



Impacto en las complicaciones con análogos de insulina ultrarrápida

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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

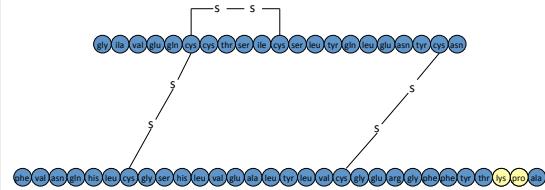
- Uso de análogos ultrarrápidos
- Diferencias con insulinas humanas
 - HbA1c
 - Hipoglicemias
- Diferencias en complicaciones crónicas

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ANÁLOGOS ULTRARRÁPIDOS

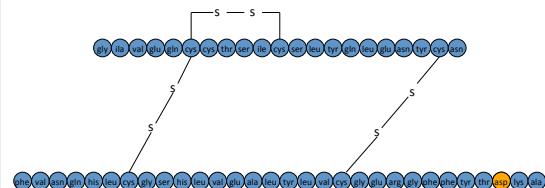
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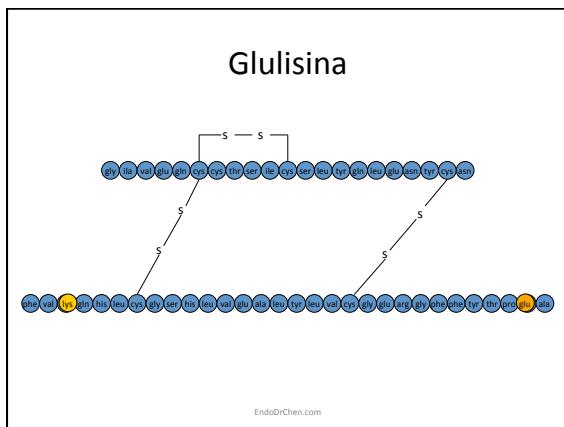


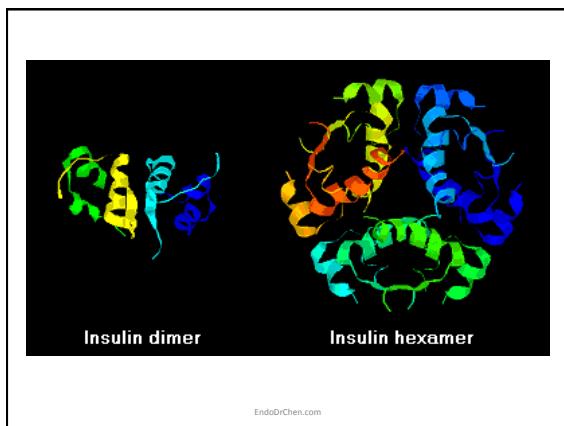
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Aspart



