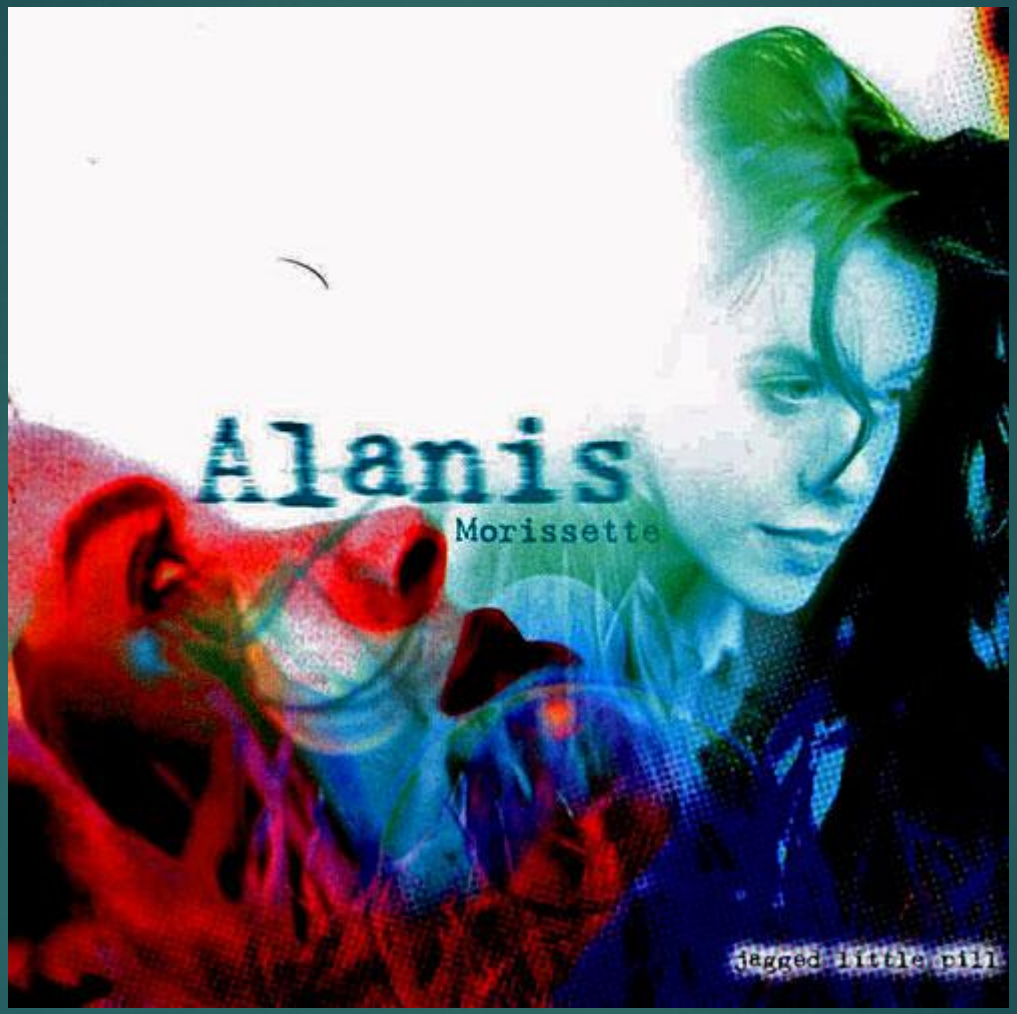
You Oughta Know

A YEAR IN THE DIABETES LITERATURE (MY TOP TEN)

DR JOHN LINDSAY

CONSULTANT PHYSICIAN

BELFAST HEALTH & SOCIAL CARE TRUST


Alanis
Morissette
jagged little pill

Best Clinical Papers?

- Best conducted and reported study?
- Most original question and results?
- Progress for the patient?
- Most likely to be quoted?
- Highest impact factor?
- Relevance to specialist or generalist?
- Published by a friend of your group?

What a choice!

- Epidemiology
- Type 1, Type 2 Diabetes
- Diabetes prevention/cure
- Complications
- Treatments
- Disease areas
- Future strategies


THE LANC
Medical innovation in the UK:
"The forging of a new social contract between health care, the medical innovation system and society will be key to the development of sustainable health-care systems that take maximum advantage of the power of modern science."
The NEW ENGLAND JOURNAL of MEDICINE
JAMA
thebmj
Thresholds for treating high blood pressure
Torture and doctors' dual obligation
Managing exacerbations of COPD
nat
Weeding out centromere
Scien
diab
Diabetolo
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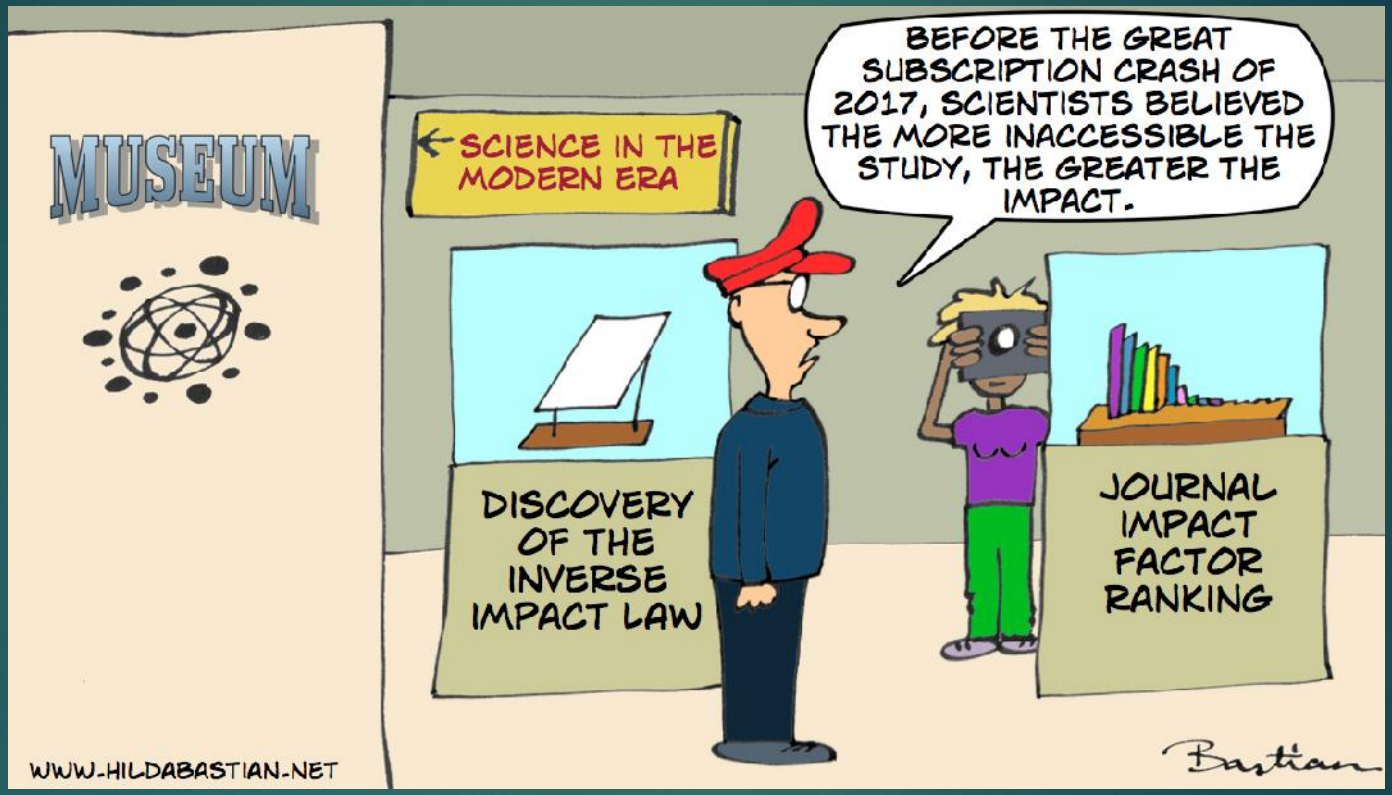
DIABET
Medici


MUSEUM
SCIENCE IN THE MODERN ERA
BEFORE THE GREAT SUBSCRIPTION CRASH OF 2017, SCIENTISTS BELIEVED THE MORE INACCESSIBLE THE STUDY, THE GREATER THE IMPACT.
DISCOVERY OF THE INVERSE IMPACT LAW
JOURNAL IMPACT FACTOR RANKING
WWW.HILDABASTIAN.NET
Bastian

Overview-my top 10!

- Epidemiology
  - Type 1 Diabetes, Scotland & USA
- Diabetes cure/prevention
  - Stem cells in T1DM
  - Topiramate/phentermine & bariatric surgery in T2DM
- Treatments in T2DM
  - Sulphonylureas and DPP4 agents
- Impact on the patient
  - EU driving license and hypo reporting
- Pregnancy
  - Glycaemic targets and insulin pumps
- Future strategies
  - Bionic pancreas

Original Investigation

Estimated Life Expectancy in a Scottish Cohort With Type 1 Diabetes, 2008-2010

Shona J. Livingstone, MSc; Daniel Levin, MSc; Helen C. Looker, MBBS; Robert S. Lindsay, FRCP; Sarah H. Wild, FRCP; Nicola Joss, MD; Graham Leese, MD; Peter Leslie, MD; Rory J. McCrimmon, FRCP; Wendy Metcalfe, MD; John A. McKnight, FRCP; Andrew D. Morris, FRCP; Donald W. M. Pearson, FRCP; John R. Petrie, MD; Sam Philip, MD; Naveed A. Sattar, FRCP; Jamie P. Traynor, MD; Helen M. Colhoun, MD; for the Scottish Diabetes Research Network epidemiology group and the Scottish Renal Registry

JAMA. 2015;313(1):37-44. doi:10.1001/jama.2014.16425

Main outcome estimated loss of life expectancy of around 11 years for women and 13 years for men at age 20 years

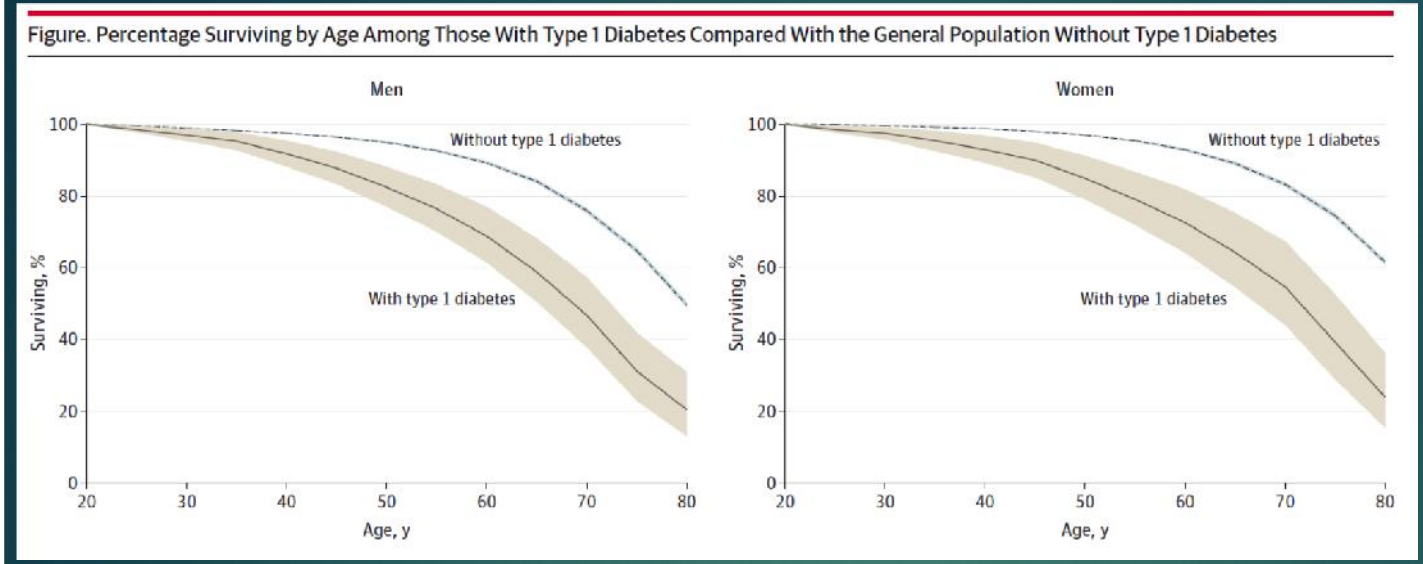
Original Investigation

Association Between 7 Years of Intensive Treatment of Type 1 Diabetes and Long-term Mortality

