



Nieuwigheden in diabetes 2018

Wim Maes



nieuwigheden

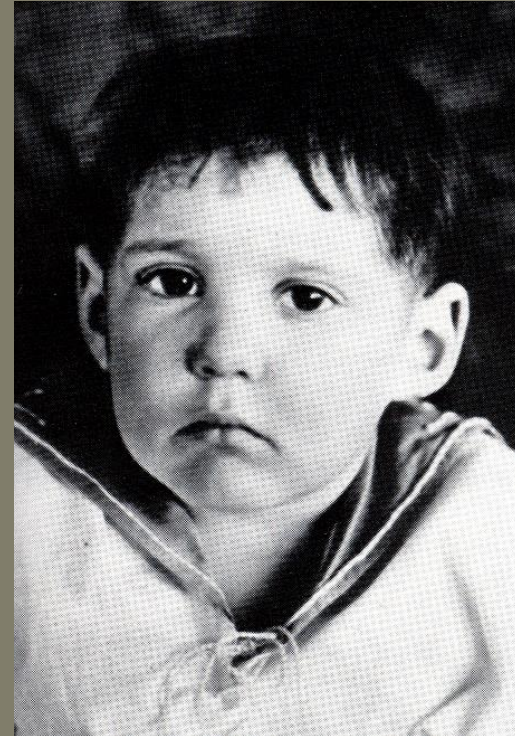
- Insulines
- Pillen
- Metingen

Het mirakel van de insuline



Patient J. Leonard Thompson,
14 jaar

December 15, 1922



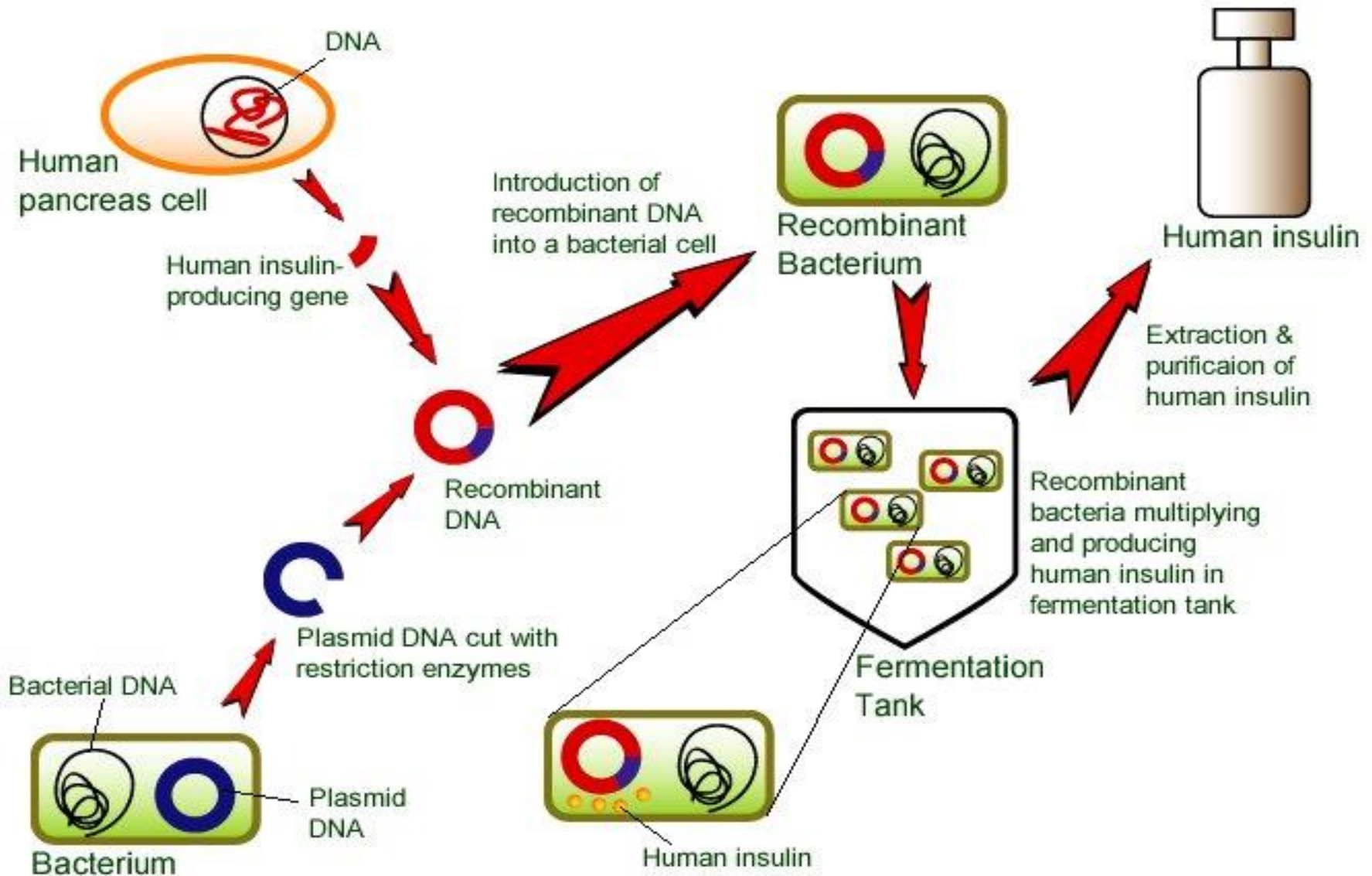
February 15, 1923

varkensinsuline



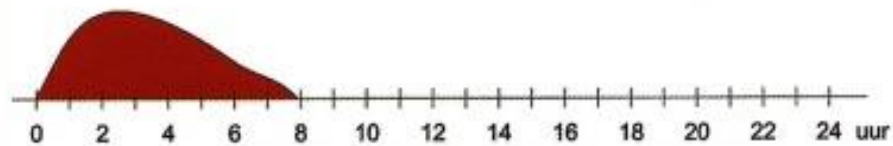
Genetic engineering

Human Insulin Production



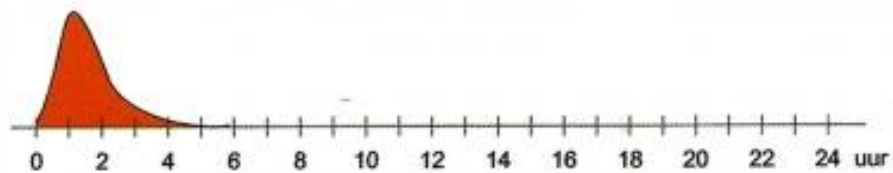
Kortwerkend humaan

- Actrapid
- Humuline Regular
- Insuman Rapid



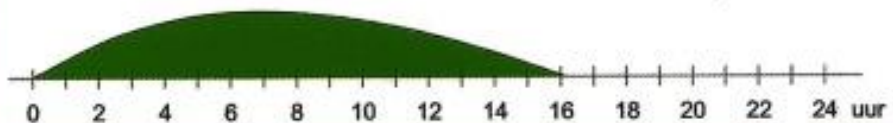
Snelwerkend analoog

- Apidra (glulisine)
- Humalog (lispro)
- Novorapid (aspart)



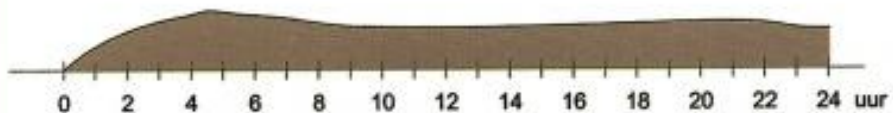
Langwerkend humaan

- Humuline NPH
- Insulatard
- Insuman Basal



Langwerkende analogen

- Lantus (glargine)

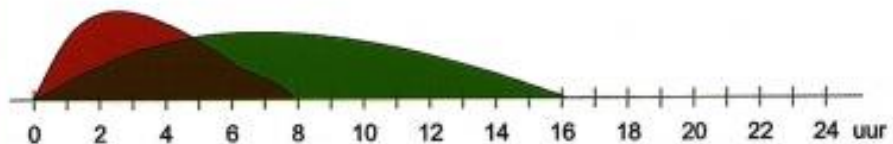


- Levemir (detemir)



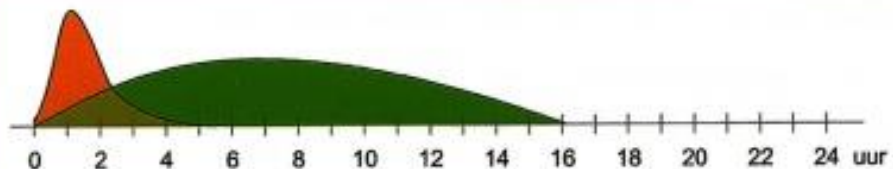
Humane mix

- Humuline NPH



Analoge mix

- Humalog Mix (lispro/lispro protamine)
- NovoMix (aspart/aspart protamine)



Humalog® 200 units/ml KwikPen™



Degludec

TOUJEO

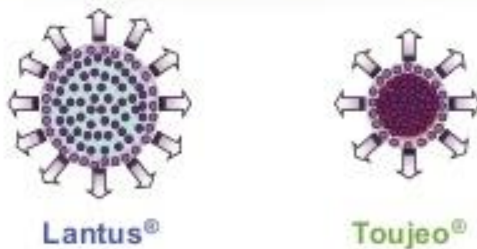


New Once-Daily Long-Acting Basal Insulin with a Unique PK/PD Profile

Reduction of Volume by 2/3

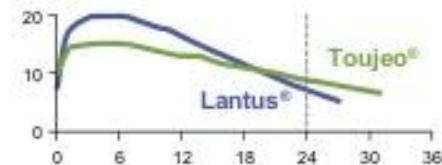


Reduction of Depot Surface Area by 1/2

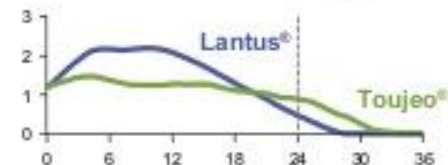


More Constant PK/PD Profile⁽¹⁾

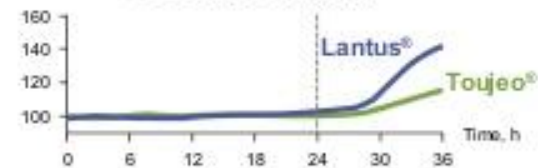
Median insulin concentration, $\mu\text{U/mL}$



Glucose infusion rate, mg/kg/min



Blood glucose, mg/dL



Confirmed or Severe Hypoglycemia per Patient per Year Significantly Lower

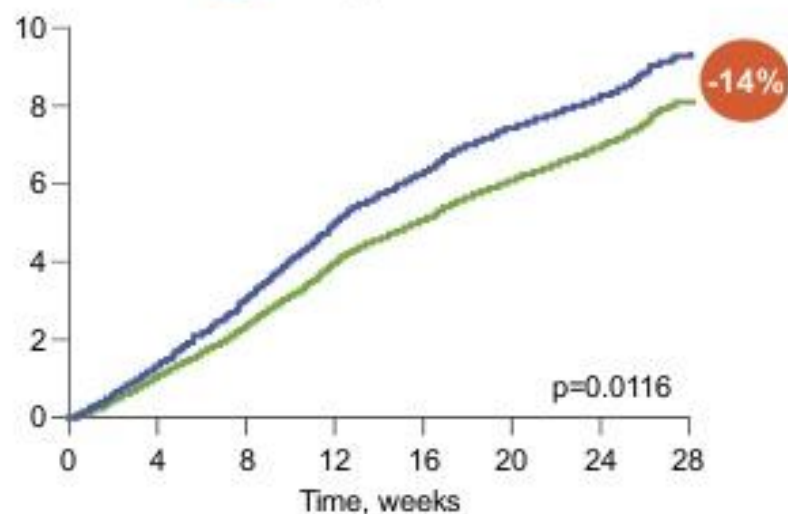
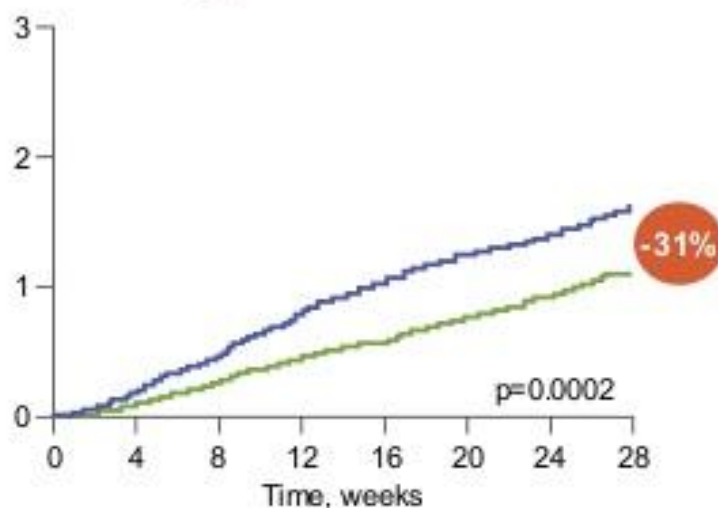
Cumulative Mean Number of Confirmed or Severe Hypoglycemia per Participant^(1,4)

Pooled analysis of EDITION 1-2-3^(1,2)

— Lantus®
— Toujeo®

● Nocturnal⁽³⁾

● At any time⁽⁴⁾



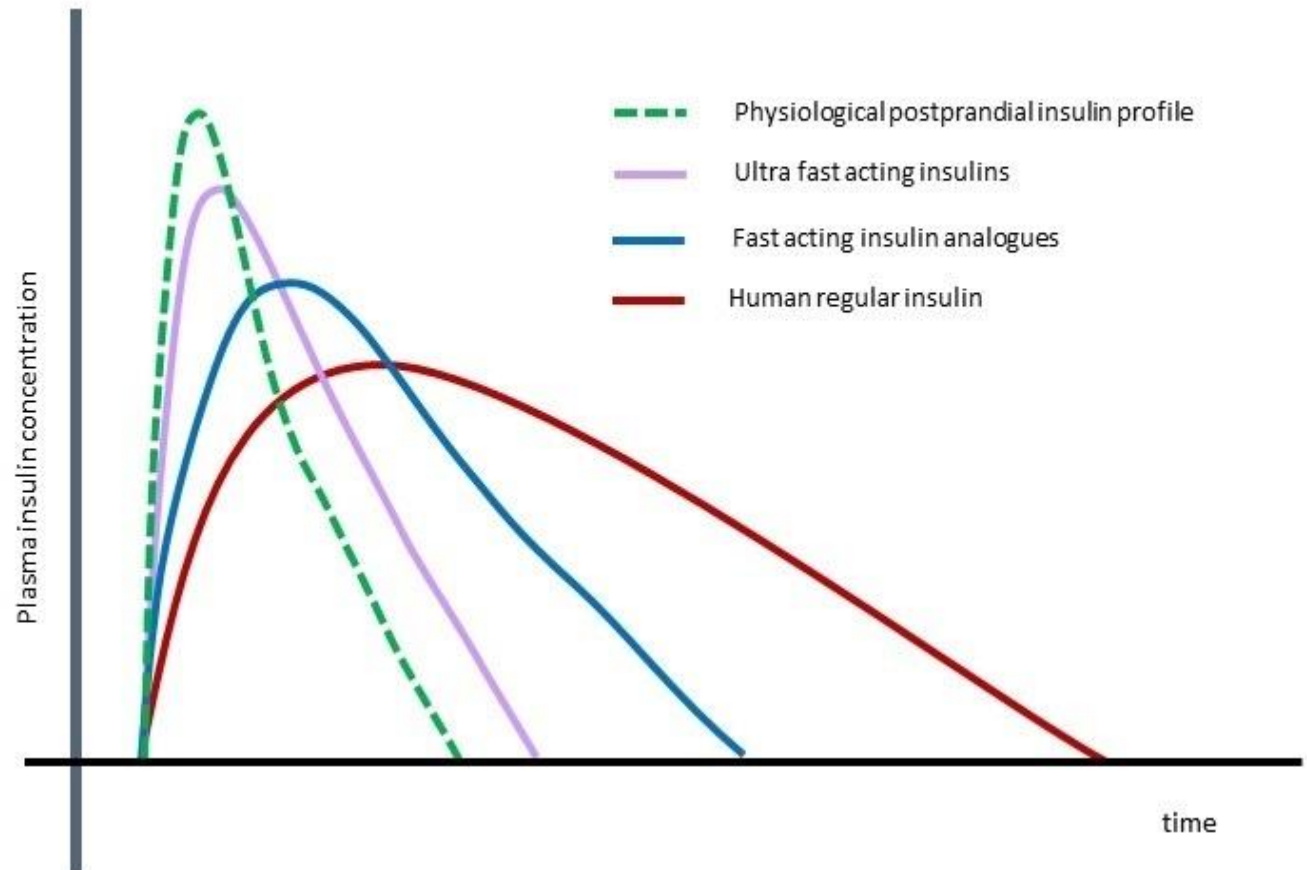
(1) Confirmed events based on plasma glucose ≤ 3.9 mmol/L (≤ 70 mg/dL); Ritzel RA, et al. Poster presented at EASD 2014; Abstract 963

(2) Peer-reviewed EDITION program publications include: Riddle MC, et al. Diabetes Care. 2014; 37:2755-62 (EDITION 1); Yki-Järvinen H, et al. Diabetes Care. 2014; 37:3235-43 (EDITION 2); Bolli GB, et al. Diabetes Obes Metab. FEB 2015; DOI: 10.1111/doms.12438 (EDITION 3)

(3) 0000-05:59h

(4) 24 h

Faster acting aspartart Fiasp

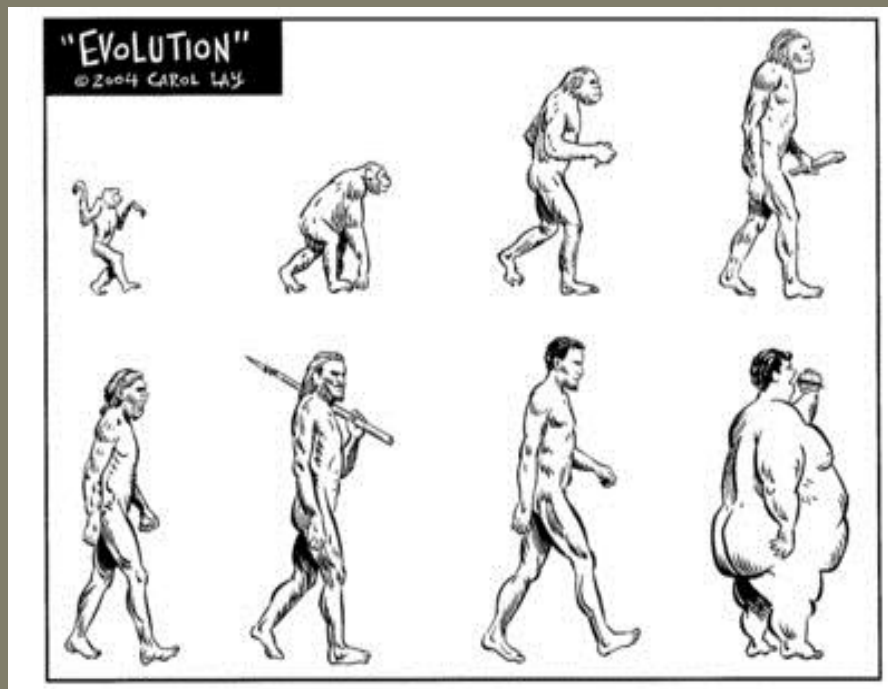
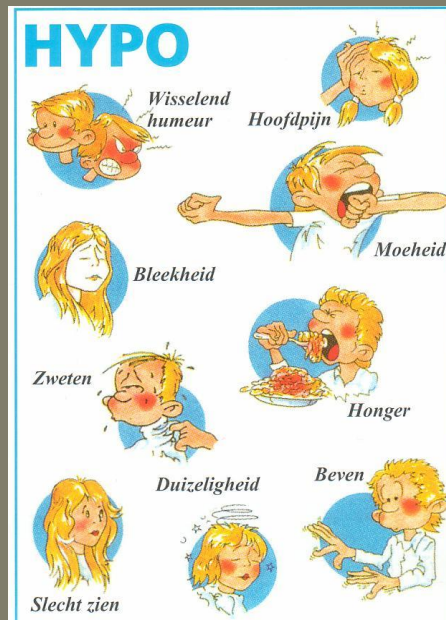


