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East and North Herts Institute of Diabetes and Endocrinology

Prevention of CVD in Diabetes

Dr Peter Winocour

3rd Herts Diabetes Conference 2016

Prevention of CVD in DM

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- 1.Type 1 DM important but separate issue
- 2. DM is NOT necessarily a CVD risk equivalent
- 3. Multiple Risk Factors amplify CV Risk
  Combined Management Delivers Benefit – Steno
- 4.Lifestyle – diet, exercise **and** smoking cessation
- 5. Lipid management – non HDLC < 2.5
- 6. Renal (GFR and albuminuria) amplify CVD risk
- 7. Aspirin only for established CVD – renal
- 8. BP targets individualised especially in elderly
- 9. CCF specific input – link with CKD-anaemia

Where is the guidance ?

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JBS3

Joint British Societies for the prevention of cardiovascular disease

Type 1 Diabetes

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- CVD risk contingent on age, duration of diabetes, HbA1c , renal status
- Statins in majority over the age of 40 ? unless just diagnosed, thin and fit with no other CVD risk
- Younger patients aged 30-40 with high CVD risk justify statins, such as long duration with renal complications , insulin resistance features or poor DM control with additional risk e.g. severe retinopathy–smoking
- Aged 18-30 only if advancing nephropathy
- Caution in women of child bearing potential

Lipids – Threshold for Initiation and Targets

- The higher non HDLC the higher the baseline risk
- There is no lower non-HDLC limit if CVD risk high
- Current non HDL cholesterol target < 2.5 mmol/l where statins initiated on basis of CVD risk
- High intensity statins (atorvastatin 80 mg) with established CVD or non HD CKD and not at target

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What about statin intolerance ?

- Alternative statin and titration trial
- Ezetimibe
- Fenofibrate – non lipaemic benefits
- Future – PCSK9I – alirocumab and evilocumab

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When to use Aspirin ?

- Secondary prevention – established CHD, PVD, non haemmorhagic CVA
- Proteinuric nephropathy and CKD3-5
- Dosage 75 mg has modest evidence base
- Potential bleeding and cancer prevention

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BP targets – ‘different strokes…’

- 140/80 for majority
- 130/70 for renal
- Role for microvascular protection with ACEI-ARB independent of BP effect
- Conservative in frail elderly
- Sick day rules

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The emerging importance of CCF Comorbidity and outcome

	Mortality		Heart Failure hospitalisation	
	HR	P value	HR	P value
Chronic kidney disease	1.50	0.0212	1.59	0.0005
Anaemia	1.69	0.0017	1.44	0.0034
Diabetes	1.74	0.0004	1.31	0.0239

Prevalence of co morbidity was the same regardless of ejection fraction

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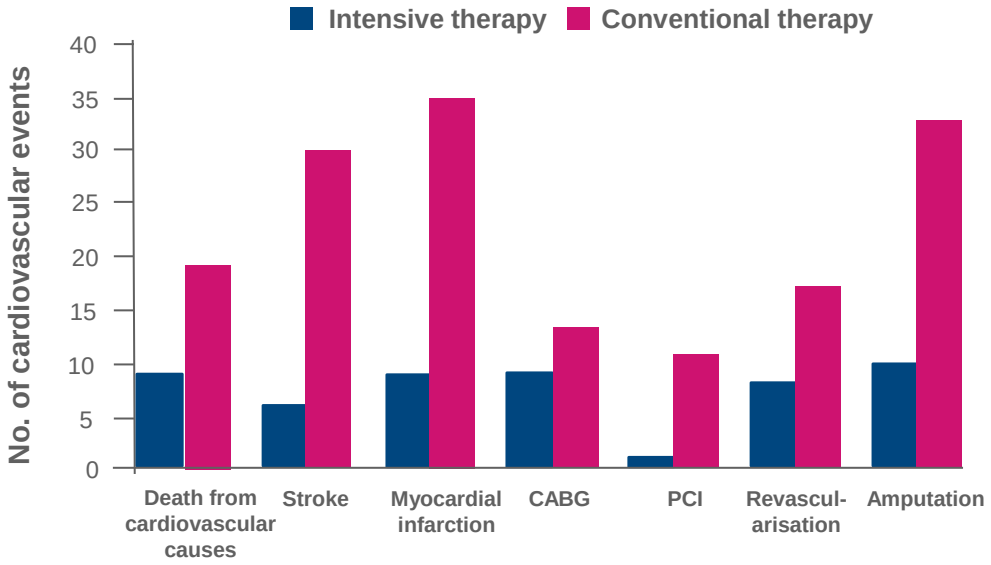
Intensified multifactorial intervention has sustained beneficial effects at stage of microalbuminuria in T2DM