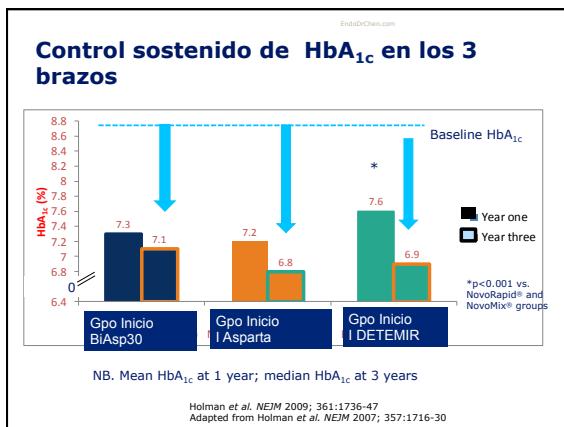
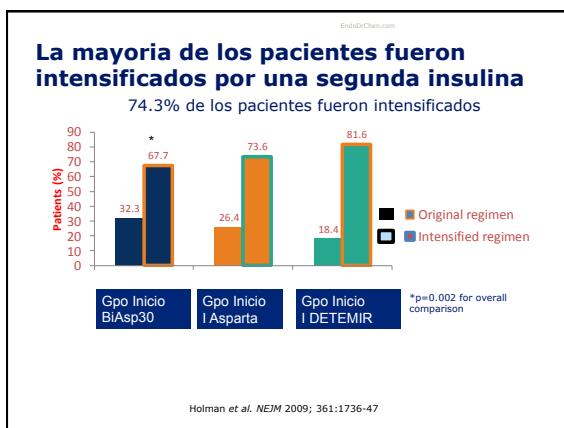
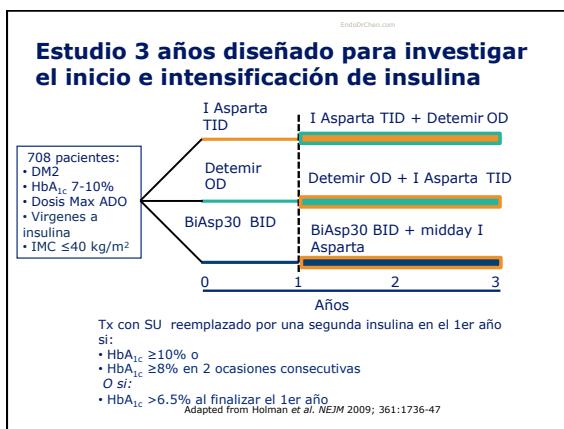
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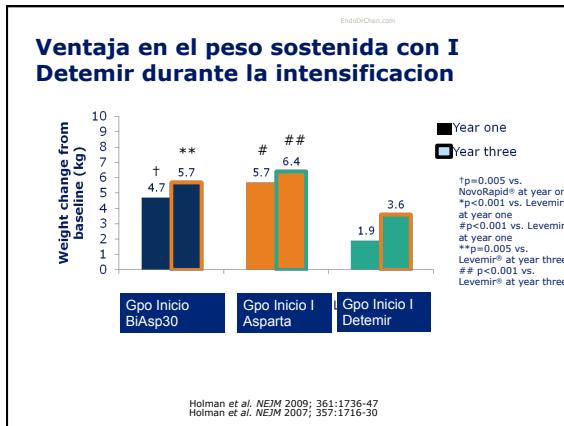
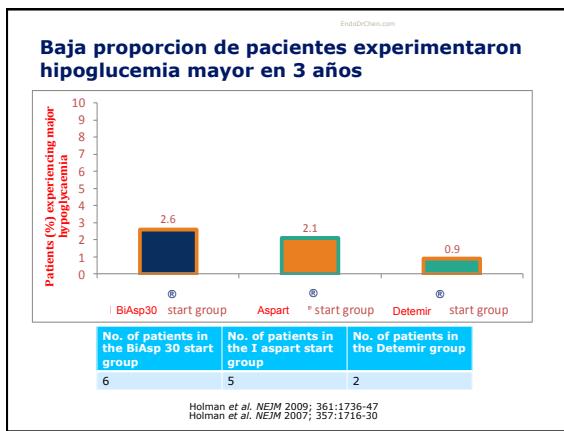
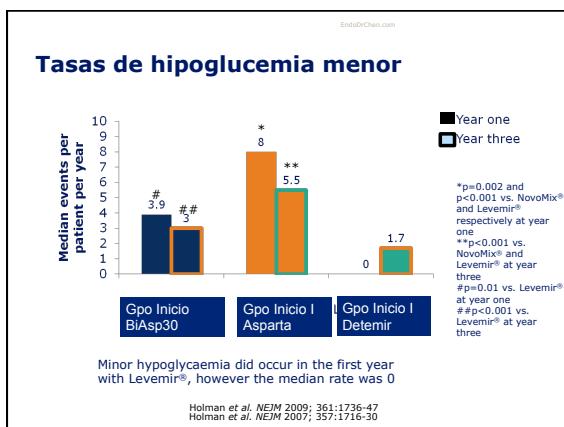


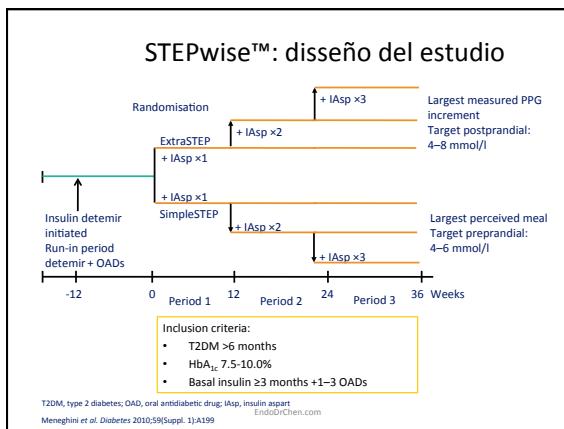
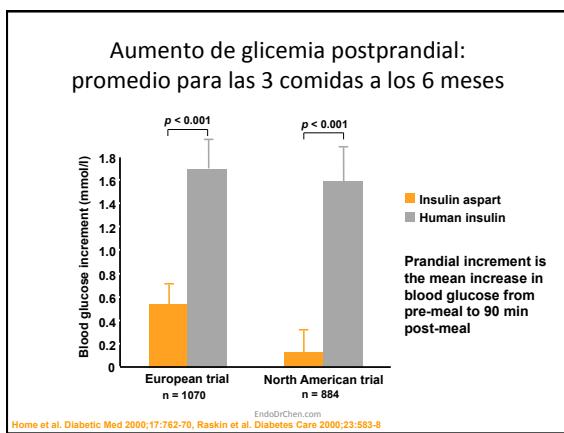
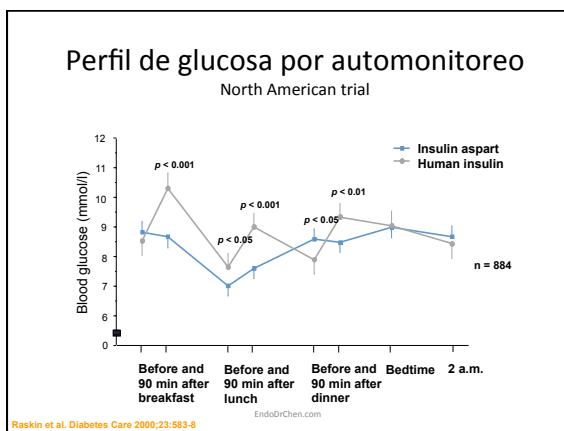