Medicaties

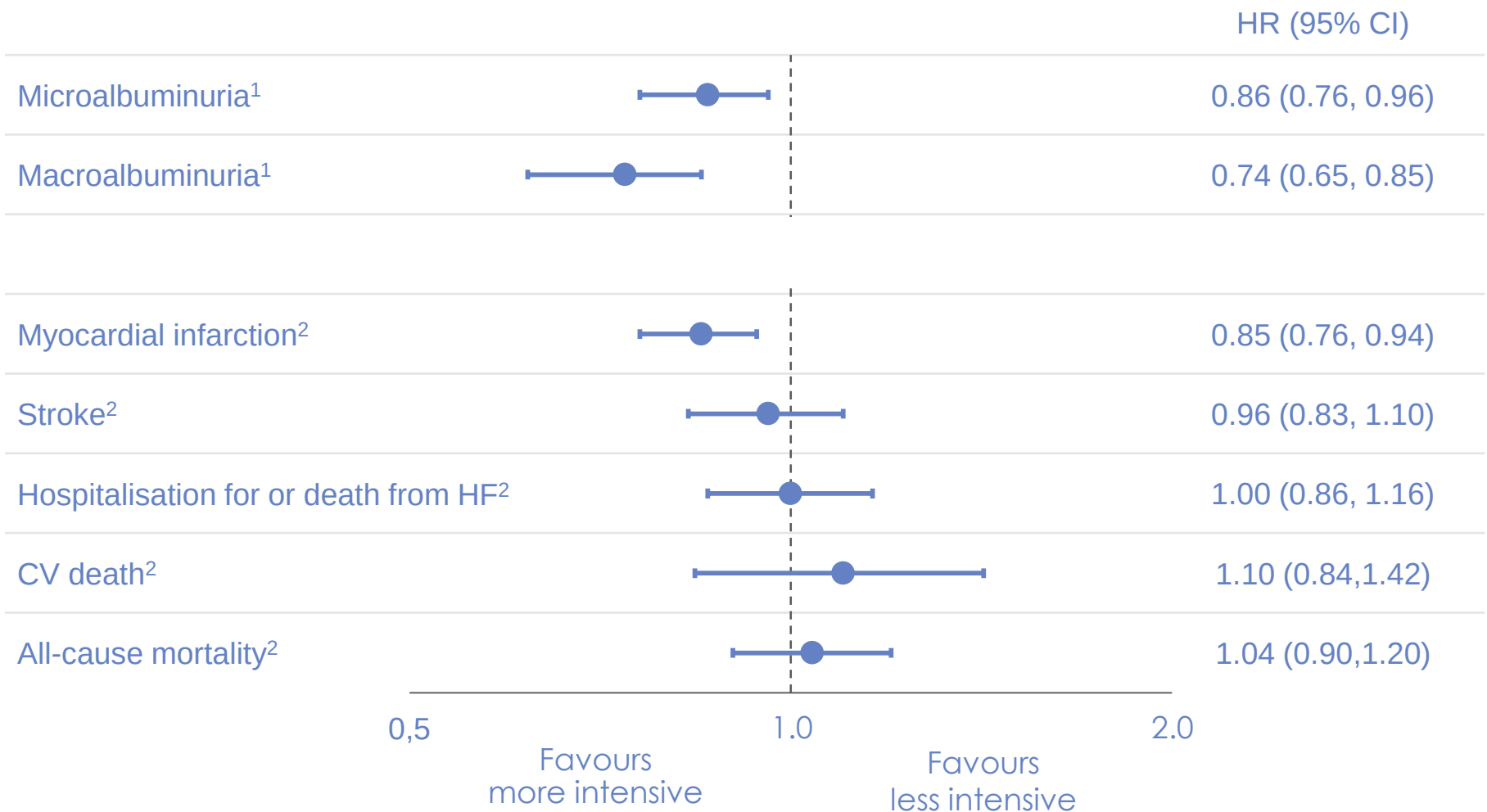
- Metformin
- Sulfonylurea
- Thiazolidinediones
- Incretines * inspuittbare
 * DPP 4 inhibitoren
- SGLT2- inhibitoren



	HbA1c	MEAN BLOOD GLUCOSE	
	test score	mg/dL	mmol/L
↑ action suggested	14.0	380	21.1
	13.0	350	19.3
↑ good	12.0	315	17.4
	11.0	280	15.6
↑ excellent	10.0	250	13.7
	9.0	215	11.9
↓	8.0	180	10.0
	7.0	150	8.2
↓	6.0	115	6.3
	5.0	80	4.7
	4.0	50	2.6



Intensive glucose-lowering therapy has limited impact on macrovascular outcomes and mortality



medicatie

1. Metformin = Glucophage, Metformax .. 500 en 850 mg

Verbetert de werking van insuline – vooral thv lever
bewaart de werking van de pancreas

gewichtsdeling

Weinig kans op hypo

Soms maag- darmlast

Mag niet bij verminderde nierwerking of zo kans op
zuurstoftekort in het bloed : lactaatacidose

EERSTE KEUZE : steeds proberen max. dosis van 3 x 850
te bereiken

metformin

Nierfunctie:

eGFR/creatinineclearance >50 ml/min:

3 x 850 mg

eGFR/creatinineclearance 50 à 30 ml/min:

2 x 500 mg

eGFR/creatinineclearance <30 ml/min:

STOP

Cave B 12 tekort !

Metformin

Bewijs dat hart- en bloedvatverwikkelingen bij type 2 diabetes verminderen

- Minder kanker !
- Invloed op prognose:
- Overlevingstijd (Britse retrospectieve studie eind 2014): diabetes gestart met metformin als eerste therapie
 - 38 % langer dan diabetes gestart met sulfonureum
- Dikkedarmkanker: minder voorkomen (-10%), minder sterfte (-32%)

medicatie

2, Pancreas stimuleren : sulfonylurea

Daonil = Euglucon: langwerkend – meer hypo's
gliclazide 80 mg 3 x 1 = Uni-diamicron 60mg : langwerkend
Amarylle : langwerkend (2-3-4 mg)
Glurenorm: kortwerkend – ook bij nierinsufficiëntie
Minidiab = Glibenese : kortwerkend
Novonorm : zeer kortwerkend – minder G-stijging- duur
(0,5-1-2 mg) 'gliniden'

Putten de pancreas verder uit

Nooit bewezen dat ze de sterfte door hart-en vaatziekten verbeteren

Kans op hypo's

medicatie

3. Thiazolidinediones = glitazones

(Avandia 4 en 8 mg) , Actos 15 en 30 mg

Werken op PPAR gamma in kern

Verbeteren de werking van insuline in lever, spier en vet

Sparen de pancreas

afremmen van de ziekte in beginfase

Duur

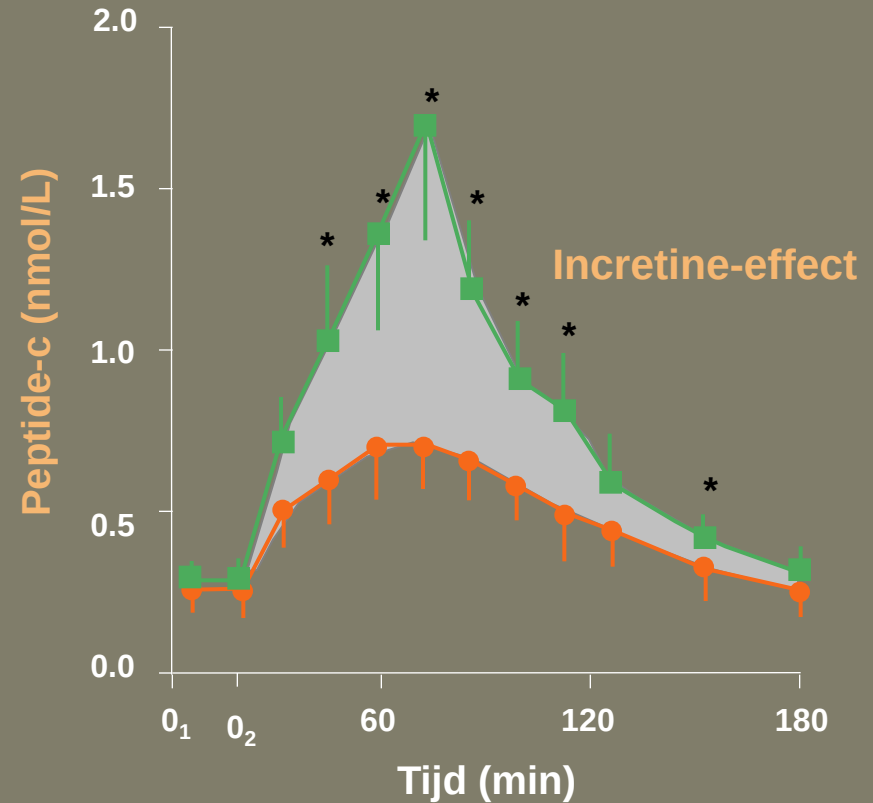
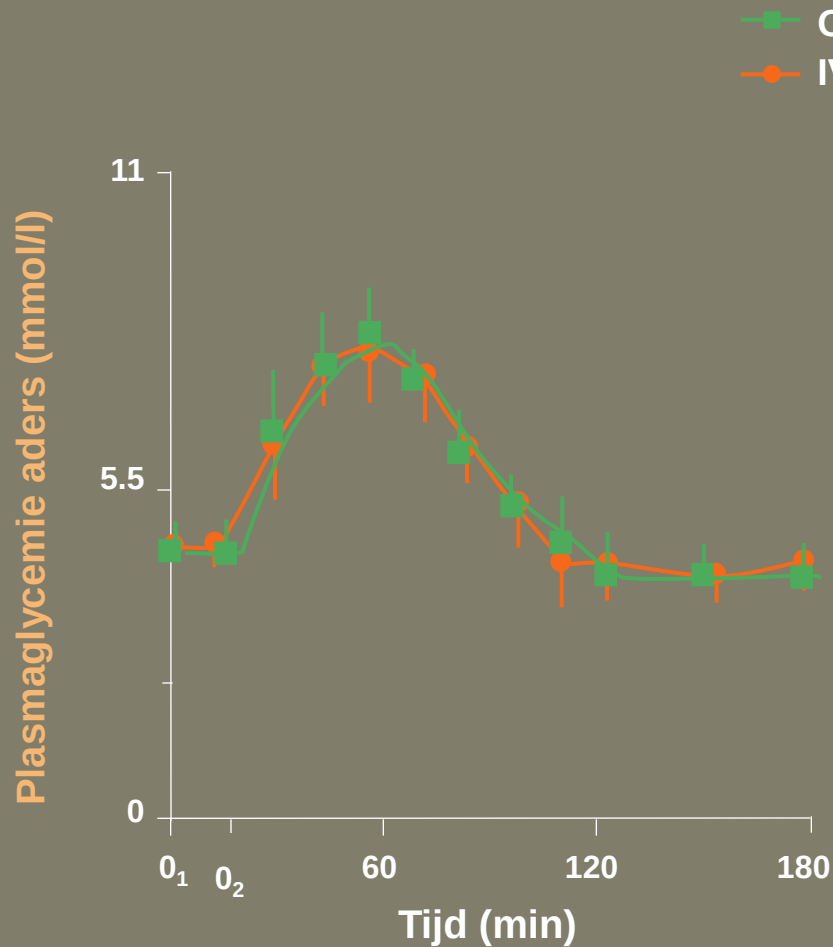
gewichtstoename, bloeddrukstijging, water ophouden

Osteoporose

meer hartinfarcten door Avandia

Het “incretine-effect”

-Glucagon like peptide I
-Glucosedependent
insulinotropic polypeptide



Studie in cross over bij niet-diabetici (n=6)
Gemiddelden $\pm$ SE; * $p \leq 0,05$; 0₁-0₂ = Perfusietijd van glucose.
(1) Nauck MA, et al.. J Clin Endocrinol Metab. 1986;63:492-498.

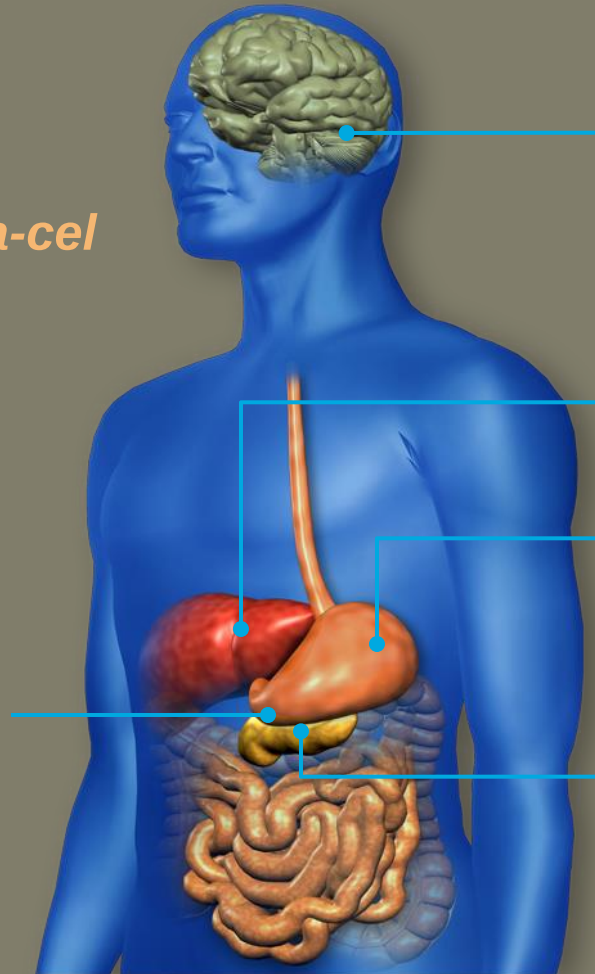
Werking Glucagon like peptide 1

Bestudeerd in continu infuus

*Verbeterd de Beta-cel
respons*

**Beta-cellen van de
pancreas :**

- Stimuleert de glucose-afhankelijke insulinesecretie
- Herstelt 1ste fase insulinesecretie



*Vermindert de nood aan
insuline van het organisme
door op verschillende plaatsen in te
werken*

Hersenen :

Stimuleert verzadiging en
vermindert voedselinname

Lever :

Vermindert de hepatische
productie van glucose

Maag :

Vertraagt de maaglediging

**Alfa-cellen
van de pancreas:**

Vermindert de post-prandiale
secretie van glucagon

1. Nabootsen van effecten van GLP-1 :

Incretine mimetica :

exenatide = BYETTA > Bydurion *

liraglutide = VICTOZA

lixisenatide = LYXUMIA ++

albiglutide = EPERZAN * ++

dulaglutide = TRULICITY *

2. Verlengen van het half-leven van GLP-1 :

DPP-4 inhibitoren

- Sitagliptin = JANUVIA
- Vildagliptin = GALVUS
- Saxagliptin = ONGLYZA
- Alogliptin = VIPIDIA
- Linagliptin = TRAJENTA

medicatie

4. DPP4 inhibitoren

Januvia, Galvus, Onglyza, Trajenta, Vipidia....

Geen hypo's

Goed verdragen

Doen gewicht niet toenemen

Duur

Afremmend effect op evolutie?

Cardiovasculair neutraal

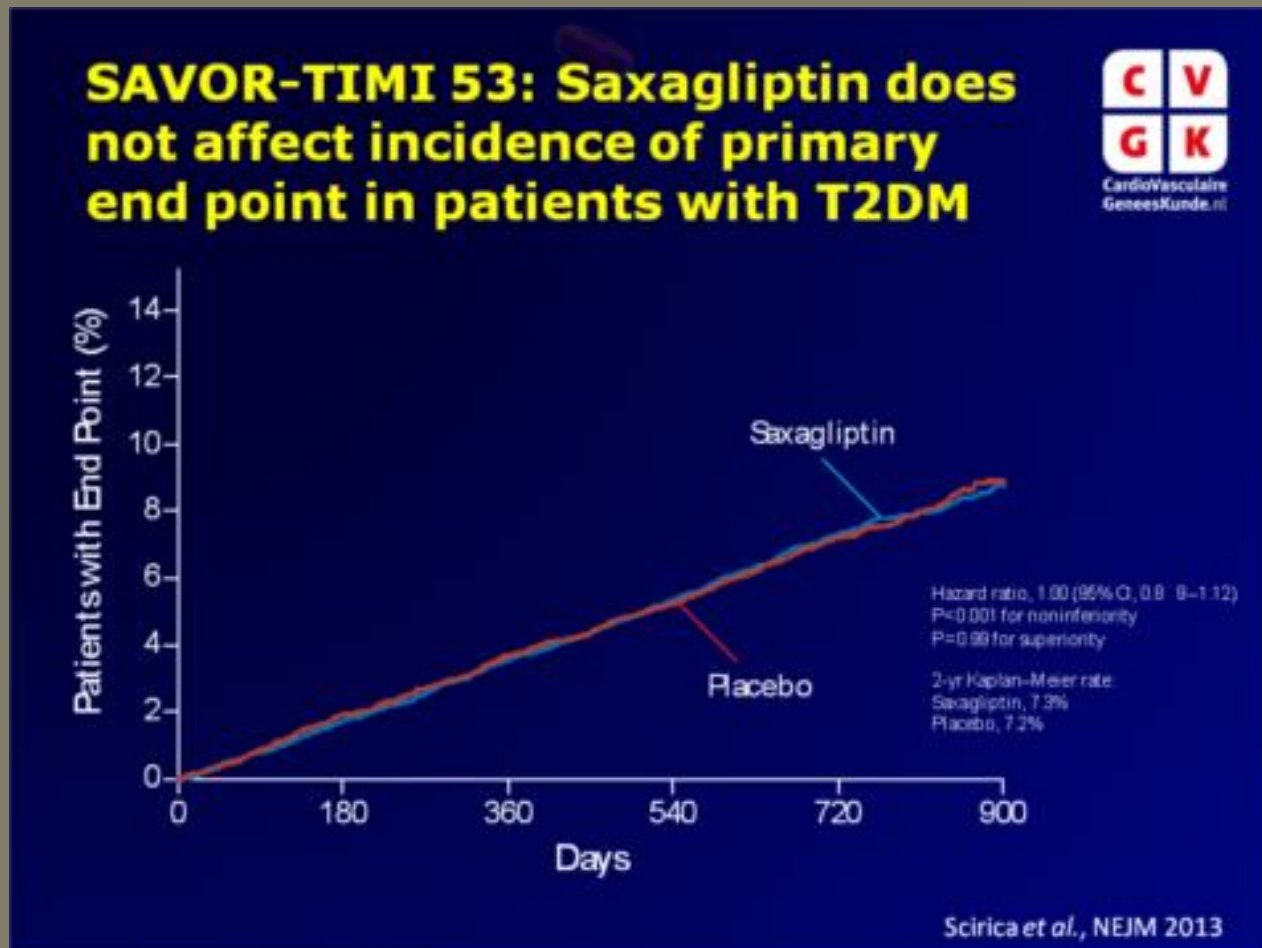
De DPP 4 inhibitoren zijn cardiovasculair neutraal

Savor TIMI study : saxagliptin (Onglyza)

Examine study : alogliptin (Vipidia)

Tecos study : sitagliptin (Januvia)

Verwacht : Carolina trial : linagliptin (Trajenta)