- In type 2 diabetes with **albuminuria**, intensified multifactorial intervention* had sustained beneficial effects on vascular complications and on rates of death[1]
- After mean of 13.3 years† 20% absolute risk reduction for death
- 21 year follow up shows median 7.9 years of life gained
- Only 80 active and 80 placebo Rx !

Number of cardiovascular disease events among patients on intensive vs. conventional therapy[1]



* tight glucose regulation and the use of renin–angiotensin system blockers, aspirin, and lipid-lowering agents

† 7.8 years of multifactorial intervention and an additional 5.5 years of follow-up

CABG=coronary artery bypass graft, PCI=Percutaneous Coronary Intervention

Reference:

1. Gæde P, Lund-Anderson H, Parving H-H, et al. N Engl J Med 2008;358:580-91 2. Gaede P et al , Diabetologia 2016.

The NEW ENGLAND JOURNAL of MEDICINE

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

This article was published on September 17, 2015, at NEJM.org.

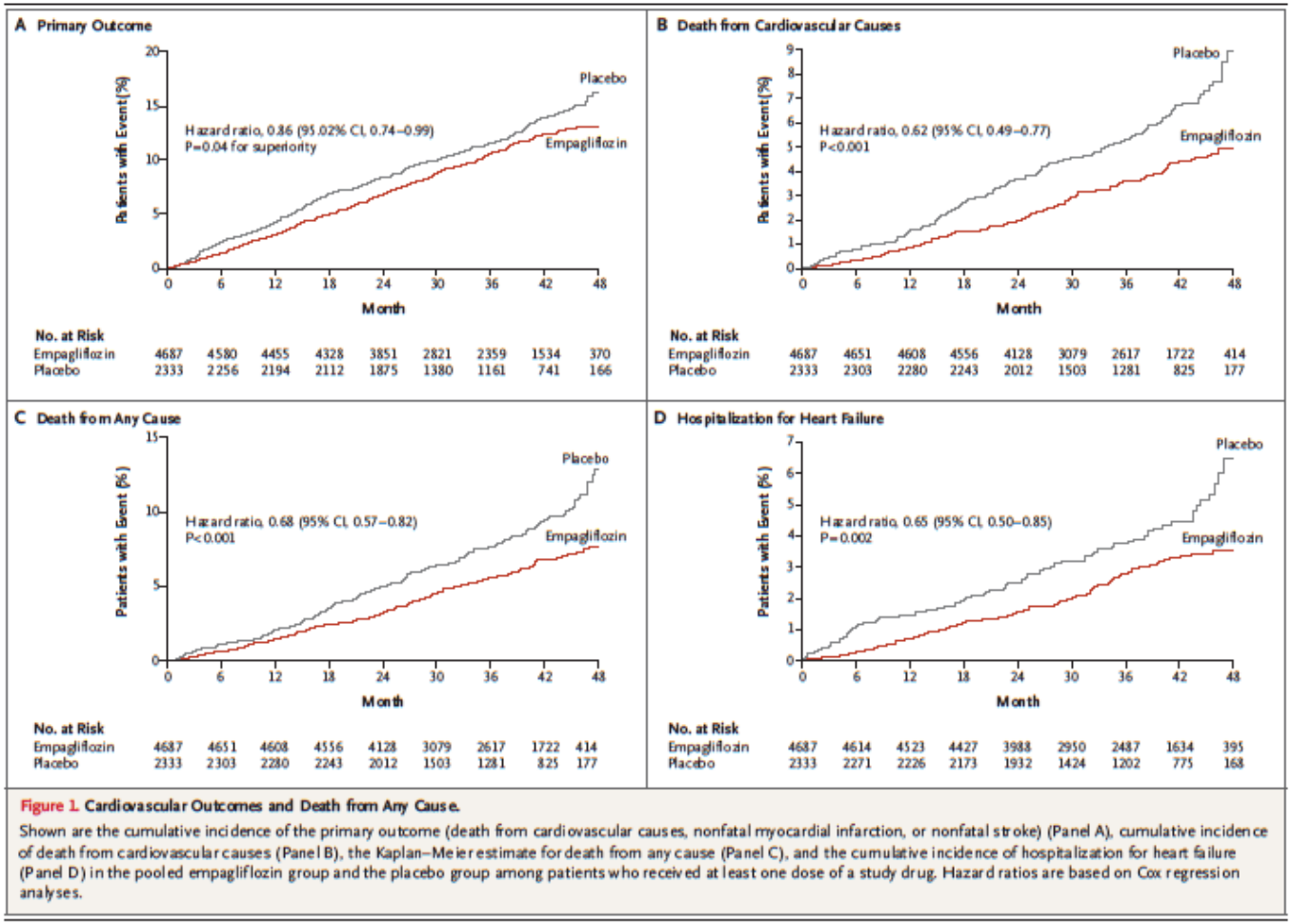


Figure 1. Cardiovascular Outcomes and Death from Any Cause.

