



## Evolución en el tratamiento de la diabetes: por qué nuevas insulinas?

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Departamento de Farmacología y Toxicología Clínica,  
Universidad de Costa Rica

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## Conflictos de interés

- He recibido honorarios por conferencias, advisory board y/o investigación clínica de:
  - Astra Zeneca
  - Novartis Pharma Logistics Inc
  - Novartis Oncology
  - Novo Nordisk
  - Merck Sharp & Dohme
  - Roche
  - Glaxo SmithKline
  - Sanofi Aventis
  - Boehringer
  - Organon

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## Agenda

- Por qué análogos?
- Son todos los análogos iguales?
- Cuál es la mejor estrategia para intensificación?
- Cuál es el futuro de las insulinas?

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## Insulinas humanas

- Descubiertas en 1921, usadas desde 1922
- Han salvado muchísimas vidas
- Limitantes
  - Farmacocinética variable
  - Tiempo de administración
  - Picos de acción
  - hipoglicemia

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## Características ideales de insulinoterapia

- Poder alcanzar metas de control
- Mínimo riesgo de hipoglicemias
- Poca variabilidad
- Que se ajuste al estilo de vida del paciente
- Buena adherencia
- Menor número de aplicaciones posibles

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Initial drug monotherapy	Healthy eating, weight control, increased physical activity
Efficacy (HbA1c)	Metformin high
Hypoglycemia	none
Weight	neutral
Side effects	GI / lactic acidosis
Costs	low

T2DM Antihyperglycemic Therapy: General Recommendations | Diabetes Care | Diabetologia | 19 April 2013 | pub ahead of print

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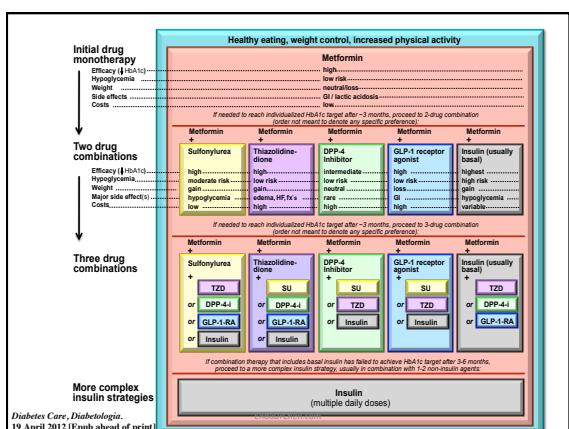
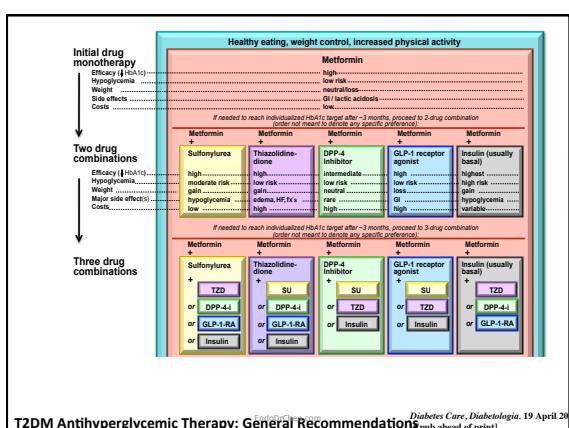
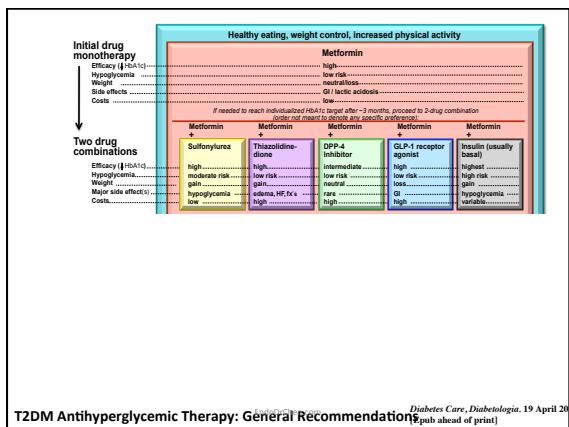
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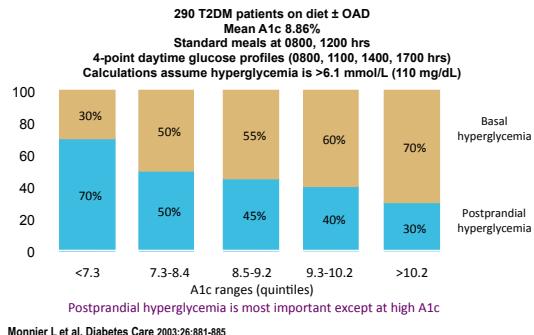
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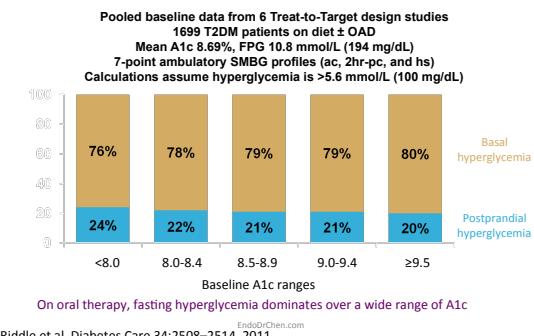
## POR QUÉ EMPEZAR CON ANÁLOGOS BASALES?