Met metformin 2*850/1000

Janumet

Eucreas

Komboglyze

Jentadueto

Vipdomet

Byetta (exenatide): 2 maal per dag

Victoza (liraglutide): 1 maal per dag

Lyxumia (lixisenatide): 1 maal per dag

Bydurion (exenatide-microsferen): 1
maal per week

Eperzan (albiglutide): 1 maal per week

Trulicity (dulaglutide): 1 maal per week



ELIXA

LEADER

SUSTAIN-6

EXSCEL

ORIGINAL ARTICLE

Lixisenatide in Patients with Type 2 Diabetes
and Acute Coronary Syndrome

The **NEW ENGLAND**
JOURNAL of MEDICINE

ESTABLISHED IN 1812

JULY 28, 2015

PAGE 375 NO. 8

Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes

ORIGINAL ARTICLE

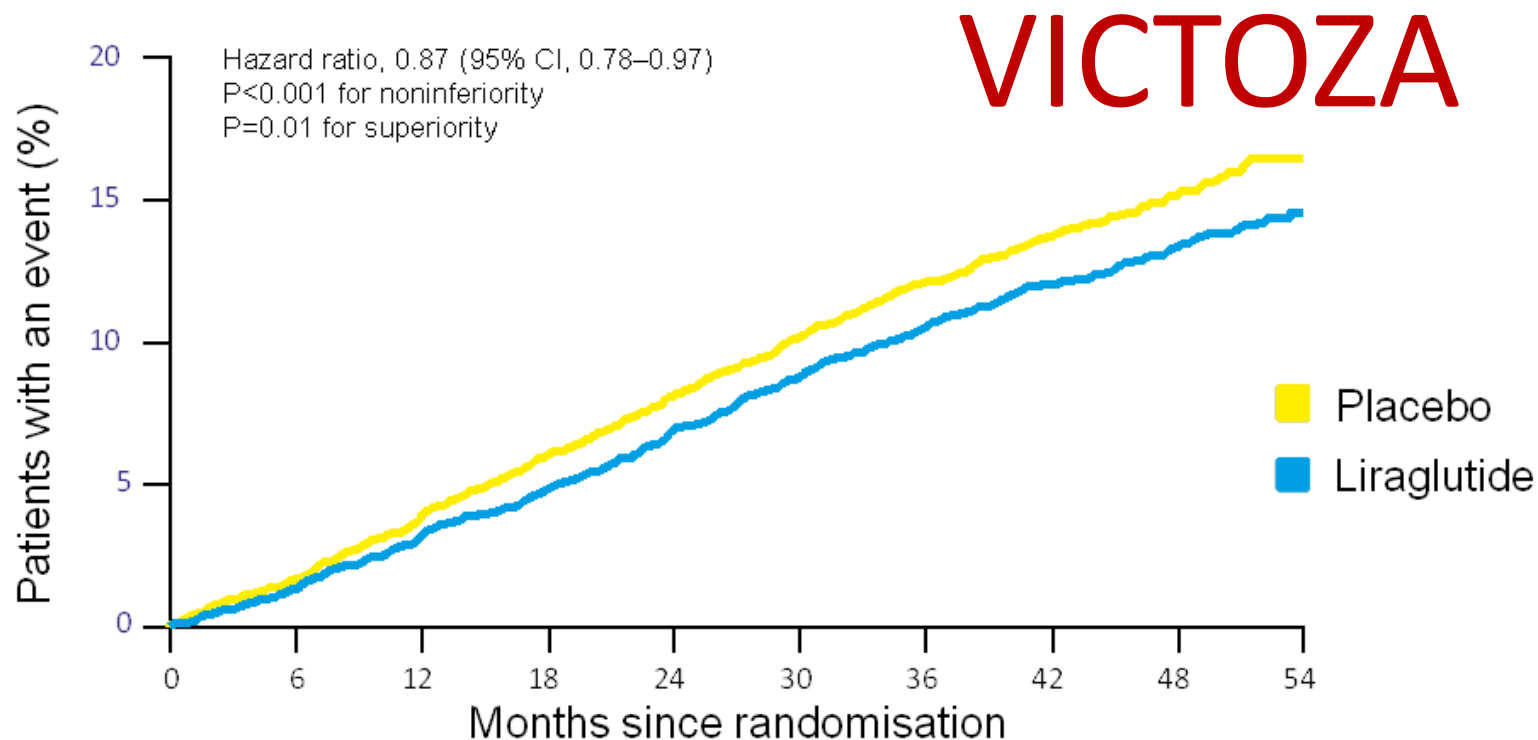
Semaglutide and Cardiovascular Outcomes
in Patients with Type 2 Diabetes

ORIGINAL ARTICLE

Effects of Once-Weekly Exenatide on
Cardiovascular Outcomes in Type 2 Diabetes

LEADER trial: Primary Outcome

First occurrence of CV death, nonfatal myocardial infarction, or nonfatal stroke in the time-to-event analysis in patients with type 2 diabetes and high CV risk.



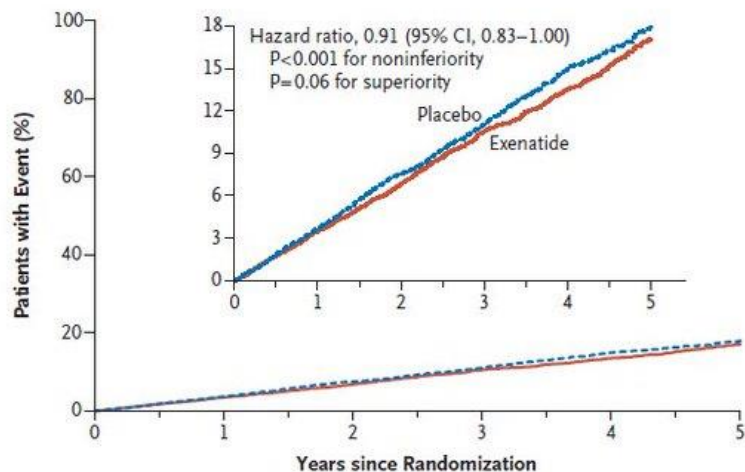
Liraglutide Effect and Action in Diabetes: Evaluation of cardiovascular outcome Results (LEADER) trial

Adapted from: Marso SP *et al.*, NEJM 2016



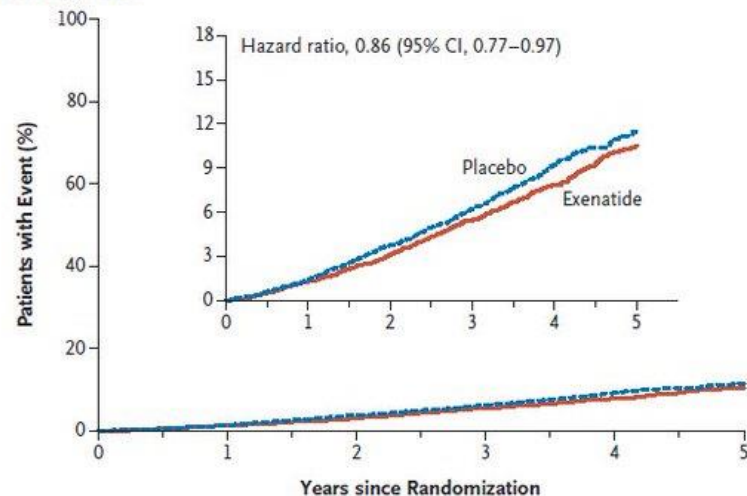
Exenatide – Bydurion : EXSCEL TRIAL

A Primary Cardiovascular Outcome



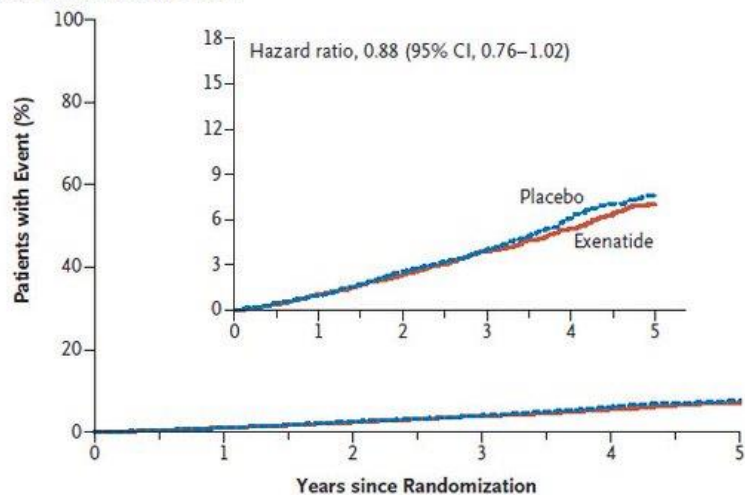
No. at Risk												
Placebo	7396	7120	6897	6565	5908	4468	3565	2961	2209	1366	687	
Exenatide	7356	7101	6893	6580	5912	4475	3595	3053	2281	1417	727	

B Death from Any Cause



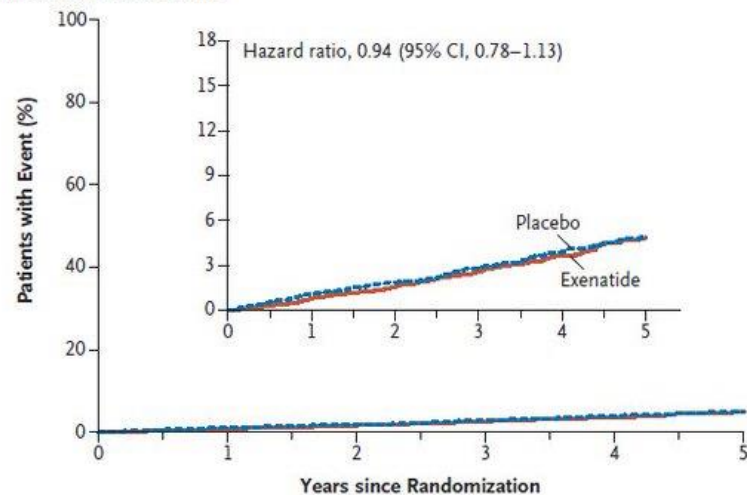
No. at Risk													
Placebo	7396	7344	7278	7058	6470	5019	4091	3478	2666	1695	892		
Exenatide	7356	7304	7234	7028	6433	4991	4095	3518	2698	1726	907		

C Death from Cardiovascular Causes

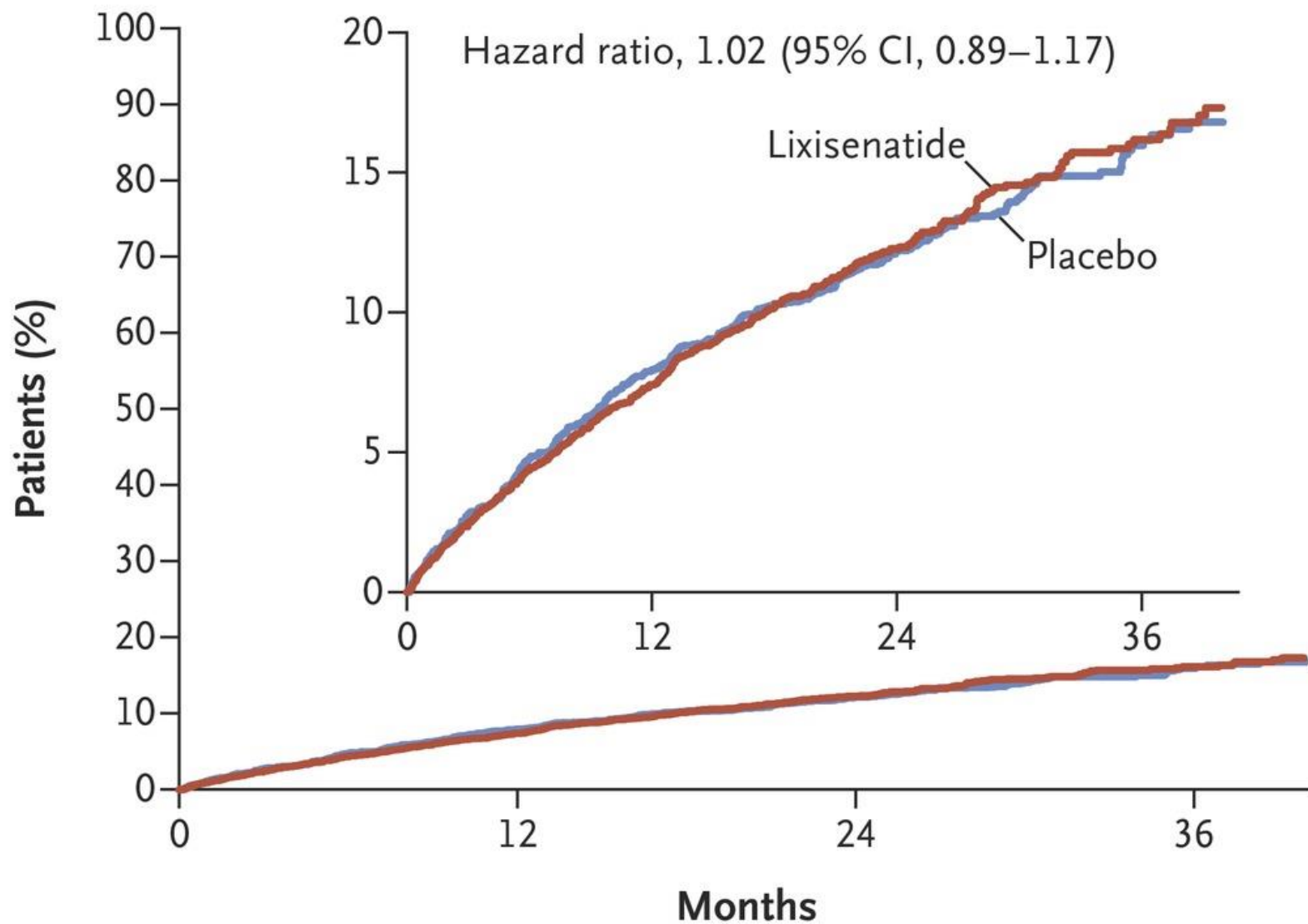


No. at Risk													
Placebo	7396	7344	7278	7058	6470	5019	4091	3478	2666	1695	907		
Exenatide	7356	7304	7234	7028	6433	4991	4095	3518	2698	1726	892		

D Hospitalization for Heart Failure



No. at Risk													
Placebo	7396	7183	7019	6743	6112	4678	3756	3156	2375	1464	735		
Exenatide	7356	7174	7023	6756	6108	4669	3790	3234	2430	1517	776		



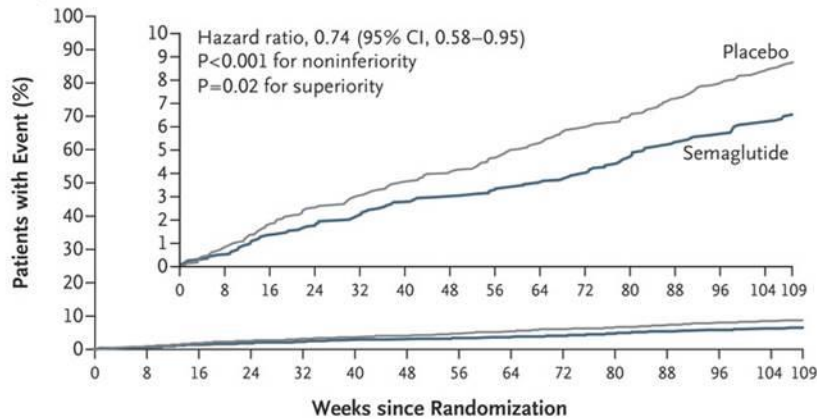
No. at Risk

Placebo	3034	2759	1566	476
Lixisenatide	3034	2785	1558	484

Semaglutide (Novo Nordisk)

SUSTAIN TRIAL

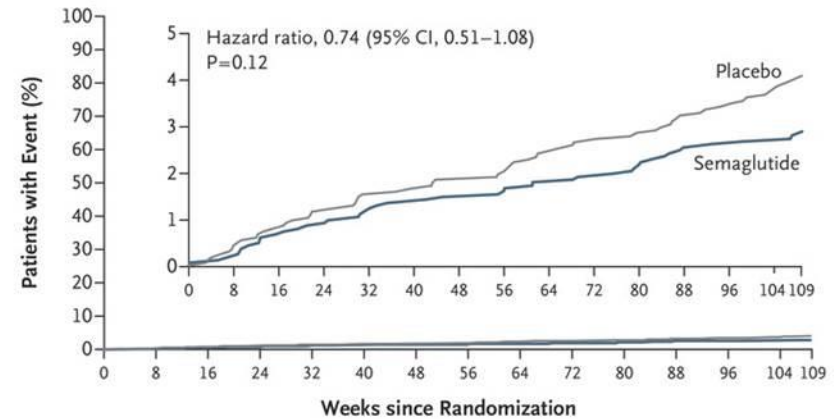
A Primary Outcome



No. at Risk

Placebo	1649	1616	1586	1567	1534	1508	1479
Semaglutide	1648	1619	1601	1584	1568	1543	1524

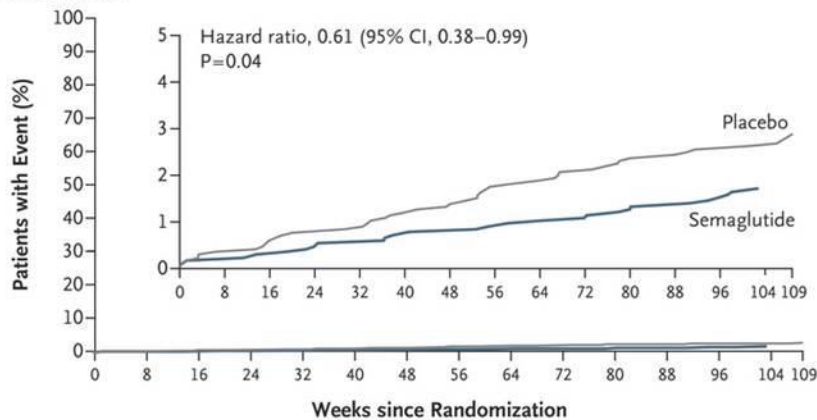
B Nonfatal Myocardial Infarction



No. at Risk

Placebo	1649	1624	1598	1587	1562	1542	1516
Semaglutide	1648	1623	1609	1595	1582	1560	1543

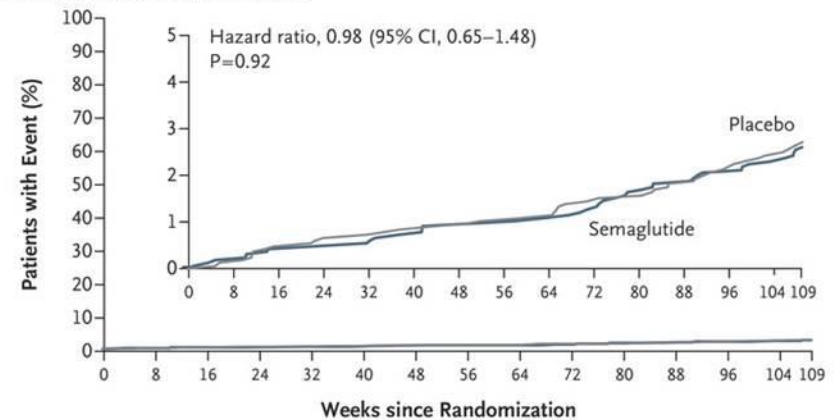
C Nonfatal Stroke



No. at Risk

Placebo	1649	1629	1611	1597	1571	1548	1528
Semaglutide	1648	1630	1619	1606	1593	1572	1558

D Death from Cardiovascular Causes



No. at Risk

Placebo	1649	1637	1623	1617	1600	1584	1566
Semaglutide	1648	1634	1627	1617	1607	1589	1579

