



Insulinización con análogos de insulina

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Conflictos de interés

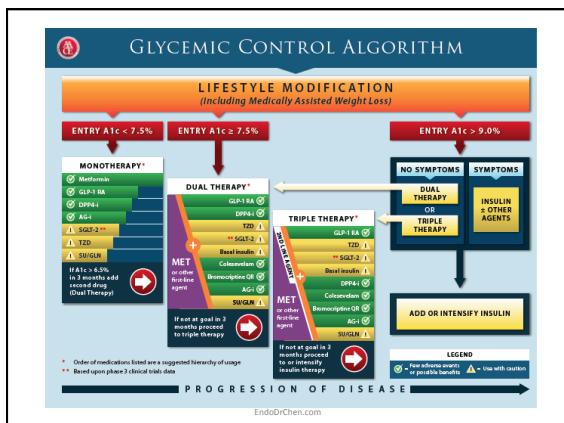
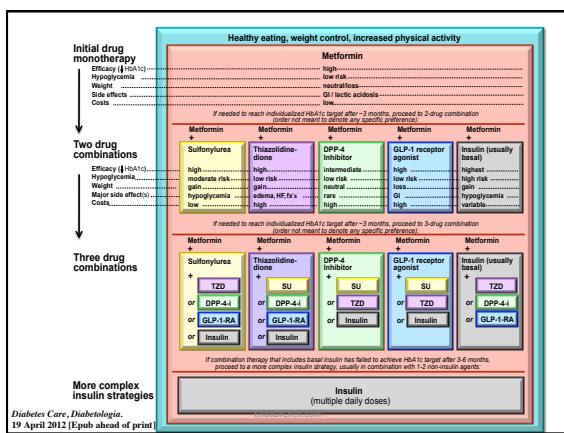
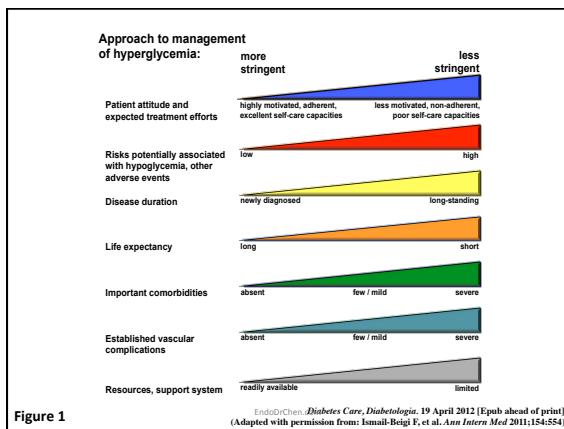
- Conferencista: Astra Zeneca, Abbott Nutrición, Novartis Oncology, Novo Nordisk, Merck Sharp & Dohme, Roche, Glaxo SmithKline, Sanofi Aventis
- Advisory Board: Novartis Oncology, Sanofi Aventis, Astra Zeneca, Novo Nordisk
- Investigación clínica: Astra Zeneca, Novartis Pharma Logistics Inc., Merck Sharp & Dohme, Glaxo SmithKline, Organon, Boehringer Ingelheim, Roche

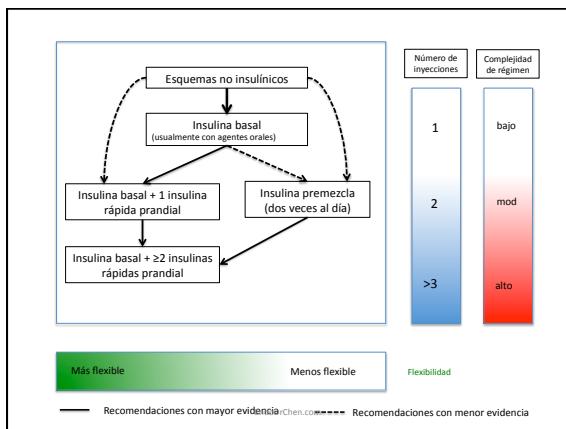
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Agenda

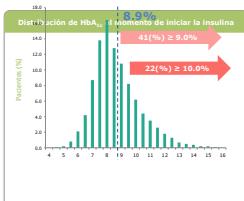
- Insulinización basal
- Diferencias entre insulinas basales
- Intensificación
- Ventajas de análogos ultrarrápidos
- Impacto en complicaciones crónicas

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Existe la necesidad de un inicio más temprano de la insulina - HbA_{1c} basal



- Los beneficios del control glucémico oportuno
- Guías de tratamiento que alientan el uso más temprano de la insulina

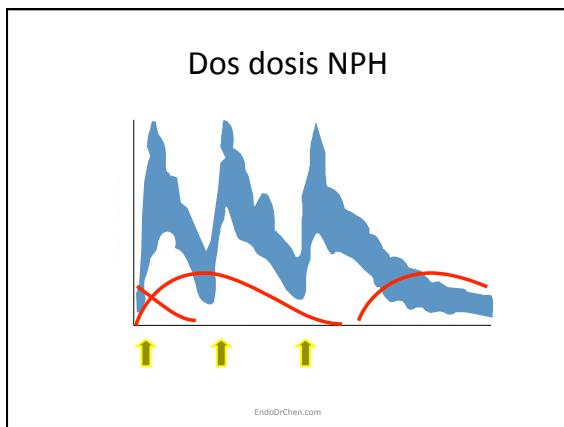
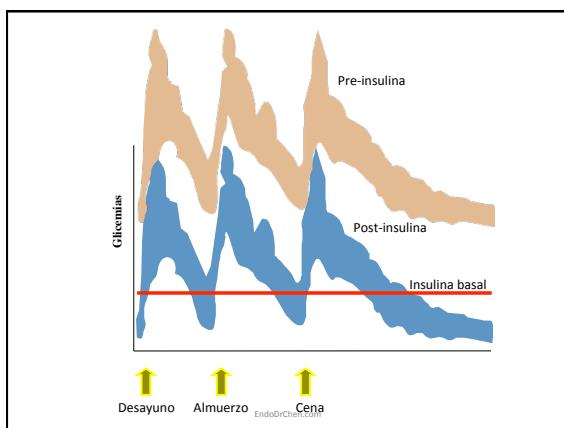
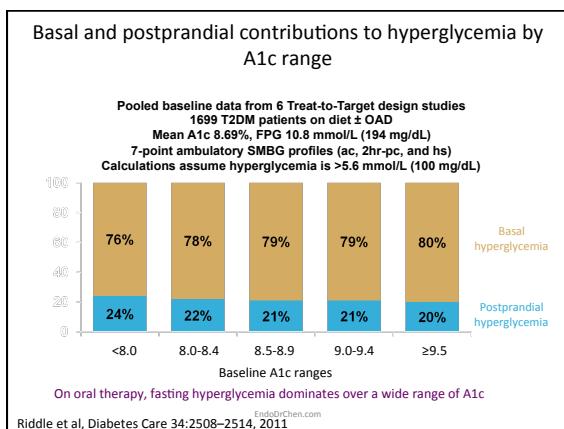
Al iniciar la insulina en SOLVE™:

Al iniciar la insulina en SOLVE™:

EndoDrChen.com Khunti et al. Diabetologia 2011; 54 (Suppl. 1): S160 and Portero

QUIÉN ES LA RESPONSABLE DE LA HIPERGLICEMIA?