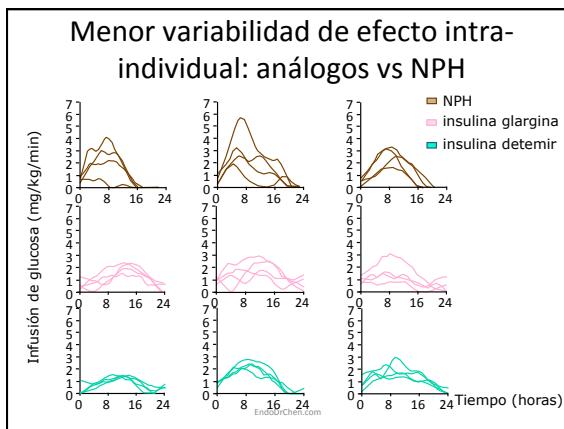
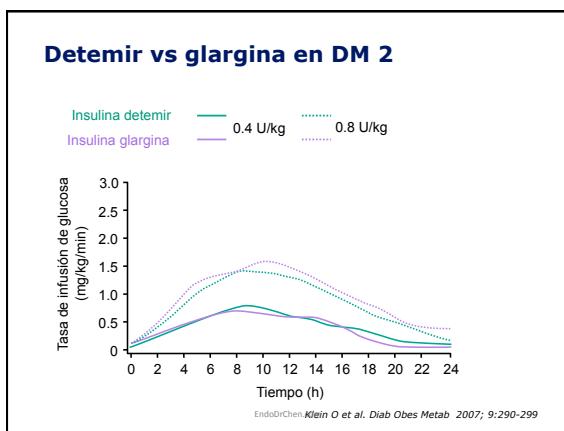
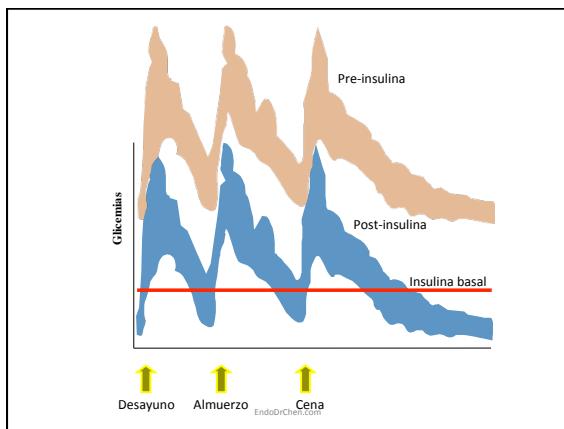
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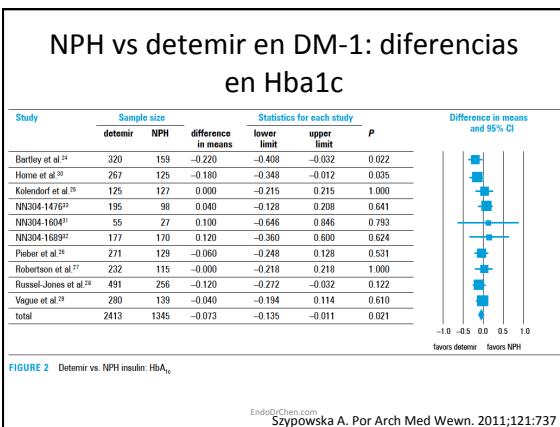
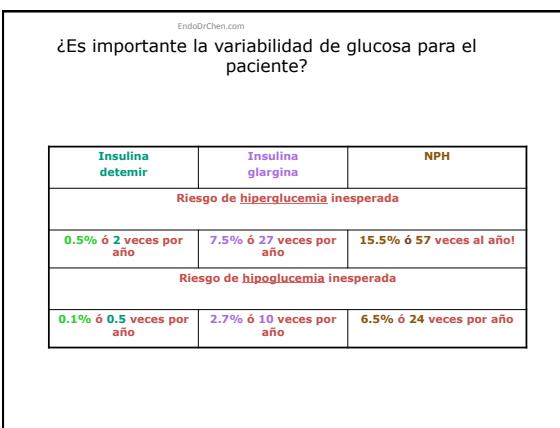
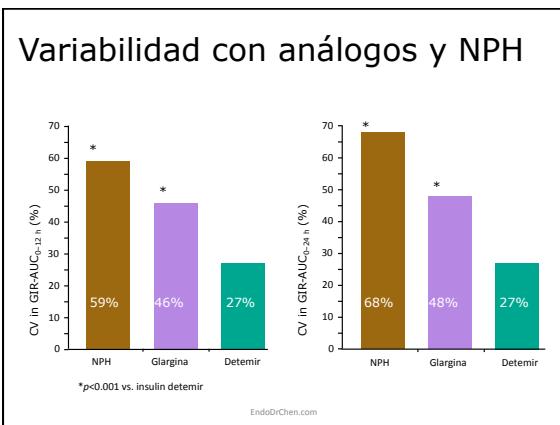
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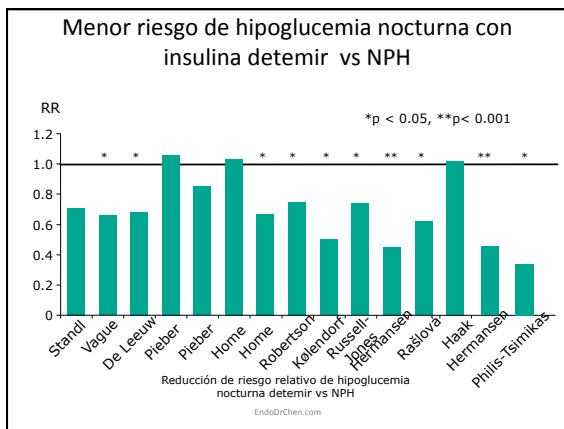
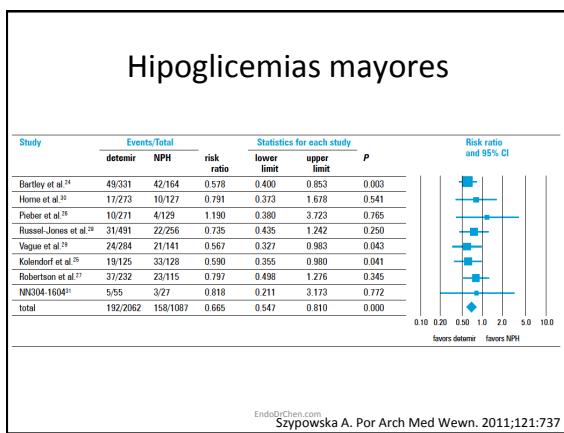
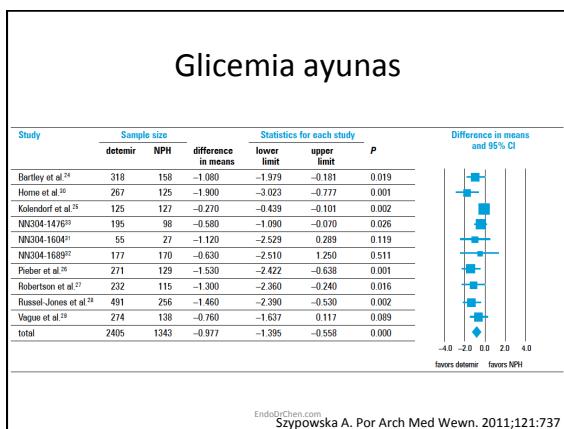


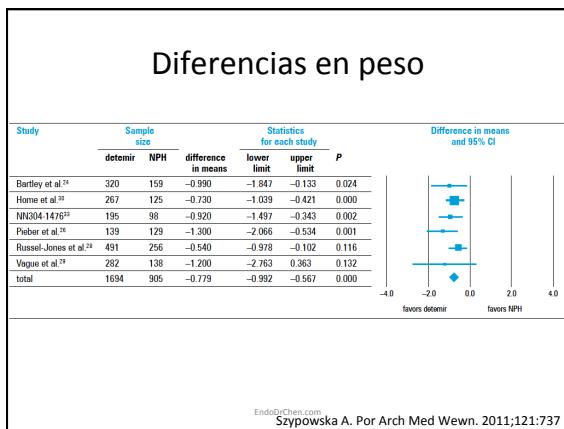
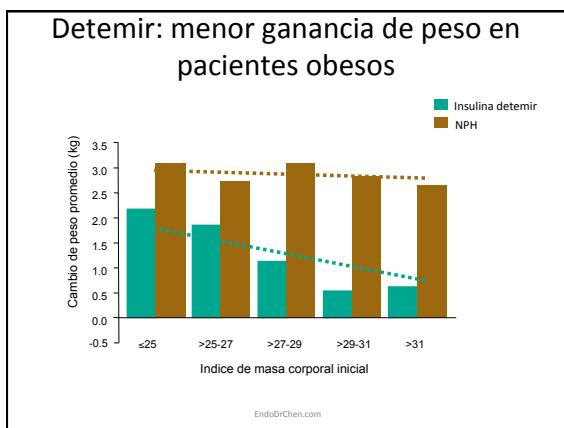
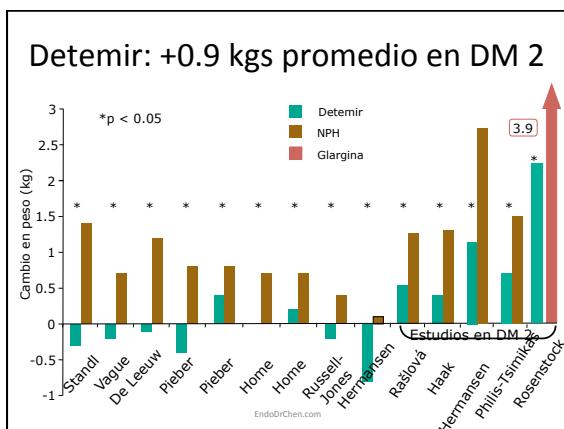
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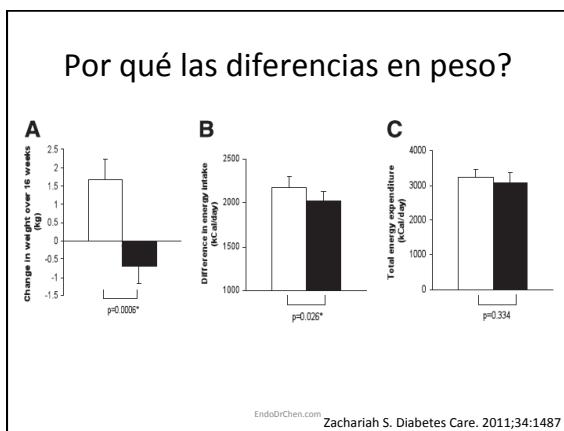








