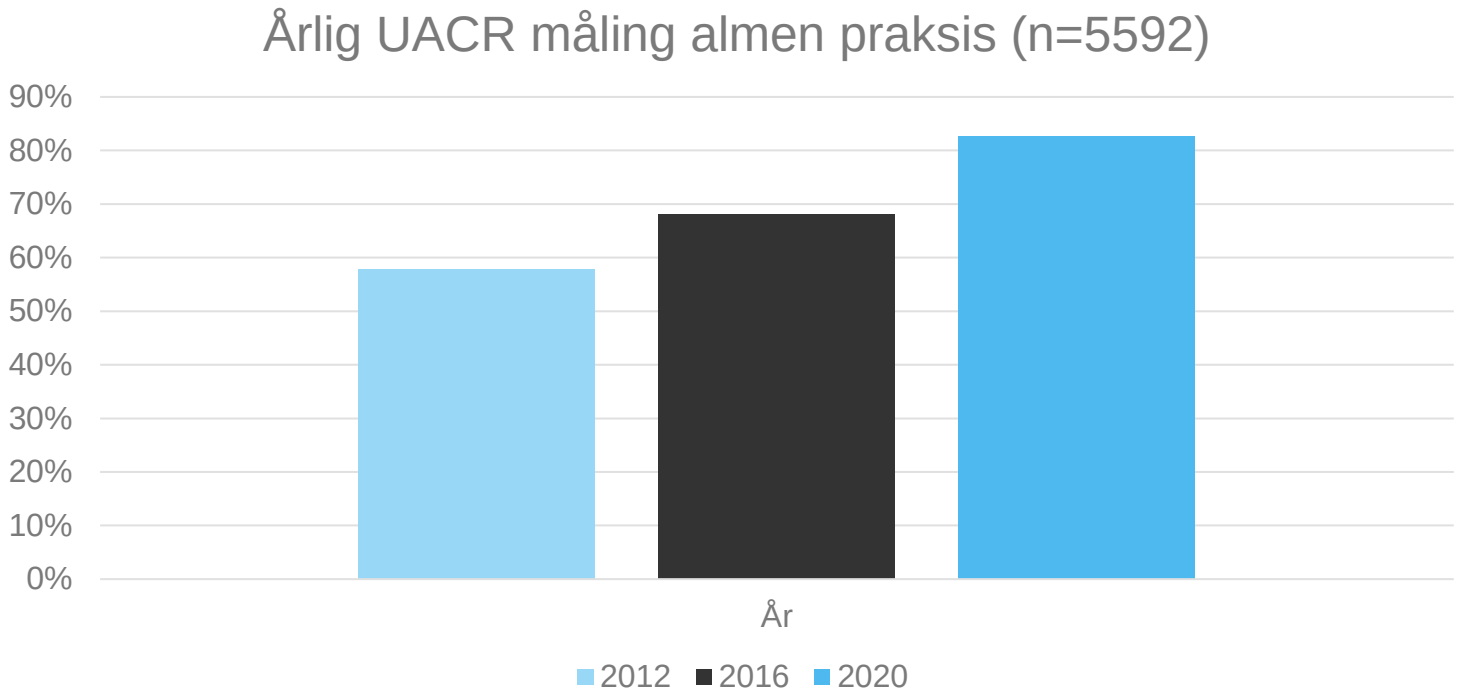


normo
< 30 mg/g

micro
30-300 mg/g

macro
> 300 mg/g

# Bedre monitorering af tegn på nyrekomplikation

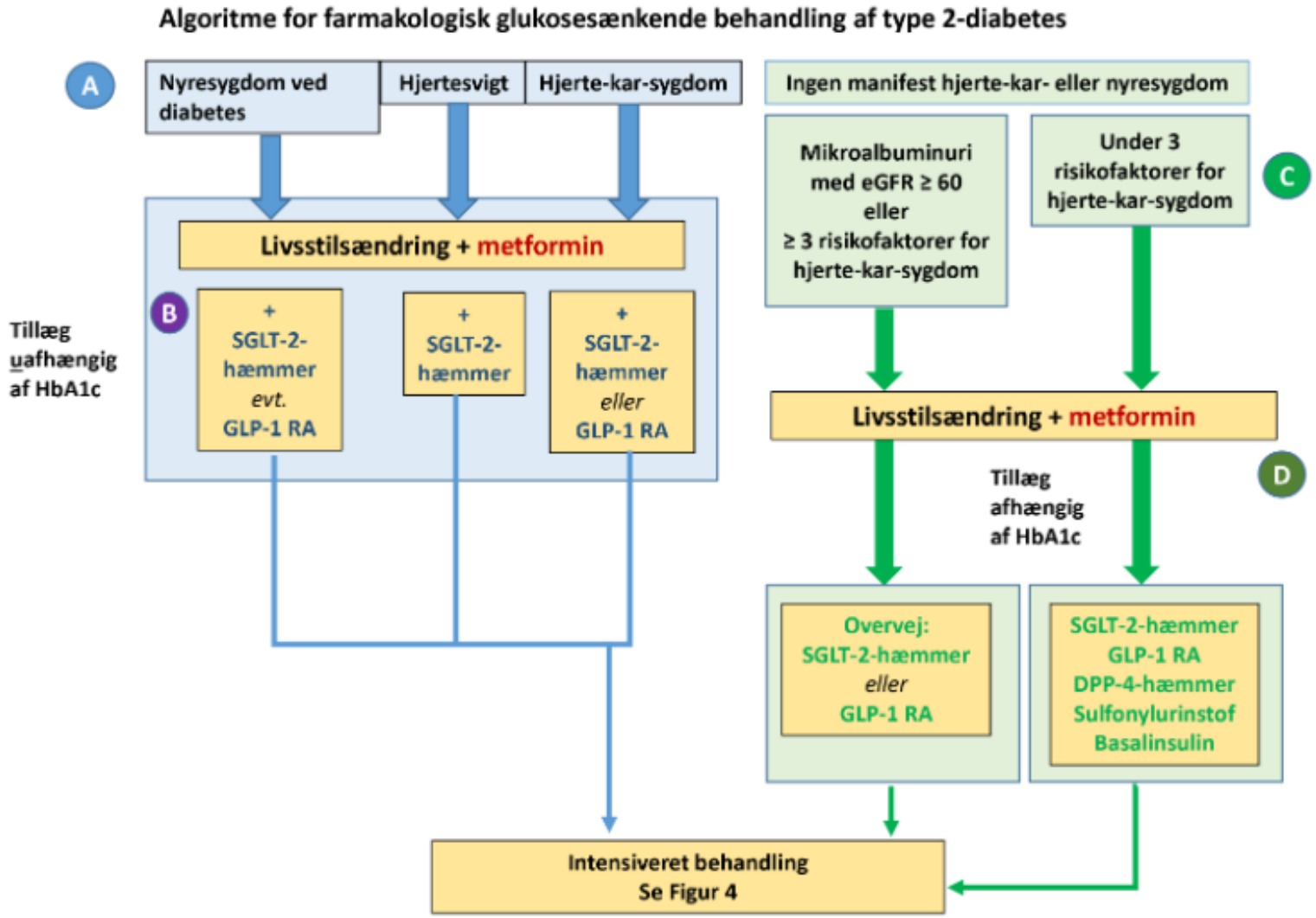



**Tabel 2. Faldende nyrefunktion (eGFR) og daglig dosis for de mest anvendte antidiabetika.**

| Antidiabetika | | eGFR ml/min/1,73 m² | | | | |
|---|---|---|---|---|---|---|
| **Klasse** | Indholdsstof | **>90** | **89 - 60** | **59 - 30** | **<30** | **Dialyse** |
| **Metformin** | metformin | 1000 mg x 2 | | 500 mg x 2 | | |
| **SGLT2i** | canagliflozin | 300 mg x 1 | | 100 mg x 1 | | |
| | dapagliflozin | 10 mg x 1* | | | | |
| | empagliflozin | 25 mg x 1* | | 10 mg x 1 | | |
| | ertugliflozin | 5-15 mg x 1 | | | | |
| **GLP1- RA** | dulaglutid | 0,75 - 1,5 mg/uge | | | | |
| | liraglutid | 0,6 – 1,8 mg/dag | | | | |
| | semaglutid | 0,5 - 1 mg/uge | | | | |
| **DPP-4i** | sitagliptin | 100 mg x 1 | | 50 mg x 1 | 25 mg x 1 | |
| | vildagliptin | 50 mg x 2 | | 50 mg x 1 | | |
| | linagliptin | 5 mg x 1 | | | | |
| **SU** | glimepirid | 1-4 mg x 1 | | halvering | | |
| | gliclazid | 30–120 mg x 1 | | halvering | | |
| **Insulin** | alle typer | *Individuel dosis – behov falder ofte med faldende GFR* | | | | |

| Uændret dosis | Dosiskorrektion | Seponering |
|---|---|---|

*Skraveret område angiver eGFR niveau hvor man kan overveje at fortsætte behandling*
**Dapagliflozin kan **opstartes** ned til eGFR 25 ml/min. Empagliflozin 10 mg kan opstartes ned til eGFR 20 ml/min ved samtidig hjertesvigt (EF<40%).*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Sulfonylurinstof
Basalinsulin
Intensiveret behandling
Se Figur 4