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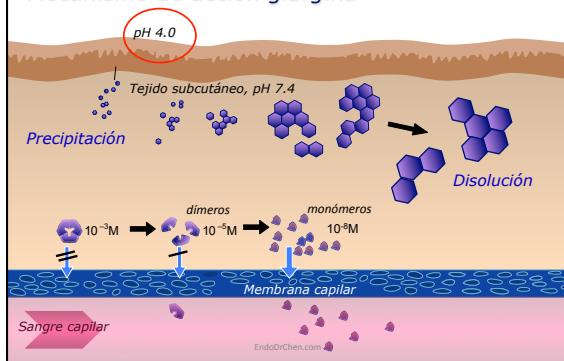


Insulinas basales

- Cuáles agentes disponibles hay?
 - NPH
 - Glargina
 - Detemir

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Mecanismo de acción glargina

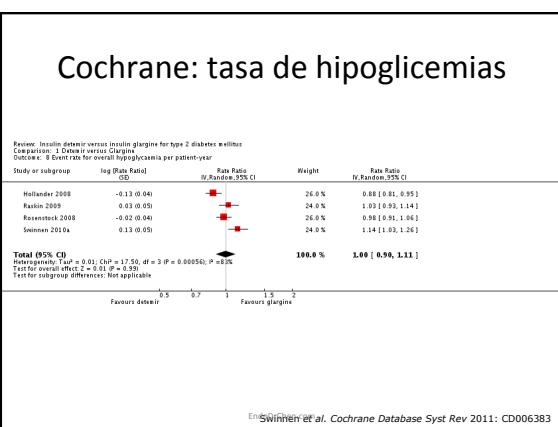
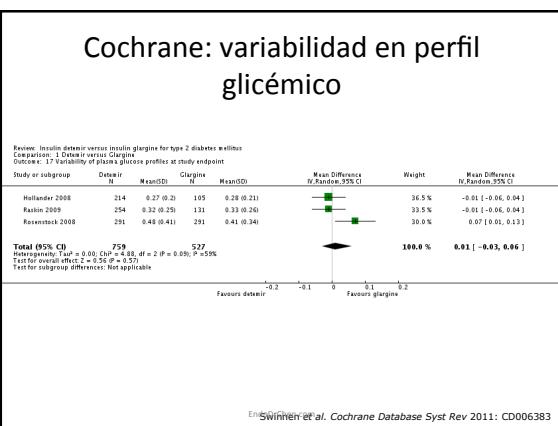
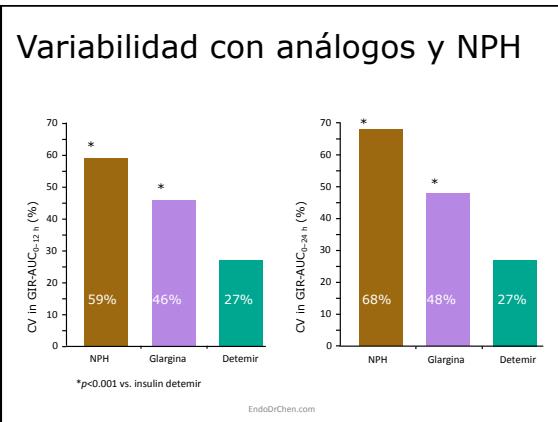


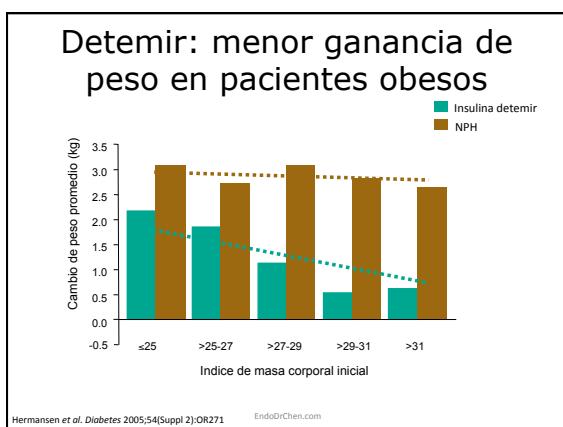
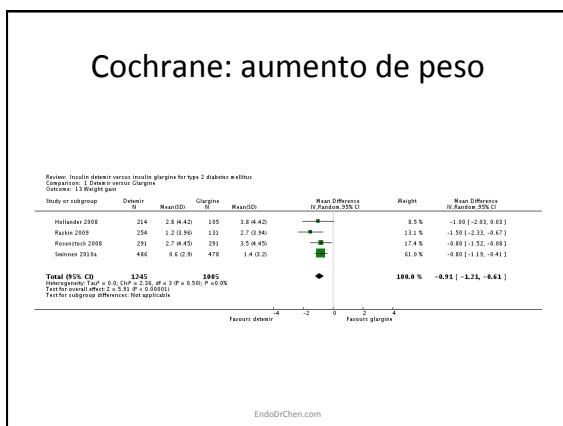
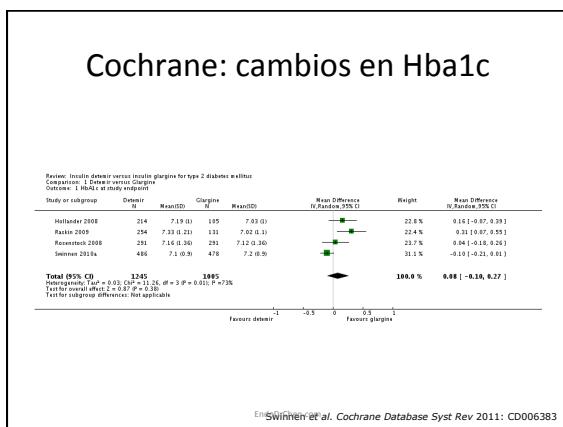
Insulina detemir

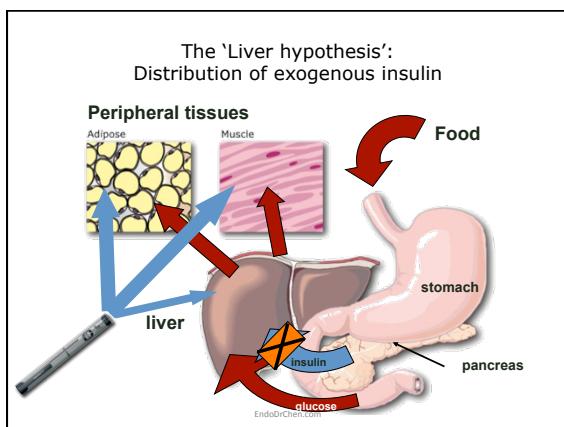
LysB29(N-tetradecanoyl)des(B30)