De SGLT-2 inhibitoren = Sodium glucose co-transporter 2 inhibitoren

- FORXIGA
INVOKANA
JARDIANCE

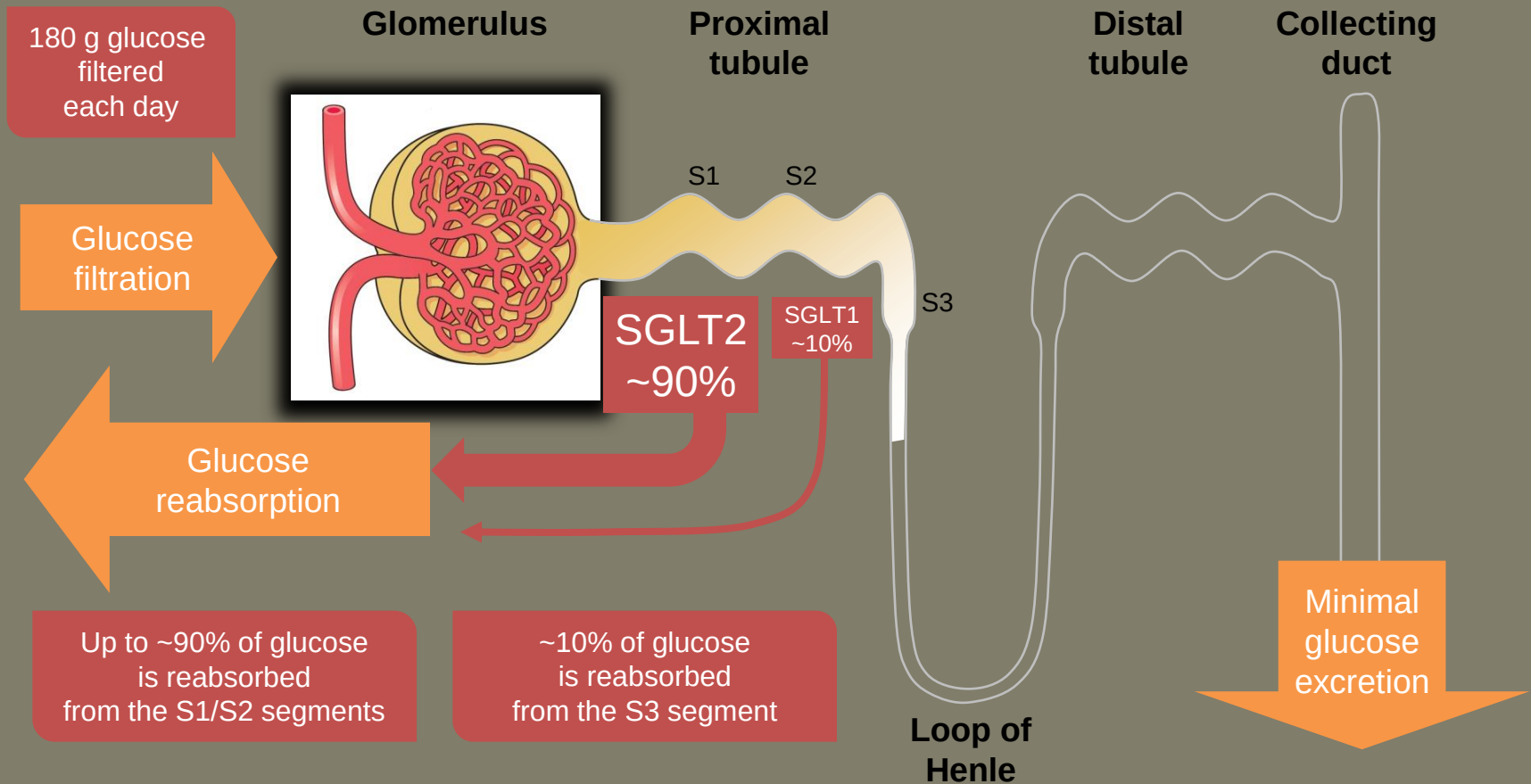


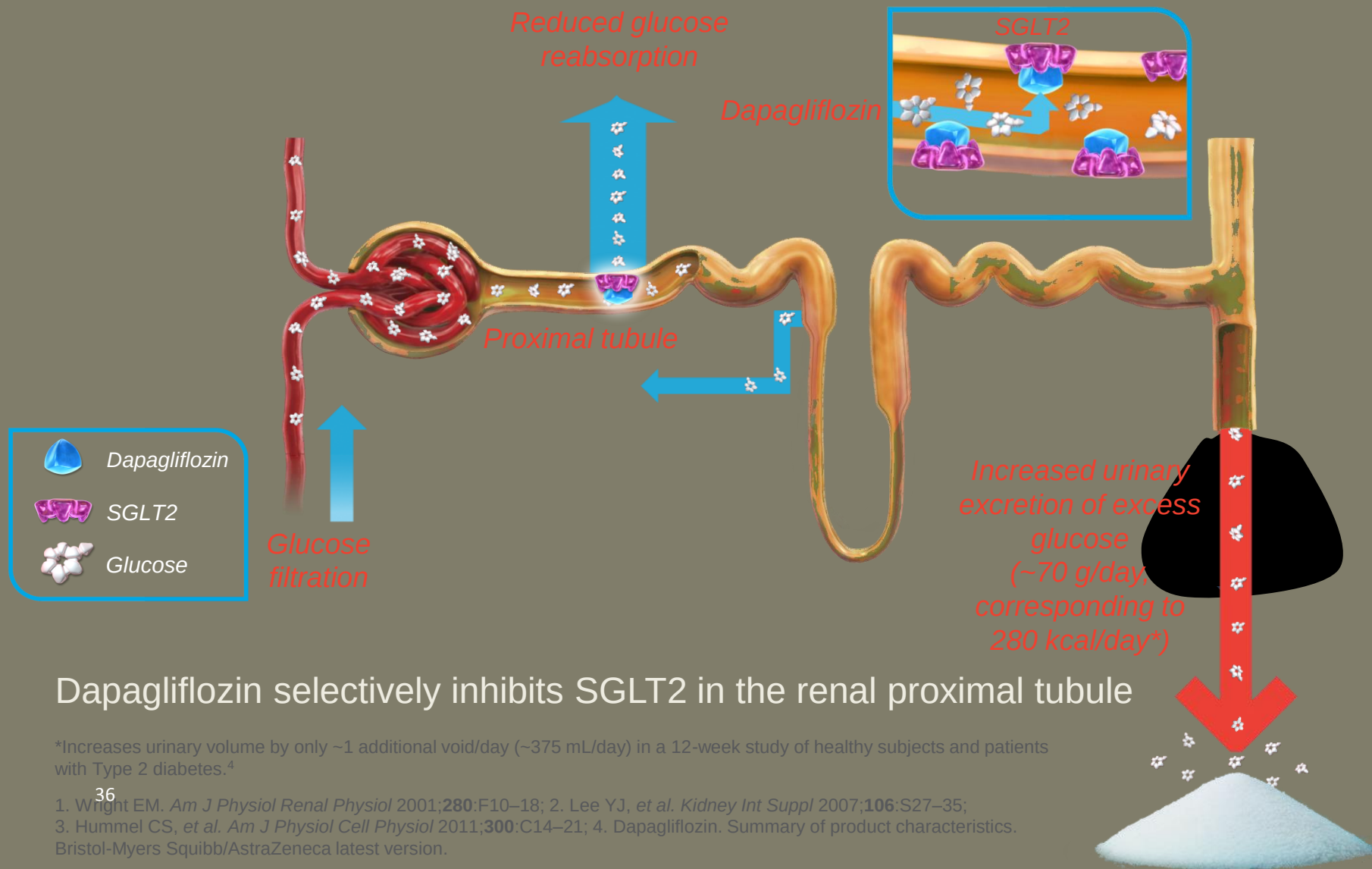
- “De suikerplaspil”



The kidneys filter and reabsorb 180 g of glucose per day

Sodium-glucose co-transporters (SGLTs) are responsible for this reabsorption in the kidneys

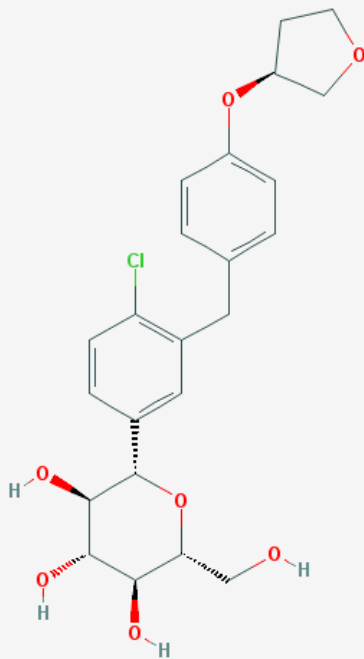




SGLT2 inhibatoren

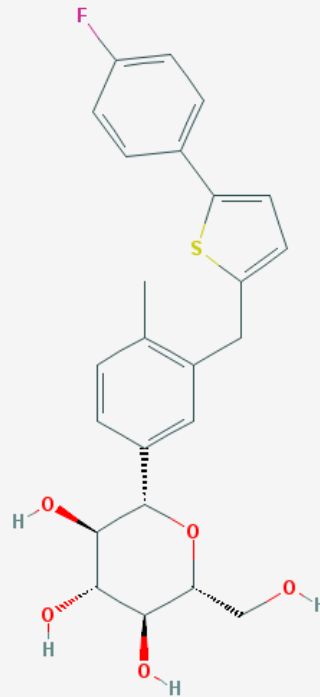
JARDIANCE

Empagliflozin



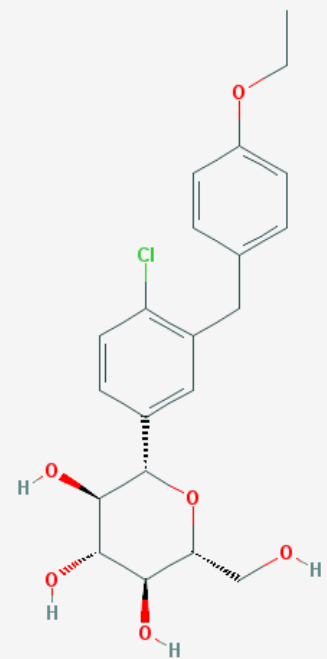
INVOKANA

Canagliflozin



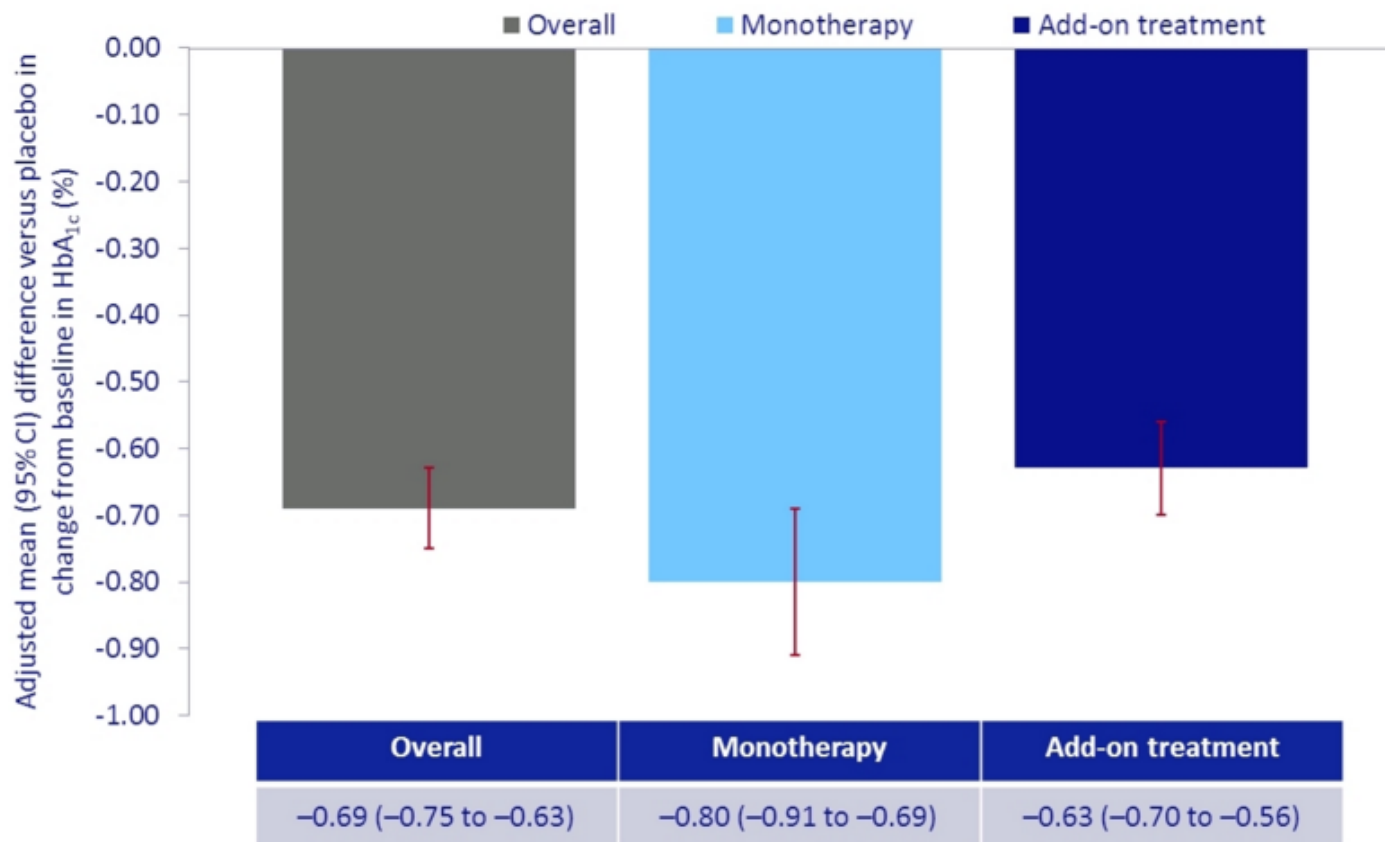
FORXIGA

Dapagliflozin



Effect van SGLT2 inhibitoren op HbA_{1c} waarden

Placebo-corrected change from baseline in HbA_{1c}

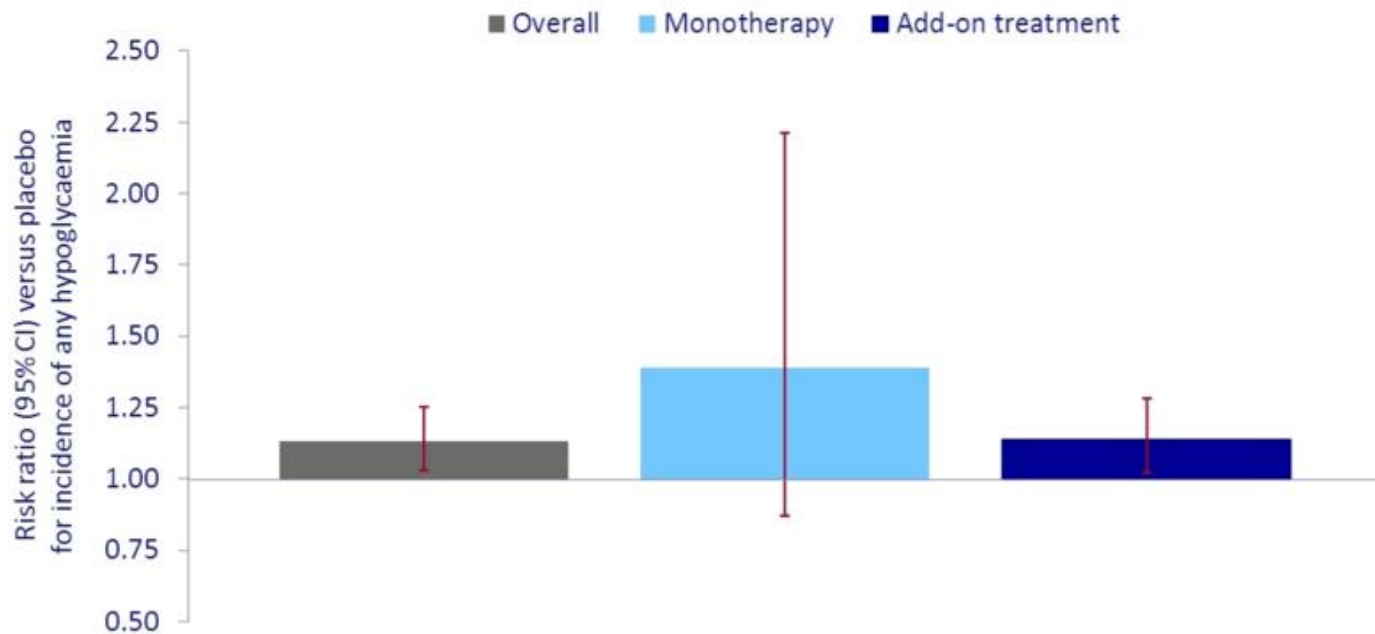


Pooled results for 20 studies of SGLT2 inhibitors as monotherapy and 35 studies as add-on treatment with ≥ 12 weeks duration from published and gray literature sources through June 30, 2014 [search strategy adapted from Vasilakou *et al.* *Ann Intern Med.* 2013(4);159:262-274]. Results are presented for the group allocated to the highest, most common dose across studies. SGLT2: sodium glucose cotransporter 2, CI: confidence interval, HbA_{1c}: haemoglobin A_{1c}.



Effect van SGLT2 inhibitoren op hypoglycemie

Risk ratio versus placebo for incidence of any hypoglycaemia



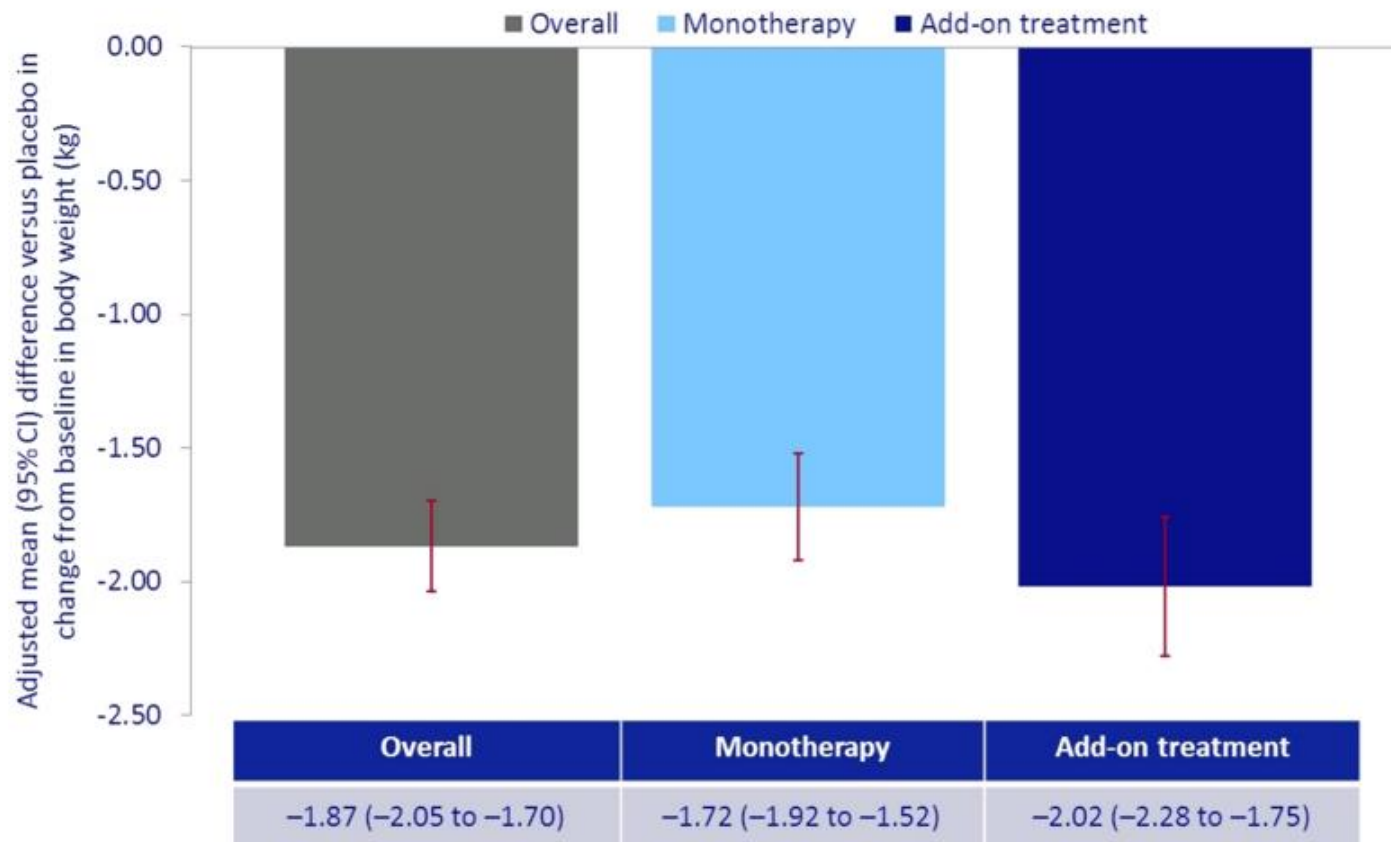
Overall	Monotherapy	Add-on treatment
1.13 (1.03 to 1.25)	1.39 (0.87 to 2.21)	1.14 (1.02 to 1.28)

Pooled results for 15 studies of SGLT2 inhibitors as monotherapy and 31 studies as add-on treatment with ≥ 12 weeks duration from published and gray literature sources through June 30, 2014 [search strategy adapted from Vasilakou *et al.* *Ann Intern Med.* 2013;159(4):262-274]. Results are presented for the group allocated to the highest, most common dose across studies. SGLT2: sodium glucose cotransporter 2, CI: confidence interval.