Writing Group for the DCCT/EDIC Research Group

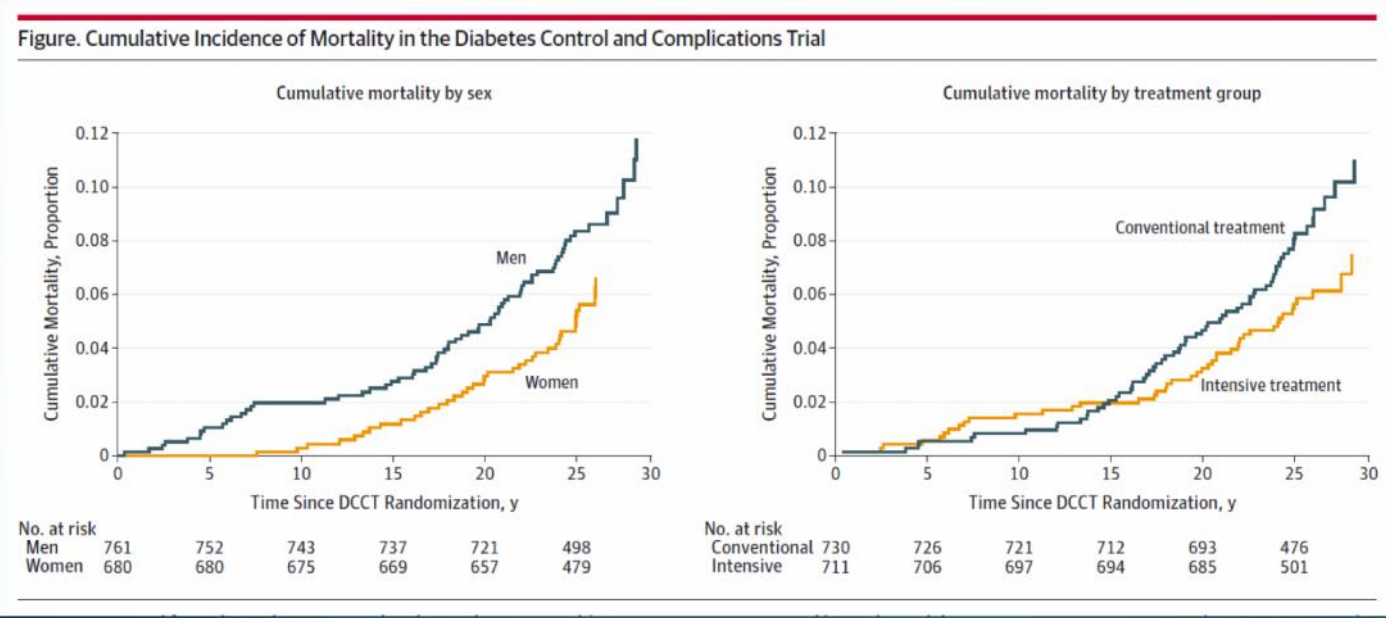
JAMA. 2015;313(1):45-53. doi:10.1001/jama.2014.16107

Lower all-cause mortality risk, intensive therapy group (HR = 0.67 [95%CI, 0.46-0.99]; *P* = .045) after 27 years of follow up



Livingstone, 2014

Life expectancy for men at 20 yrs, additional 46.2 yrs; for women additional 48.1 yrs



Lower all-cause mortality risk, intensive therapy group (HR = 0.67) after 27 years of follow up

DCCT-EDIC, 2014

Generation of Functional Human Pancreatic β Cells In Vitro

Felicia W. Pagliuca,[1,3] Jeffrey R. Millman,[1,3] Mads Gürtler,[1,3] Michael Segel,[1] Alana Van Dervort,[1] Jennifer Hyoje Ryu,[1] Quinn P. Peterson,[1] Dale Greiner,[2] and Douglas A. Melton[1,*]

[1]Department of Stem Cell and Regenerative Biology, Harvard Stem Cell Institute, Harvard University, 7 Divinity Avenue, Cambridge, MA 02138, USA

[2]Diabetes Center of Excellence, University of Massachusetts Medical School, 368 Plantation Street, AS7-2051, Worcester, MA 01605, USA

[3]Co-first author

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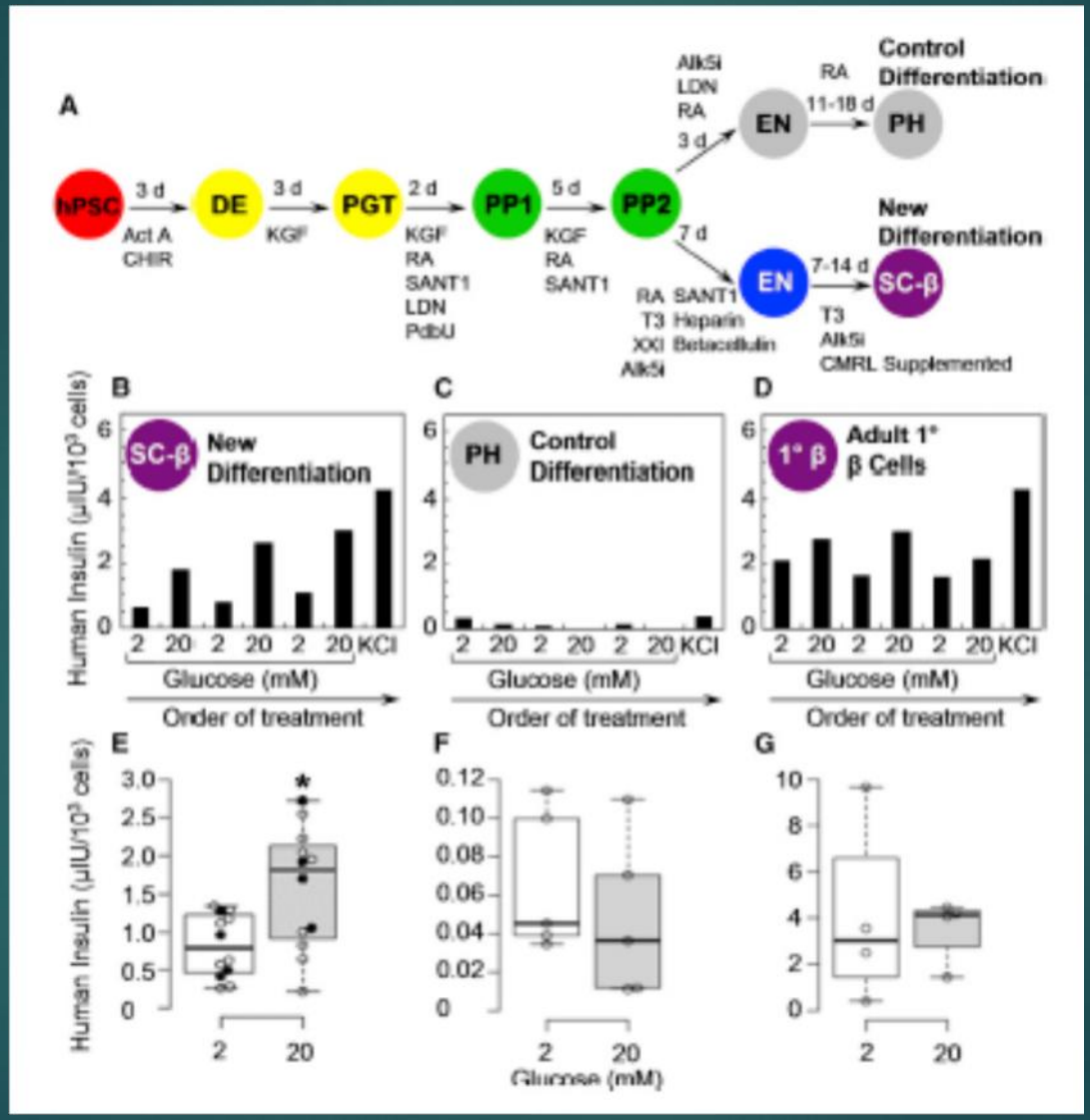
http://dx.doi.org/10.1016/j.cell.2014.09.040

The generation of insulin-producing pancreatic β cells from stem cells in vitro would provide an unprecedented cell source for drug discovery and cell transplantation therapy in diabetes. However, insulin-producing cells previously generated from human pluripotent stem cells (hPSC) lack many functional characteristics of bona fide β cells. Here, we report a scalable differentiation protocol that can generate hundreds of millions of glucose-responsive β cells from hPSC in vitro. These stem-cell-derived β cells (SC-β) express markers found in mature β cells, flux Ca^{2+} in response to glucose, package insulin into secretory granules, and secrete quantities of insulin comparable to adult β cells in response to multiple sequential glucose challenges in vitro. Furthermore, these cells secrete human insulin into the serum of mice shortly after transplantation in a glucose-regulated manner, and transplantation of these cells ameliorates hyperglycemia in diabetic mice.

Cell *159*, 428–439, October 9, 2014

Figure 1. SC-β Cells Generated In Vitro Secrete Insulin in Response to Multiple Sequential High-Glucose Challenges like Primary Human β Cells



Cell *159*, 428–439, October 9, 2014

Prevention of Type 2 Diabetes in Subjects With Prediabetes and Metabolic Syndrome Treated With Phentermine and Topiramate Extended Release

W. Timothy Garvey,[1] Donna H. Ryan,[2] Robert Henry,[3] Nancy J.V. Bohannon,[4] Hermann Toplak,[5] Michael Schwiers,[6] Barbara Troupin,[7] and Wesley W. Day[7]

Diabetes Care 2014;37:912–921 | DOI: 10.2337/dc13-1518

Bariatric Surgery versus Intensive Medical Therapy for Diabetes — 3-Year Outcomes

Philip R. Schauer, M.D., Deepak L. Bhatt, M.D., M.P.H., John P. Kirwan, Ph.D., Kathy Wolski, M.P.H., Stacy A. Brethauer, M.D., Sankar D. Navaneethan, M.D., M.P.H., Ali Aminian, M.D., Claire E. Pothier, M.P.H., Esther S.H. Kim, M.D., M.P.H., Steven E. Nissen, M.D., and Sangeeta R. Kashyap, M.D., for the STAMPEDE Investigators*

N ENGL J MED 370;21 NEJM.ORG MAY 22, 2014

Original Investigation

Association of Bariatric Surgery With Long-term Remission of Type 2 Diabetes and With Microvascular and Macrovascular Complications

Lars Sjöström, MD, PhD; Markku Peltonen, PhD; Peter Jacobson, MD, PhD; Sofie Ahlin, MD, PhD; Johanna Andersson-Assarsson, PhD; Åsa Anveden, MD; Claude Bouchard, PhD; Björn Carlsson, MD, PhD; Kristjan Karason, MD, PhD; Hans Lönroth, MD, PhD; Ingmar Näslund, MD, PhD; Elisabeth Sjöström, MD; Magdalena Taube, PhD; Hans Wedel, PhD; Per-Arne Svensson, PhD; Kajsa Sjöholm, PhD; Lena M. S. Carlsson, MD, PhD