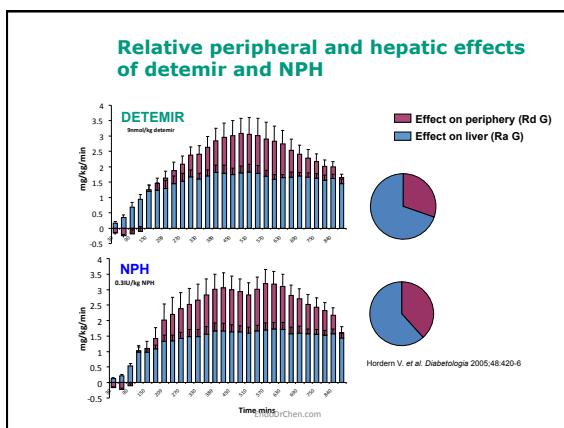
- C14 ácido graso (ácido mirístico)
- Solución cristalina
- pH neutro
- 1 IU = 24 nmol

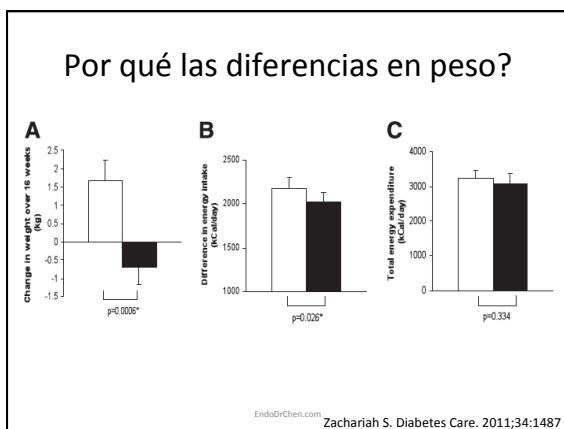
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Efectos centrales de la insulina

- Insulina actúa como señal de saciedad
- La administración intranasal de insulina en mujeres produce saciedad
- El ácido graso del detemir puede facilitar su paso al cerebro a través de la BHE

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Van Golen LW. Diabetes Care. 2013;36:4050

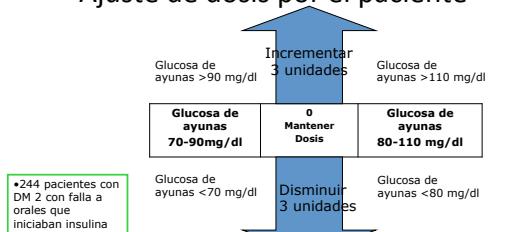
Estudios de flujo cerebral: NPH vs detemir

	CMR _{glu}			CBF		
	NPH	Detemir	P	NPH	Detemir	P
Total gray matter	0.15 ± 0.02	0.16 ± 0.02	0.2	0.31 ± 0.05	0.34 ± 0.05	0.06
Regions of interest						
OFC L				0.38 ± 0.06	0.40 ± 0.08	0.2
OFC R				0.39 ± 0.07	0.41 ± 0.08	0.3
Insula L				0.40 ± 0.07	0.44 ± 0.09	0.04
Insula R				0.39 ± 0.08	0.43 ± 0.08	0.05
Putamen L				0.40 ± 0.07	0.44 ± 0.09	0.04
Putamen R				0.40 ± 0.06	0.45 ± 0.09	0.02
Caudate L	0.19 ± 0.05	0.20 ± 0.04	0.0	0.34 ± 0.06	0.37 ± 0.08	0.08
Caudate R	0.19 ± 0.04	0.20 ± 0.03	0.2	0.31 ± 0.06	0.36 ± 0.09	0.02
Striatum				0.37 ± 0.06	0.42 ± 0.09	0.02
Thalamus L				0.39 ± 0.06	0.43 ± 0.07	0.07
Thalamus R				0.38 ± 0.06	0.43 ± 0.08	0.04
Cingulate ant L				0.36 ± 0.07	0.39 ± 0.09	0.03
Cingulate ant R				0.38 ± 0.07	0.41 ± 0.09	0.04
Cingulate post L				0.38 ± 0.06	0.41 ± 0.08	0.1
Cingulate post R				0.39 ± 0.06	0.43 ± 0.08	0.02

Data are mean ± SD unpaired data, n = 24 for CMR_{glu} and n = 18 for CBF. OFC, orbitofrontal cortex; post, posterior; R, right.

Van Golen LW. Diabetes Care. 2013;36:4050

Insulina basal: Ajuste de dosis por el paciente



Ajuste cada 3er día según el promedio de la glucosa de ayunas

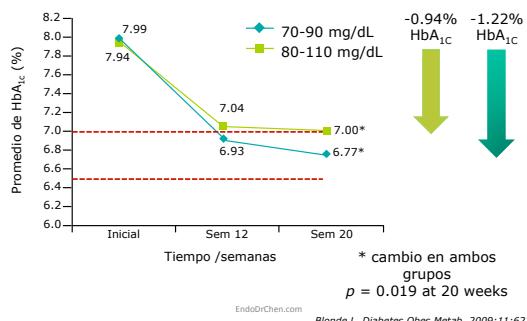
Diabétés Óbes Metab. Jun 2009;11(6):623-631

Metas de tratamiento

Meta	Glicemia ayunas	Glicemias postprandiales
<6.5%	70-110 mg/dl	<140 mg/dl
<7%	80-140 mg/dl	<180 mg/dl

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Ajuste de dosis por el paciente mejoría en HbA_{1c}: estudio Titrate



Basal Insulin: Percent of patients with HbA1c < 7%

29 trials, with 17,588 patients

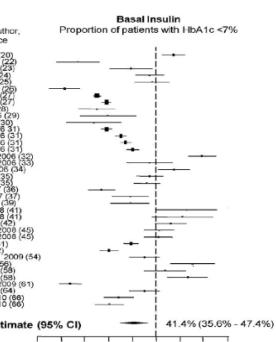
HbA_{1c} < 7% was achieved in
41.4% (95% CI, 35.6–47.4%).

Predictors of response:
 - first insulin treatment,
 - lower insulin dose
 - use of 2 oral drugs

Hypoglycemic events: 0 to
4.71 events/patient/30 days

Weight gain ~1.75 kg
(1.2-2.1)

Final Insulin dose: 0.48
(0.4-0.57)

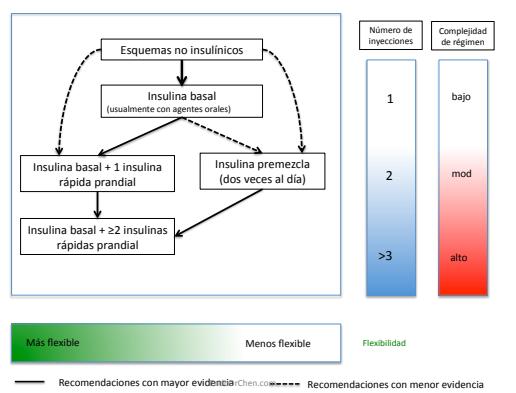


Giugliano et al. Diabetes Research & Clinical Practice 92

(2011) 1-10

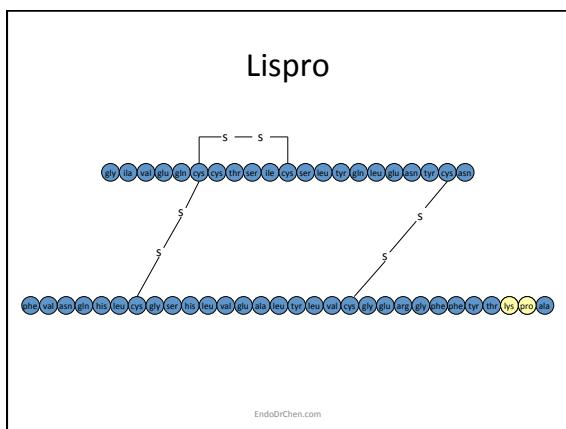
QUÉ PASA SI PERSISTE CON HBA1C ALTO A PESAR DE TENER GLICEMIA EN AYUNAS ÓPTIMO?