Effect van SGLT2 inhibitoren op lichaamsgewicht

Placebo-corrected change from baseline in body weight

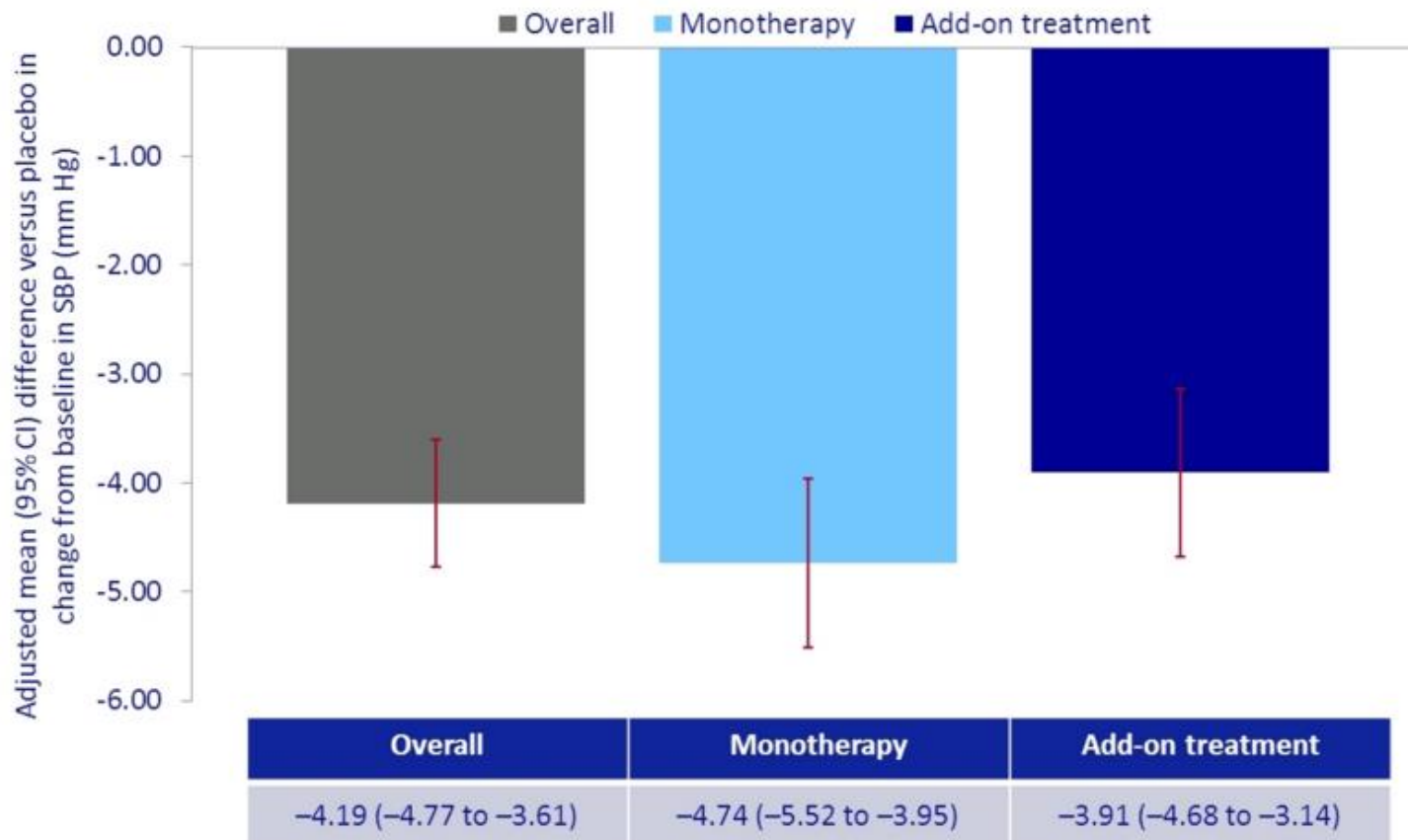


Pooled results for 18 studies of SGLT2 inhibitors as monotherapy and 28 studies as add-on treatment with ≥ 12 weeks duration from published and gray literature sources through June 30, 2014 [search strategy adapted from Vasilakou et al. *Ann Intern Med.* 2013;159(4):262-274]. Results are presented for the group allocated to the highest, most common dose across studies. SGLT2: sodium glucose cotransporter 2, CI: confidence interval.



Effect van SGLT2 inhibitoren op bloeddruk

Placebo-corrected change from baseline in systolic blood pressure (SBP)



Pooled results for 16 studies of SGLT2 inhibitors as monotherapy and 29 studies as add-on treatment with ≥ 12 weeks duration from published and gray literature sources through June 30, 2014 [search strategy adapted from Vasilakou *et al.* *Ann Intern Med.* 2013;159(4):262-274]. Results are presented for the group allocated to the highest, most common dose across studies. SGLT2: sodium glucose cotransporter 2, CI: confidence interval.

Tsapas A. *et al.* 2014. Presented at: European Association for the Study of Diabetes, September 15-19, 2014; Vienna, Austria (<http://www.easdvirtualmeeting.org/resources/will-they-change-the-landscape>)

Vasilakou D. *et al.*, *Ann Intern Med* 2013;159(4):262-274

ORIGINAL ARTICLE

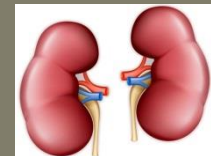
Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Bernard Zinman, M.D., Christoph Wanner, M.D., John M. Lachin, Sc.D.,
David Fitchett, M.D., Erich Bluhmki, Ph.D., Stefan Hantel, Ph.D.,
Michaela Mattheus, Dipl. Biomath., Theresa Devins, Dr.P.H.,
Odd Erik Johansen, M.D., Ph.D., Hans J. Woerle, M.D., Uli C. Broedl, M.D.,
and Silvio E. Inzucchi, M.D., for the EMPA-REG OUTCOME Investigators

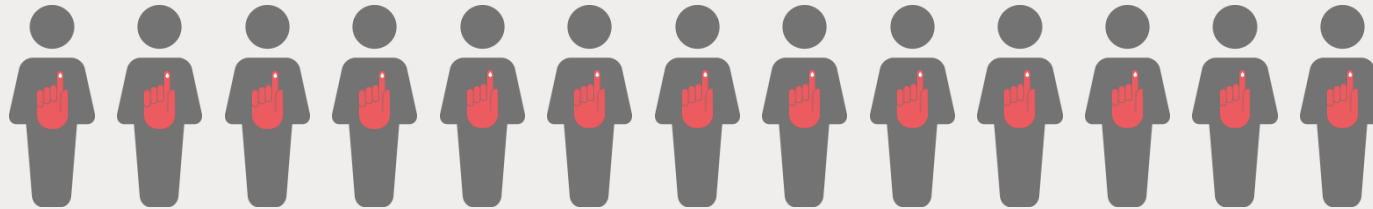
ORIGINAL ARTICLE

Empagliflozin and Progression of Kidney Disease in Type 2 Diabetes

Christoph Wanner, M.D., Silvio E. Inzucchi, M.D., John M. Lachin, Sc.D.,
David Fitchett, M.D., Maximilian von Eynatten, M.D.,
Michaela Mattheus, Dipl. Biomath., Odd Erik Johansen, M.D., Ph.D.,
Hans J. Woerle, M.D., Uli C. Broedl, M.D., and Bernard Zinman, M.D.,
for the EMPA-REG OUTCOME Investigators*



EMPA-REG OUTCOME®: een grote cardiovasculaire outcome studie in type 2 diabetes patiënten



Randomisatie
7020 type 2 diabetes patiënten



Placebo



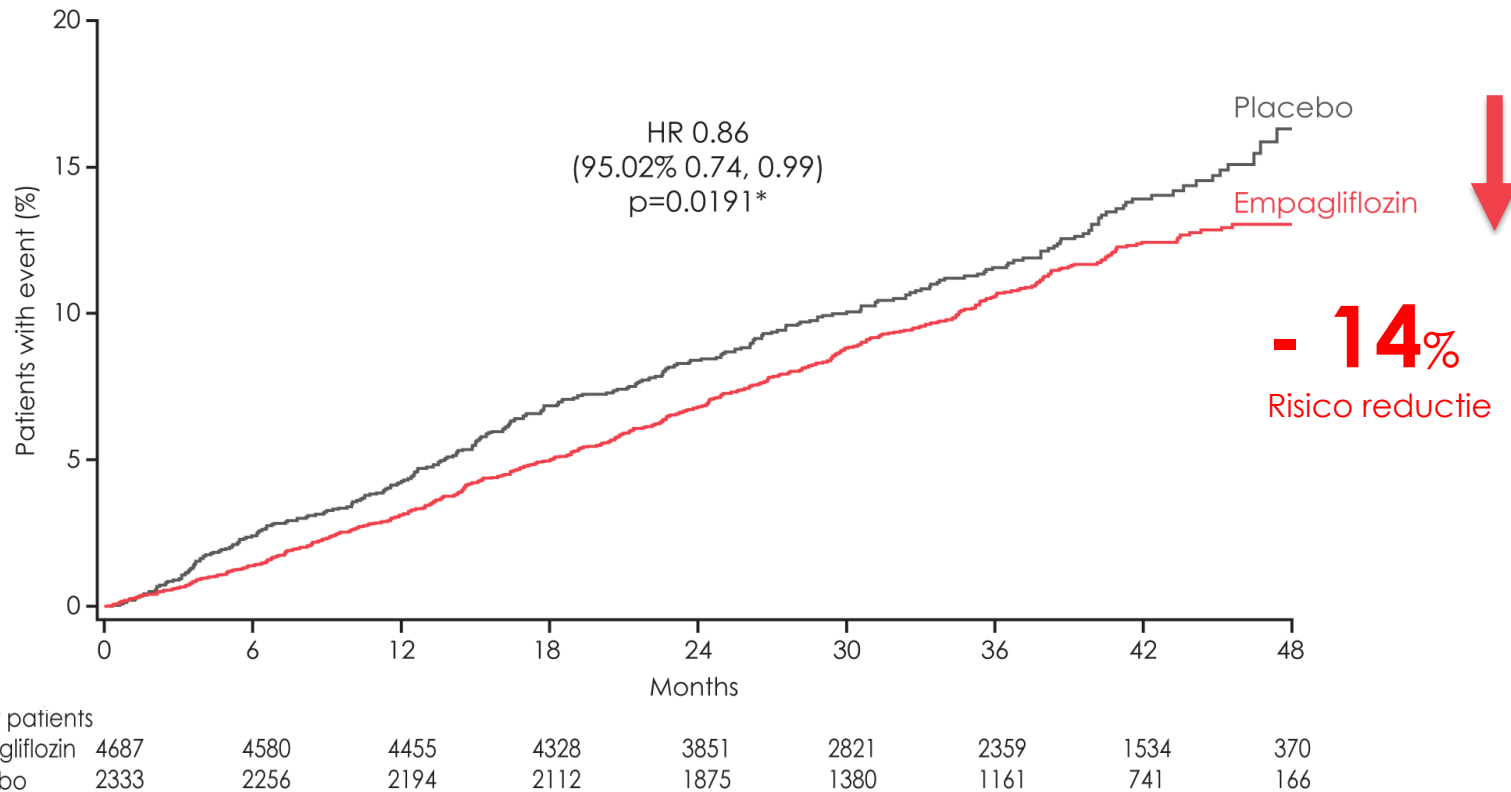
Empagliflozine
10 mg



Empagliflozine
25 mg

Bovenop een standaard behandeling

Primaire uitkomst: 3-punts-MACE

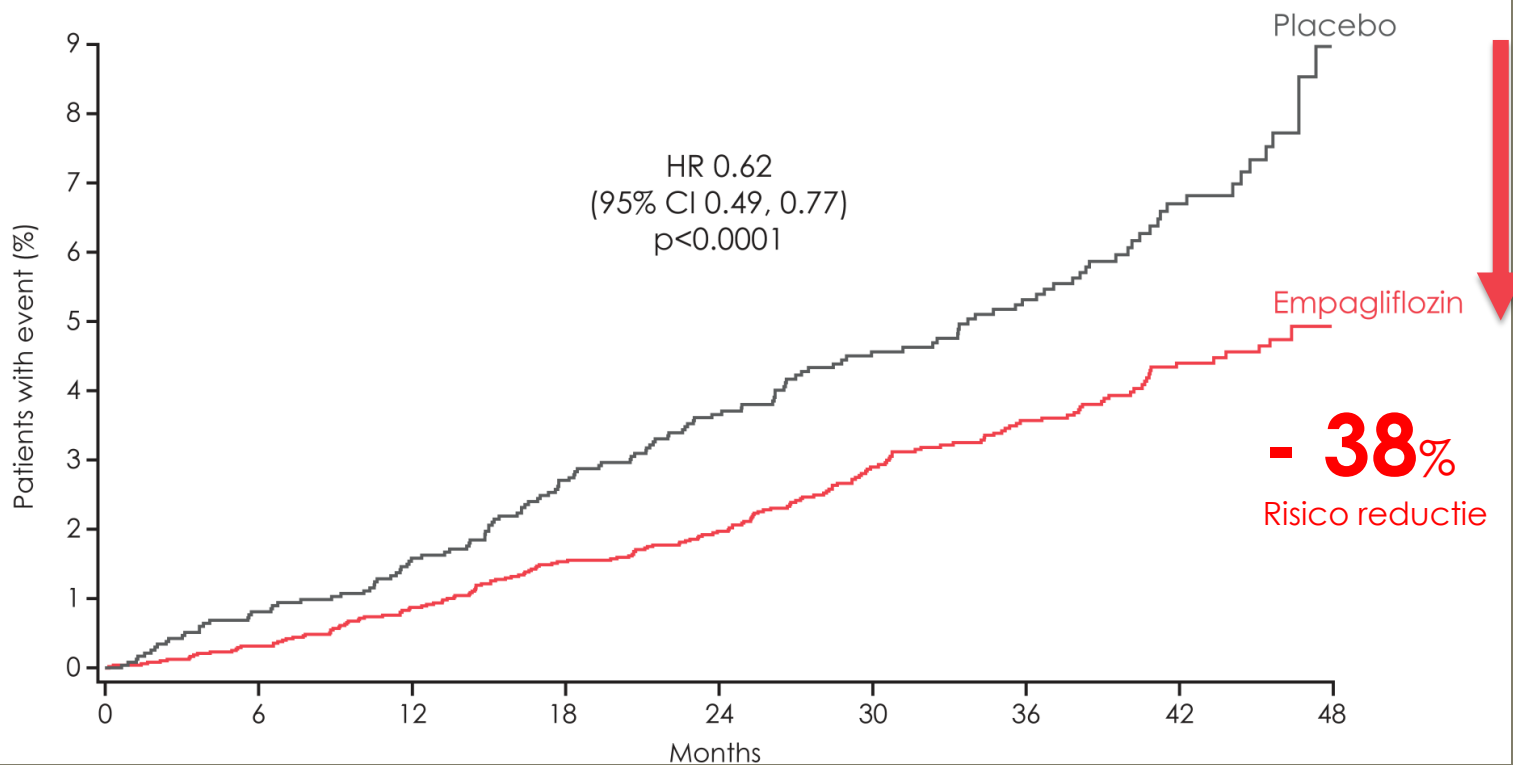


Cumulative-incidencefunctie. MACE, Major Adverse Cardiovascular Event (ernstige cardiovasculaire ongewenste gebeurtenis); HR, hazard ratio.

*Er vond dubbelzijdige toetsing op superioriteit plaats (statistische significantie werd aangegeven indien $p \leq 0,0498$)



Cardiovasculaire sterfte



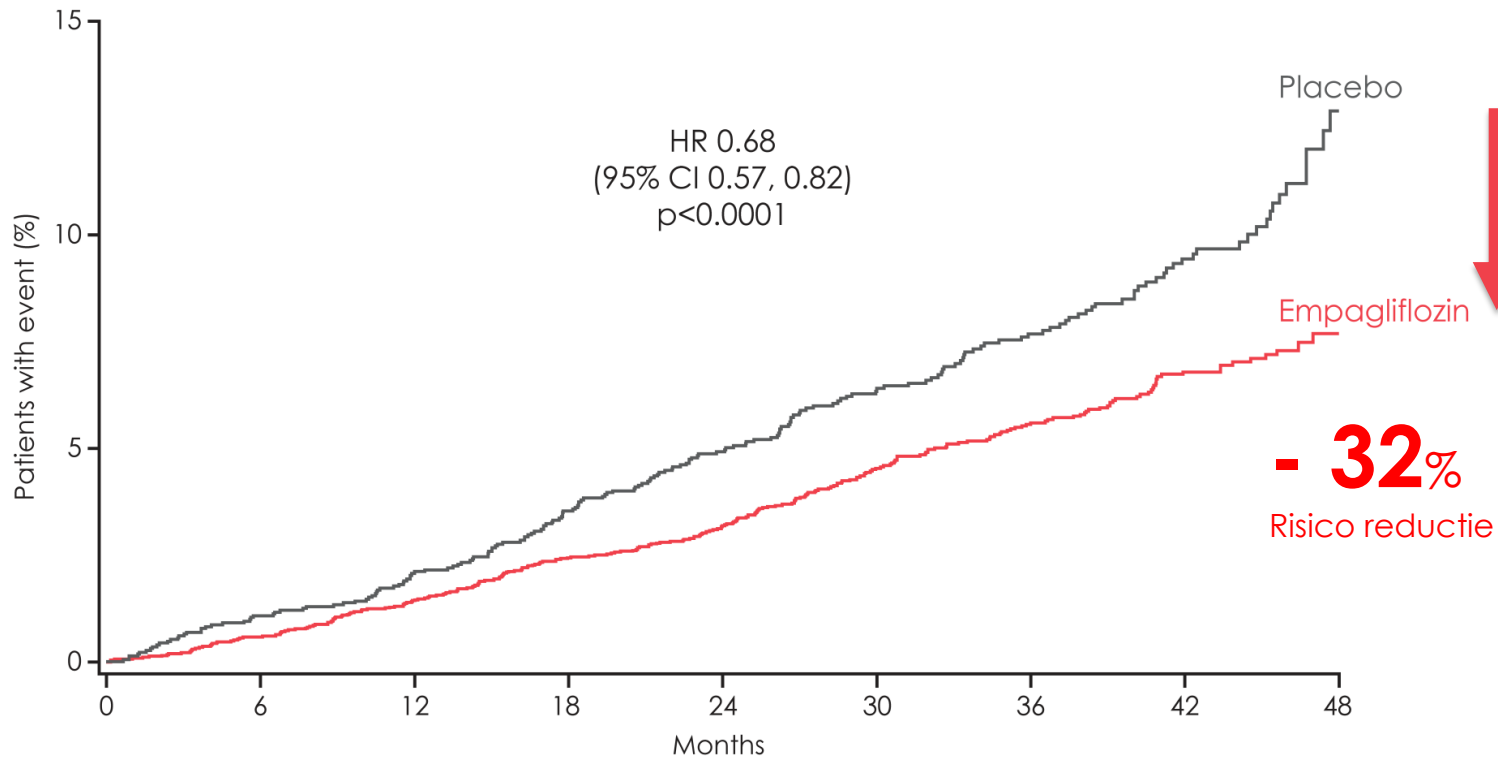
No. of patients

Empagliflozin	4687	4651	4608	4556	4128	3079	2617	1722	414
Placebo	2333	2303	2280	2243	2012	1503	1281	825	177