JAMA. 2014;311(22):2297-2304. doi:10.1001/jama.2014.5988

Prevention of Type 2 Diabetes in Subjects With Prediabetes and Metabolic Syndrome Treated With Phentermine and Topiramate Extended Release

W. Timothy Garvey,[1] Donna H. Ryan,[2] Robert Henry,[3] Nancy J.V. Bohannon,[4] Hermann Toplak,[5] Michael Schwiers,[6] Barbara Troupin,[7] and Wesley W. Day[7]

Diabetes Care Volume 37, April 2014

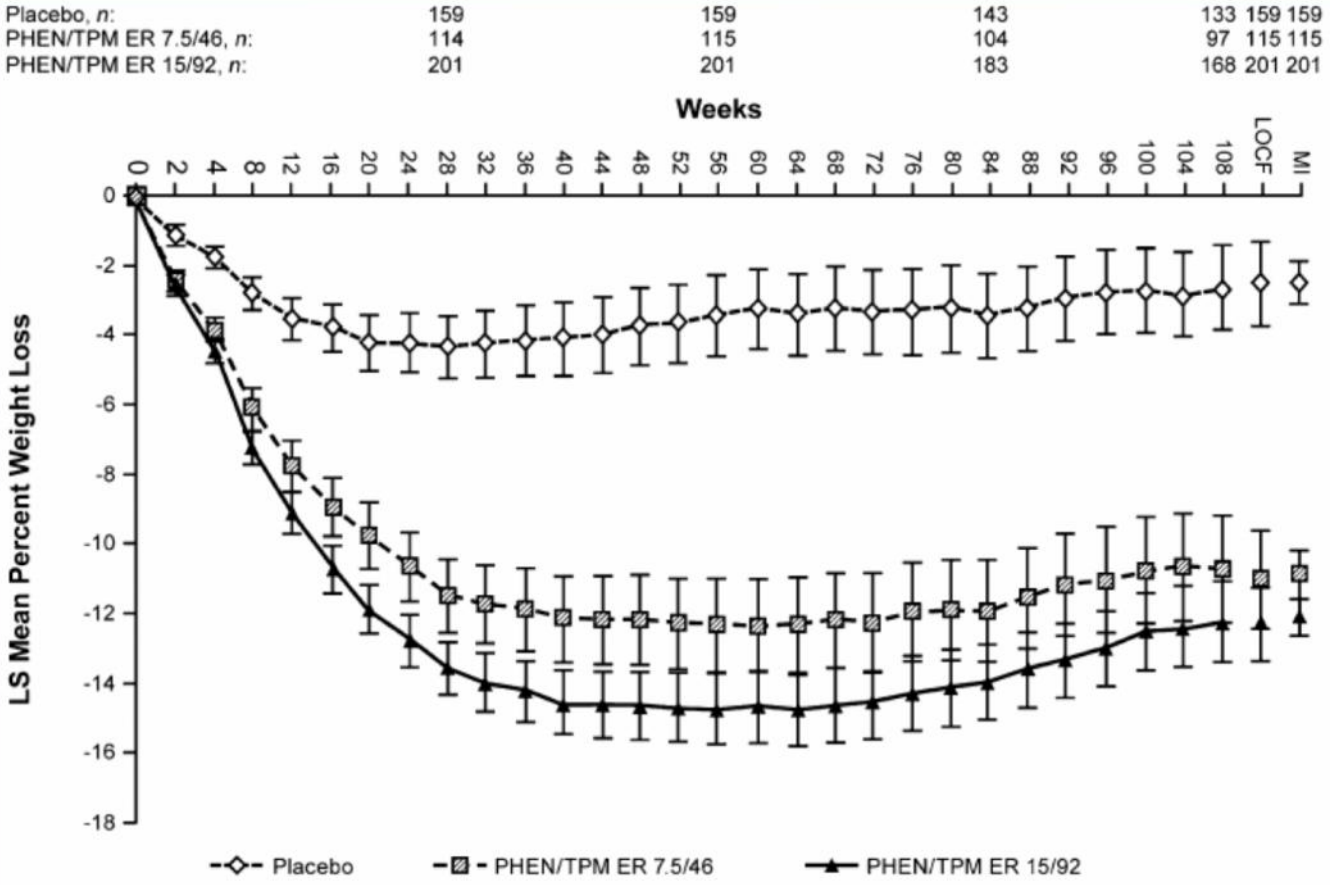


Figure 1—Percent weight loss from baseline to week 108 in the cohort with prediabetes and/or MetS at baseline. Least squares mean percent weight loss in the ITT population of subjects with prediabetes and/or MetS. $P < 0.0001$ vs. placebo for all time points assessed. LS, least squares.

-2.5%

-10.9%

-12.1%

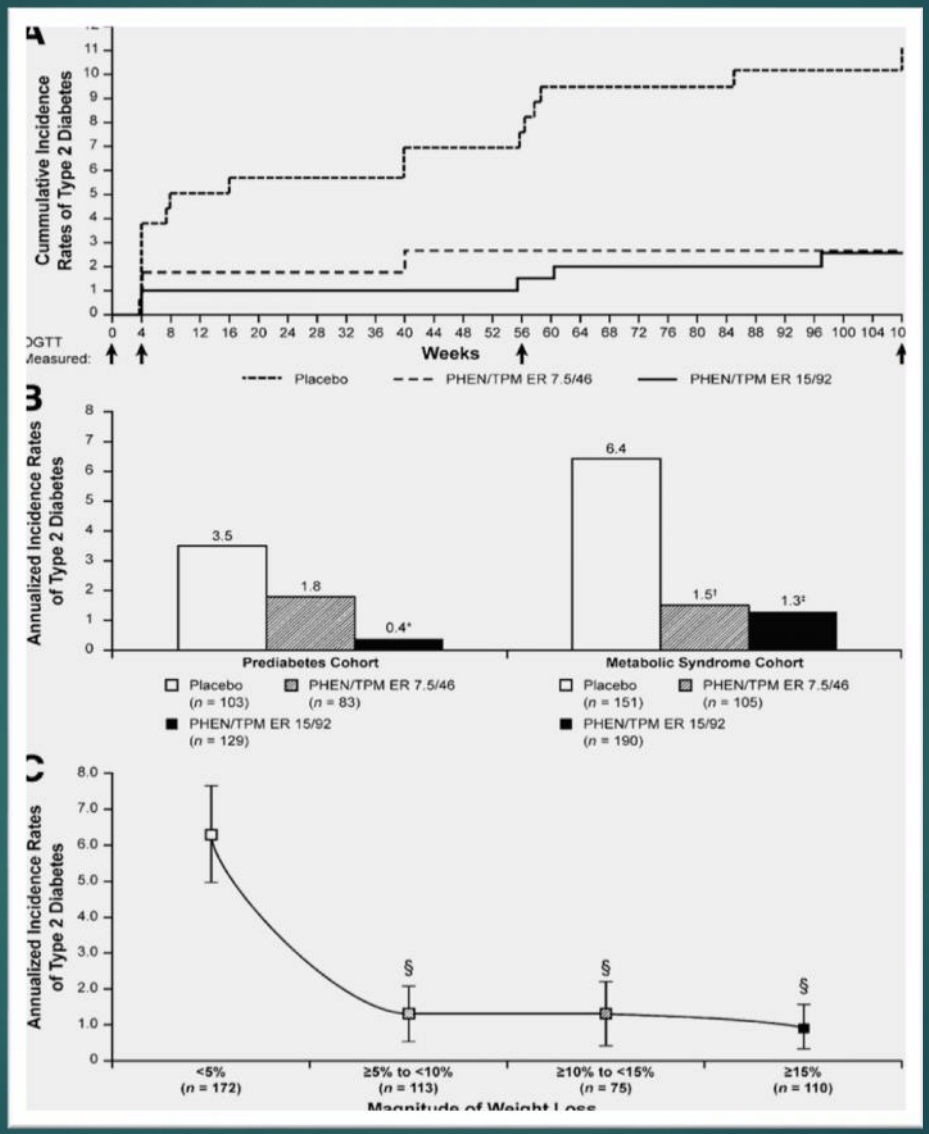
Phentermine/Topiramate Extended release plus lifestyle modification

Pre-diabetes group

48.6% Low dose

88.6% High dose

PHEN/TPM ER vs. placebo



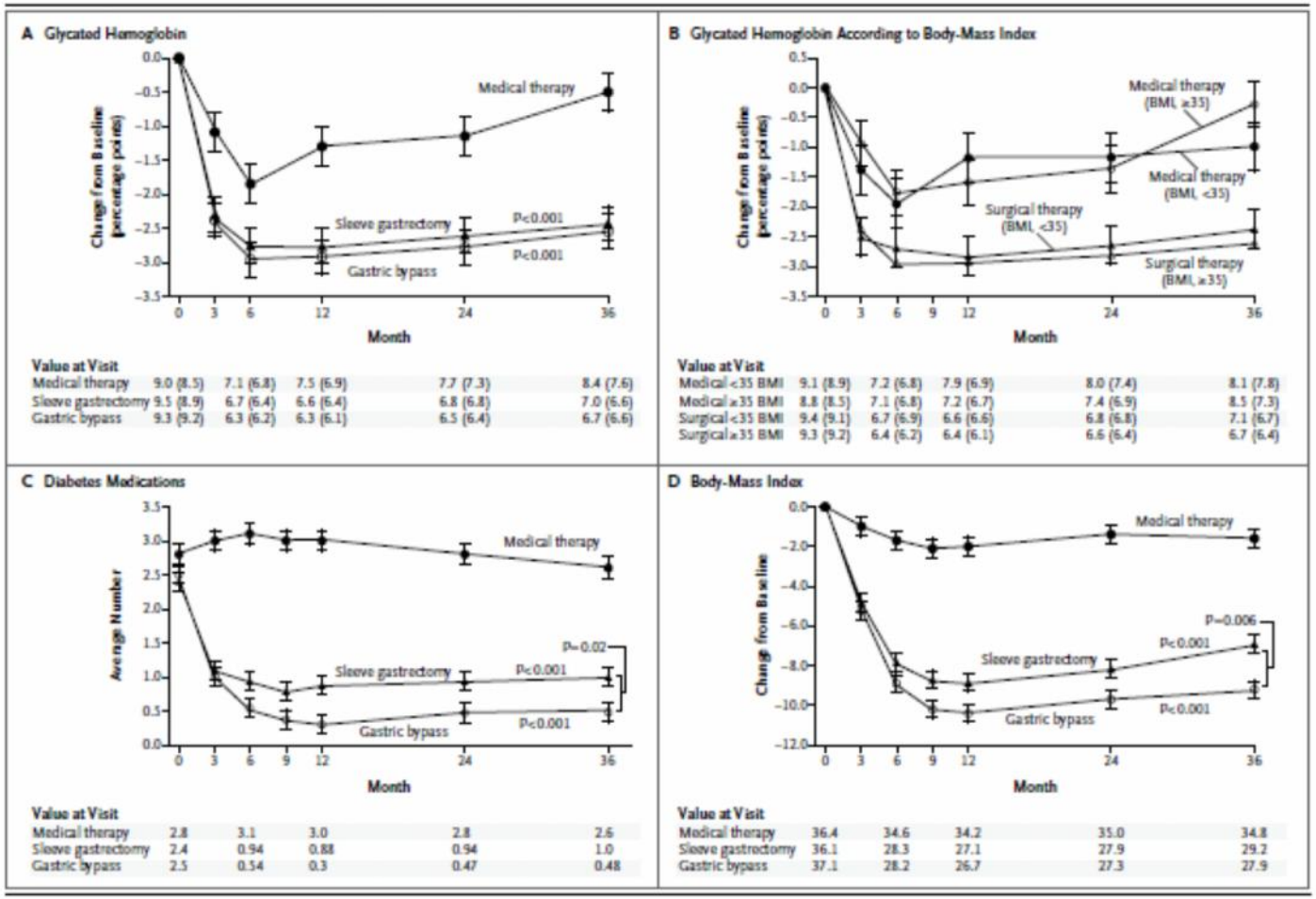
MetS group

76.6% Low dose

79.7% High dose

Diabetes Care 2014;37:912–921

STAMPEDE Trial



At 3 years, primary end point was met by 5% (med gp), v.s. 38% gastric-bypass group (P<0.001), 24% sleeve-gastrectomy group (P = 0.01)