Shown are the cumulative incidence of the primary outcome (death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke) (Panel A), cumulative incidence of death from cardiovascular causes (Panel B), the Kaplan–Meier estimate for death from any cause (Panel C), and the cumulative incidence of hospitalization for heart failure (Panel D) in the pooled empagliflozin group and the placebo group among patients who received at least one dose of a study drug. Hazard ratios are based on Cox regression analyses.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes

Steven P. Marso, M.D., Gilbert H. Daniels, M.D., Kirstine Brown-Frandsen, M.D., Peter Kristensen, M.D., E.M.B.A., Johannes F.E. Mann, M.D., Michael A. Nauck, M.D., Steven E. Nissen, M.D., Stuart Pocock, Ph.D., Neil R. Poulter, F.Med.Sci., Lasse S. Ravn, M.D., Ph.D., William M. Steinberg, M.D., Mette Stockner, M.D., Bernard Zinman, M.D., Richard M. Bergenstal, M.D., and John B. Buse, M.D., Ph.D., for the LEADER Steering Committee on behalf of the LEADER Trial Investigators*

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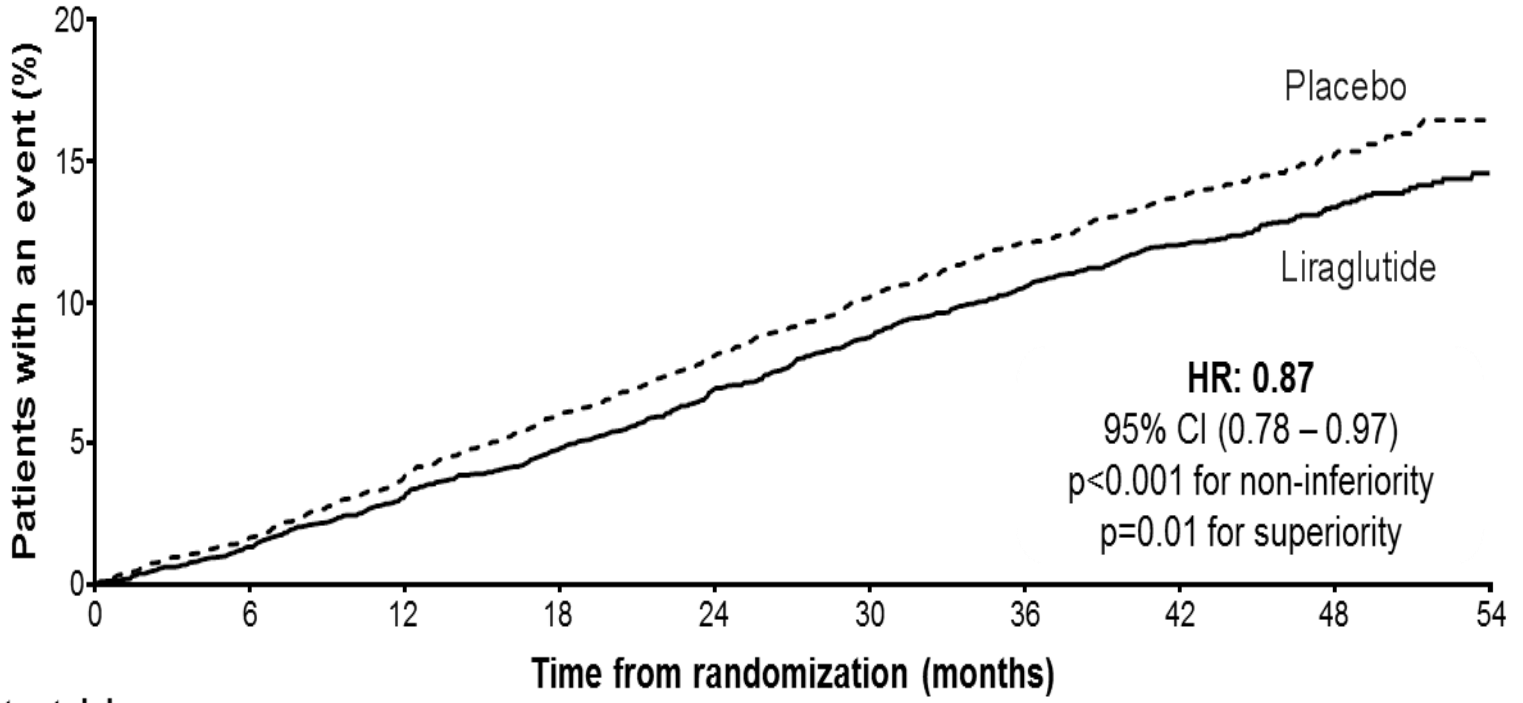
LEADER: Primary outcome