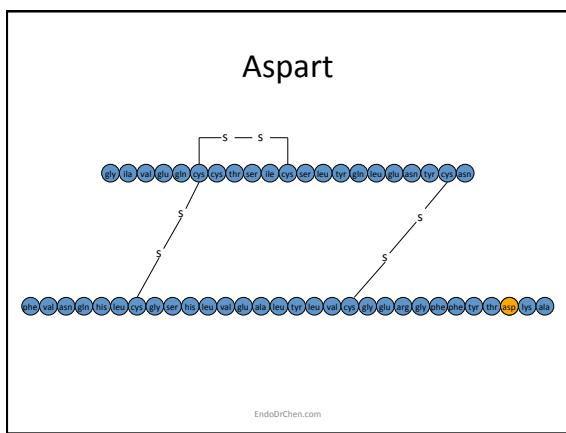
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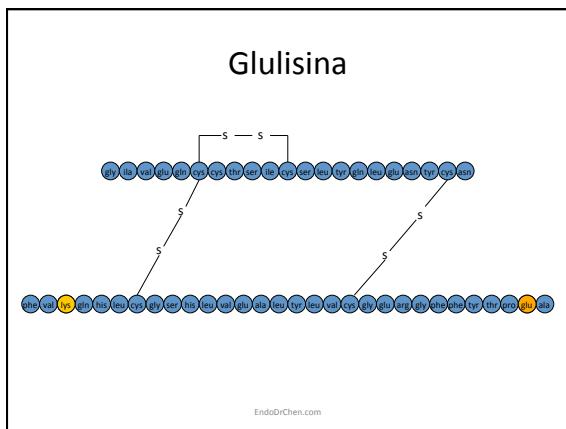


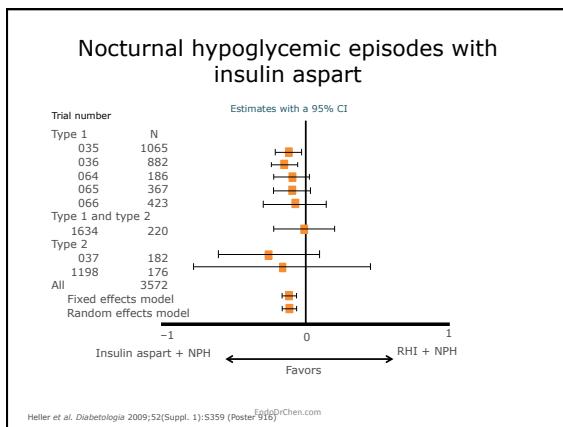
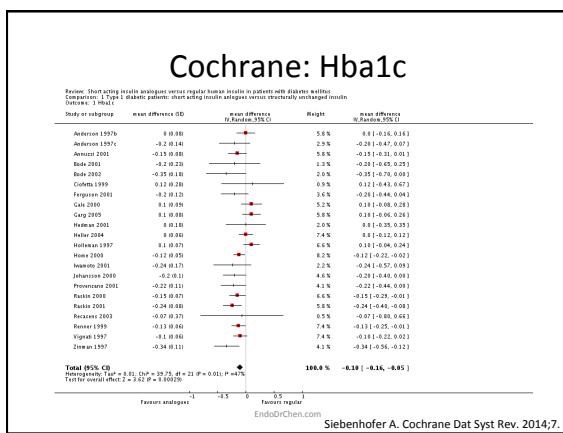
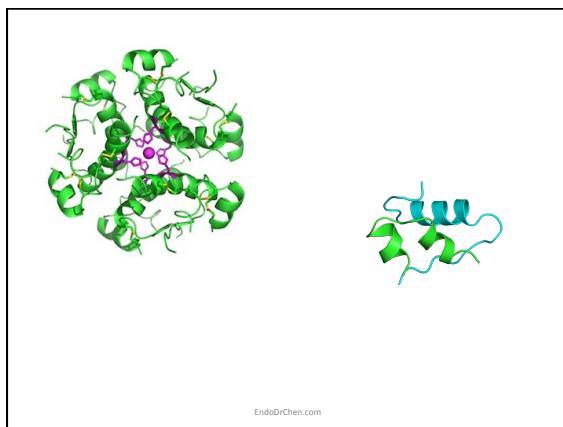
ANÁLOGOS ULTRARRÁPIDOS