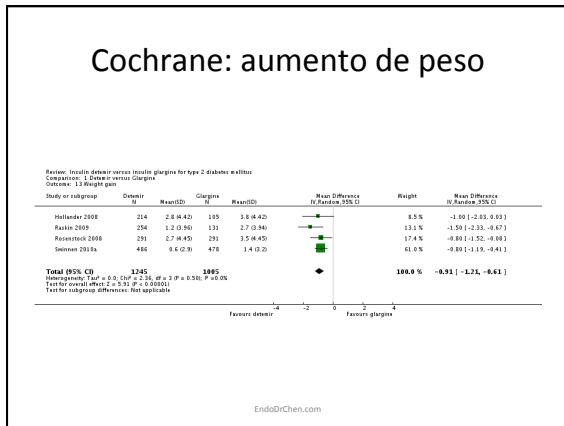


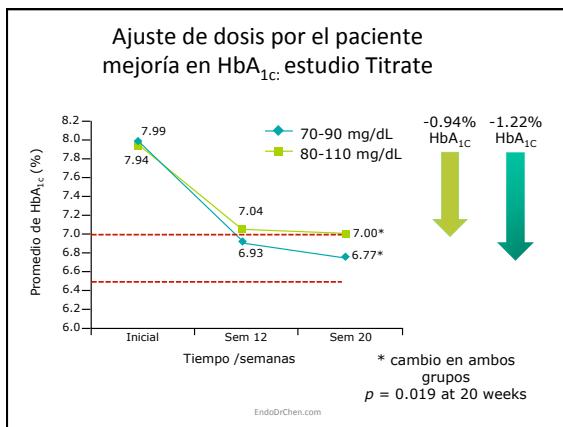
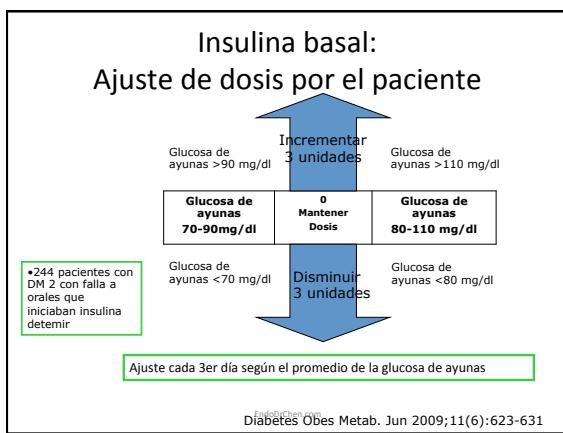
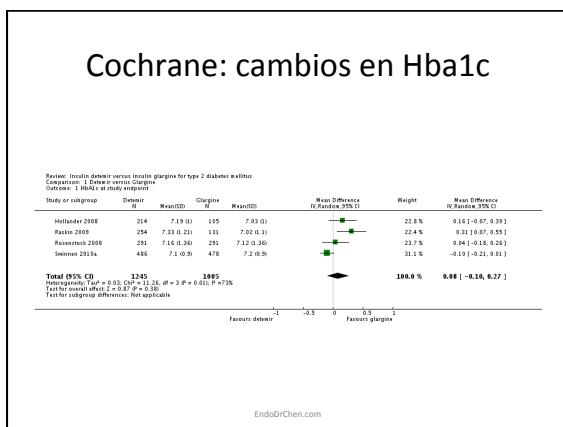


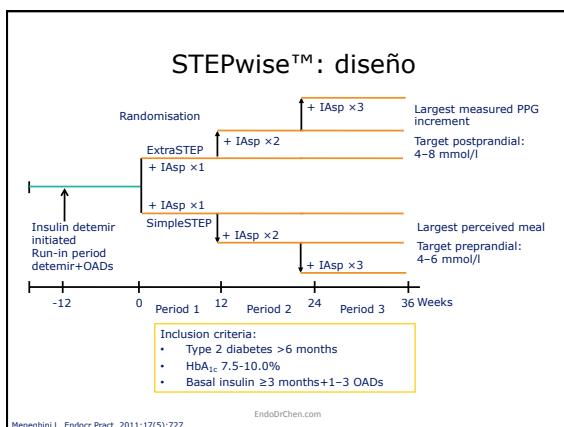
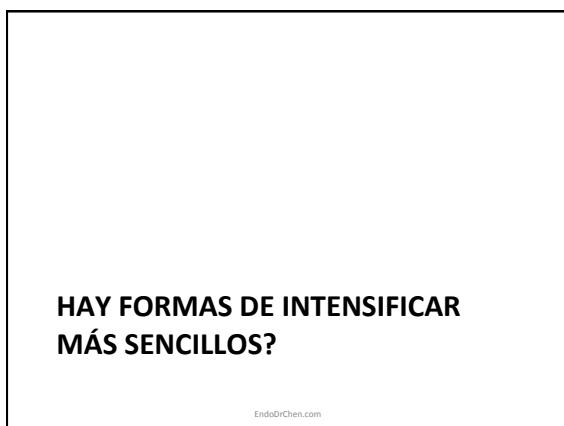
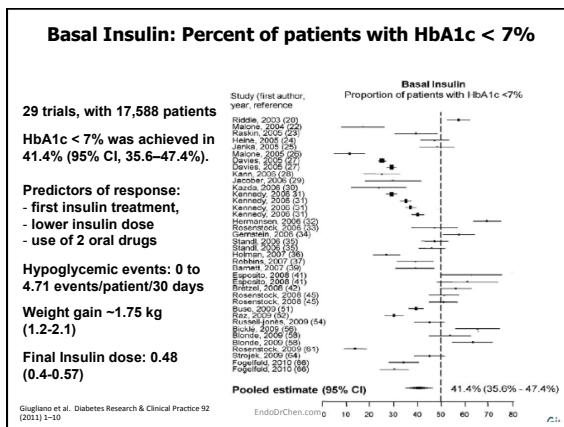
## Diferencias en peso