Cumulatieve-incidentiefunctie. HR, hazard ratio

Mortaliteit door alle oorzaken



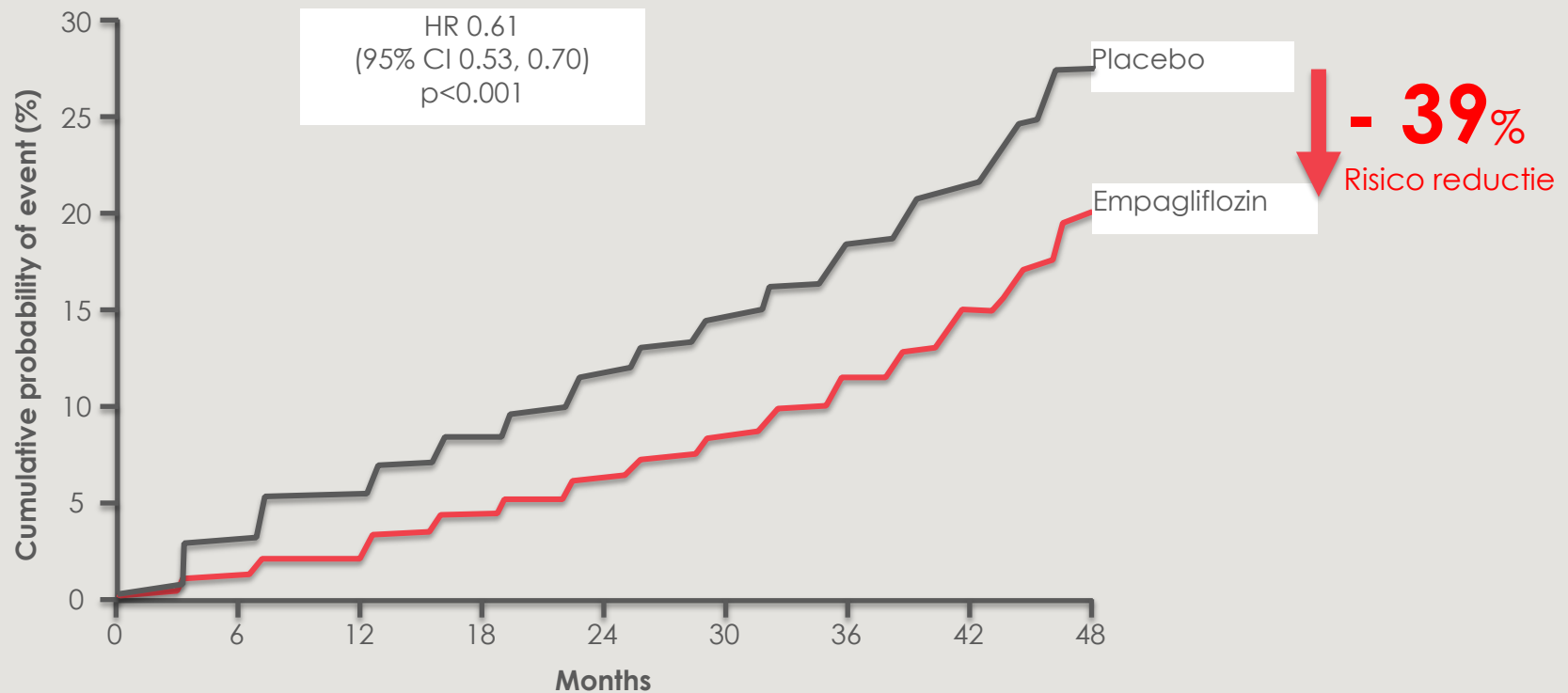
No. of patients								
Empagliflozin	4687	4651	4608	4556	4128	3079	2617	1722
Placebo	2333	2303	2280	2243	2012	1503	1281	825

Kaplan-Meierschatting. HR, hazard ratio



EMPA-REG OUTCOME®: renale uitkomsten

Empagliflozine reduceert het optreden of verergeren van nefropathie*



*gedefiniëerd als nieuw optreden van macroalbuminurie, verdubbeling van serum creatinine (vergezeld van eGFR [MDRD] ≤ 45 mL/min/1.73 m²), initiatie van niervervangingstherapie of overlijden tgv. nieraandoening

Samenvatting renale eindpunten EMPA-REG OUTCOME®



 **-38% RR**

Progressie naar
macroalbuminurie

 **-44% RR**

Verdubbeling van
serum creatinine*

 **-55% RR**

Initiatie van
niervervangings-
therapie
(vb. dialyse)



RR: risico reductie

*vergezeld van eGFR (MDRD) ≤ 45 mL/min/1.73 m²



Empagliflozine: multifactoriële effecten



↓ **0,7%**

HbA1c daling



↓ **1,9 kg**

Gewichtsdeling



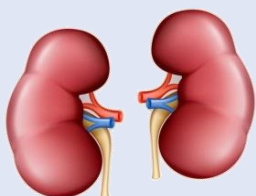
↓ **-38% RR**

Cardiovasculair
overlijden



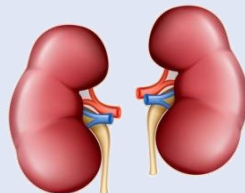
↓ **-35% RR**

Hospitalisatie
voor hartfalen



↓ **-38% RR**

Progressie naar
macroalbuminurie



↓ **-44% RR**

Verdubbeling van
serum creatinine*

RR: risico reductie

*in combinatie met eGFR (MDRD) ≤ 45 mL/min/1.73 m²

Participating countries

590 sites in 42 countries





Home

Hulpdiensten

Nieuws

Patiënten

Opname en verblijf

Artsen

Raadplegingen

Medische diensten

Verpleegafdelingen

Paramedische diensten

Omkaderende diensten

Brochures & Co

Info en route

Kwaliteit en

patiëntveiligheid

Bezoekers

Bestuur

Vacatures

Professionelen

WZC Den Olm

Maes Toon



Specialisme: Endocrinologie/Diabetologie

Consultatie:
(Na afspraak)

Ma		Di		Wo		Do		Vr		Za
VM	NM	VM	NM	VM	NM	VM	NM	VM	NM	VM

Afspraken: 015/ 50 51 11

Secretariaat: 015 50 57 19 (diabetessecretariaat)

Verwante pagina's:

[Raadpleging Endocrinologie - diabetologie](#)[Dienst Endocrinologie en diabetes](#)

Curriculum

Toon Maes behaalde in 2007 het diploma van arts aan de Katholieke Universiteit van Leuven. Nadien volgde hij een opleiding tot specialist algemene inwendige ziekten te UZ Leuven, AZ St.-Dimpna in Geel, en Imperial college in Londen. In 2011-2013 voltooide hij een subspecialisatie te UZ Leuven tot specialist in de diabetologie-endocrinologie. Sinds september 2013 is hij voltijds werkzaam in het Imeldaziekenhuis. Daarnaast is hij deeltijds staflid te UZ Leuven, als consulent op de raadpleging algemene endocrinologie.

Naast de algemene endocrinologie (hypofyseproblematiek, bijnierpathologie, schildklier en bijschildklier, ...) heeft hij een bijzondere interesse in de diabetologie, en meer bepaald in nieuwe technologieën en medicatie binnen dit domein. Hij is binnen het Imeldaziekenhuis dan ook mee verantwoordelijk voor verschillende klinische studies die deze nieuwe toepassingen implementeren. Tenslotte staat hij mee in voor het coördineren van het multidisciplinaire begeleidingsproject voor obesitas "Grandioos", en de begeleiding van patiënten die



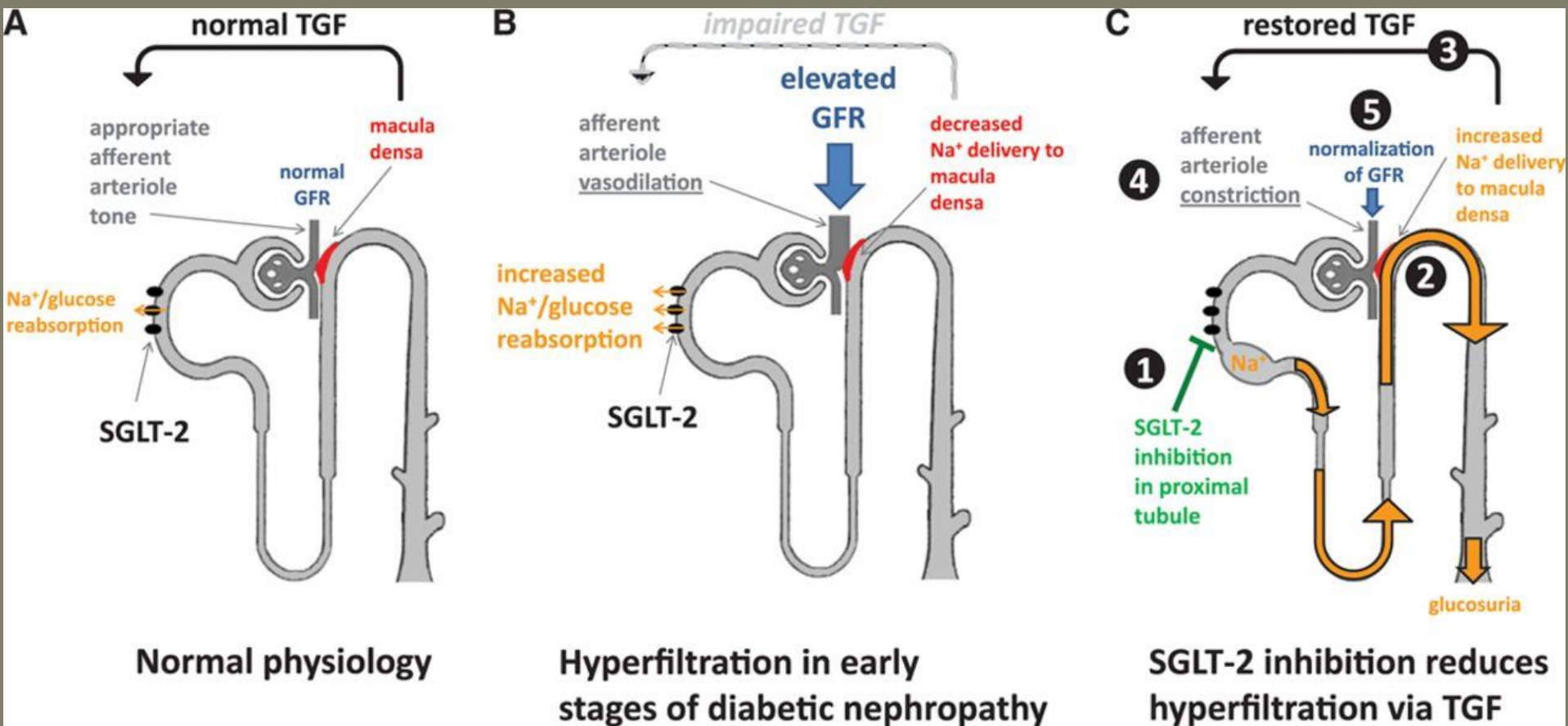
Voordelen en nadelen

- Voordelen

- Weinig hypo's
 - Gewichtsdeling
 - Bloeddrukdeling
 - Goede outcome
- EMPAREG study

- Nadelen

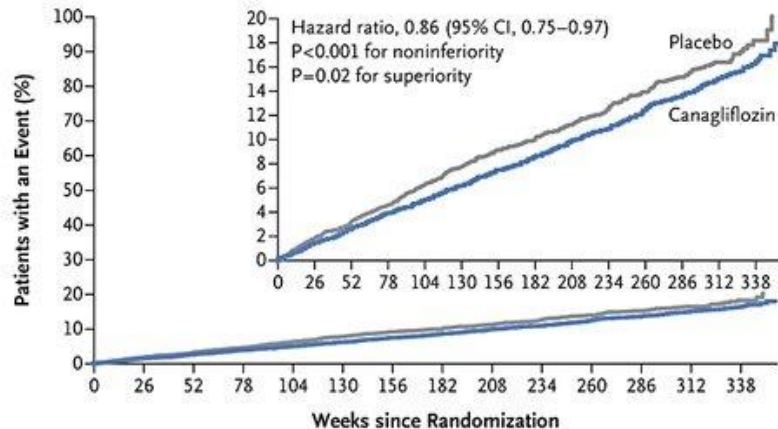
- Meer genitale infecties – meer blaasontstekingen
- Terugbetaling aan te vragen
- Niet zo verminderde nierfunctie (= niet bij ouderen ?)
- Soms ondervulling bv bij inname waterafdrifters



CANVAS TRIAL

betere populatie dan de empareg

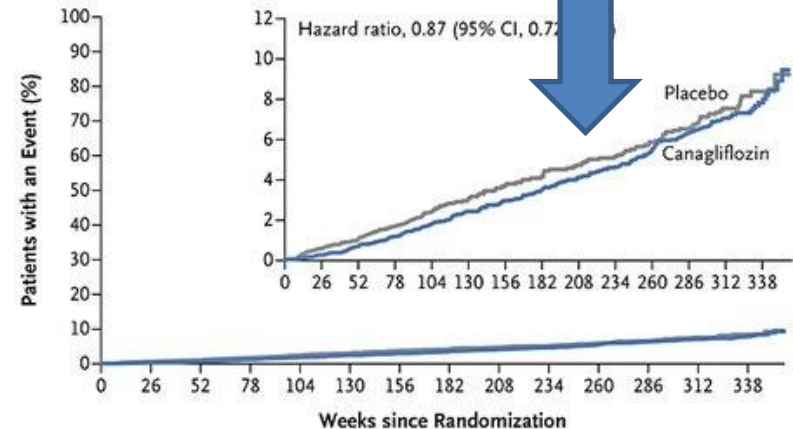
A Death from Cardiovascular Causes, Nonfatal Myocardial Infarction, or Nonfatal Stroke



No. at Risk

Placebo	4347	4239	4153	4061	2942	1626	1240	1217	1187	1156	1120	1095	789	216
Canagliflozin	5795	5672	5566	5447	4343	2984	2555	2513	2460	2419	2363	2311	1661	448

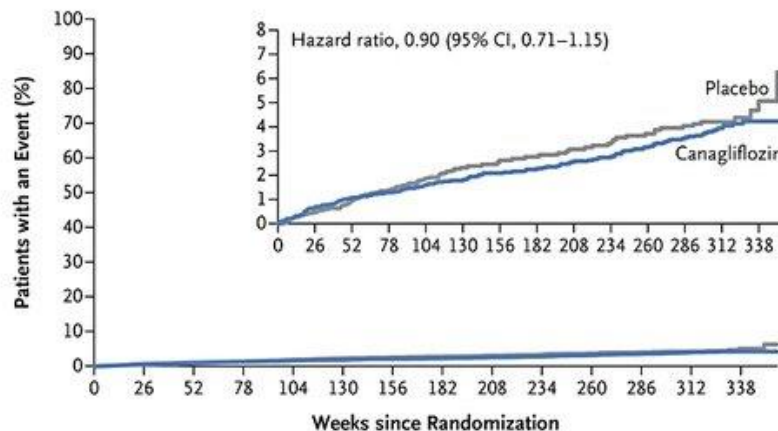
B Death from Cardiovascular Causes



No. at Risk

Placebo	4347	4316	4279	4236	3119	1759	1356	1344	1328	1310	1292	1280	924	258
Canagliflozin	5795	5768	5723	5679	4576	3182	2761	2736	2710	2687	2651	2615	1904	532

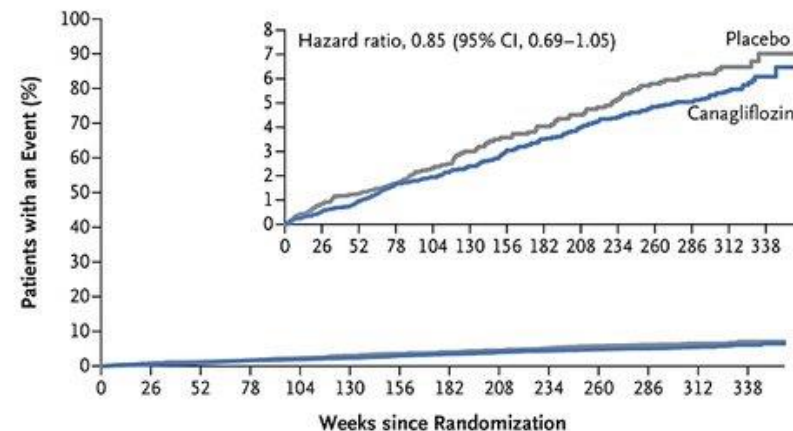
C Nonfatal Stroke



No. at Risk

Placebo	4347	4270	4197	4123	3004	1667	1274	1255	1232	1208	1177	1155	829	232
Canagliflozin	5795	5702	5615	5530	4414	3043	2621	2588	2543	2511	2464	2415	1751	481

D Nonfatal Myocardial Infarction



No. at Risk

Placebo	4347	4256	4187	4109	2986	1647	1255	1233	1207	1179	1146	1126	812	223
Canagliflozin	5795	5711	5625	5513	4405	3029	2602	2565	2516	2476	2425	2382	1728	468

Canagliflozin in type 2 diabetes

Reduces CV events



3.2% → 2.7%
(percent of patients/year)

Increases amputations



0.3% → 0.6%
(percent of patients/year)

Reduces renal events*



0.9% → 0.6%
(percent of patients/year)

Increases other adverse events

Fractures, genital infections, volume depletion, ?ketoacidosis

CANVAS

[nejm.org/doi/full/10.1056/NEJMoa1611925](https://doi.org/10.1056/NEJMoa1611925)

*renal death, renal replacement therapy, eGFR ↓40%

Prepared by: Ricky Turgeon & Judy Xie

July 10, 2017

RWE: CVD-REAL: SGLT2i vs OGLD



Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

Lower Risk of Heart Failure and Death in Patients Initiated on Sodium-Glucose Cotransporter-2 Inhibitors Versus Other Glucose-Lowering Drugs

The CVD-REAL Study (Comparative Effectiveness of Cardiovascular Outcomes in New Users of Sodium-Glucose Cotransporter-2 Inhibitors)

Kosiborod et al. 2017, Circulation, 136: 249-259

First presented at the 66th Annual Scientific Session of the ACC, Washington, DC, March 17–19, 2017



Data sources



Truven MarketScan Claims & Encounters and linked Medicare



National full-population registries



National full-population registries



National full-population registries



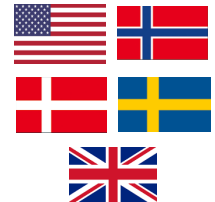
Clinical Practice Research Datalink (CPRD) and
The Health Improvement Network (THIN)



Diabetes Patienten Verlaufsdokumentation (DPV) initiative

hHF

All cause death



Population studied

Inclusion criteria

New users receiving SGLT-2 inhibitors or other glucose-lowering drugs

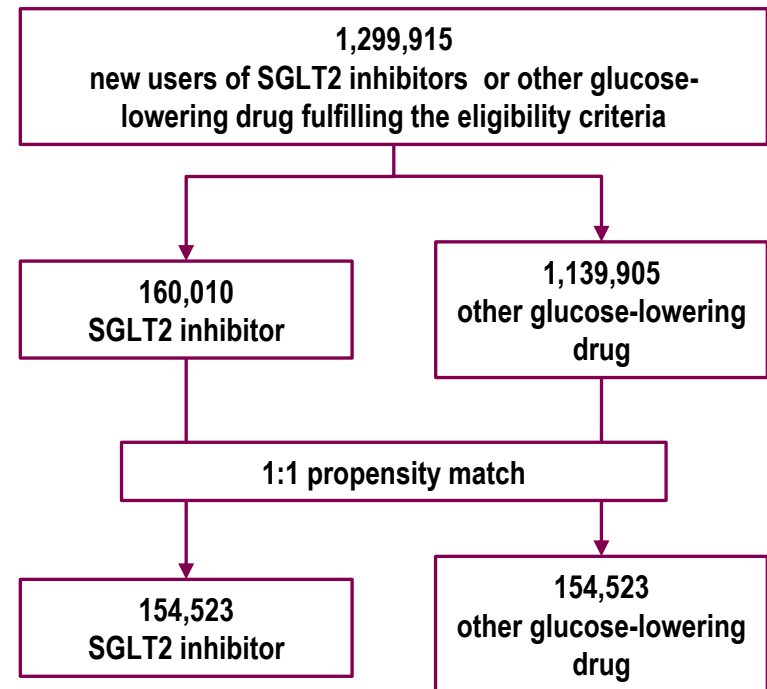
- Established type II diabetes mellitus on or prior to the index date
- ≥ 18 years old
- >1 year* historical data available prior to the index date