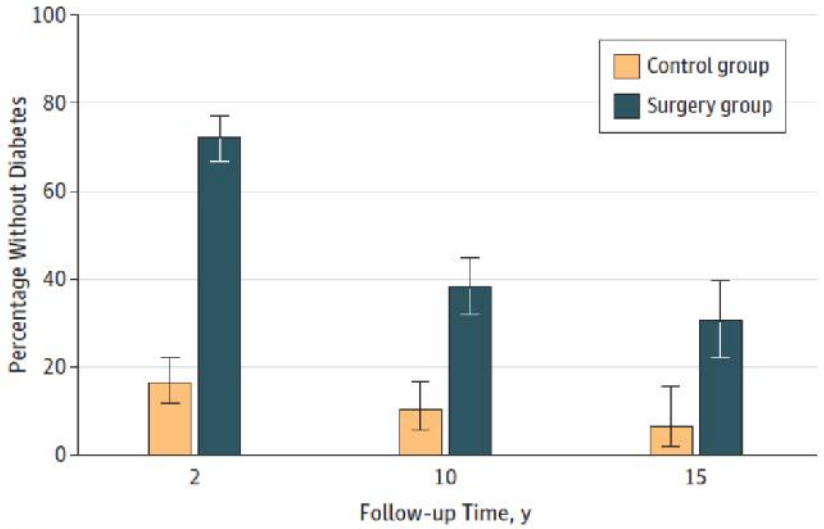
N ENGL J MED 370;21 NEJM.ORG MAY 22, 2014

Original Investigation

Association of Bariatric Surgery With Long-term Remission of Type 2 Diabetes and With Microvascular and Macrovascular Complications

Lars Sjöström, MD, PhD; Markku Peltonen, PhD; Peter Jacobson, MD, PhD; Sofie Ahlin, MD, PhD; Johanna Andersson-Assarsson, PhD; Åsa Anveden, MD; Claude Bouchard, PhD; Björn Carlsson, MD, PhD; Kristjan Karason, MD, PhD; Hans Lönroth, MD, PhD; Ingmar Näslund, MD, PhD; Elisabeth Sjöström, MD; Magdalena Taube, PhD; Hans Wedel, PhD; Per-Arne Svensson, PhD; Kajsa Sjöholm, PhD; Lena M. S. Carlsson, MD, PhD

Figure 1. Prevalence of Diabetes Remission in the Bariatric Surgery and Control Groups



Total participants			
Control	207	135	62
Surgery	303	236	115
Odds ratio (95% CI)	13.3 (8.5-20.7)	5.3 (2.9-9.8)	6.3 (2.1-18.9)

Diabetes remission rates:

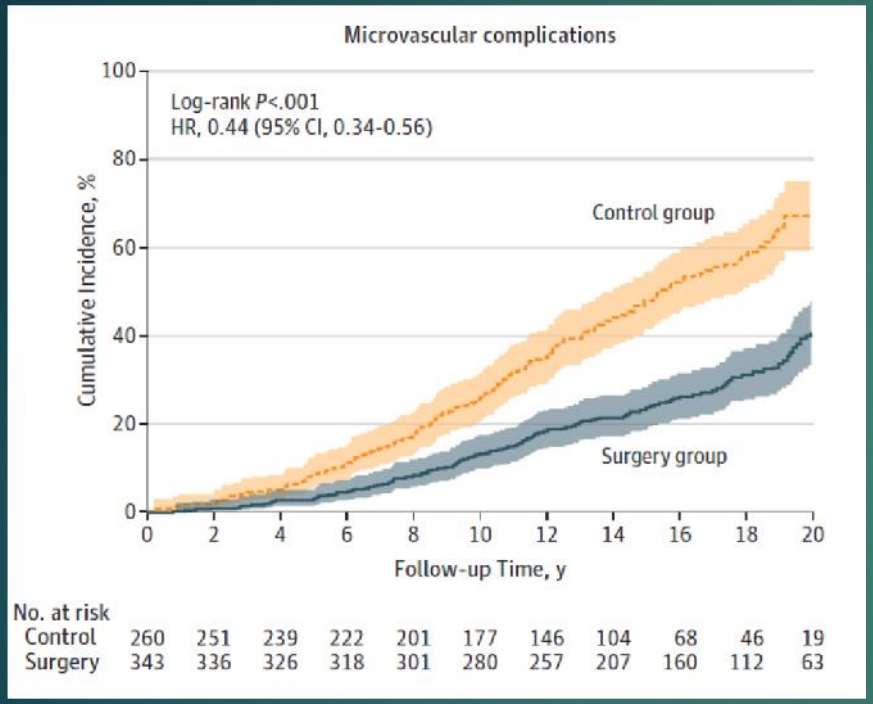
72.3% v.s. 16.4% for bariatric surgery v.s. controls at 2 yrs ($P < 0.001$)

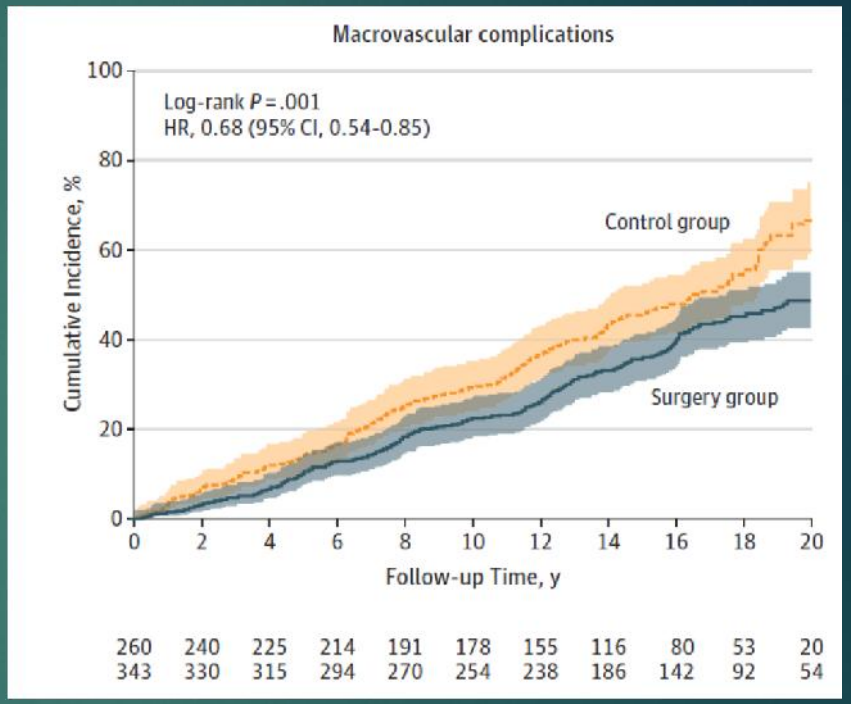
30.4% v.s. 6.5% for bariatric surgery v.s. controls and at 15 yrs ($P < 0.001$)

Banding, n= 61; vertical banding, n=227; bypass, n=55.

JAMA. 2014;311(22):2297-2304. doi:10.1001/jama.2014.5988

Bariatric surgery & diabetes complications





HR, 0.44; $P < 0.001$

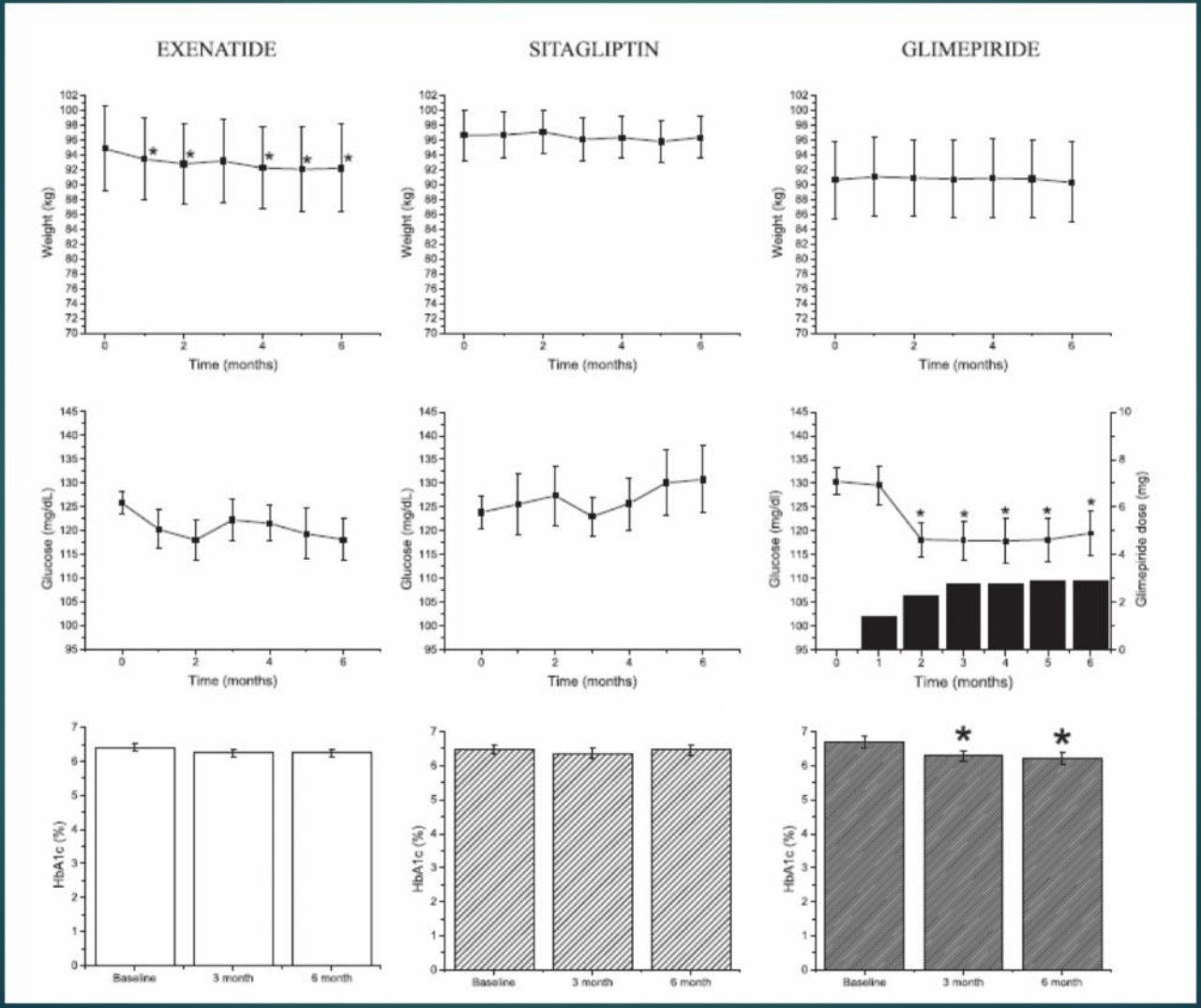
HR, 0.68; $P = 0.001$

CONCLUSIONS AND RELEVANCE In this very long-term follow-up observational study of obese patients with type 2 diabetes, bariatric surgery was associated with more frequent diabetes remission and fewer complications than usual care. These findings require confirmation in randomized trials.