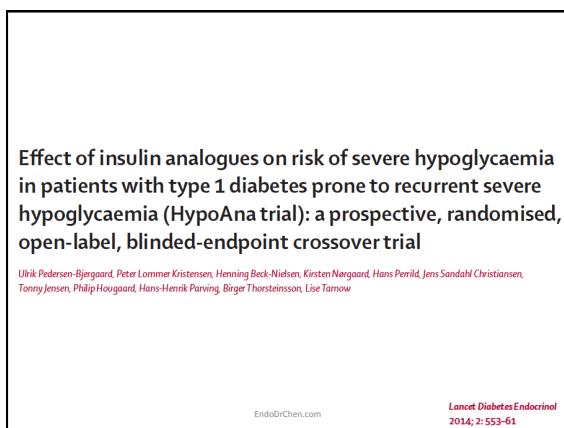
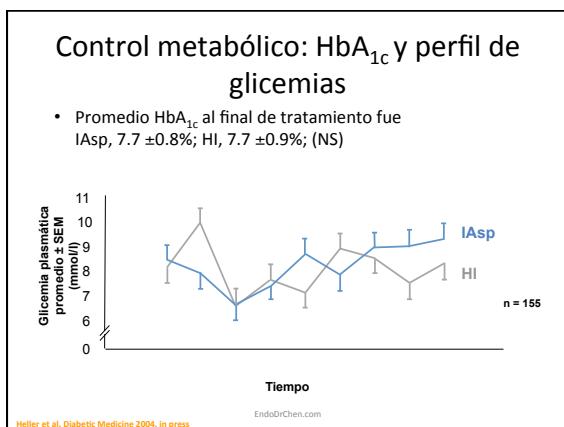
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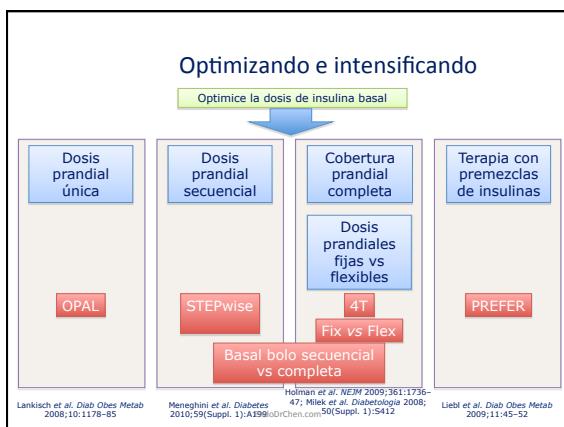
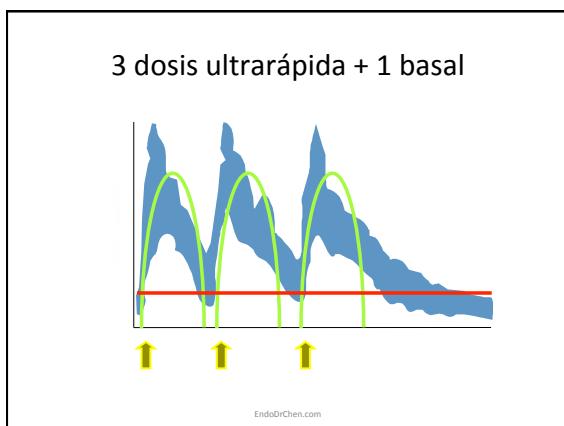
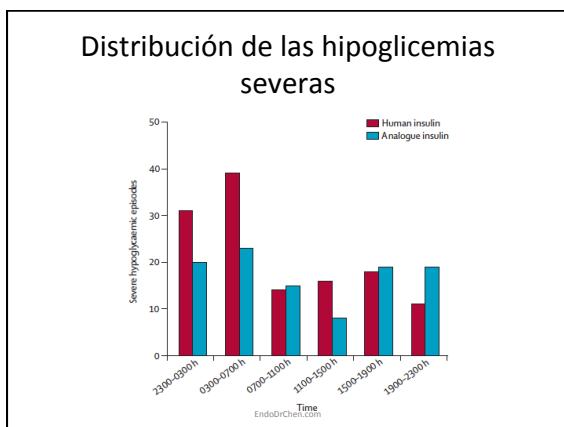
Tasa de hipoglicemias severas

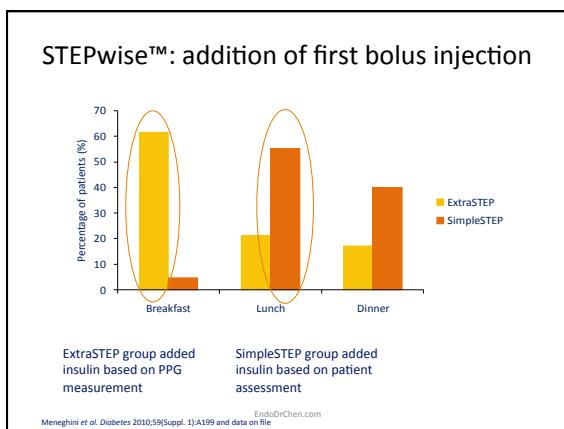
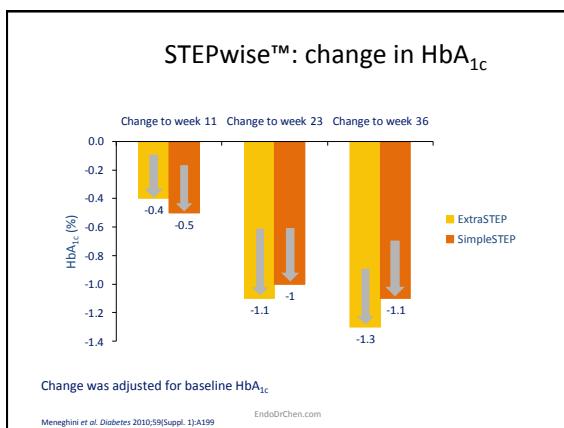
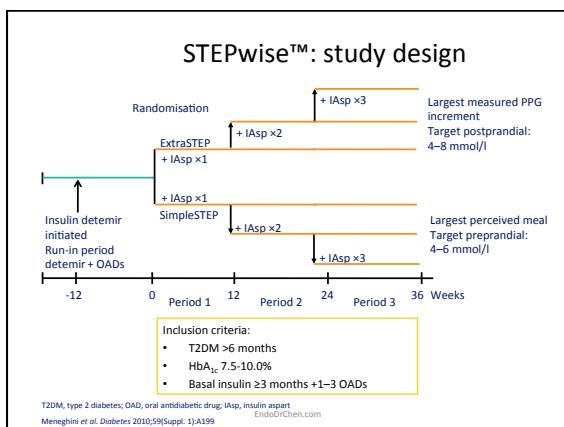
	On analogue insulin treatment	On human insulin treatment	p value
Number of severe hypoglycaemic events	105	136	–
Causality (Whipple's triad)			0.14
Definite	31 (30%)	53 (39%)	–
Probable	74 (70%)	83 (61%)	–
NNT 2 pacientes en 1 año para evitar una hipoglicemia severa			
With convulsions or fits	18 (17%)	25 (18%)	0.87
Treatment with intramuscular glucagon or intravenous glucose	12 (11%)	28 (21%)	0.080
External assistance required	27 (26%)	45 (33%)	0.26
Use of health-care resources			
Emergency call	16 (15%)	28 (21%)	0.31
Health-care professional	21 (20%)	33 (24%)	0.53
Hospital admission	2 (2%)	0	0.19

Data are number of events (%) or mean (SD).

Table 3: Causality and severity of severe hypoglycaemic events in the intention-to-treat population

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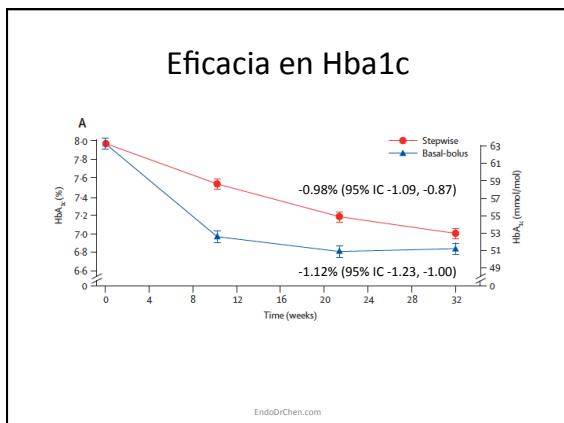




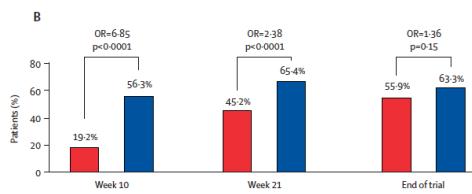
Procedimientos

- Basal bolo:
 - 2 u de insulina aspart con cada comida
- Stepwise:
 - 4 u insulina aspart con la mayor comida agregando un segundo bolo a la semana 11 o tercer bolo a la semana 22 si hba1c >7%
 - Mayor comida: definido como la comida con mayor contenido de carbohidrato determinado por el paciente