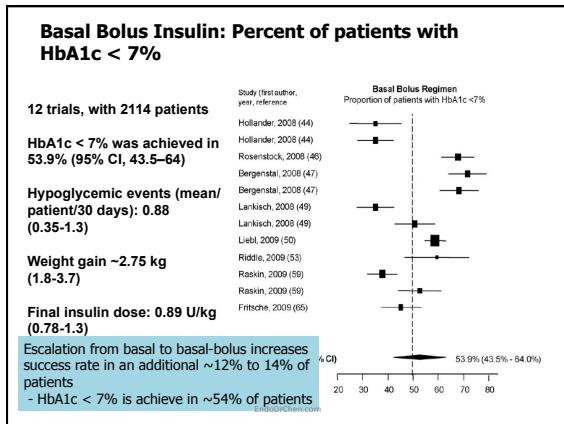
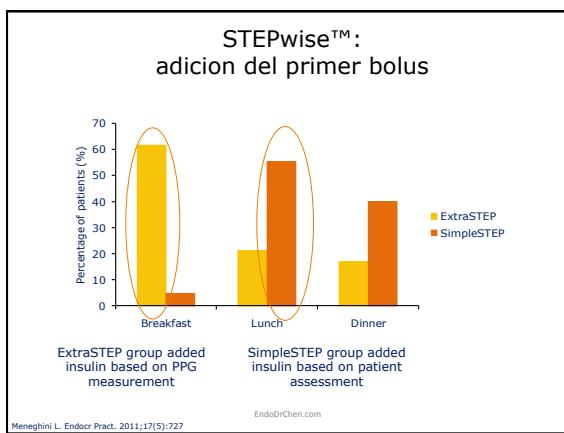
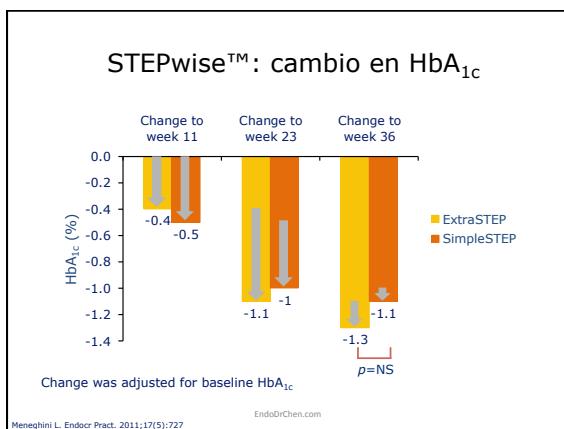
- Mayor efecto hepático y menos periférico?
  - Menos lipogénesis?
  - El ácido graso lo puede hacer menos soluble a través del endotelio y por lo tanto menos acceso a tejidos periféricos
  - Mayor efecto anorexígeno central?

EndoDrChen.com Zachariah S. Diabetes Care. 2011;34:1487





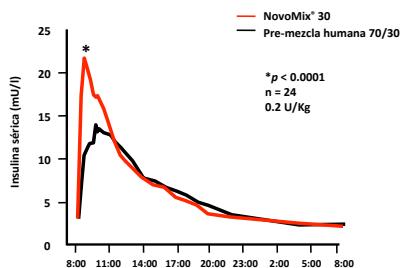




## BASAL BOLUS VS PREMEZCLAS

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**NovoMix30 en individuos normales:**  
absorción más rápida y mayor pico de concentración  
comparado con la pre-mezcla humana



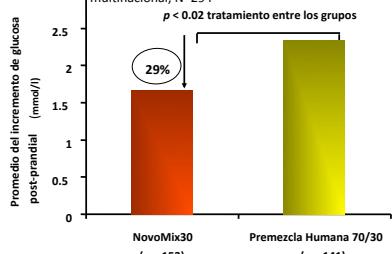
\* $p < 0.0001$   
 $n = 24$   
0.2 U/Kg

Estudio aleatorizado, doble ciego, cruzado, 48 hs.  
Jacobson L et al. Eur J Clin Pharm 2000;56:399-403

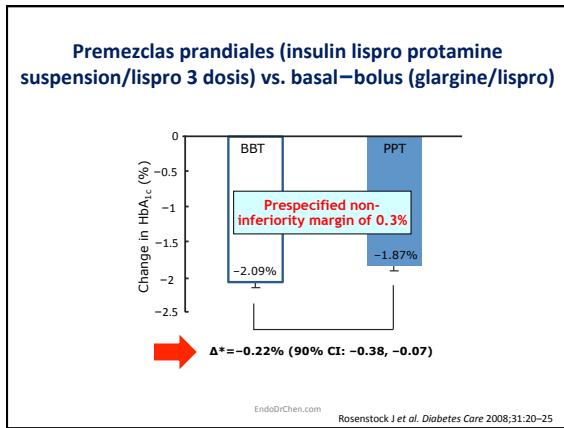
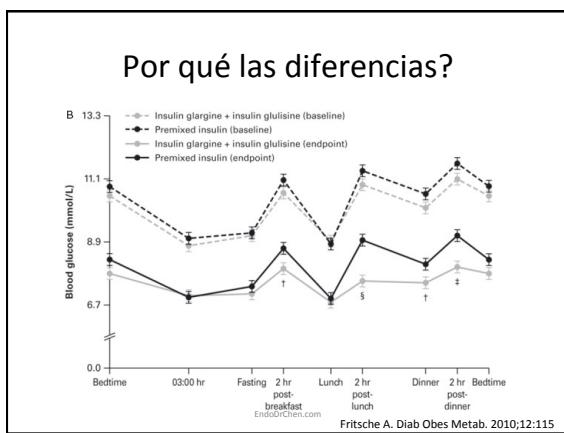
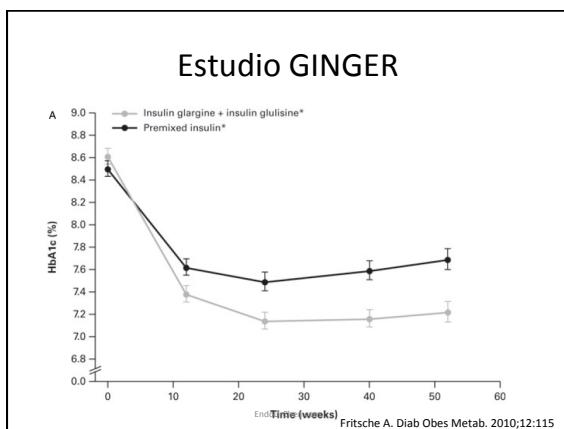
**NovoMix30 en DM2 después de 3 meses**  
vs. Humana 70/30: disminución significativa de la excurción

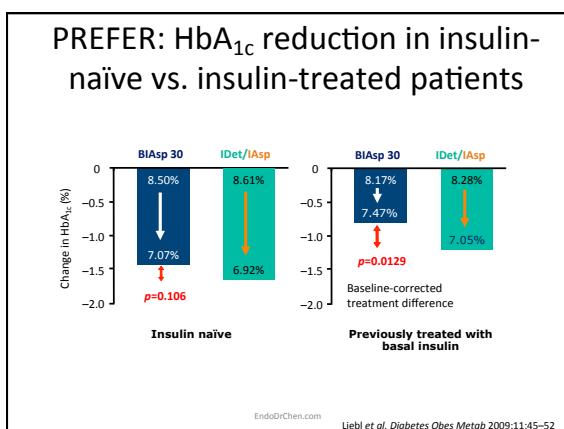
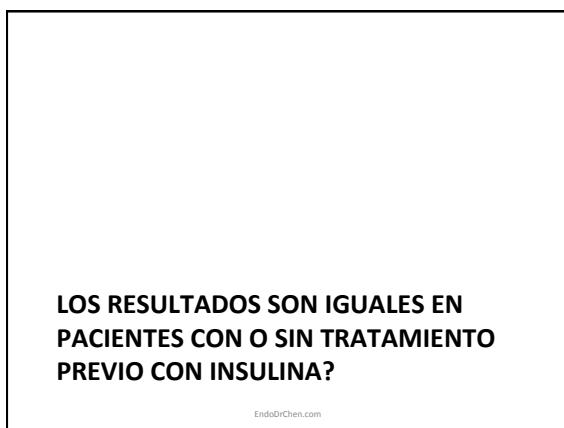
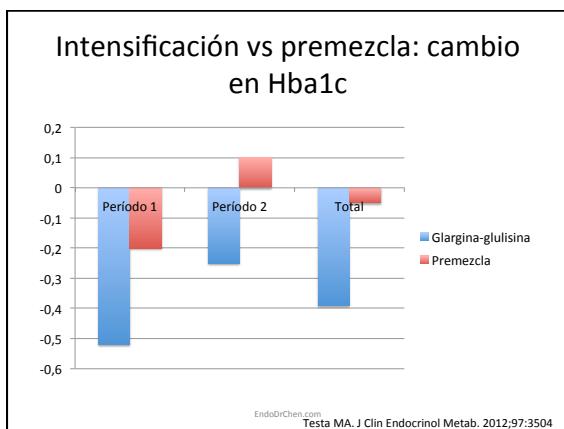
glucémica post-prandial