Effect of Exenatide, Sitagliptin, or Glimepiride on β-Cell Secretory Capacity in Early Type 2 Diabetes

Lalitha Gudipaty,[1] Nora K. Rosenfeld,[1] Carissa S. Fuller,[1] Robert Gallop,[2] Mark H. Schutta,[1] and Michael R. Rickels[1]

Diabetes Care 2014;37:2451–2458 | DOI: 10.2337/dc14-0398



Glucose potentiated arginine test

Table 2—Measures of β-cell secretory capacity, β-cell sensitivity to glucose, insulin sensitivity, and glucagon secretion derived from the GPA test

	Exenatide (n = 14)			Sitagliptin (n = 12)			Glimepiride (n = 14)		
	Baseline	6 months[a]	Δ	Baseline	6 months[a]	Δ	Baseline	6 months[a]	Δ
AIR_{arg} (μU/mL)	52 ± 14	52 ± 11	−0.2 ± 9	35 ± 4	34 ± 6	−2 ± 7	44 ± 6	42 ± 4	−2 ± 7
AIR_{pot} (μU/mL)	138 ± 31	108 ± 21	−30 ± 20†	83 ± 12	80 ± 15	−2 ± 8	97 ± 16	119 ± 19	22 ± 12
AIR_{max} (μU/mL)	214 ± 60	188 ± 34	−25 ± 50‡	149 ± 20	158 ± 30	9 ± 21	133 ± 19	202 ± 35*	69 ± 33
PG_{50} (mg/dL)	175 ± 13	190 ± 14	25 ± 20	226 ± 12	209 ± 16	−5 ± 24	168 ± 17	182 ± 10	10 ± 26
M (mg · kg^{-1} · min^{-1})	5.5 ± 0.3	5.8 ± 0.4	0.27 ± 0.4	5.4 ± 0.4	5.3 ± 0.4	−0.1 ± 0.4	5.5 ± 0.4	5.8 ± 0.4	0.35 ± 0.4
I (μU/mL)	41 ± 13	39 ± 9	−2 ± 9	22 ± 2	23 ± 4	1 ± 3	28 ± 7	26 ± 2	−2 ± 5
M/I (mg · kg^{-1} · min^{-1}/μU/mL)	0.3 ± 0.1	0.3 ± 0.1	−0.01 ± 0.0	0.3 ± 0.0	0.3 ± 0.1	0.04 ± 0.1	0.3 ± 0.1	0.3 ± 0.1	−0.04 ± 0.0
AGR_{arg} (pg/mL)	60 ± 12	63 ± 8	3 ± 17	77 ± 13	60 ± 11	−17 ± 6	40 ± 9	62 ± 8	22 ± 17
AGR_{inh} (pg/mL)	63 ± 12	58 ± 13	−3 ± 6	64 ± 13	55 ± 16	−10 ± 10	46 ± 7	59 ± 7	11 ± 7
AGR_{min} (pg/mL)	51 ± 12	52 ± 12	2 ± 5‡	55 ± 8	59 ± 19	4 ± 21	37 ± 6	59 ± 8*	21 ± 8

Data are means ± SE. Δ, change from baseline to 6 months with each value. [a]Final visits after 6 months of therapy were conducted following a 5- to 7-day drug washout. *$P < 0.05$ when comparing values within each group. †$P < 0.05$ when comparing Δ between the exenatide and glimepiride groups. ‡$P \leq 0.1$ (statistical trend) when comparing Δ between exenatide and glimepiride groups.

B-cell secretory capacity
B-cell sensitivity to glucos

CONCLUSIONS

After 6 months of treatment, exenatide or sitagliptin had no significant effect on functional β-cell mass as measured by β-cell secretory capacity, whereas glimepiride appeared to enhance β- and α-cell secretion.

Sulfonylurea in combination with insulin is associated with increased mortality compared with a combination of insulin and metformin in a retrospective Danish nationwide study

Ulrik M. Mogensen · Charlotte Andersson · Emil L. Fosbøl · Tina K. Schramm · Allan Vaag · Nikolai M. Scheller · Christian Torp-Pedersen · Gunnar Gislason · Lars Køber

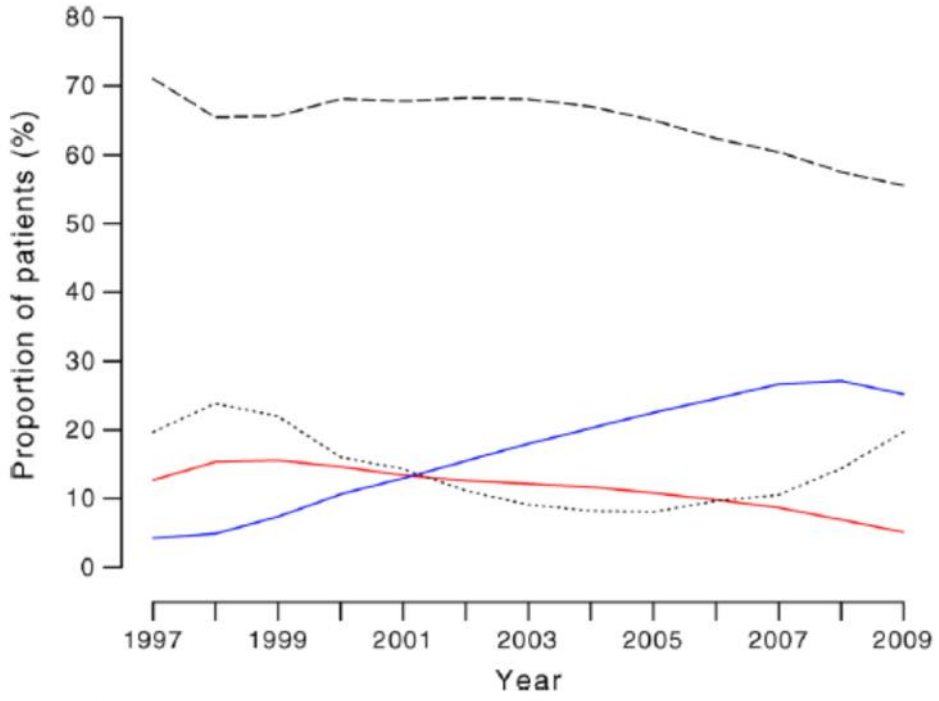


Fig. 2 Use of SU+insulin compared with other dual therapies according to year. Red line, SU+insulin; blue line, metformin+insulin; dashed line, metformin+SU; dotted line, other dual therapy

1997-2009

11,081 SU + Insulin

16,910 Metformin + Insulin users

Diabetologia (2015) 58:50–58

Table 2 Crude incidence rates per 1,000 person-years for mortality, cardiovascular death and a composite endpoint of stroke, MI and cardiovascular death

Variable	Insulin +					
	Glibenclamide	Gliclazide	Glimepiride	Glipizide	Tolbutamide	Metformin
All-cause mortality						
Events	99	63	524	72	30	774
Person-years	880	830	5,469	588	237	33,193
Crude incidence rates	112 (92–137)	76 (59–97)	96 (87–104)	122 (97–154)	126 (88–181)	23 (22–25)
Cardiovascular death						
Events	36	19	188	20	9	325
Person-years	880	830	5,469	588	237	33,193
Crude incidence rates	40 (29–56)	23 (15–36)	34 (30–40)	33 (22–52)	38 (20–73)	9.8 (8.8–10.9)
Composite endpoint						
Events	52	36	265	37	13	650
Person-years	850	809	5,321	578	235	32,451
Crude incidence rate	61 (47–80)	46 (32–62)	49 (44–56)	64 (46–88)	55 (32–95)	20 (18.6–21.6)

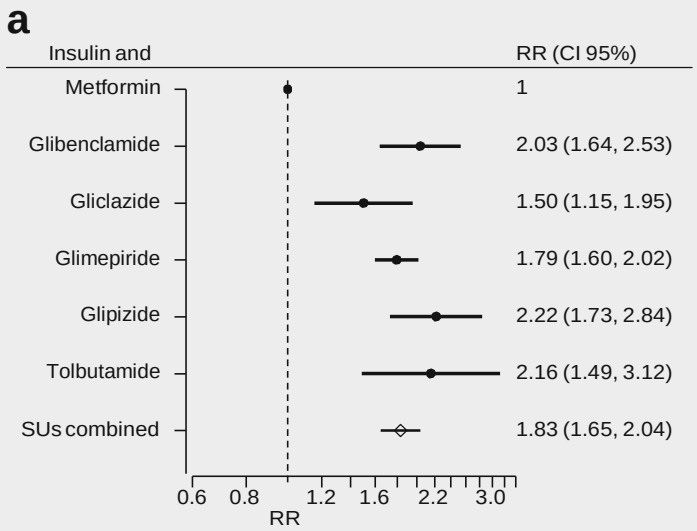
Table 3 Crude incidence rates for hypoglycaemia

Variable	Insulin +					
	Glibenclamide	Gliclazide	Glimepiride	Glipizide	Tolbutamide	Metformin
Hypoglycaemia						
Events	20	17	118	10	5	206
Person-years	880	830	5,469	588	237	33,193
Crude incidence rate per 1,000 person-years	23 (16–37)	20 (12–34)	21 (18–26)	17 (9–31)	21 (9–51)	6 (5–7)

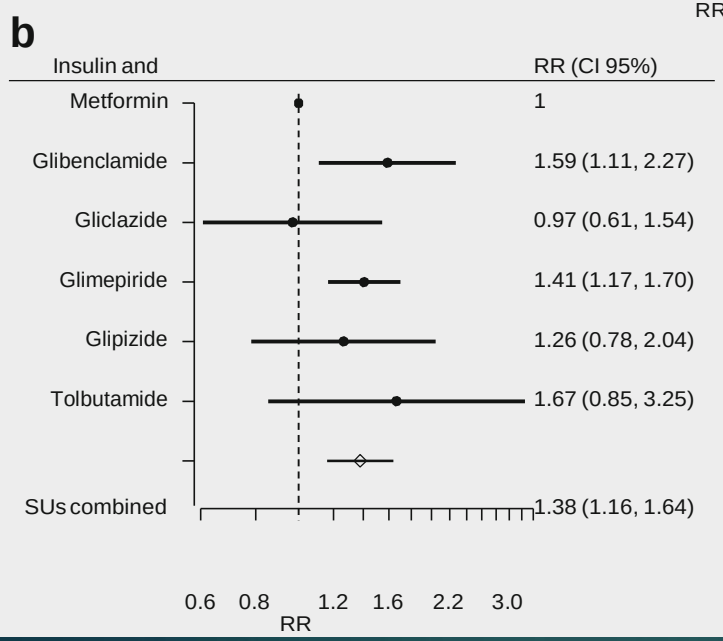
Diabetologia (2015) 58:50–58

RRs and 95% CIs associated with the use of insulin in combination with SUs or metformin