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Pacientes que alcanzaron Hba1c <7%



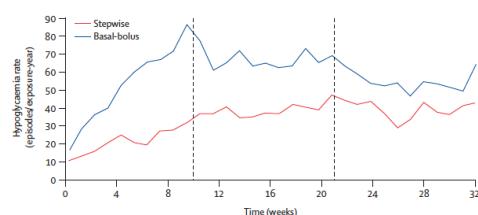
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Requerimientos de insulina

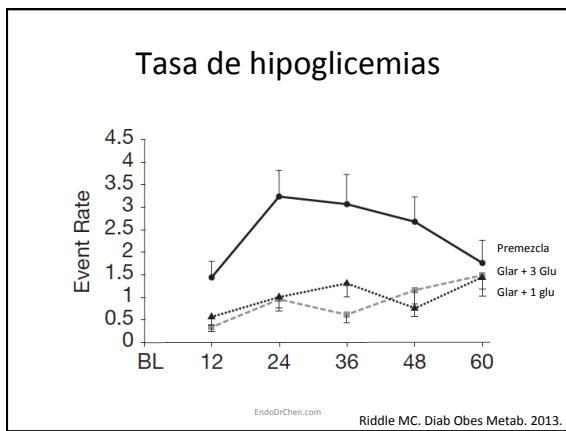
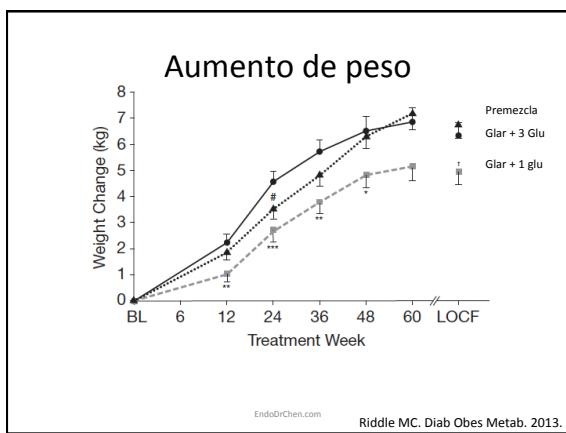
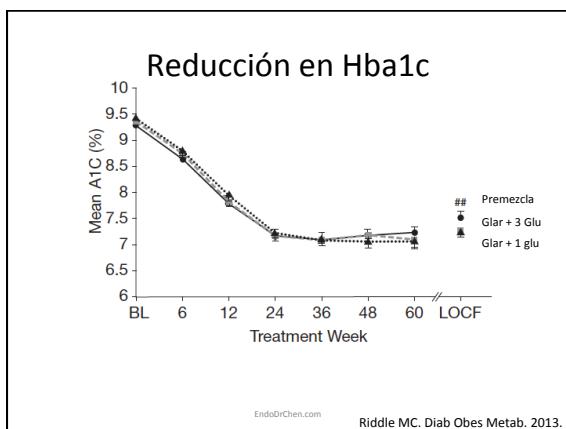
- Basal bolus: 0.6 u/kg de bolo
- Stepwise: 0.5 u/kg de bolo
 - 17% requirieron un sólo bolo
 - 27% requirieron 2 bolos
 - 40% requirieron 3 bolos
- En ambos grupos, la insulina basal fue 0.6 u/kg

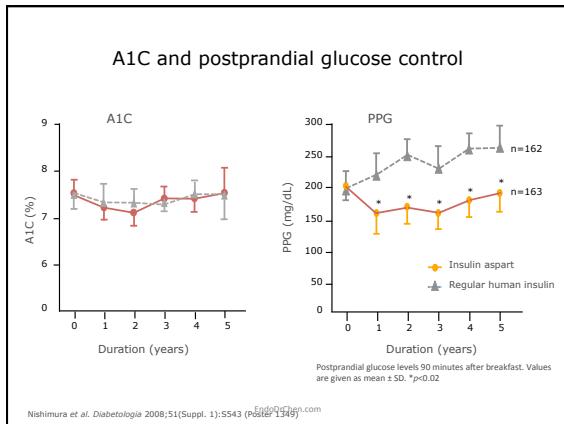
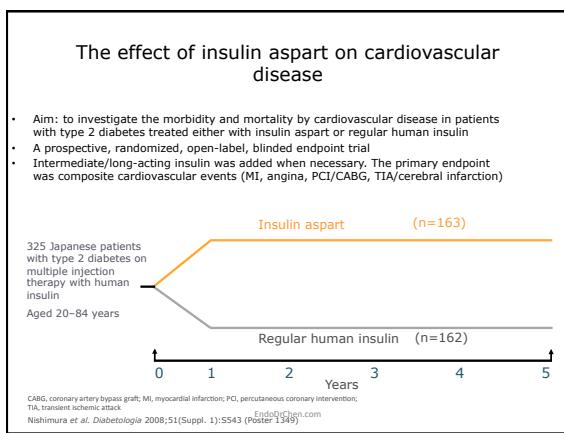
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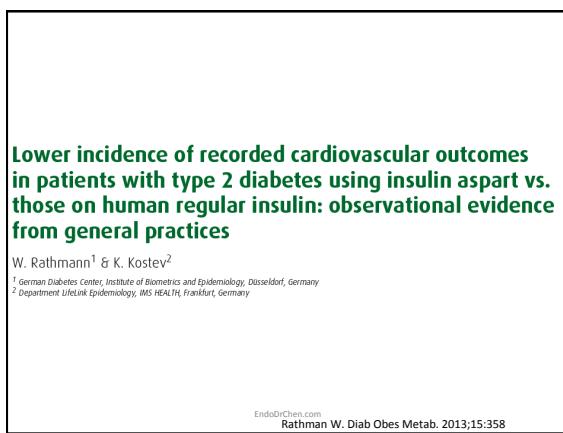
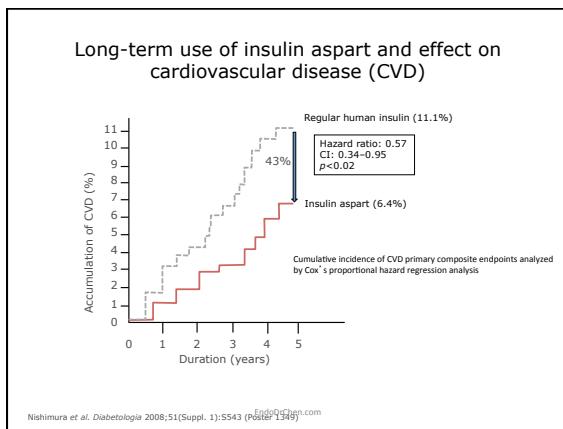
Hipoglicemia