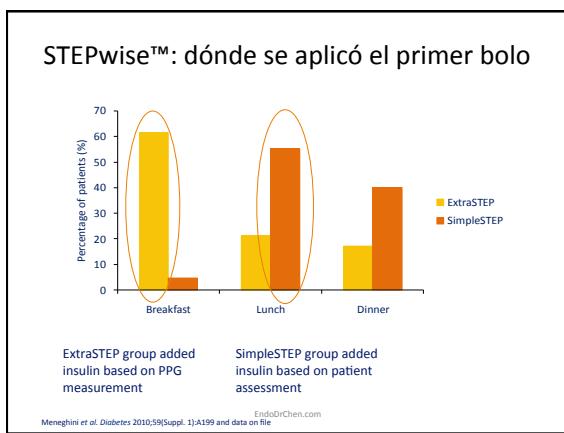
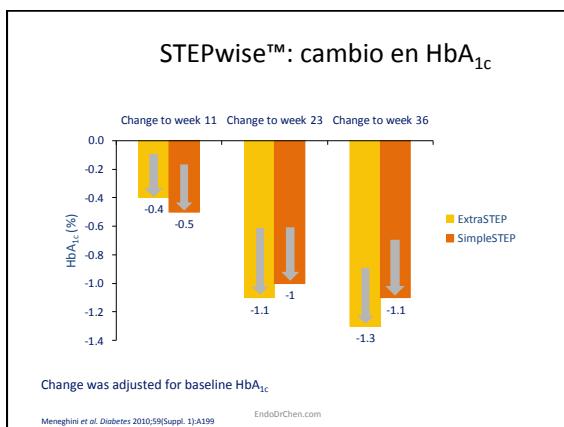
**INTENSIFICACIÓN BASAL-BOLUS,
CUÁL ES LA EVIDENCIA?**

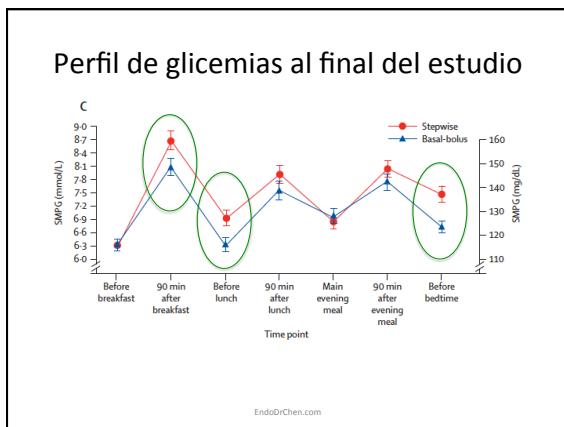
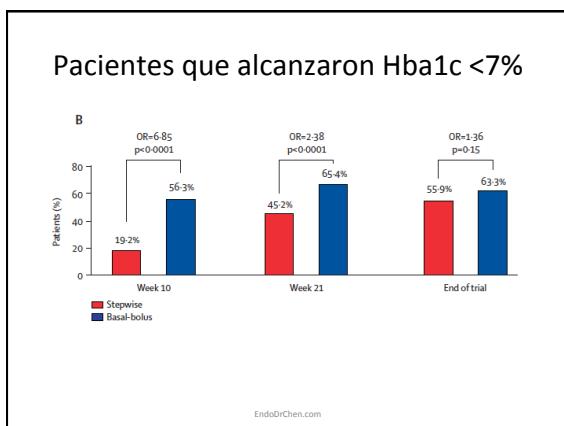
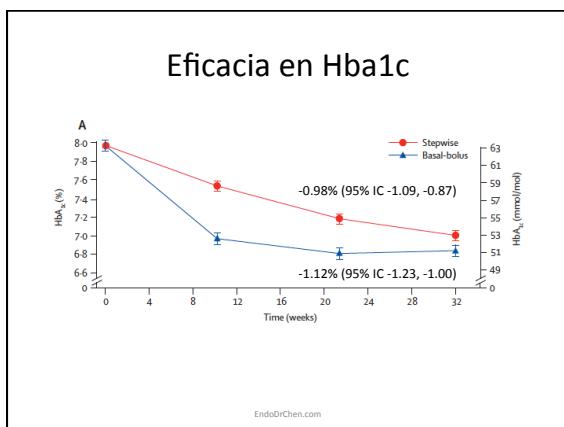
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Requerimientos de insulina