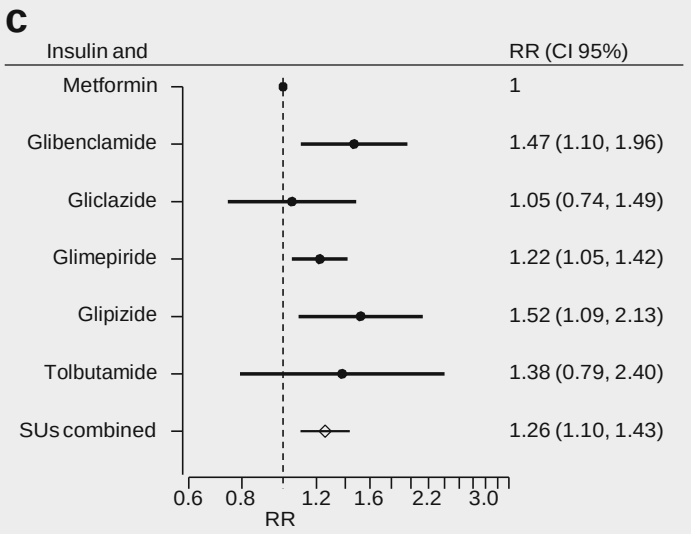
All-cause mortality



CV death

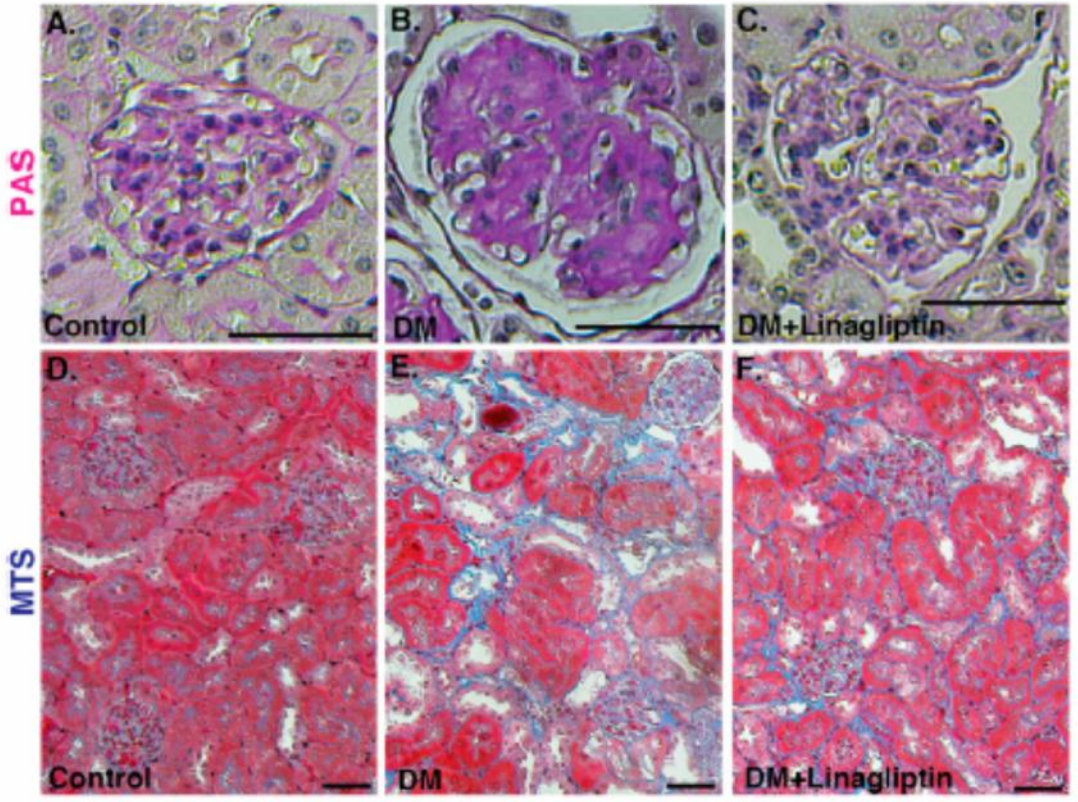


Composite acute MI, stroke and CV death



Linagliptin-Mediated DPP-4 Inhibition Ameliorates Kidney Fibrosis in Streptozotocin-Induced Diabetic Mice by Inhibiting Endothelial-to-Mesenchymal Transition in a Therapeutic Regimen

Diabetes 2014;63:2120–2131 | DOI: 10.2337/db13-1029



Keizo Kanasaki,[1] Sen Shi,[1] Megumi Kanasaki,[1] Jianhua He,[1] Takako Nagai,[1] Yuka Nakamura,[2] Yasuhito Ishigaki,[2] Munehiro Kitada,[1] Swayam Prakash Srivastava,[1] and Daisuke Koya[1]

DPP4 inhibition/renal fibrosis

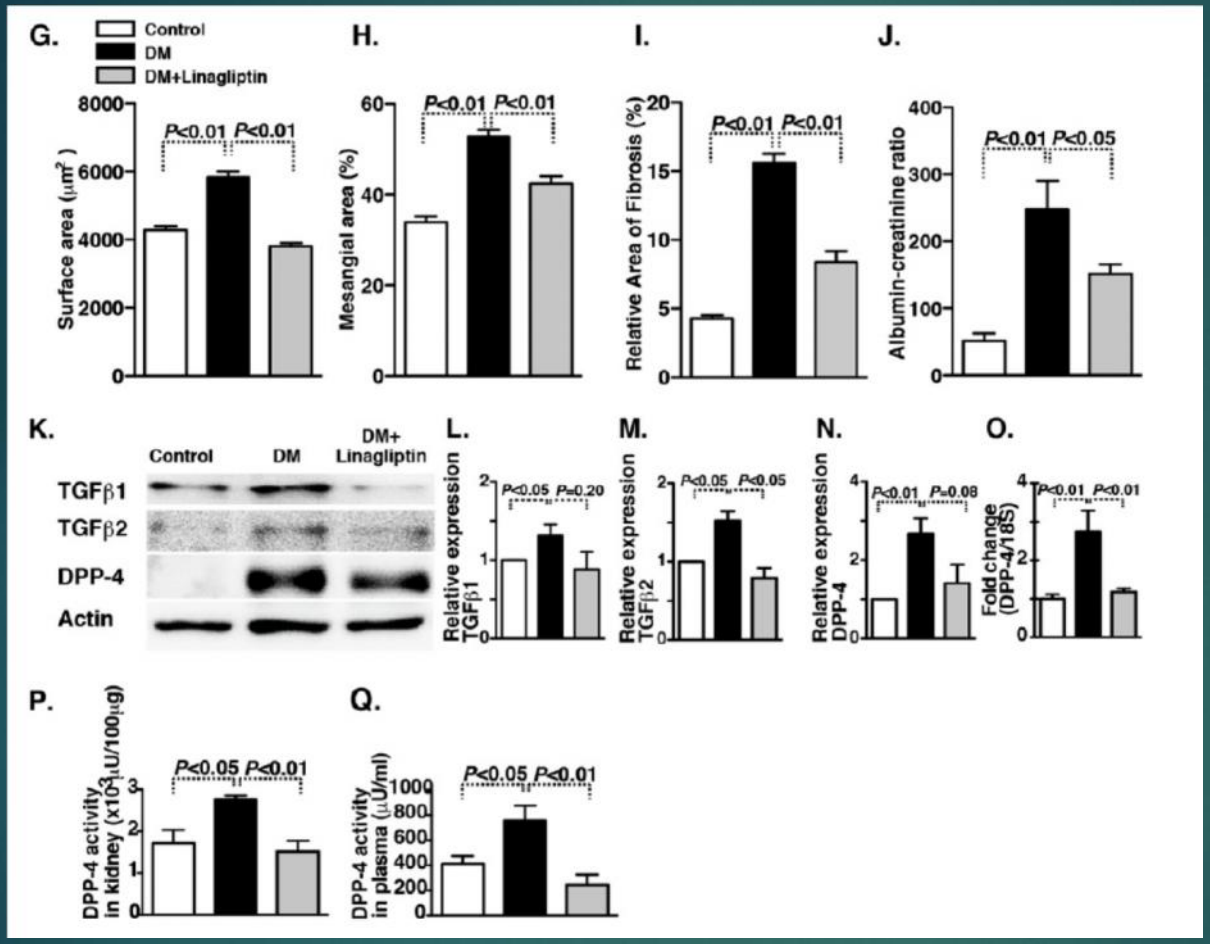


Figure 2—Inhibition of DPP-4 by linagliptin in diabetic kidneys is associated with the amelioration of kidney fibrosis. *A–C*: PAS staining for glomeruli. *D–F*: MTS staining in the indicated group of mice. Scale bar, 50 μm. *G–I*: A morphometric analysis of the kidney histology was performed as described in the RESEARCH DESIGN AND METHODS. Control, $n = 5$; DM, $n = 7$; DM+linagliptin, $n = 5$ were analyzed. *J*: Urine albumin excretion was analyzed by albumin-creatinine ratios. Control, $n = 5$; DM, $n = 8$; DM+linagliptin, $n = 6$ were analyzed. *K*: Western blot analysis for TGF-β1, TGF-β2, and DPP-4. A representative blot from four independent experiments is shown. *L–N*: Densitometric analysis of indicated protein expression relative to actin levels is shown. $n = 4$ in each group were analyzed. *O*: qPCR analysis for DPP-4 in the kidney from six mice in each group. DPP-4 activity measurements in kidney (control, $n = 3$; DM, $n = 6$; DM+linagliptin, $n = 6$) (*P*) and plasma (all $n = 6$) (*Q*) were analyzed. The graphs in the figure are expressed as mean ± SEM. DM, diabetic mice.

The Influence of New European Union Driver's License Legislation on Reporting of Severe Hypoglycemia by Patients With Type 1 Diabetes

Ulrik Pedersen-Bjergaard,[1,2] Louise Færch,[1] Marie-Louise Allingbjerg,[1] Rikke Agesen,[1,2] and Birger Thorsteinsson[1,2]

Diabetes Care 2015;38:29–33 | DOI: 10.2337/dc14-1417

Table 2—Temporal development in rates of severe hypoglycemia as indicated in medical records, HbA_{1c} levels, and insulin treatment regimens

	Year		
	2010	2011	2012
Data coverage (%)	81.7	65.4	66.1
Severe hypoglycemia			
Mean rate per patient-year	0.36	0.47	0.19
Range	0–7	0–11	0–5
Insulin doses (IU/day)	51.2 (22.0)	49.8 (21.9)	49.5 (22.1)
Insulin regimen			
Analog basal-bolus	113 (36.6)	125 (40.5)	128 (41.4)
Human basal-bolus	48 (15.5)	46 (14.9)	41 (13.3)
Mixed basal-bolus	55 (17.8)	48 (15.5)	55 (17.8)
CSII	28 (9.1)	38 (12.3)	49 (15.9)
Other	65 (21.0)	52 (16.8)	36 (11.6)
HbA_{1c} (%)	8.0 (1.1)	7.8 (1.1)	7.7 (1.0)
HbA_{1c} (mmol/mol)	64 (12)	62 (12)	61 (11)

Data are presented as mean (SD) or *n* (%) unless otherwise indicated.