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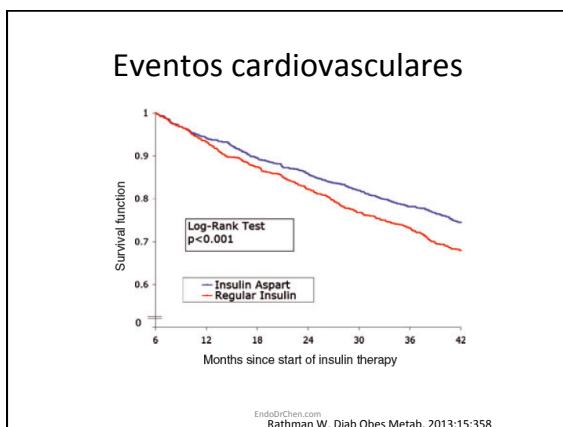






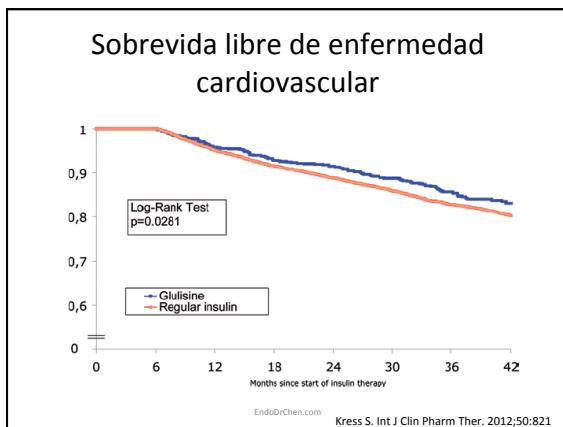
Variables	Insulin aspart	Regular insulin
N	3154	3154
Age (years)	60.0 (10.2)	60.0 (10.2)
Diabetes treatment period (practice) (years)	2.2 (2.5)	2.2 (2.5)
Males (%)	57.4	57.4
Private health insurance (%)	5.8	5.8
Diabetologist treatment (%)	42.1*	32.6*
Region (West Germany) (%)	73.1*	78.6*
Urban residency(%)	26.6	26.2
Antidiabetic treatment(%)		
Biguanides	26.2	26.1
Sulphonylureas	13.5*	19.7*
Acarbose	4.1*	6.0*
NPH insulin	47.6*	67.9*
Long-acting analogues	50.7*	27.6*
Co-medication(%)		
Antihypertensives	59.4	62.5
Lipid-lowering drugs	32.0	28.6
Antithrombotic agents	20.9	23.4

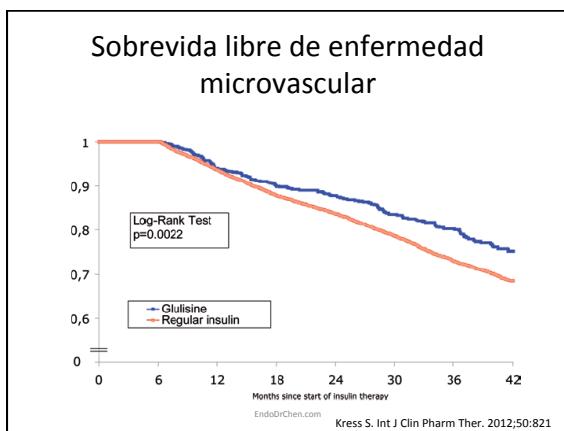
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Rathman W. Diab Obes Metab. 2013;15:358



Variables	Insulin glulisine	Regular insulin
n	952	11,157
Age (y)	60.7 (11.2)*	64.7 (10.9)*
Observational period prior to the index date (y)	2.6 (3.7)*	1.6 (3.0)*
Males (%)	54.3	52.4
Diabetologist treatment (%)	43.0	44.5
Private health insurance (%)	9.8*	3.5*
Region (West Germany) (%)	71.5*	68.2*
Urban residency ^a (%)	26.5	25.6
Antidiabetic treatment ^b (%):		
Any oral antidiabetics	41.3*	33.1*
Sulfonylureas	18.3	16.4
Biguanides	34.0*	27.2*
Acarbose	7.4*	4.2*
NPH insulin	25.6*	64.6*
Long-acting insulin analogs	74.5*	30.7*
Co-Medication ^c (%):		
Antihypertensives	55.5	56.3
Lipid-lowering drugs	32.3	30.1
Antithrombotic agents	17.7*	21.7*

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Kress S. Int J Clin Pharm Ther. 2012;50:821

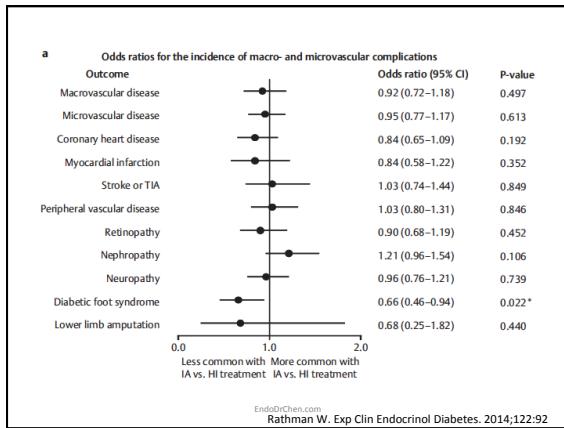




Características basales

Variable	IA N=2764 ^a	HI N=4193 ^b	p-value ^c
duration of follow-up on IA or HI treatment from index date [days], mean (SD)	1891 (698)	1835 (608)	0.266
age [years], mean (SD)	61.0 (11.3)	64.7 (10.5)	<0.001
males [%]	58.3	53.5	0.006
private health insurance [%]	8.0	33	<0.001
treated by diabetologist [%]	72.5	22.7	0.024
treated in West Germany [%]	73.8	71.3	0.022
urban residency (> 100 000 inhabitants) [%]	23.6	22.8	0.411
type of insulin treatment [%]			
multiple daily injection therapy	88.2	86.0	0.008
use of long-acting insulin analogue	53.6	29.8	<0.001
HbA1c treatment before the index date ^d	25.7	9.7	<0.001
concomitant oral medications ^e [%]			
biguanides	50.5	53.2	0.028
sulfonylureas	26.1	36.5	<0.001
diuretics	46.7	52.8	<0.001
B-blockers	49.6	55.2	<0.001
calcium channel blockers	35.2	38.1	0.016
ACE inhibitors	57.6	62.5	<0.001
angiotensin II receptor antagonists	28.2	26.7	0.177
lipid-lowering agents	52.1	52.3	0.907
acetyle salicylic acid	35.1	38.8	0.002

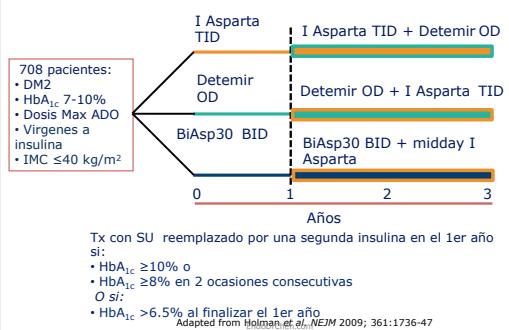
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Rathman W. Exp Clin Endocrinol Diabetes. 2014;122:92



INTENSIFICACIÓN BASAL-BOLUS, CUÁL ES LA EVIDENCIA?