- 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

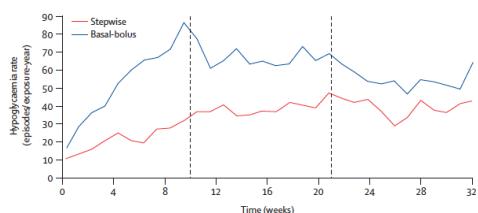
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Satisfacción

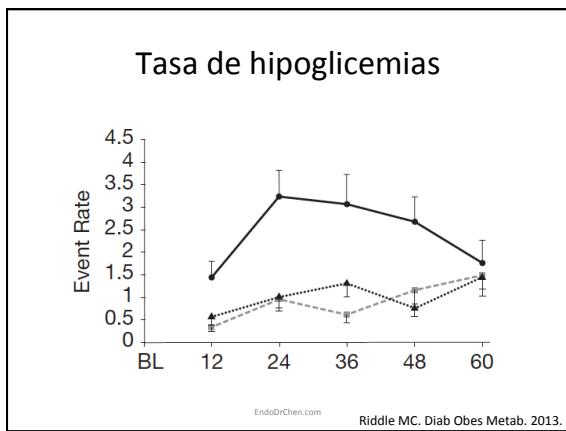
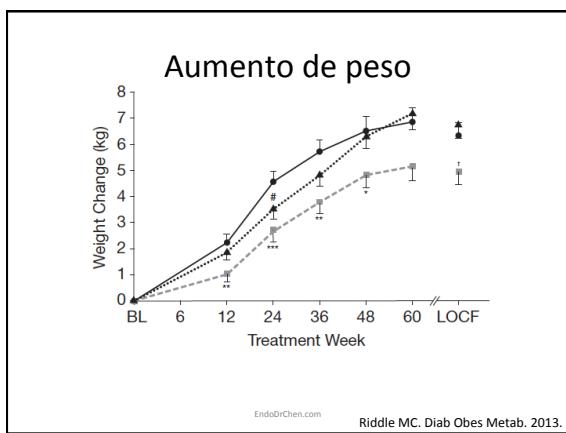
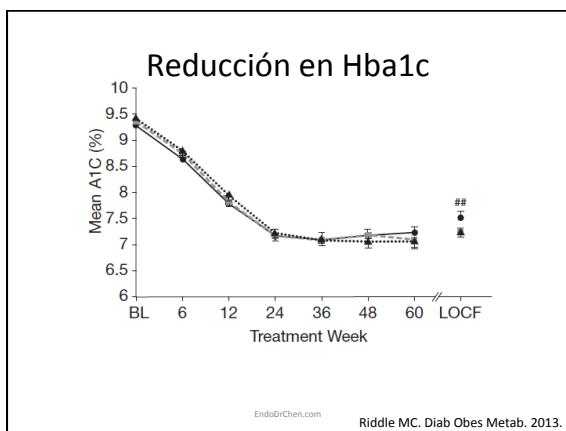
- En general mayor satisfacción con el stepwise comparado con el basal bolus, menos carga del tratamiento y mayor percepción de eficacia

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Hipoglicemia



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COMPARACIÓN CON INSULINAS HUMANAS

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SOSTENIBILIDAD CONTROL A LARGO PLAZO

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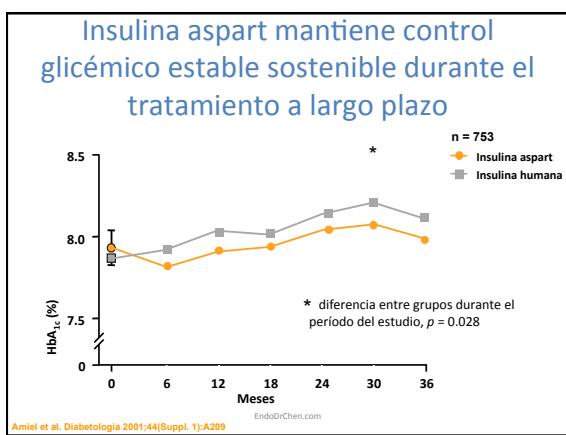
Diseño del estudio