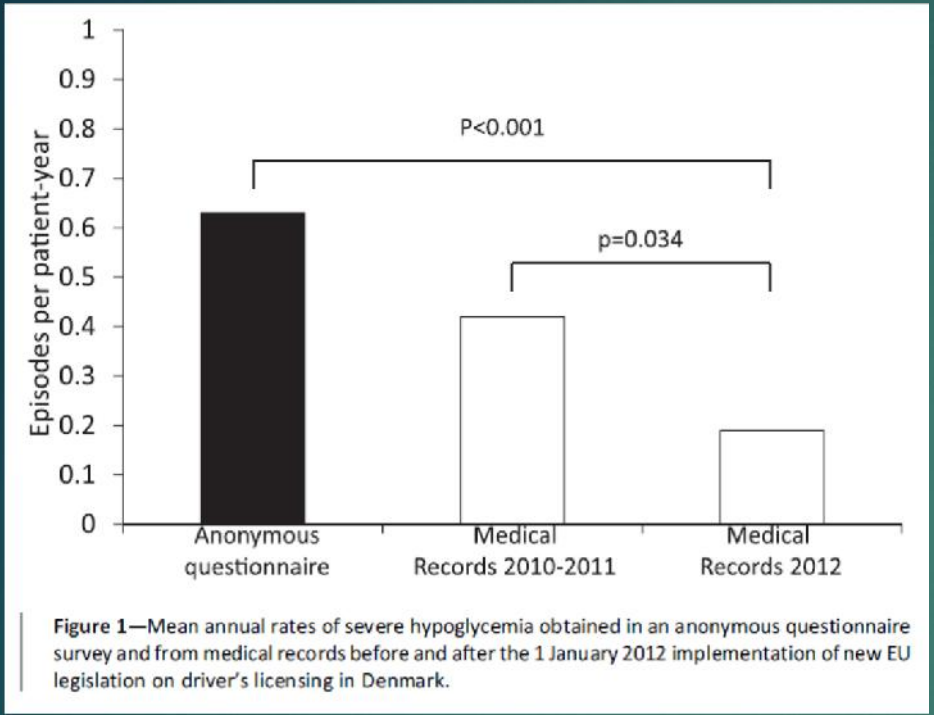


Figure 1—Mean annual rates of severe hypoglycemia obtained in an anonymous questionnaire survey and from medical records before and after the 1 January 2012 implementation of new EU legislation on driver's licensing in Denmark.

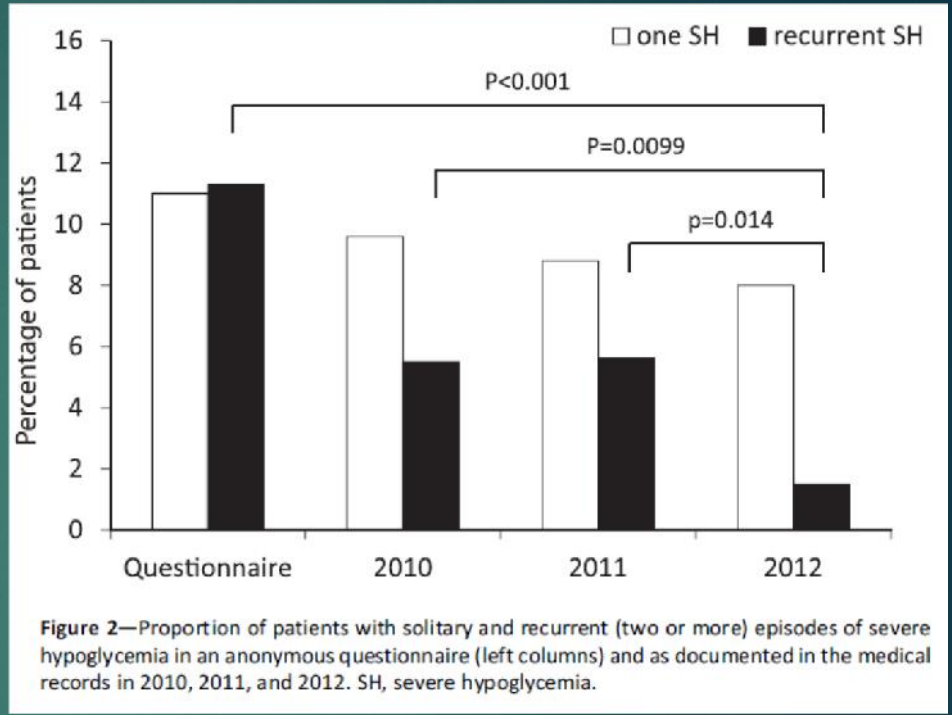


Figure 2—Proportion of patients with solitary and recurrent (two or more) episodes of severe hypoglycemia in an anonymous questionnaire (left columns) and as documented in the medical records in 2010, 2011, and 2012. SH, severe hypoglycemia.

Reported rates of severe hypoglycemia in the medical records were reduced by 55% in 2012 compared with the prior years (P = 0.034)

The proportion of subjects reporting recurrent episodes was grossly reduced from 5.6 to 1.5% (P = 0.014)

Compared with anonymous reporting in the questionnaire, the rate of severe hypoglycemia in 2012 was 70% lower (P < 0.001)

Glycemic Targets in the Second and Third Trimester of Pregnancy for Women With Type 1 Diabetes

Michael J.A. Maresh,[1] Valerie A. Holmes,[2] Christopher C. Patterson,[2] Ian S. Young,[2] Donald W.M. Pearson,[3] James D. Walker,[4] and David R. McCance,[5] for the Diabetes and Pre-eclampsia Intervention Trial Study Group

Diabetes Care 2015;38:34–42 | DOI: 10.2337/dc14-1755

Table 1—Maternal characteristics and glycemic control in 725 participants

Age (years), mean (SD)	29.6 (5.6)
BMI (kg/m^2), mean (SD)*	27.4 (4.7)
Diabetes duration (years), mean (SD)	14.5 (8.2)
Primiparous, *n* (%)	361 (49.8)
Smoker, *n* (%)	139 (19.2)
Social class: head of household in professional or managerial/technical occupation, *n* (%)†	297 (46.0)
Nonwhite ethnicity, *n* (%)	26 (3.6)
Education (years), mean (SD)	14.0 (2.8)
A1C [% (mmol/mol)], mean (SD)‡	
First antenatal visit	7.8 (1.4)/62 (15)
26 weeks' gestation	6.7 (0.8)/50 (9)
34 weeks' gestation	6.6 (0.7)/48 (7)
Mean fasting/preprandial capillary glucose (mmol/L), mean (SD)§	
26 weeks' gestation	6.4 (1.8)
34 weeks' gestation	6.0 (1.7)
Mean 1-h postprandial capillary glucose (mmol/L), mean (SD)‖	
26 weeks' gestation	7.5 (2.4)
34 weeks' gestation	7.2 (2.3)

*Based on *n* = 708 results. †Based on *n* = 646 results. ‡Based on *n* = 698/576/505 results at first antenatal visit/26 weeks' gestation/34 weeks' gestation. §Based on *n* = 610/546 results at 26 weeks' gestation/34 weeks' gestation. ‖Based on *n* = 484/447 results at 26 weeks' gestation/34 weeks' gestation.

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Table 2—Adverse pregnancy outcomes by A1C category at 26 weeks' gestation

	A1C at 26 weeks					
	<6.0% (<42 mmol/mol) (*n* = 101)	6.0–6.4% (42–47 mmol/mol) (*n* = 176)	6.5–6.9% (48–52 mmol/mol) (*n* = 128)	7.0–7.4% (53–58 mmol/mol) (*n* = 98)	7.5+% (59+ mmol/mol) (*n* = 73)	*P* value for trend
Pre-eclampsia						
No. (%)	8/101 (8)	23/176 (13)	29/128 (23)	24/98 (24)	17/73 (23)	
OR (95% CI)	1.0 (Reference)	1.7 (0.8–4.1)	3.4‡ (1.5–7.8)	3.8‡ (1.6–8.9)	3.5‡ (1.4–8.7)	<0.001
OR (95% CI)*	1.0 (Reference)	2.0 (0.8–4.9)	4.3‡ (1.7–10.8)	4.6‡ (1.8–12.0)	5.1‡ (1.9–14.1)	<0.001
LGA (>90th centile)						
No. (%)	36/99 (36)	88/175 (50)	73/128 (57)	60/98 (61)	46/73 (63)	
OR (95% CI)	1.0 (Reference)	1.8† (1.1–2.9)	2.3‡ (1.4–4.0)	2.8§ (1.6–4.9)	3.0§ (1.6–5.6)	<0.001
OR (95% CI)*	1.0 (Reference)	1.7† (1.0–3.0)	2.5‡ (1.4–4.5)	3.2§ (1.7–6.1)	3.7§ (1.8–7.5)	<0.001
Cesarean section delivery						
No. (%)	67/101 (66)	125/176 (71)	85/128 (66)	76/98 (78)	46/73 (63)	
OR (95% CI)	1.0 (Reference)	1.2 (0.7–2.1)	1.0 (0.6–1.7)	1.8 (0.9–3.3)	0.9 (0.5–1.6)	0.90
OR (95% CI)*	1.0 (Reference)	1.1 (0.6–2.0)	1.1 (0.6–2.0)	2.0 (1.0–3.9)	1.0 (0.5–1.9)	0.48
Neonatal hypoglycemia requiring glucose infusion						
No. (%)	20/99 (20)	42/170 (25)	49/124 (40)	39/95 (41)	30/70 (43)	
OR (95% CI)	1.0 (Reference)	1.3 (0.7–2.4)	2.6‡ (1.4–4.7)	2.8‡ (1.5–5.2)	3.0‡ (1.5–5.9)	<0.001
OR (95% CI)*	1.0 (Reference)	1.5 (0.8–2.9)	2.9‡ (1.5–5.6)	3.5§ (1.7–7.2)	3.8§ (1.7–8.2)	<0.001
Hyperbilirubinemia requiring phototherapy						
No. (%)	13/99 (13)	25/173 (14)	26/127 (20)	28/96 (29)	20/71 (28)	
OR (95% CI)	1.0 (Reference)	1.1 (0.5–2.3)	1.7 (0.8–3.5)	2.7‡ (1.3–5.7)	2.6† (1.2–5.7)	<0.001
OR (95% CI)*	1.0 (Reference)	1.4 (0.6–2.9)	2.1 (0.9–4.5)	3.7‡ (1.7–8.3)	3.8‡ (1.6–8.9)	<0.001
Delivery before 37 weeks						
No. (%)	21/101 (21)	51/176 (29)	48/128 (38)	50/98 (51)	33/73 (45)	
OR (95% CI)	1.0 (Reference)	1.6 (0.9–2.8)	2.3‡ (1.3–4.2)	4.0§ (2.1–7.4)	3.1§ (1.6–6.1)	<0.001
OR (95% CI)*	1.0 (Reference)	1.6 (0.8–2.9)	2.5‡ (1.3–4.8)	5.1§ (2.6–10.2)	3.8§ (1.8–8.0)	<0.001
Composite adverse neonatal outcome						
No. (%)	8/101 (8)	21/176 (12)	25/128 (20)	27/98 (28)	16/73 (22)	
OR (95% CI)	1.0 (Reference)	1.6 (0.7–3.7)	2.8† (1.2–6.6)	4.4§ (1.9–10.3)	3.3† (1.3–8.1)	<0.001
OR (95% CI)*	1.0 (Reference)	1.6 (0.7–4.1)	3.2‡ (1.3–8.0)	6.7§ (2.6–17.0)	4.4‡ (1.6–12.3)	<0.001

*Adjusted for age, BMI, years of education, social class, ethnicity, parity, current smoking, duration of diabetes, microalbuminuria before pregnancy, vitamin treatment group, and center. †$P < 0.05$, ‡$P < 0.01$, §$P < 0.001$.