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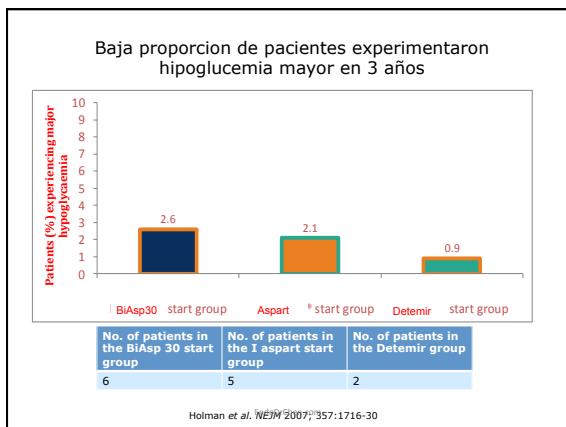
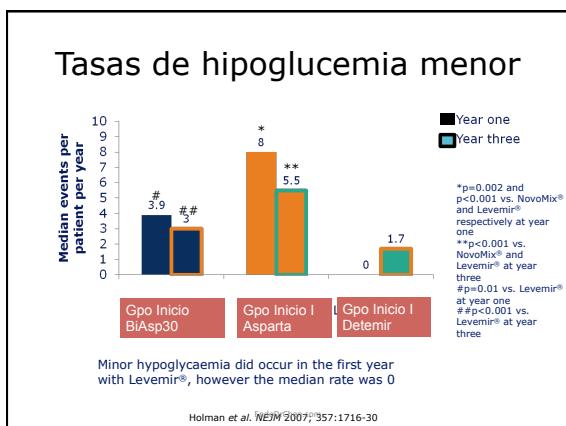
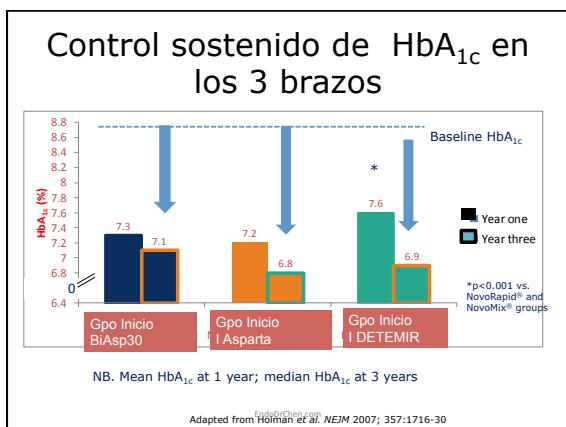
Estudio 3 años diseñado para investigar el inicio e intensificación de insulina

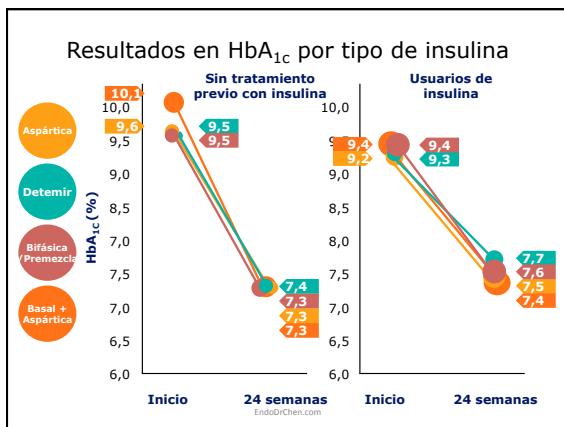
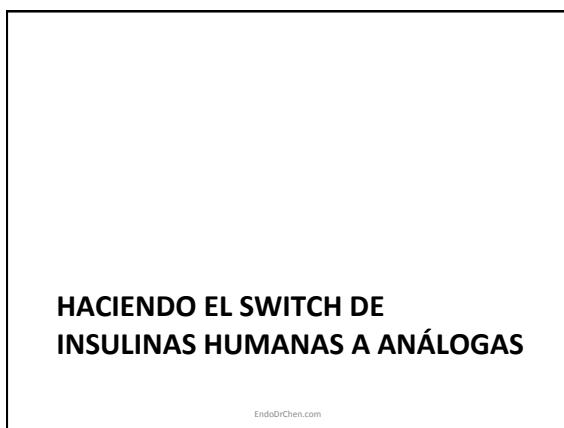
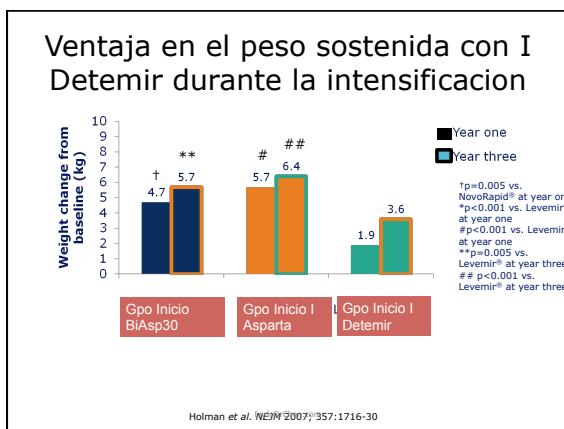


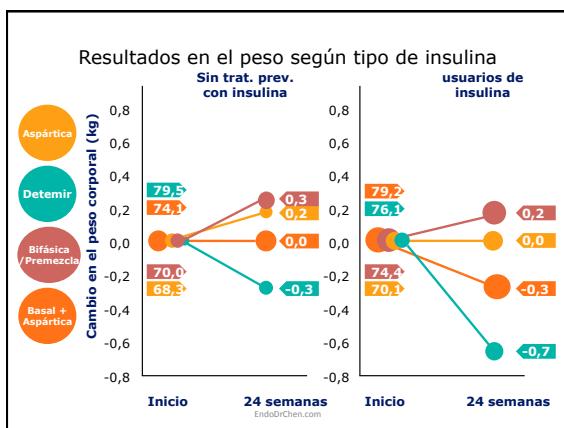
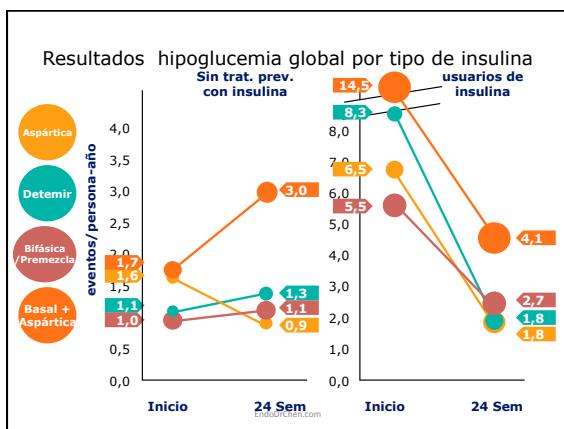
La mayoría de los pacientes fueron intensificados por una segunda insulina



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CONCLUSIONES