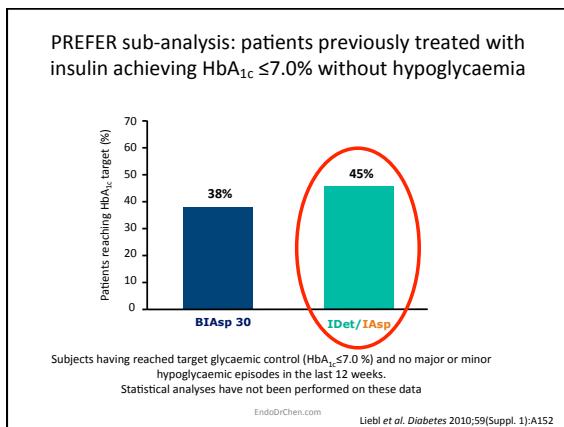
Estudio abierto, randomizado, 12 semanas, grupos paralelos, DMT1 y DMT2,  
multinacional, N=294



Boehm B et al. Diabet Med 2002;19(5):393-399







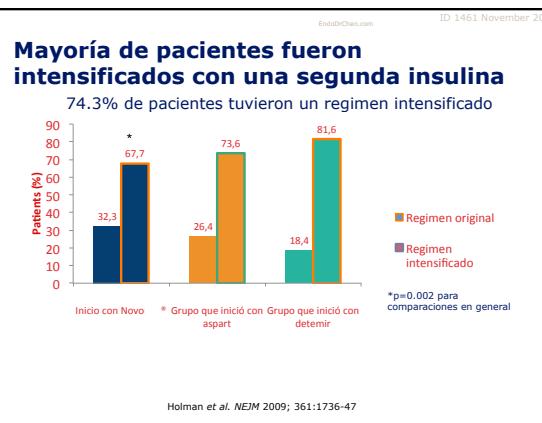
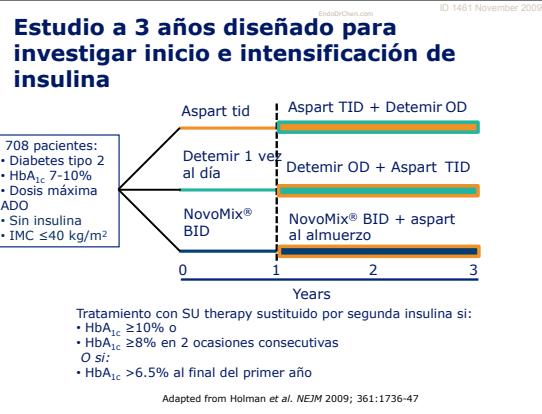
**POR LO TANTO, HAY ALGÚN PAPEL  
PARA LAS PREMEZCLAS? CUÁNDΟ  
UTILIZARLOS?**

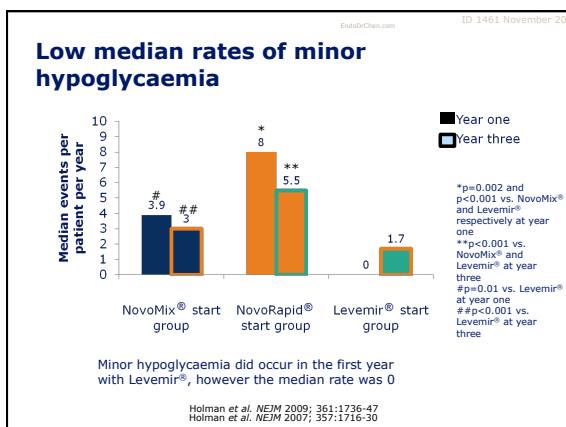
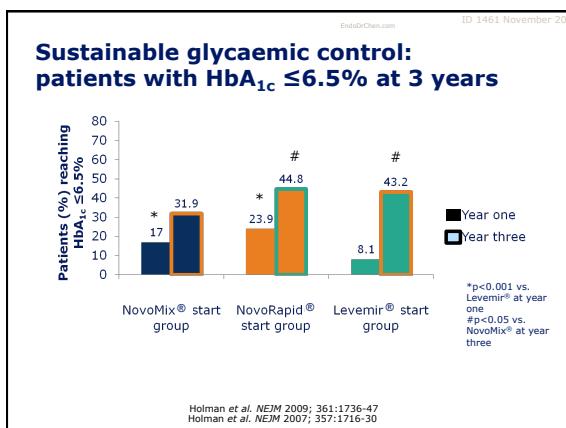
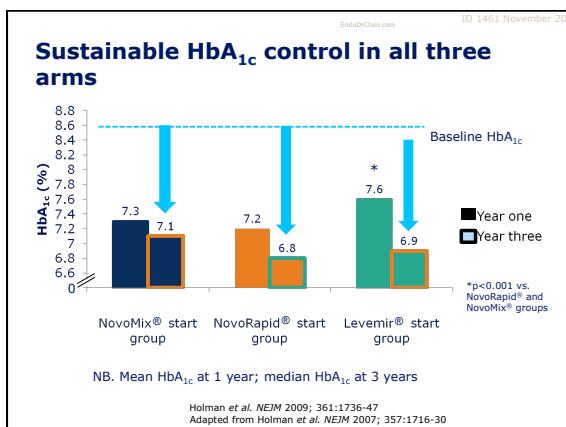
## Papel de premezclas

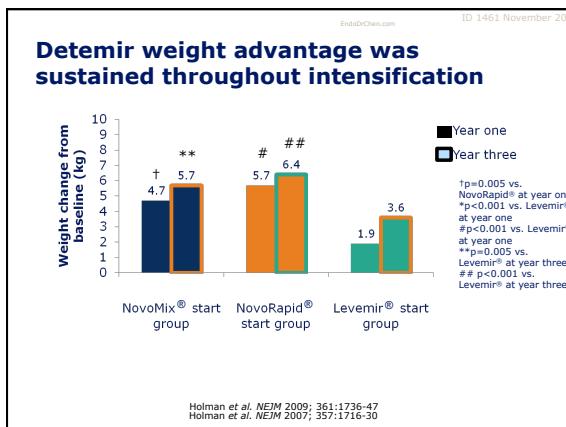
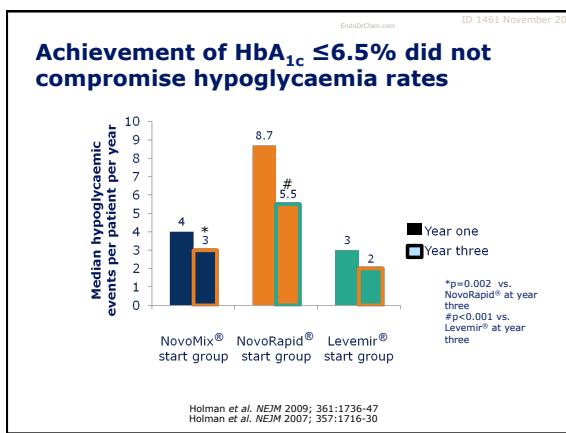
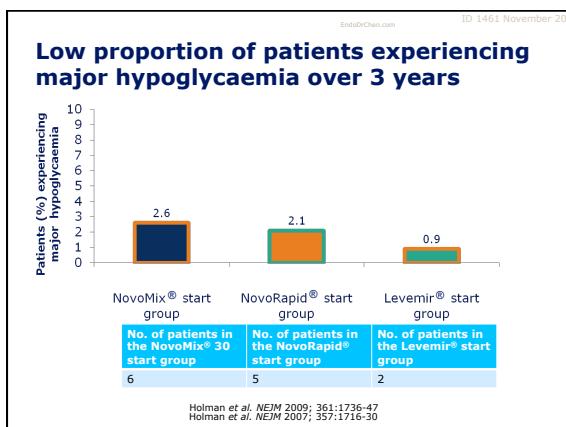
- Dependencia del paciente
    - Metas de control glicémico más laxas
    - Facilidad de administración
    - Dispositivo
    - Menor cantidad de aplicaciones al día
    - El que no está totalmente insulinopénico y aún tiene alguna reserva pancreática