Insulin pump use in pregnancy is associated with lower HbA_{1c} without increasing the rate of severe hypoglycaemia or diabetic ketoacidosis in women with type 1 diabetes

Melissa M. Kallas-Koeman · Jason M. Kong · Jennifer A. Klinke · Sonia Butalia · Abhay K. Lodha · Ken I. Lim · Qiuli M. Duan · Lois E. Donovan

Table 2 Maternal outcomes in pregnancies >20 weeks' gestation according to mode of insulin therapy

Outcome	MDI (n=218)	Insulin pump (n=113)	p value[a]
HbA_{1c}, % (mmol/mol), mean ± SD (n)			
First trimester average	7.60±1.38 (60±15.1) (182)	6.90±0.71 (52±7.8) (97)	<0.001
Second trimester average	6.83±0.99 (51±10.8) (202)	6.34±0.56 (46±6.1) (105)	<0.001
Third trimester average	6.81±0.85 (51±9.3) (168)	6.49±0.52 (47±5.7) (83)	0.002
Severe hypoglycaemia, n (%)			
1+ event	18/237 (7.6)	9/113 (8.0)	0.90
Total events	35	17	–
Diabetic ketoacidosis, n (%)	7/237 (3.0)	2/112 (1.8)	0.72
Hypertension in pregnancy, n (%)			
Gestational hypertension or pre-eclampsia	56/198 (28.3)	22/103 (21.4)	0.19
Pre-eclampsia only	12/198 (6.1)	6/103 (5.8)	0.93
Weight gain, kg, mean ± SD (n)	15.2±6.2 (206)	16.3±8.7 (107)	0.18
Delivery mode, n (%)			
Caesarean	140/218 (64.2)	78/113 (69.0)	0.38
Vaginal	56/218 (25.7)	29/113 (25.7)	–
Assisted vaginal	22/218 (10.1)	6/113 (5.3)	–
Primary Caesarean birth, n (%)	152/213 (71.4)	81/112 (72.3)	0.86

[a] Student's t test for continuous variables and χ^2 tests of association for categorical variables

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Glycaemic control

Table 3 Proportion of women achieving a mean HbA_{1c} ≤6.1% and ≤7.0% in each trimester of pregnancy according to mode of insulin therapy

Trimester	HbA_{1c}≤6.1% (43 mmol/mol)			HbA_{1c} ≤7.0% (53 mmol/mol)		
	MDI	Insulin pump	*p* value[a]	MDI	Insulin pump	*p* value[a]
First, *n* (%)	17/206 (8.3)	11/109 (10.1)	0.59	79/206 (38.4)	68/109 (62.4)	<0.001
Second, *n* (%)	44/207 (21.3)	43/111 (38.7)	<0.001	143/207 (69.1)	100/111 (90.1)	<0.001
Third, *n* (%)	28/168 (16.7)	22/86 (25.6)	0.09	113/168 (67.3)	73/86 (84.9)	0.003

[a] χ^2 tests of association

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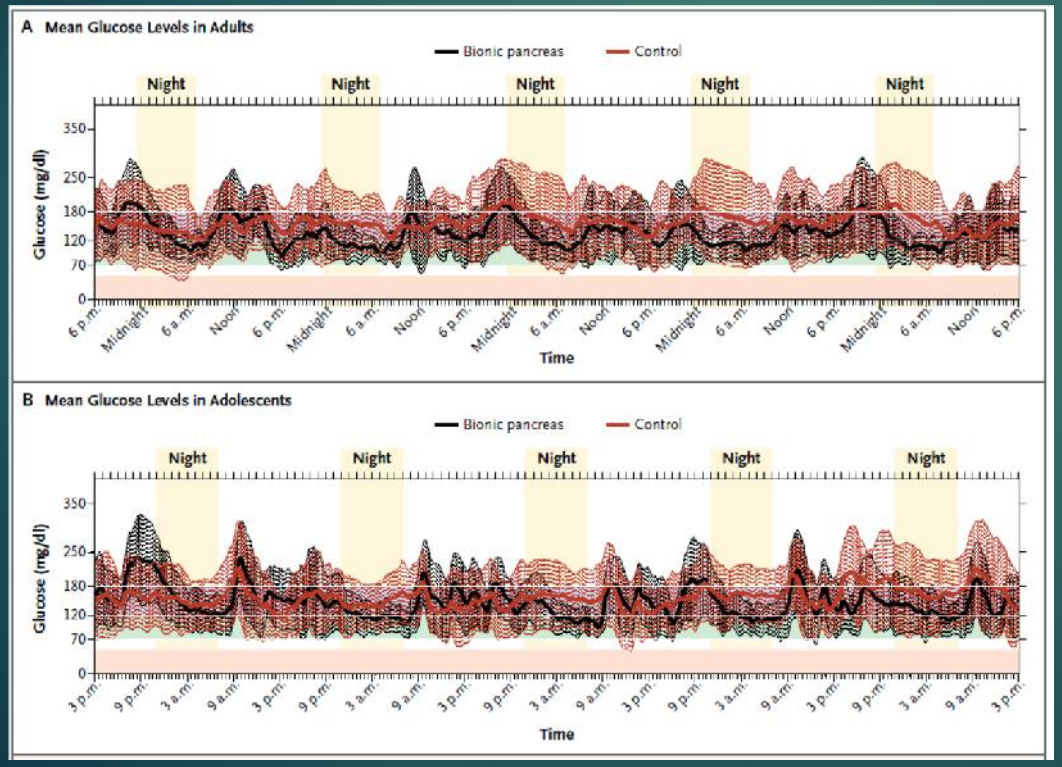
ORIGINAL ARTICLE

Outpatient Glycemic Control with a Bionic Pancreas in Type 1 Diabetes

Steven J. Russell, M.D., Ph.D., Firas H. El-Khatib, Ph.D., Manasi Sinha, M.D., M.P.H., Kendra L. Magyar, M.S.N., N.P., Katherine McKeon, M.Eng., Laura G. Goergen, B.S.N., R.N., Courtney Balliro, B.S.N, R.N., Mallory A. Hillard, B.S., David M. Nathan, M.D., and Edward R. Damiano, Ph.D.



Bionic-pancreas v.s. control pump period

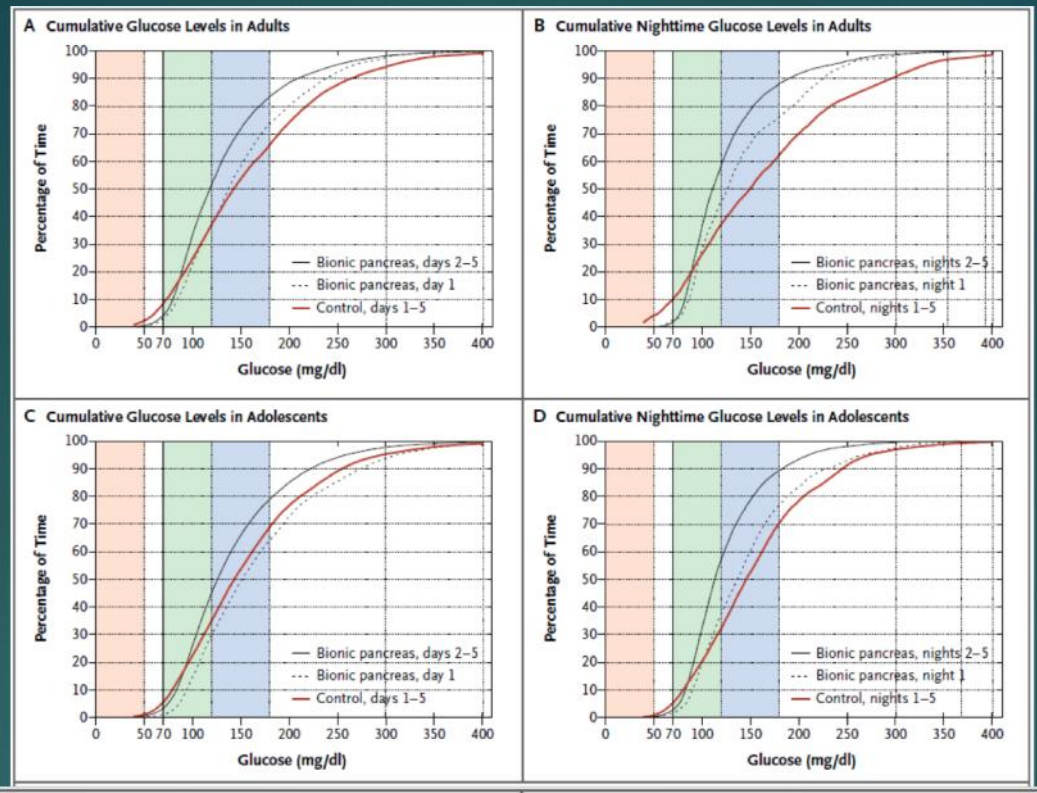
Mean glucose 7.4 vs 8.8 mmol/l in adult study (p=0.01)

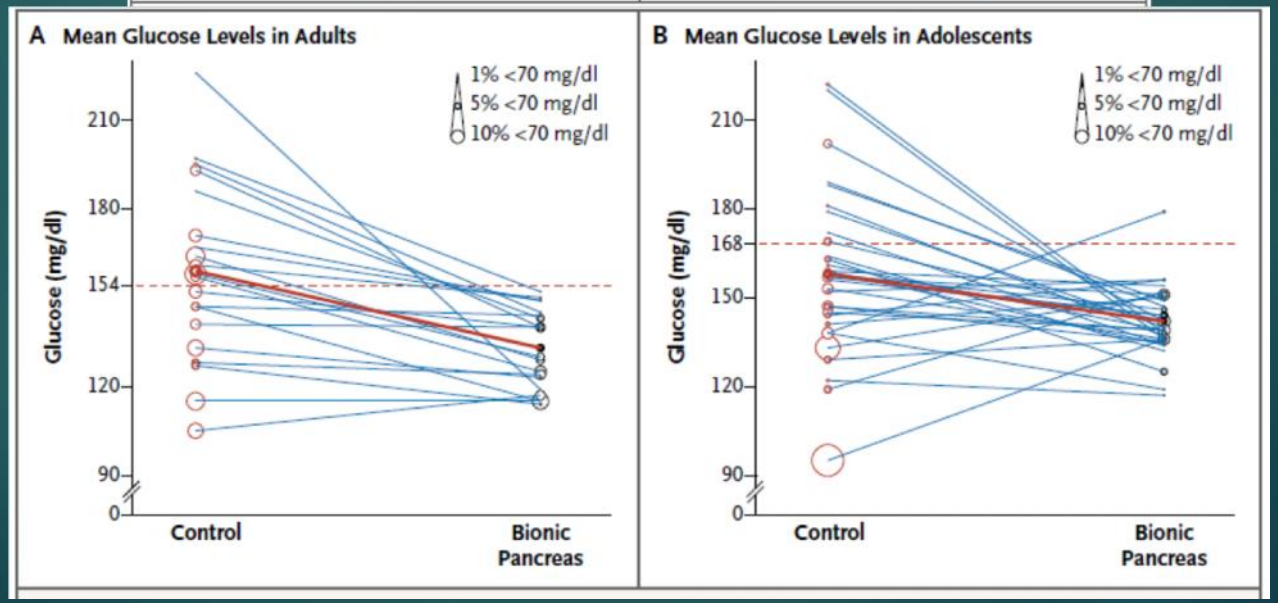
% time with hypoglycaemia 4.1% v.s. 7.3% (p =0.01)

Mean glucose 7.7 v.s. 8.7 mmol/l in adolescents (p=0.004)

% time with hypoglycaemia similar at 6.1% and 7.6% (p=0.23)

N ENGL J MED 371;4 NEJM.ORG JULY 24, 2014


A Cumulative Glucose Levels in Adults
B Cumulative Nighttime Glucose Levels in Adults
C Cumulative Glucose Levels in Adolescents
D Cumulative Nighttime Glucose Levels in Adolescents
Percentage of Time
Glucose (mg/dl)
Bionic pancreas, days 2–5
Bionic pancreas, day 1
Control, days 1–5
Bionic pancreas, nights 2–5
Bionic pancreas, night 1
Control, nights 1–5


A Mean Glucose Levels in Adults
B Mean Glucose Levels in Adolescents
1% <70 mg/dl
5% <70 mg/dl
10% <70 mg/dl
Glucose (mg/dl)
Control
Bionic Pancreas

Summary & Conclusions

- Trends in epidemiology and intervention trials
- Examined the role of stem cells, new therapies and surgical strategies for diabetes cure/prevention
- Reviewed treatment efficacy and risks of current oral agents
- Potential impact of new agents and renal complications
- Challenges in supporting patients with driving legislation
- New studies on glycaemic targets and treatment for diabetes in pregnancy
- Technological innovations with bionic pancreas