- **Diseño:** abierto, controlado, multicéntrico, multinacional con extensión
- **Duración:** 6 meses + 30 meses
- **Objetivo:** evaluar seguridad y eficacia de IAsp vs HI en pacientes con diabetes tipo 1
- **Regimen:**
 - Insulina prandial: IAsp o HI 3x día
 - Insulina basal: 1 o 2 inyecciones de NPH

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Características demográficas		
	IAsp	HI
No. pacientes	567	186
Sexo (% masculino)	58	59
Caucásicos (%)	99	98
Tabaquistas (%)	23	33
Edad (años)	38 ±11	40 ±12.2
IMC (kg/m ²)	25 ± 3	25 ±3
Duración de DM (años)	15 ±10	16 ±11

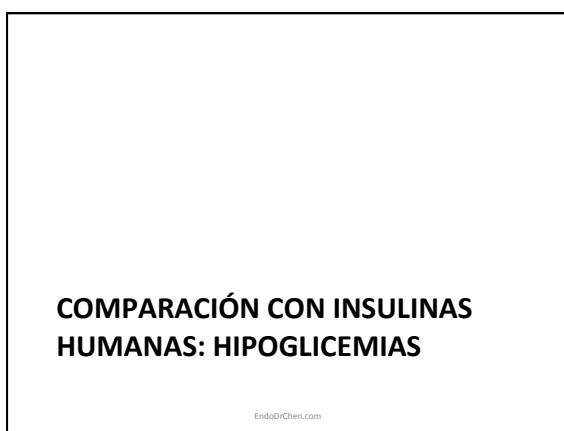
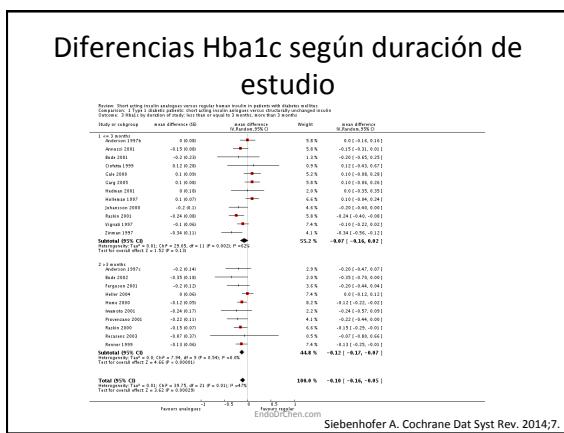
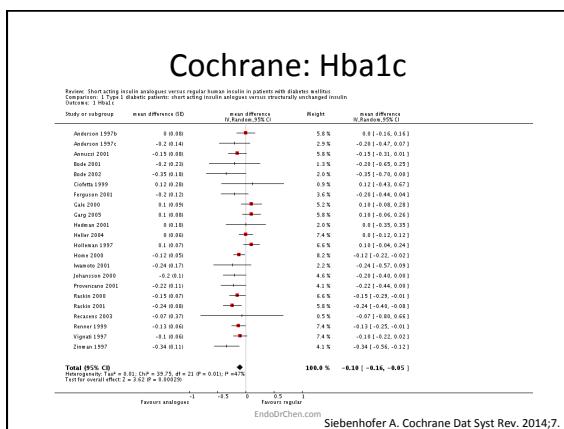
Amiel et al. Diabetologia 2001;44(Suppl. 1):A209



Episodios de hipoglicemia
El riesgo de hipoglicemia mayor no fue diferente entre ambos grupos