CV death, non-fatal myocardial infarction, or non-fatal stroke



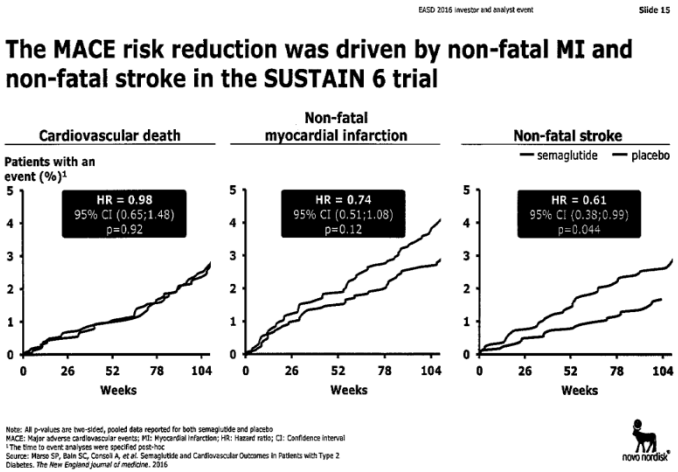
Patients at risk

Liraglutide	4668	4593	4496	4400	4280	4172	4072	3982	1562	424
Placebo	4672	4588	4473	4352	4237	4123	4010	3914	1543	407

The primary composite outcome in the time-to-event analysis was the first occurrence of death from cardiovascular causes, non-fatal myocardial infarction, or non-fatal stroke. The cumulative incidences were estimated with the use of the Kaplan–Meier method, and the hazard ratios with the use of the Cox proportional-hazard regression model. The data analyses are truncated at 54 months, because less than 10% of the patients had an observation time beyond 54 months. CI: confidence interval; CV: cardiovascular; HR: hazard ratio.

Presented at the American Diabetes Association 76th Scientific Sessions, Session 3-CT-SY24. June 13 2016, New Orleans, LA, USA.

SUSTAIN CVD events- Semaglutide Weekly GLP1



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Prevention of CVD in DM - The future

- 1.? Potential role for gliflozins for heart failure and renoprotection in DM at high risk for CVD
- ? No impact on empa on IHD or CVA
- 2. ? Potential role for GLP1 analogues in IHD-CVA reduction in DM at high risk for CVD as alternative to intensive insulin based regime
- No impact of GLP-1 analogues on CCF
- 3. Statins-ACEI or ARBs and occasional use of PCSK9 and ASA
- Potassium sparing therapies ?

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