Exclusion criteria

- Patients with type 1 diabetes
- Patients with gestational diabetes

Statistical methods

- Propensity score¹ developed for 'being initiated on an SGLT-2 inhibitor' within each country to minimize confounding by indication
- Patients in the SGLT-2 inhibitor and other glucose-lowering drug groups matched 1:1 by propensity score



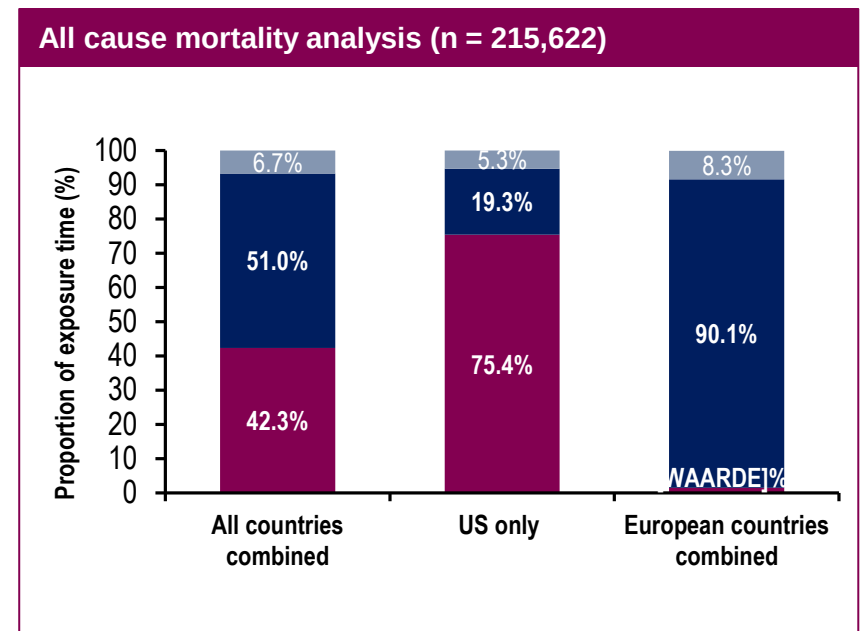
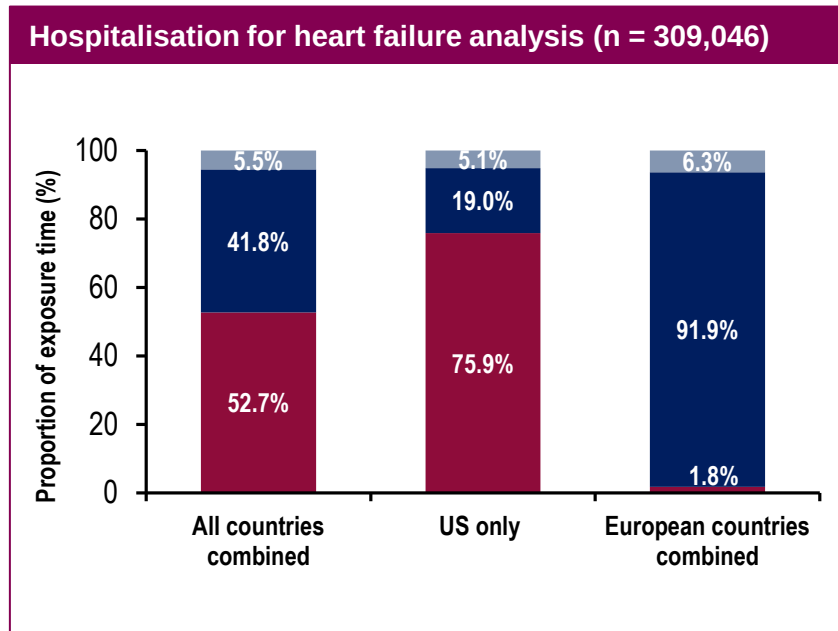
*In Germany, > 6 months.

¹ A non-parsimonious propensity score attempts to minimize confounding by including all observed variables that may have affected treatment assignment for the outcomes of interest

Kosiborod et al. 2017, Circulation, 136: 249-259



CVD-REAL: Contributions of individual SGLT2 inhibitors



■ Canagliflozin
 ■ Dapagliflozin
 ■ Empagliflozin



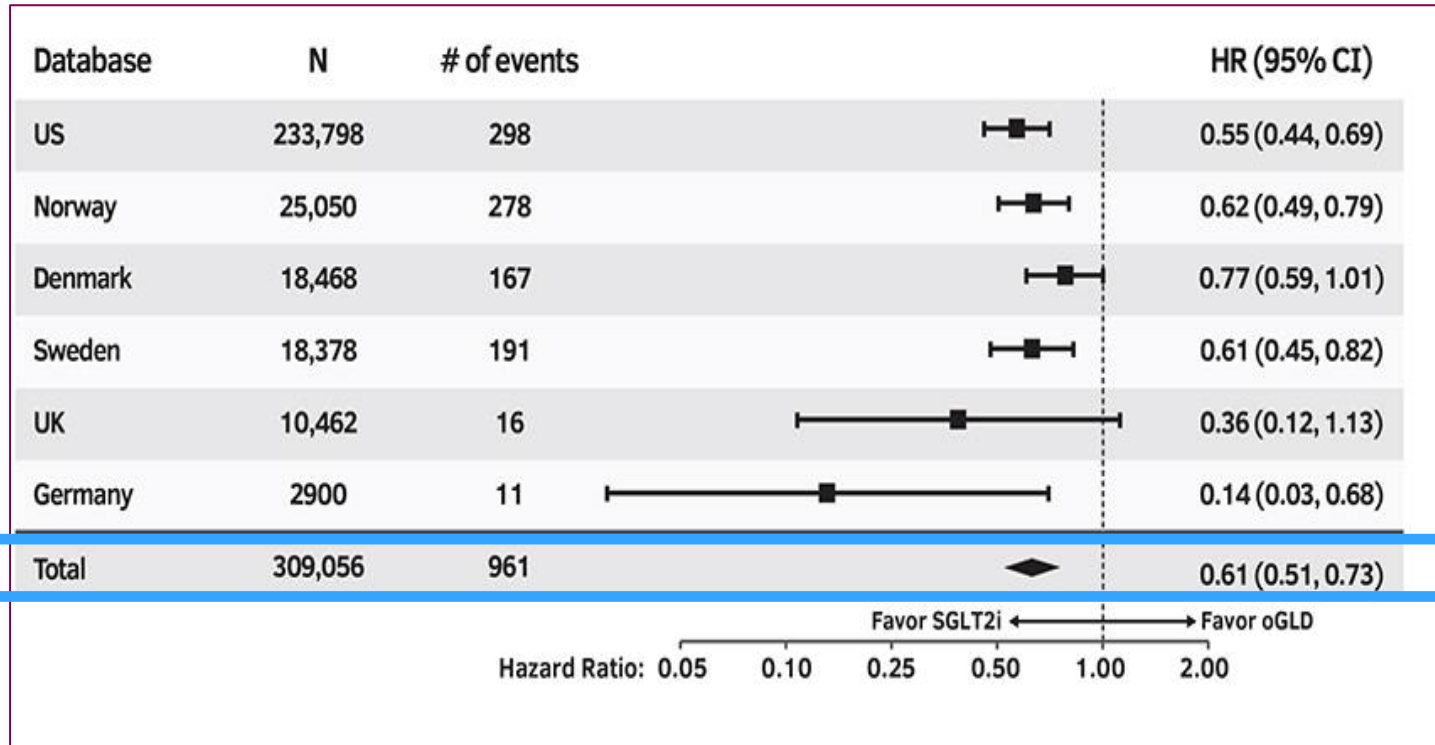
Baseline characteristics (1/2)

	SGLT2 inhibitor* N=154,523	Other glucose-lowering drug* N=154,523
Age (years), mean (SD)	57.0 (9.9)	57.0 (10.1)
Women	68,419 (44.3)	68,770 (44.5)
Established cardiovascular disease	20,043 (13.0)	20,302 (13.1)
Acute myocardial infarction	3792 (2.5)	3882 (2.5)
Unstable angina	2529 (1.6)	2568 (1.7)
Heart failure	4714 (3.1)	4759 (3.1)
Atrial fibrillation	5632 (3.6)	5698 (3.7)
Stroke	6347 (4.1)	6394 (4.1)
Peripheral arterial disease	5239 (3.4)	5229 (3.4)
Microvascular disease	42,214 (27.3)	42,221 (27.3)
Chronic kidney disease	3920 (2.5)	4170 (2.7)

~87% primary prevention



Hospitalization for heart failure: primary analysis



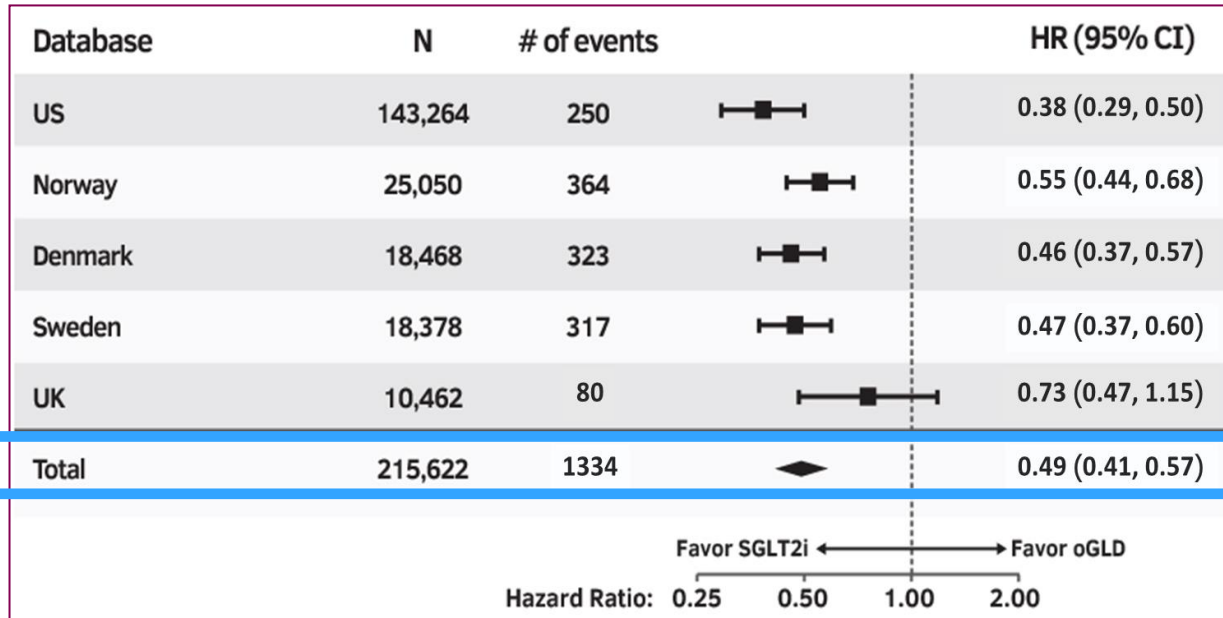
P-value for SGLT2 inhibitor vs other glucose-lowering drug: <0.001

Heterogeneity p-value: 0.169

Data are on treatment, unadjusted - Kosiborod et al. 2017, Circulation, 136: 249-259



All cause death



-51%

P-value for SGLT2 inhibitor vs other glucose-lowering drug: <0.001

Heterogeneity p-value: 0.089

Data are on treatment, unadjusted. This data analysis did not include Germany as data for all-cause death were not available from the DPV database.

Kosiborod et al. 2017, Circulation, 136: 249-259



ADA/EASD richtlijnen 2016

Mono-therapy

Efficacy*
Hypo risk
Weight
Side effects
Costs*

Healthy eating, weight control, increased physical activity, and diabetes education

Metformin

high
low risk
neutral / loss
GI / lactic acidosis
low

If HbA_{1c} target not achieved after ~3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- and disease-specific factors):

Dual therapy†

Efficacy*
Hypo risk
Weight gain
Side effects
Costs*

Metformin +	Metformin +	Metformin +	Metformin +	Metformin +	Metformin +
Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)
high efficacy moderate risk gain weight hypoglycemia low costs	high efficacy low risk gain weight edema, HF, fxs low costs	intermediate efficacy low risk neutral weight rare side effects high costs	intermediate efficacy low risk loss weight GU, dehydration high costs	high efficacy low risk loss weight GI side effects high costs	highest efficacy high risk gain weight hypoglycemia variable costs

If HbA_{1c} target not achieved after ~3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- and disease-specific factors):

Triple therapy

Metformin +	Metformin +	Metformin +	Metformin +	Metformin +	Metformin +
Sulfonylurea + TZD or DPP-4-i or SGLT2-i or GLP-1-RA or Insulin [§]	Thiazolidinedione + SU or DPP-4-i or SGLT2-i or GLP-1-RA or Insulin [§]	DPP-4 inhibitor + SU or TZD or SGLT2-i or Insulin [§]	SGLT2 inhibitor + SU or TZD or DPP-4-i or Insulin [§]	GLP-1 receptor agonist + SU or TZD or Insulin [§]	Insulin (basal) + TZD or DPP-4-i or SGLT2-i or GLP-1-RA

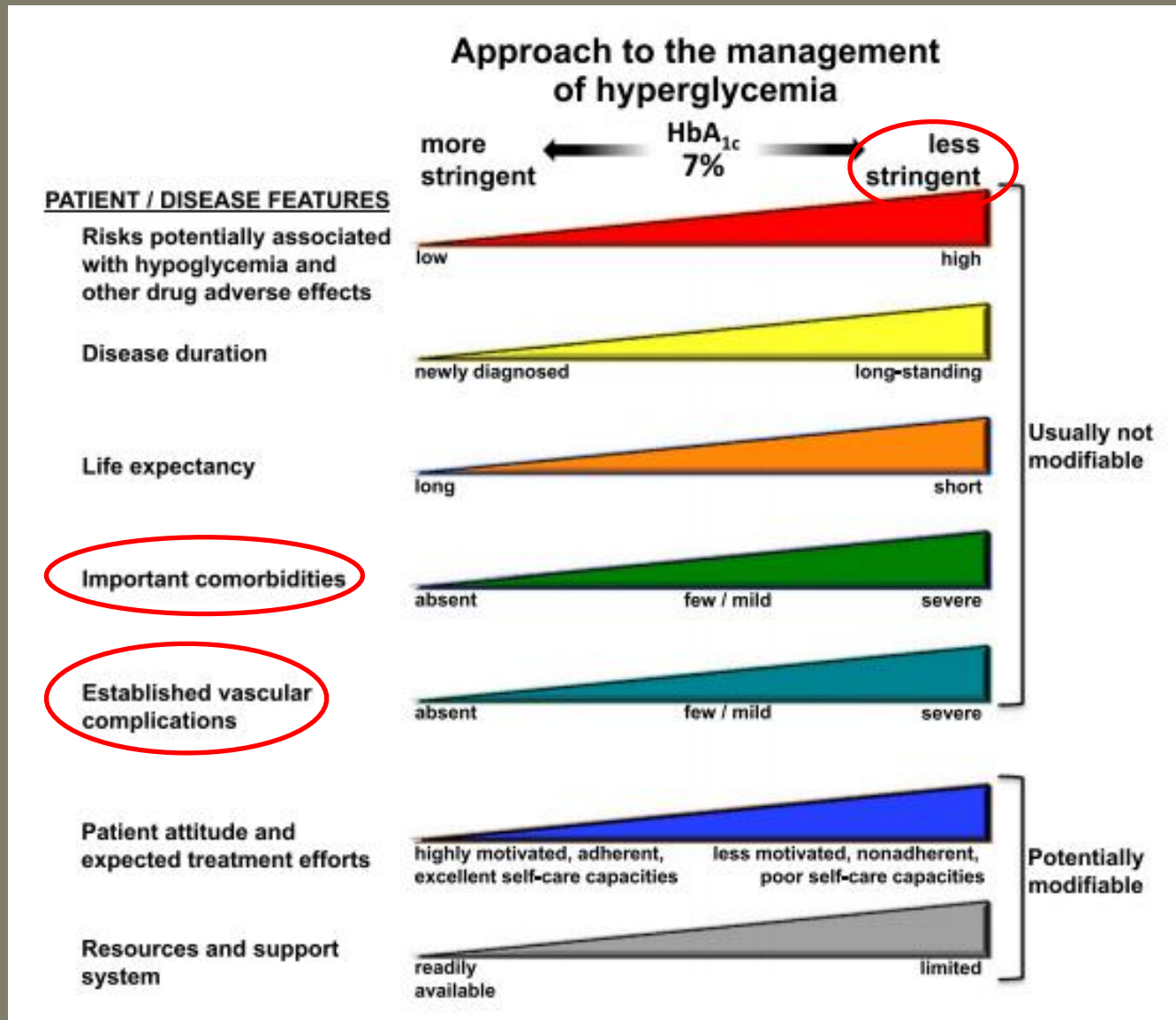
If HbA_{1c} target not achieved after ~3 months of triple therapy and patient (1) on oral combination, move to injectables; (2) on GLP-1-RA, add basal insulin; or (3) on optimally titrated basal insulin, add GLP-1-RA or mealtime insulin. In refractory patients consider adding TZD or SGLT2-i:

Combination injectable therapy†

Metformin +
Basal insulin + Mealtime insulin or GLP-1-RA

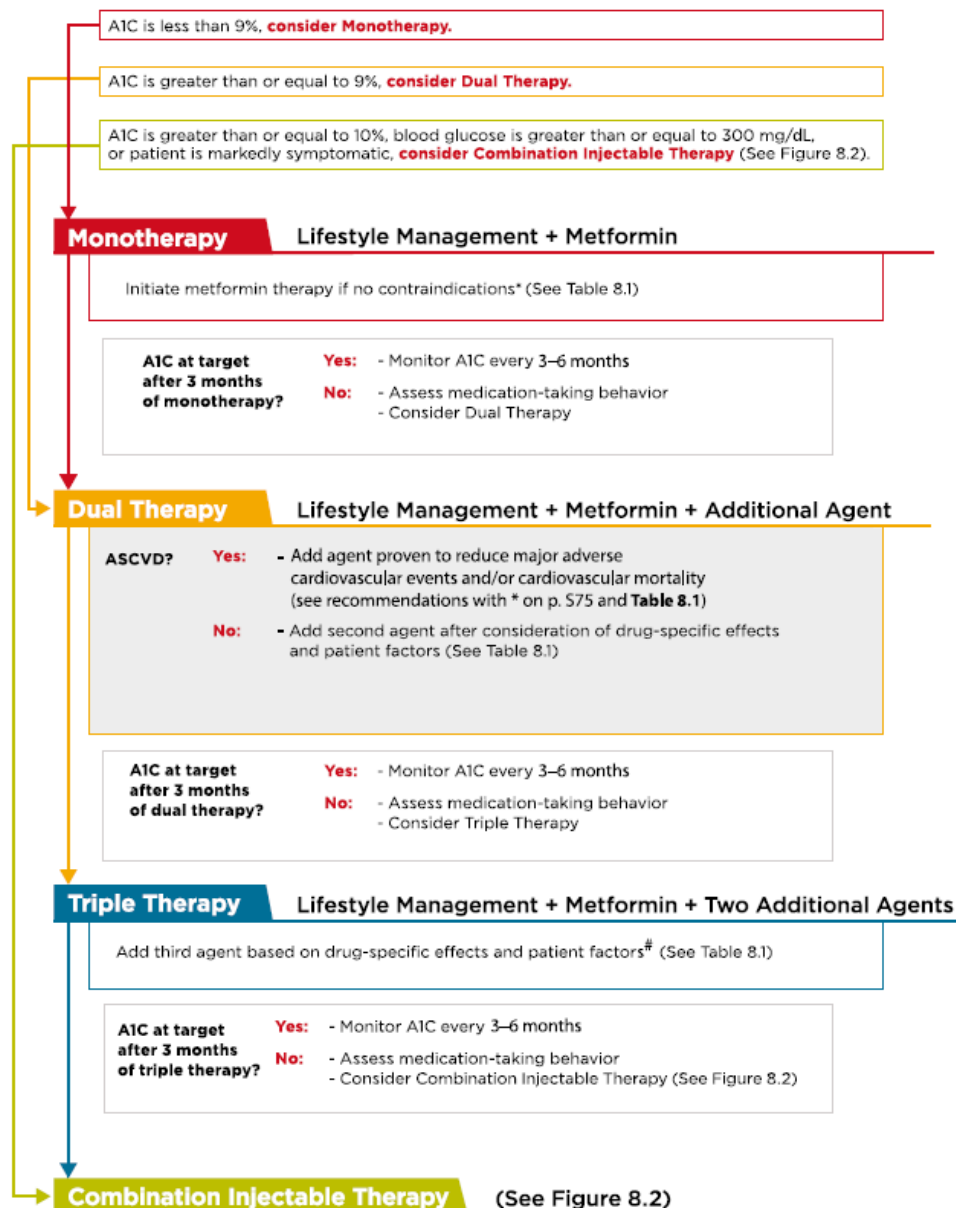
Diabetes Care, 2015; 38(suppl 1)

Geïndividualiseerde aanpak !!!