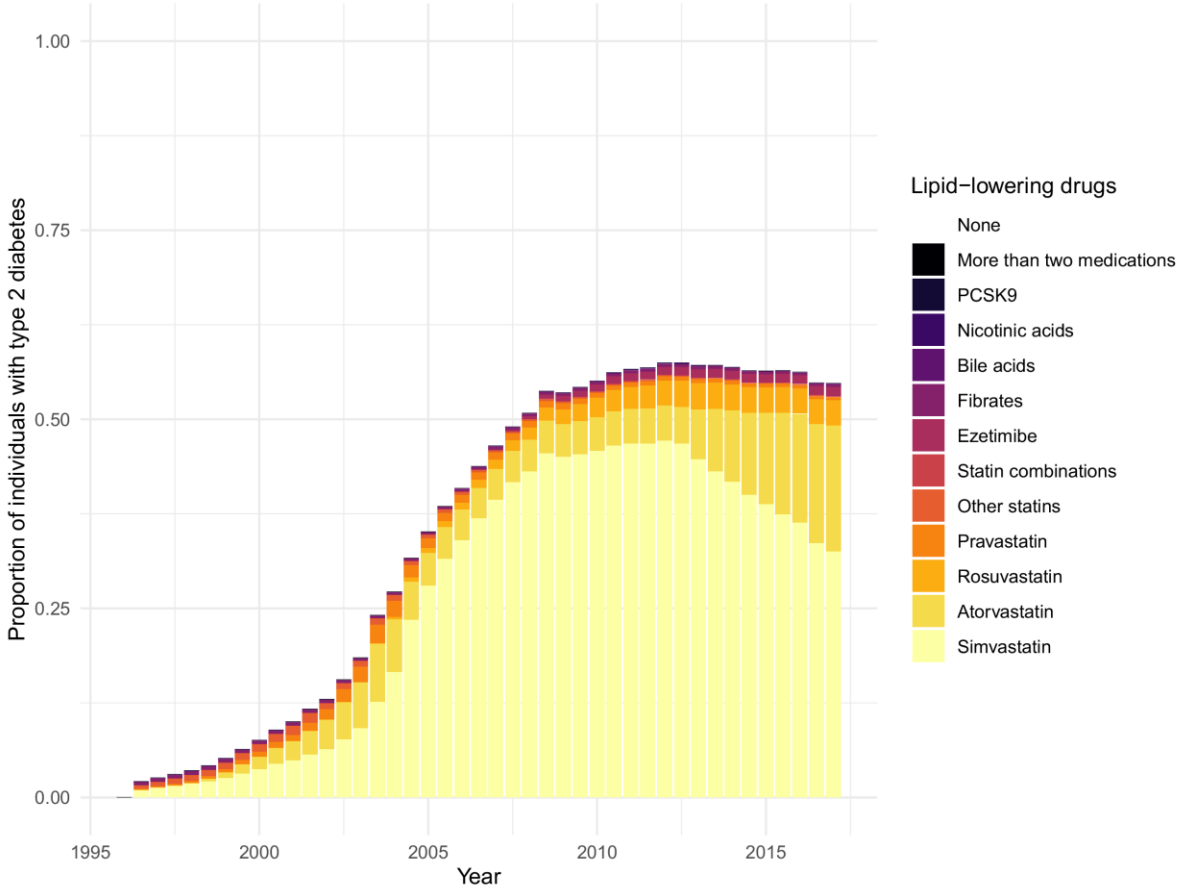
Karakterisér

Individualisér

# Individualiser

- Alder
- Økonomi
- Komorbiditet
- Standardbehandling

# For få henter kolesterolmedicin!





Hanan Amadid et al. DOM 2021

# Hvem skal have ….

- magnyl?
- Basalinsulin?
- SGLT2 + GLP1?
- Finerenon?
- Statin?
- Metformin?

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# Tag-med-hjem-beskeder

- Karakterisér & Individualisér
- Nye behandlinger finerenon og tirzepatid
- Glem ikke standarden!