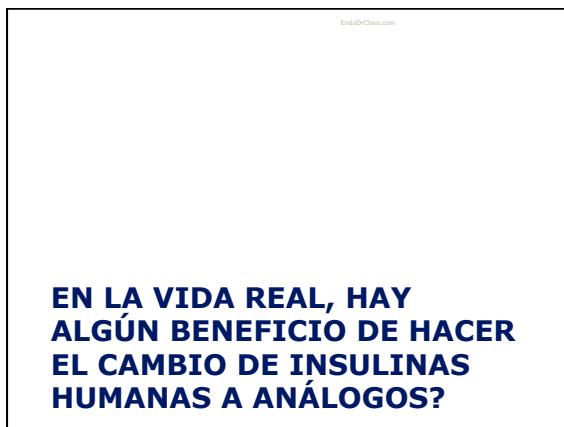
## HAY ALGUNA ESTRATEGIA MÁS EFECTIVA?

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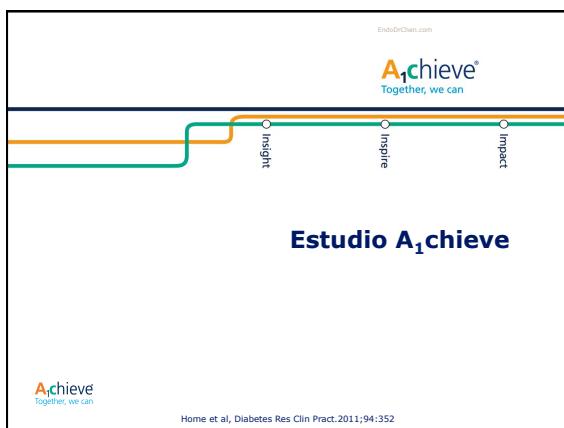
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**Características de la cohorte completa al inicio del estudio**

	Total	Sin terapia farmacológica	Sólo ADOs	Insulina ± ADOs
N	66.726	6.010	38.862	21.854
Porcentaje del total	-	9	58	33
Sexo M/F (%)	55,6/44,4	60,9/39,1	56,8/43,2	51,9/48,1
Edad (años)	54,0 (12,0)	51,8 (14,4)	53,5 (11,1)	55,6 (12,5)
Peso (kg)	72,9 (15,0)	67,3 (12,7)	72,4 (14,6)	75,3 (15,9)
IMC (kg/m <sup>2</sup> )	27,1 ( 5,0)	25,2 ( 4,2)	26,9 ( 4,7)	27,9 ( 5,5)
Duración de la diabetes (años)	8,0 ( 6,2)	2,6 ( 4,9)	7,2 ( 5,2)	10,8 ( 6,8)
HbA <sub>1c</sub> (%)	9,5 ( 1,8)	10,2 ( 2,3)	9,5 ( 1,7)	9,4 ( 1,8)

Promedio (DE), número o porcentaje; ADOs, antidiabéticos orales

Holman et al. NEM 2009; 361:1736-47  
Home et al, Diabetes Res Clin Pract.2011;94:352  
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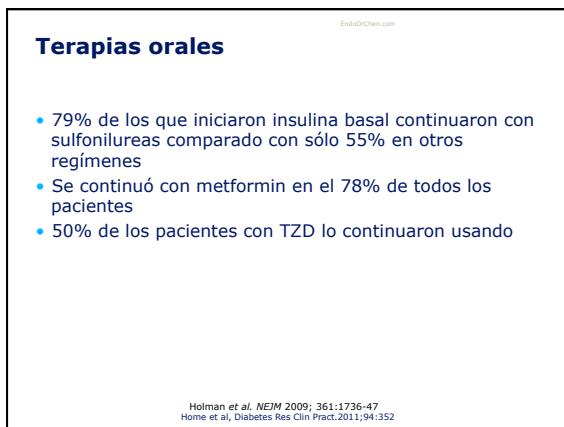
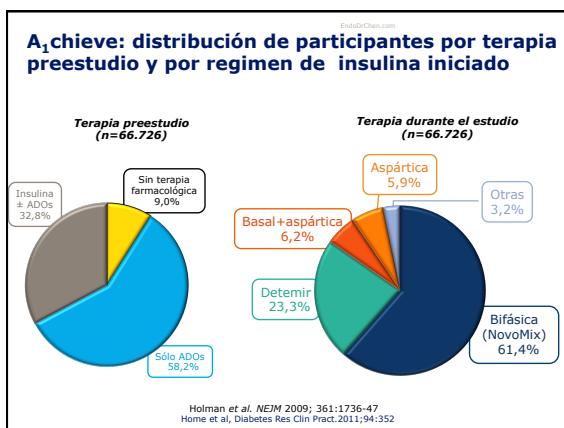
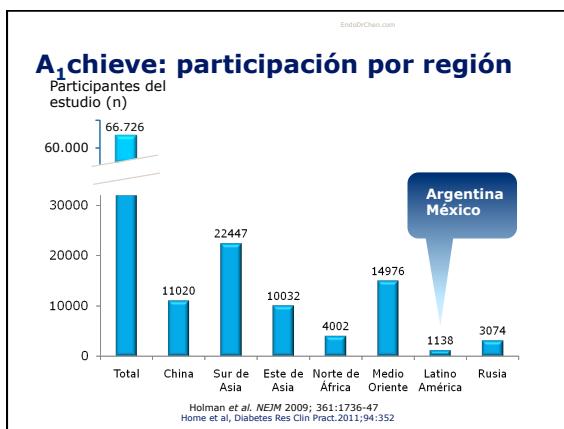
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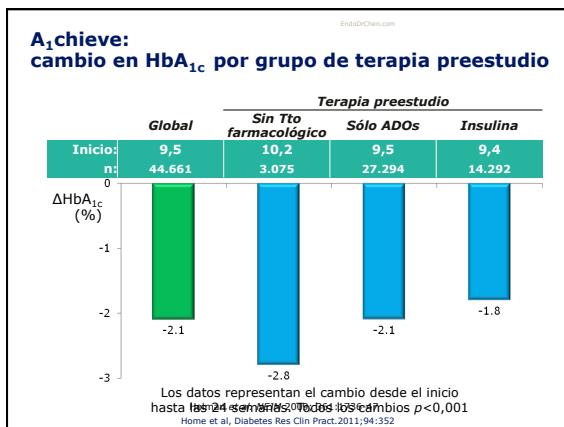
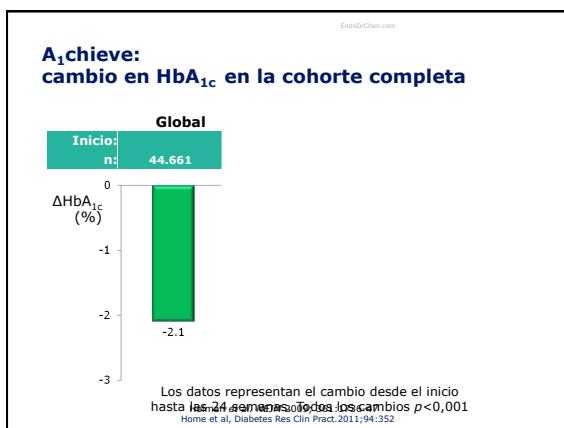
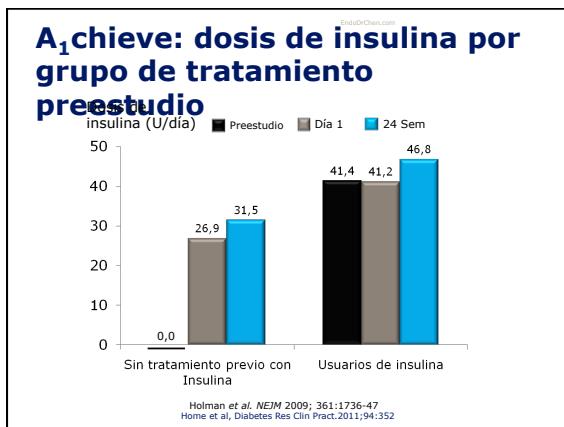