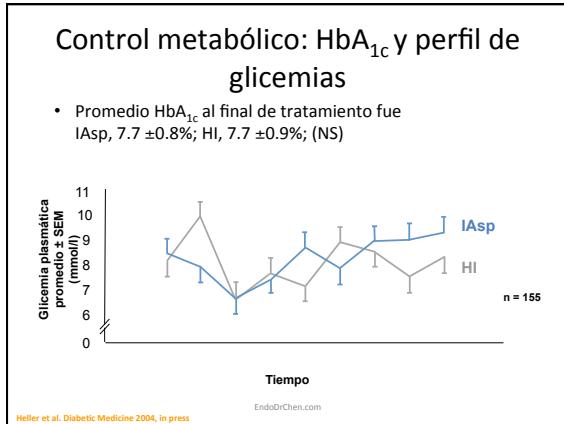
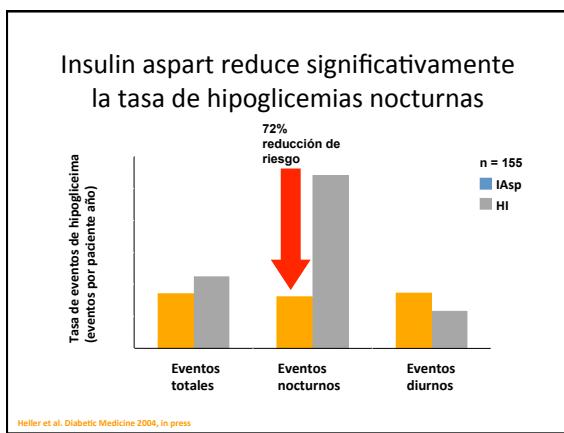
	IAsp	HI	RR (IAsp/HI) [95% CI], p
Mayor	820	261	1.00 [0.72–1.39], NS
Menor	25260	6546	1.24 [1.09–1.39], p = 0.02

Amiel et al. Diabetologia 2001;44(Suppl. 1):A209



Tasas de hipoglicemias			
	IAsp n (rate per patient-year)	HI n (rate per patient-year)	RR (95% CI) IAsp vs HI
Episodios mayores: NOCTURNO	9 (0.80)	31 (2.70)	0.28 (0.13–0.59) $p = 0.001$
Episodios mayores: DIURNO	29 (0.86)	20 (0.58)	1.38 (0.78–2.45) $p = 0.27$
Episodios mayores: TOTAL	38 (0.85)	51 (1.12)	0.72 (0.47–0.99) $p = 0.12$
Episodios menores	1590 (35.8)	1752 (38.2)	0.93 (0.87–1.00) $p = 0.048$

McCloskey
Heller et al. Diabetic Medicine 2004, in press
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Effect of insulin analogues on risk of severe hypoglycaemia in patients with type 1 diabetes prone to recurrent severe hypoglycaemia (HypoAna trial): a prospective, randomised, open-label, blinded-endpoint crossover trial

Ulrik Pedersen-Bjergaard, Peter Løkke Kristensen, Henning Beck-Nielsen, Kirsten Norgaard, Hans Perild, Jens Sandahl Christiansen, Tonny Jensen, Philip Hougaard, Hans-Henrik Parving, Birger Thorsteinsson, Lise Tamow

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Lancet Diabetes Endocrinol
2014; 2: 553-61

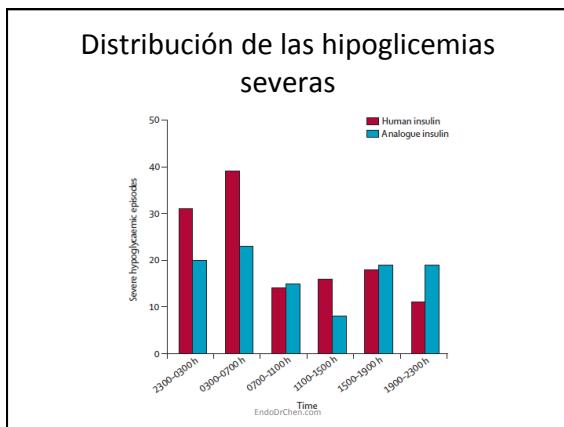
Tasa de hipoglicemias severas

	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%)	..
Possible	34 (32%)	43 (32%)	..
Probable	40 (38%)	30 (22%)	..
NNT 2 pacientes en 1 año para evitar una hipoglicemia severa			
With convulsions or fits	18 (17%)	25 (18%)	0.97
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

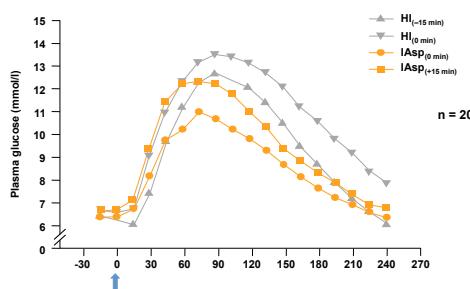
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COMPARACIÓN CON INSULINAS HUMANAS: FLEXIBILIDAD

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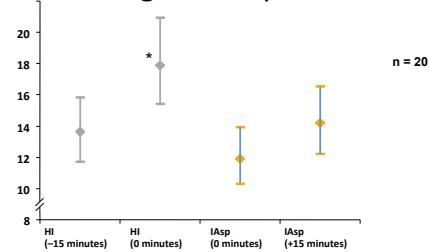
Perfil de glicemias plasmática



Brunner et al. Diabet Med. 2000 May;17(5):371-5.