Updated treatment guidelines 2018

At diagnosis, initiate lifestyle management, set A1C target and initiate pharmacologic treatment based on A1C



ADA richtlijnen 2018

Zo HbA1c > 10 % of glycaemie > 300 mg% : insuline op te starten

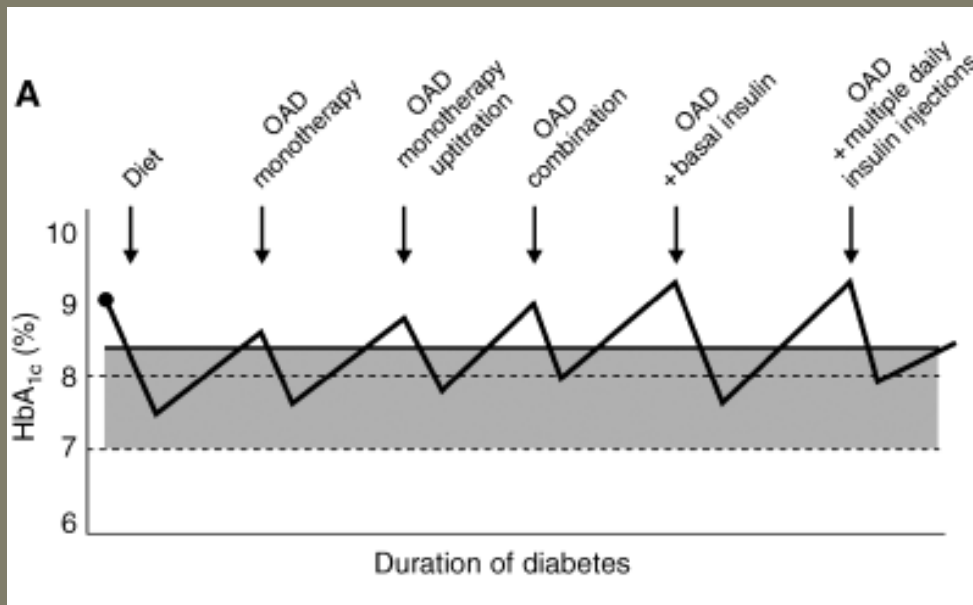
Zo HbA1c > 9 % : start 2 medicaties

Controle van HbA1c na 3 maand : zo target niet gehaald :
combinatie

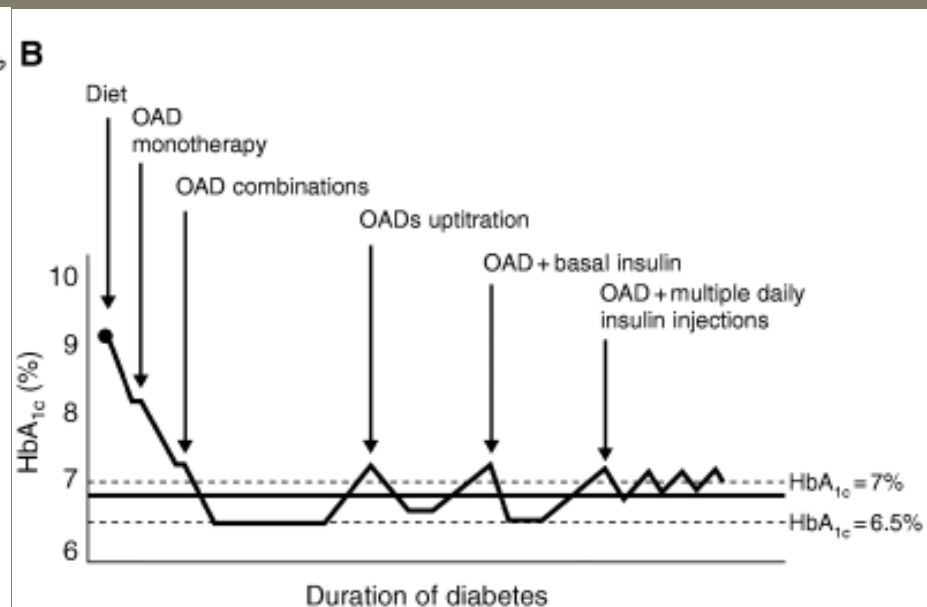
Zo bewijs van atheromatose: naast metformin kiezen voor een
medicatie die cardiovasculaire outcome verbetert :

- Liraglutide
- empaglifozine (evtl canaglifozine)

Conservatief management: Traditionele stapsgewijze aanpak



Pro-actief management: Vroege combinatie aanpak



OAD: oral antidiabetic drug

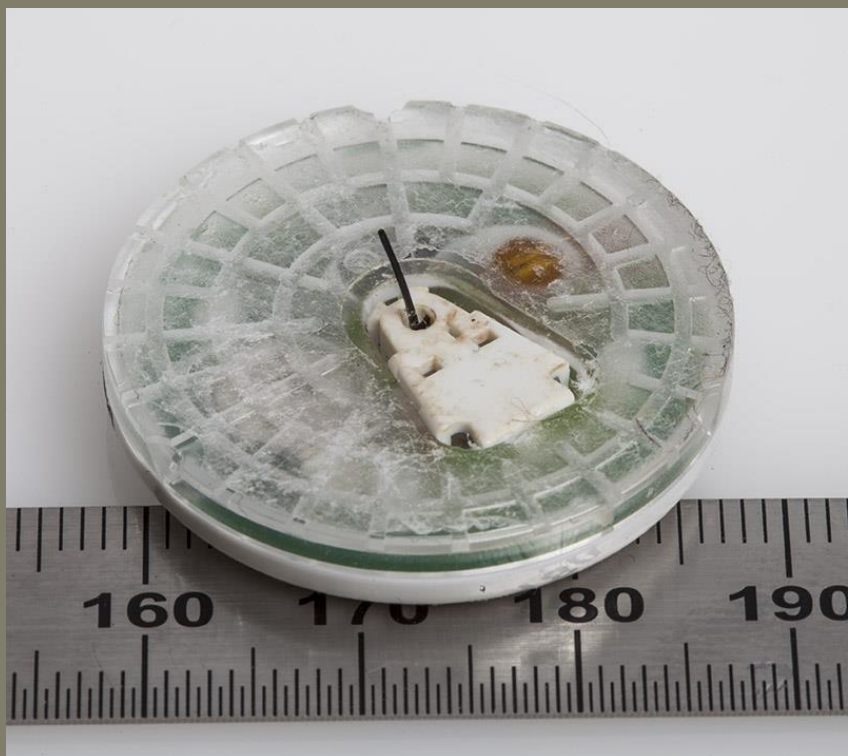
prijs

Glucophage 850 mg	0,077 euro
Uni-diamicron 60	0,162 euro
Trajenta 5 mg	1,31 euro
Jardiance 10 mg	1,46 euro
Insulatard 20 E	0,38 euro
Novomix 30 flexpen	0,57 euro
Lantus 20 E	0,66 euro
Victoza 1.2 mg	3,52 euro
1,8 mg	5,28 euro
Trulicity 1,5 mg	28 euro per week = 4 euro per dag

Alternatief voor vingerprik









De FreeStyle Libre meter: functionaliteiten

Touchscreen

Makkelijk te gebruiken

Bloedglucosewaarden

Geeft de laatste bloedglucose waarde op basis van een scan

Glucose Trend Peil

Geeft de richting aan qua evolutie van de bloedglucose

Laatste 8 uren bloedglucose

Laat toe om betere beslissingen te nemen inzake diabetes management

90-dagen geheugen

Laat toe om 90 dagen terug in de tijd te gaan voor een correcte evaluatie



Kleurenscherm

Voor een betere gebruikservaring

Glucose en opmerkingen

De patiënt kan zelf zijn glucose en insuline loggen, alsook zijn activiteiten monitoren

USB poort

Nodig om de meter op te laden en om data door te geven aan de FS Libre software

Test strip poort

De traditionele meting van bloedglucose en ketonen met strips blijft mogelijk



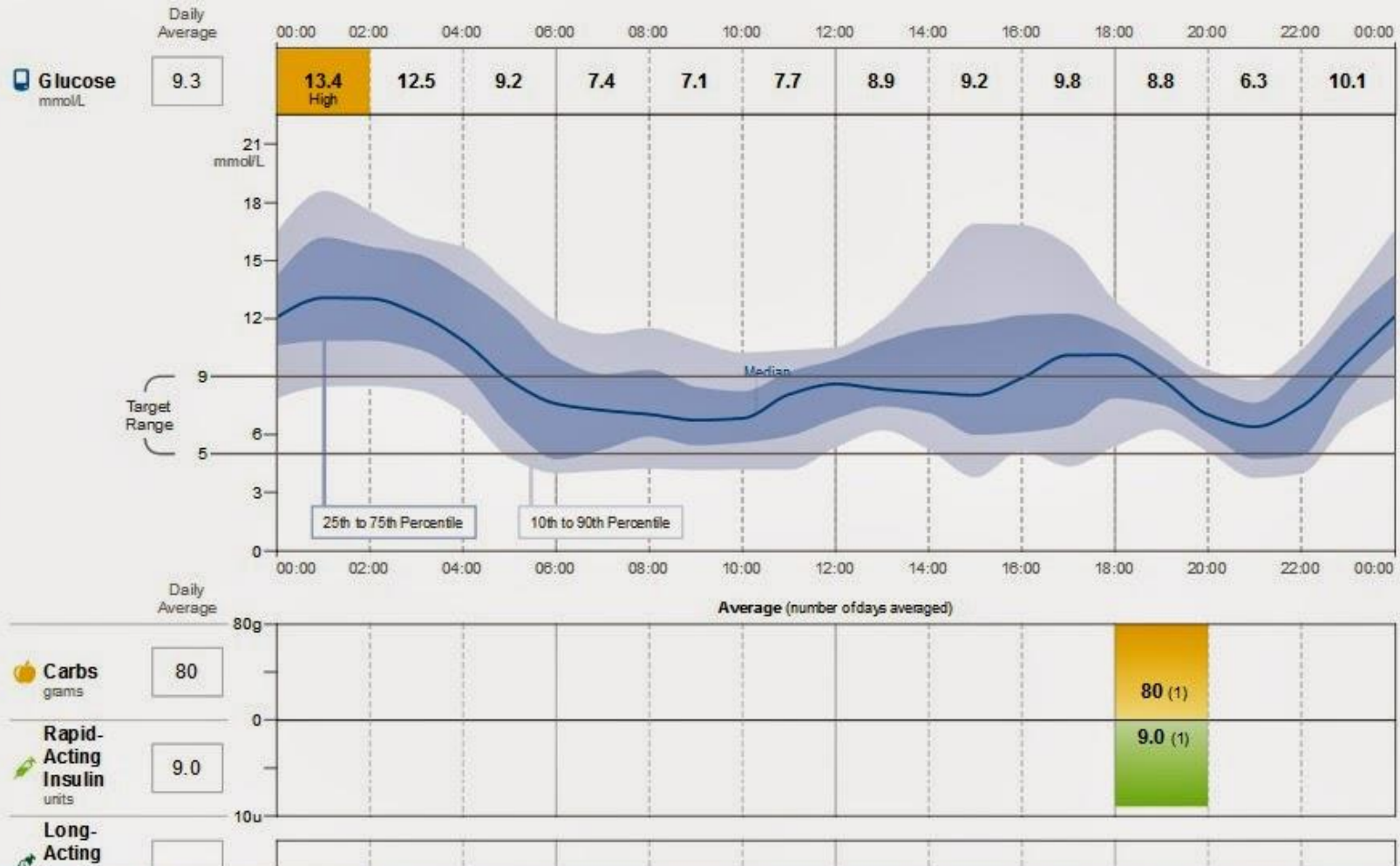
1/2



Back

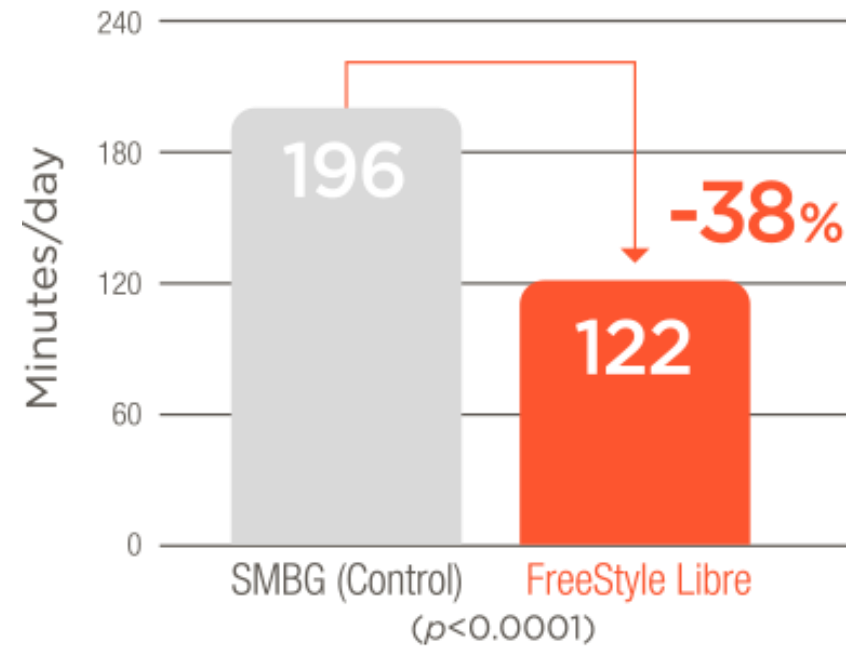
Save

12 September 2014 - 20 September 2014 (9 days)

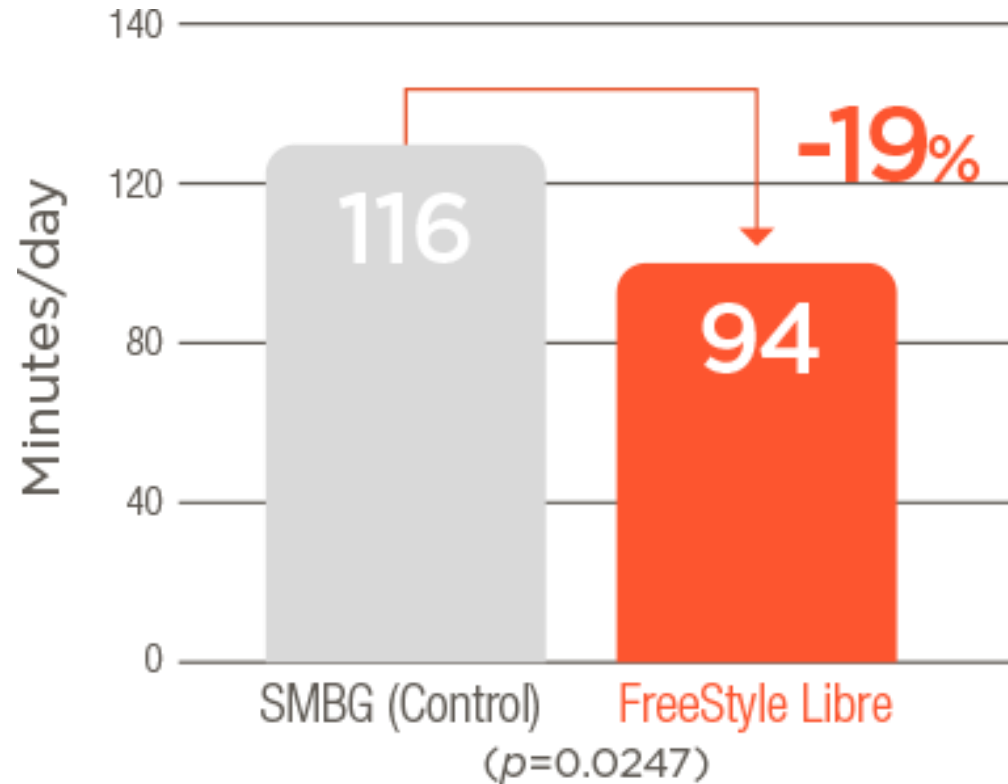
Estimated A1c **7.5%** or **58 mmol/mol**PAGE: 1 / 2
DATE: 2014/09/20DATA SOURCE: FreeStyle Libre 2.1.2
FreeStyle Libre 1.0

IMPACT STUDY

Tijd onder de 70 mg/dl



Tijd boven 240 mg /dl



Geen verandering in HbA1c !

Loskomen

goed wachten (5 min) na gebruik van alcoholdoekje
skin tac wipes

19 euro/50

Gewone pleisters

Opsite flexifix



Armband
'AnnaPS '



Eczeem

Cortisone zalf

Corticoïd spray

LAG TIME

'5 min'

Eerste 12 uur minder accuraat

Geen alarm

Obsessie

Angst : te veel corrigeren

Geen wondermiddel !



terugbetaling

- **Vanaf 1 juli 2016 zijn patiënten ingedeeld in 3 groepen**
- **GROEP A:** Type 1 diabetes of afwezigheid functie van de pancreas.
- **GROEP B:**
Type 2 diabetes op intensieve insulinetherapie (3 of meer injecties per dag),
Zwangerschapsdiabetes behandeld met insuline
- of mensen met diabetes na orgaantransplantatie of tijdens dialyse behandeld met insuline.
- **GROEP C:**
Mensen met type 2 diabetes op 1 of 2 injecties per dag die kunnen nu alleen nog tijdelijk in conventie komen naar aanleiding van een bijkomende ernstige ziekte. Heel wat van die personen zullen uit de (vroegere) conventie vallen en zullen moeten gevolgd worden in een **zorgtraject** diabetes
- Zwangerschapsdiabetes zonder insuline
- Vrouwen, met diabetes en zonder insulinetherapie, die wensen zwanger te worden.
- *De conventie in groep C is in tijd beperkt tot 6 maand (maar kan zo nodig uitzonderlijk verlengd worden).*

Kostprijs

- **Groep A : sensoren gratis 2,2 per maand
afleestoestel gratis (60 euro)**

- **Patiënten uit groep B en C**

krijgen vingerprik strips verder zoals vroeger,
90 à 120 per maand voor groep B

25 per maand (dus 5 minder dan vroeger) voor groep C .

Ze kunnen ook kiezen voor de Freestyle Libre

groep B aan de prijs van 2,52 euro per dag (75euro per m)

groep C aan 3,49 euro per dag. (100 euro per m)

Treatment of type 2 diabetes: is it still all about glucose?