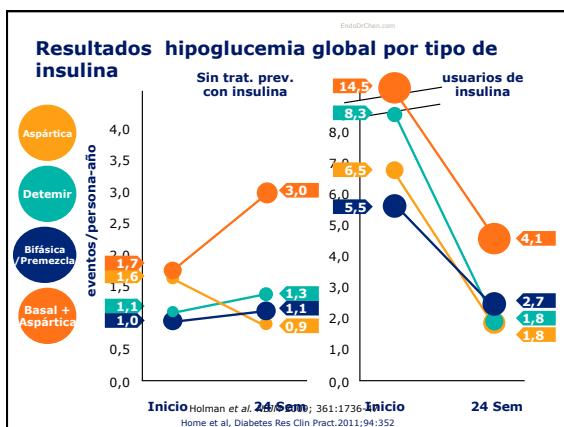
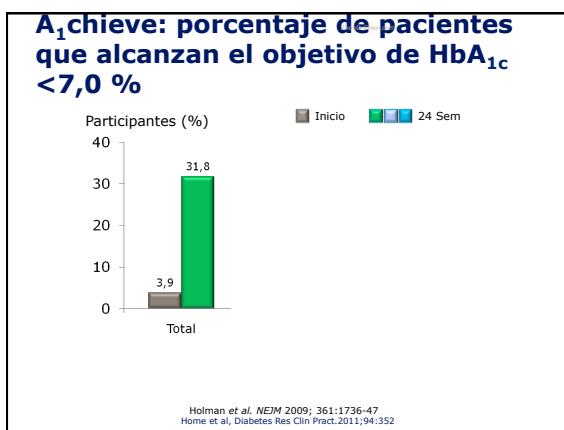
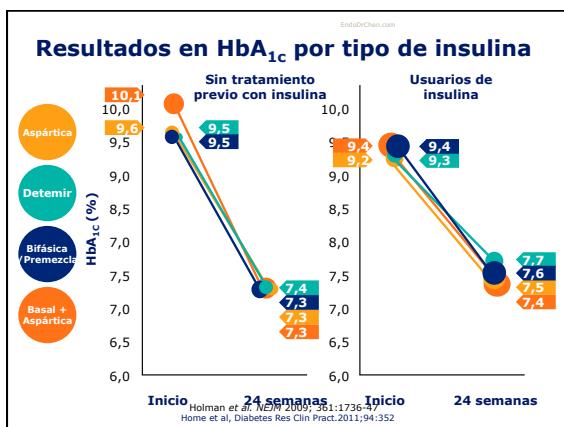
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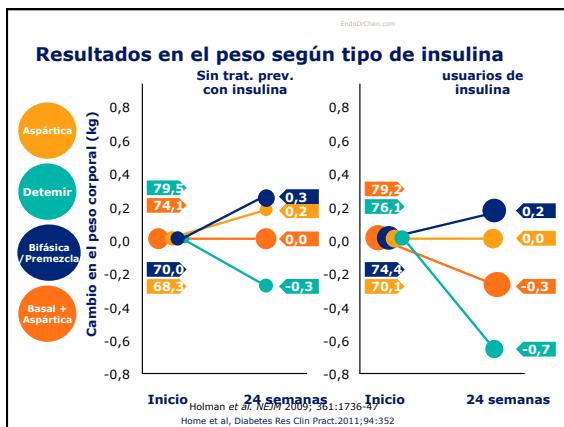
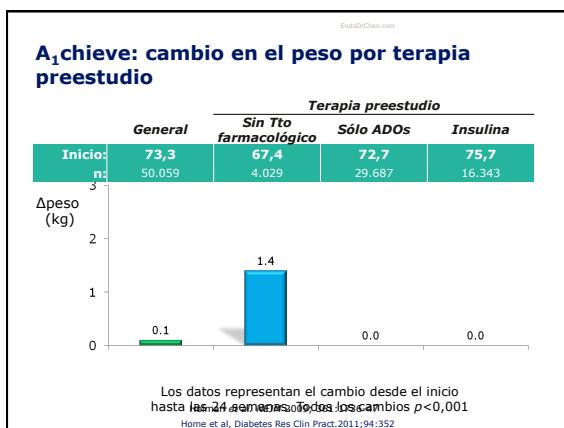
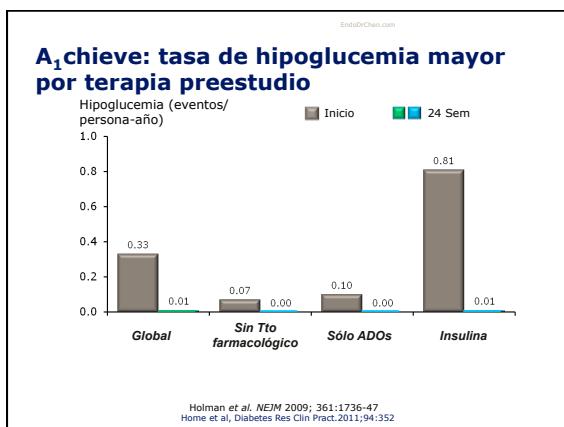