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Excusión de glicemia plasmática

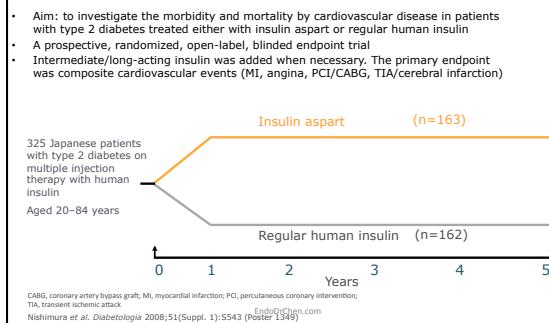


Brunner et al. Diabet Med. 2000 May;17(5):371-5.

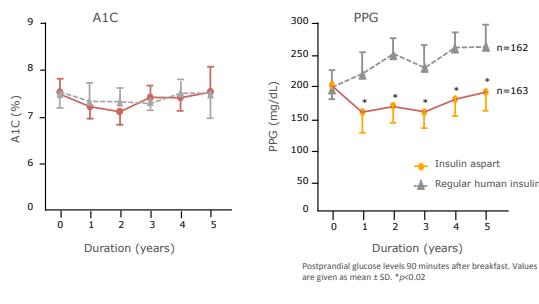
ANÁLOGOS ULTRARRÁPIDOS Y COMPLICACIONES CRÓNICAS

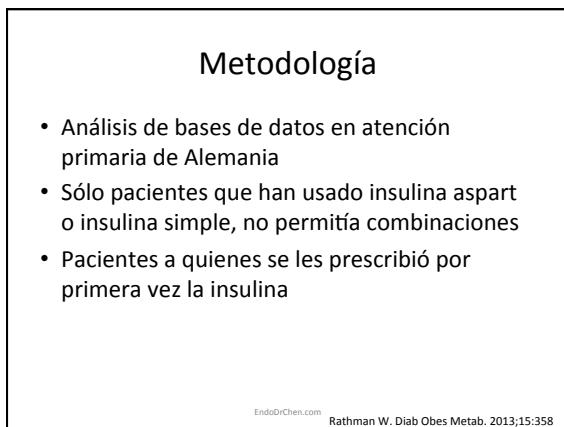
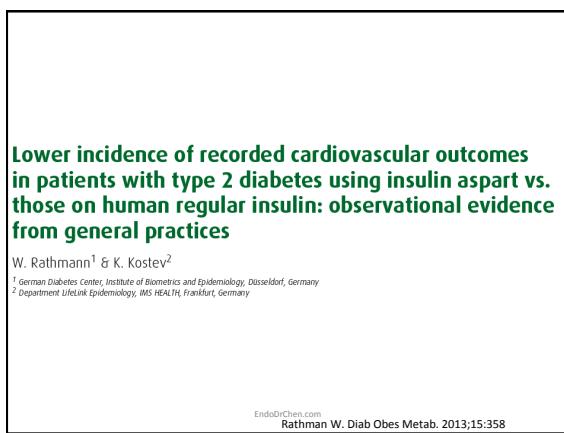
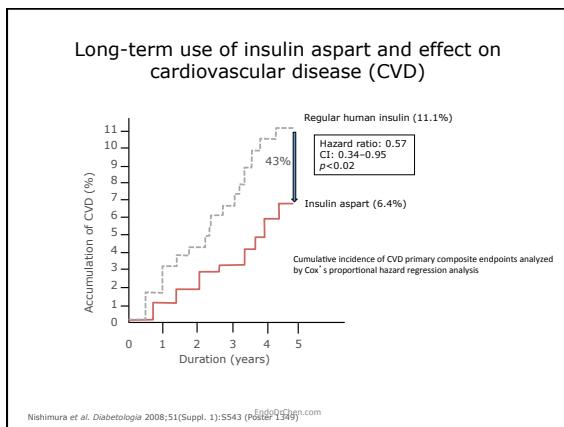
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The effect of insulin aspart on cardiovascular disease