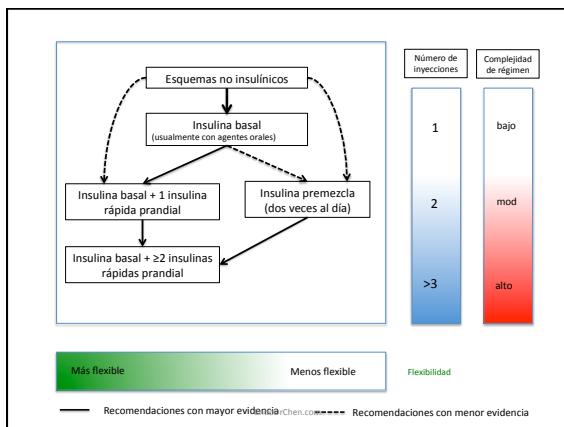
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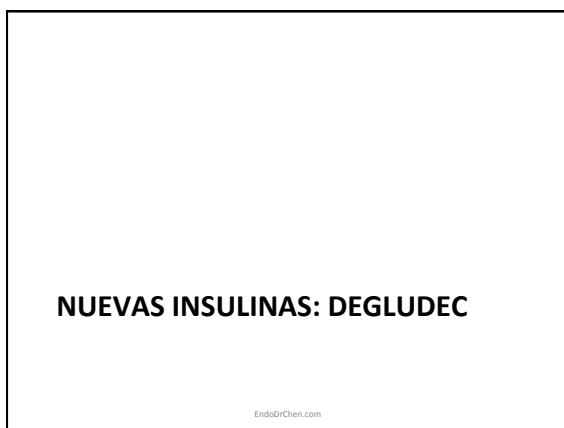
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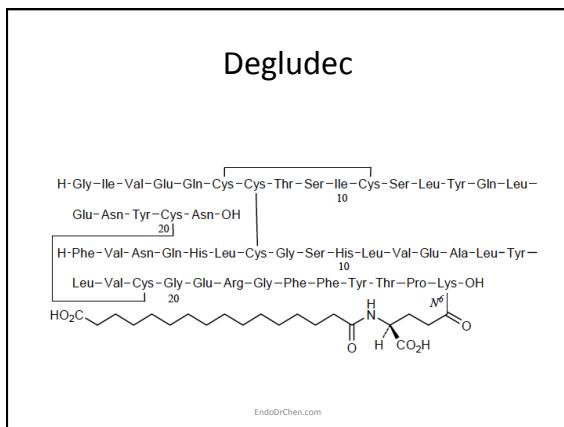
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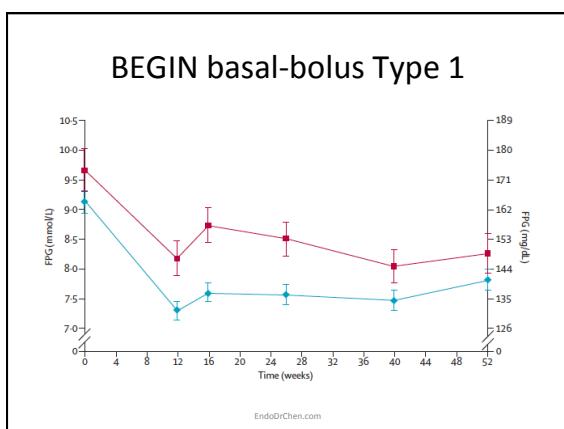
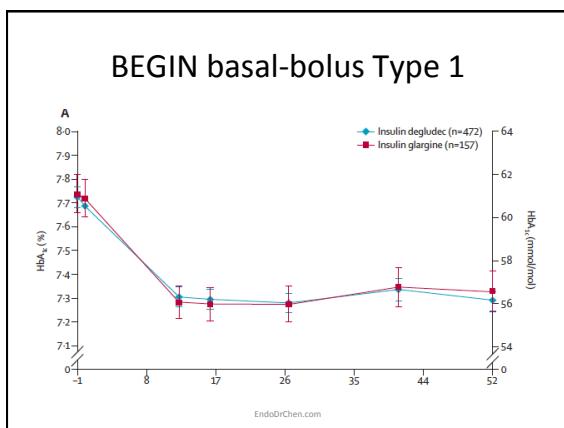
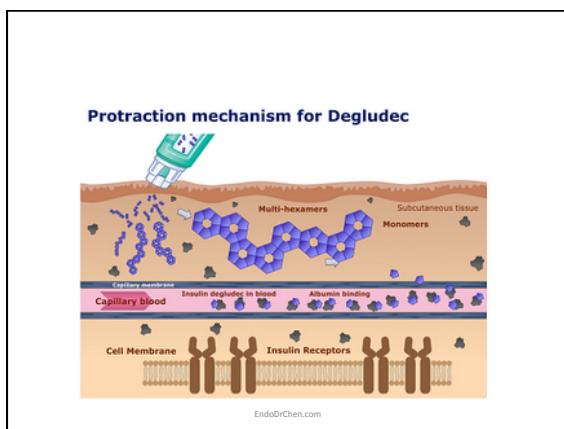
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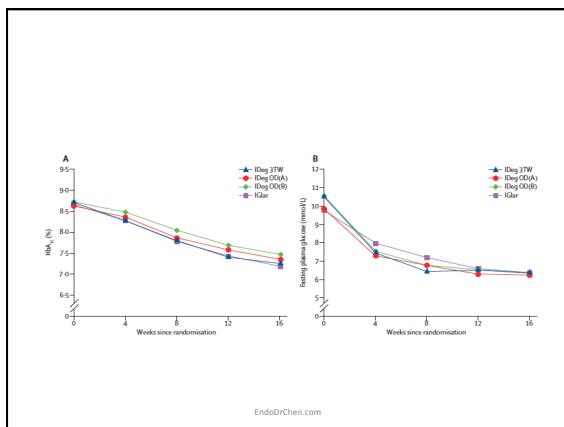
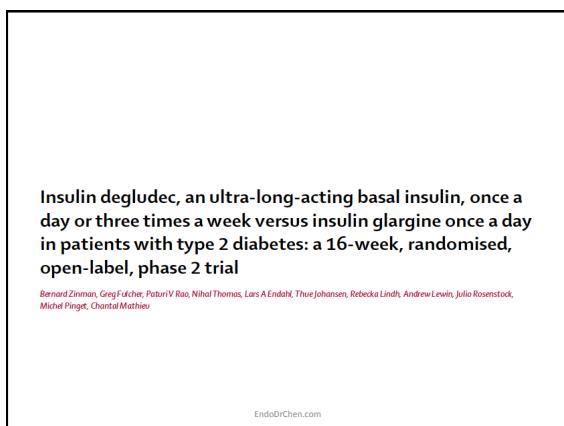


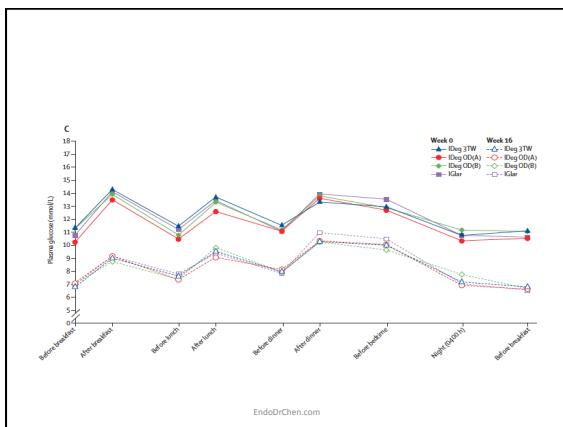
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BEGIN basal-bolus Type 1					
	Insulin degludec (U/kg; n=470)	Insulin glargine (U/kg; n=154)	Mean ratio* of insulin degludec to insulin glargine	Estimated treatment ratio† of insulin degludec to insulin glargine (95% CI)	p value
<b>Basal insulin (degludec or glargine)</b>					
Pretrial	0.37 (0.01)	0.36 (0.01)	--	--	--
Week 1	0.35 (0.01)	0.33 (0.01)	--	--	--
Week 52	0.35 (0.01)	0.39 (0.02)	0.91	0.86 (0.81-0.92)	<0.0001
<b>Bolus insulin aspart (at mealtimes)</b>					
Week 1	0.36 (0.01)	0.38 (0.01)	--	--	--
Week 52	0.40 (0.01)	0.44 (0.02)	0.90	0.90 (0.83-0.98)	0.016
<b>Total insulin (basal + bolus)</b>					
Week 1	0.72 (0.01)	0.71 (0.02)	--	--	--
Week 52	0.75 (0.02)	0.82 (0.03)	0.91	0.89 (0.84-0.93)	<0.0001

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## Conclusiones

- Las terapias análogas basales son una forma eficaz y segura de iniciar insulinas en pacientes que fallan a antidiabéticos orales
- No todos los análogos se comportan igual
- Hay formas más sencillas de intensificar como es el basal plus
- Nuevas insulinas en desarrollo que tienen duración de acción aún más prolongada

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## Preguntas...

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