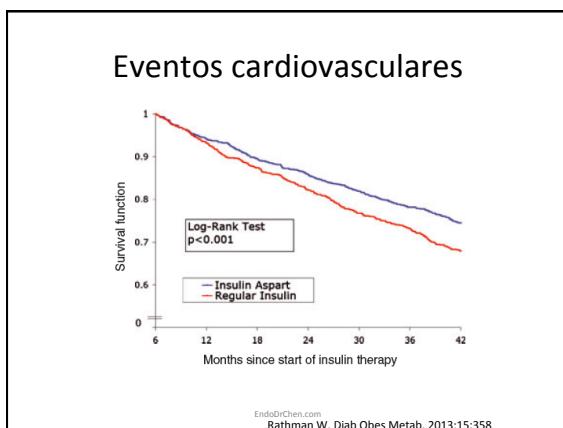
A1C and postprandial glucose control





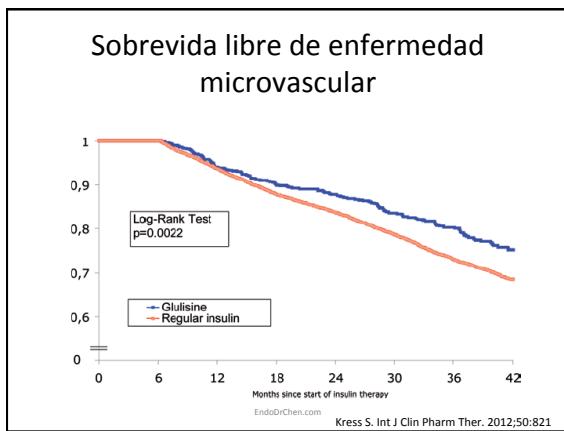
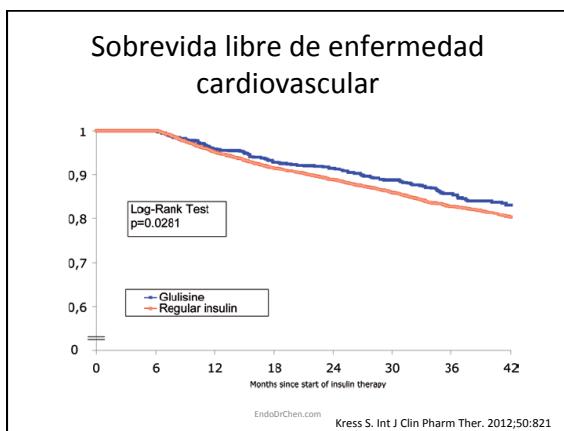
Variables	Insulin aspart	Regular insulin
N	3154	3154
Age (years)	60.0 (10.2)	60.0 (10.2)
Diabetes treatment period (practice) (years)	2.2 (2.5)	2.2 (2.5)
Males (%)	57.4	57.4
Private health insurance (%)	5.8	5.8
Diabetologist treatment (%)	42.1*	32.6*
Region (West Germany) (%)	73.1*	78.6*
Urban residency(%)	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*

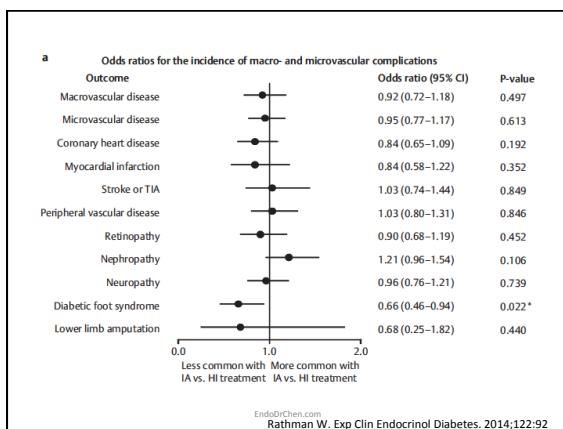
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Kress S. Int J Clin Pharm Ther. 2012;50:821



Características basales

Variable	IA N= 2764 ^b	HI N= 4193 ^b	p-value ^c
duration of follow-up on IA or HI treatment from index date [days], mean (SD)	1.891 (698)	1.835 (608)	0.266
age [years], mean (SD)	61.0 (11.3)	64.7 (10.5)	<0.001
males [%]	56.9	53.5	0.006
private health insurance [%]	8.0	3.3	<0.001
treated by diabetologist [%]	23.5	22.7	0.424
treated by General practitioner [%]	73.8	71.3	0.022
urban residence (>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
HI/IA treatment before the index date ^d	25.7	9.7	<0.001
concomitant oral medications* [%]			
biguanides	50.5	53.2	0.038
sulfonylurea	26.1	36.5	<0.001
metformin	46.7	53.8	<0.001
β-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
acetethyl salicylic acid	35.1	38.8	0.002

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



Conclusiones

- Los esquemas basal plus pueden ser una alternativa para intensificación en DM-2
- Los análogos de insulina ultrarrápidos ofrecen control glicémico sostenible con menor riesgo de hipoglicemias
- Conveniencia en horarios de administración
- Algunos cohortes muestran reducción de complicaciones microvasculares y cardiovasculares

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Preguntas...
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