



Cuándo es el momento para iniciar y cuál es la mejor insulina para diabéticos tipo 2?

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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
 - Abbott Nutrición

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Agenda

- Cuándo es el momento de insulinizar?
- Cómo podemos empezar a insulinar?
- Cuándo y cómo intensificar el uso con insulinas?

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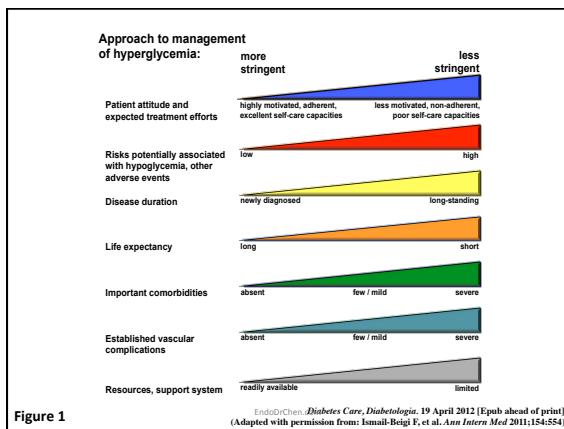
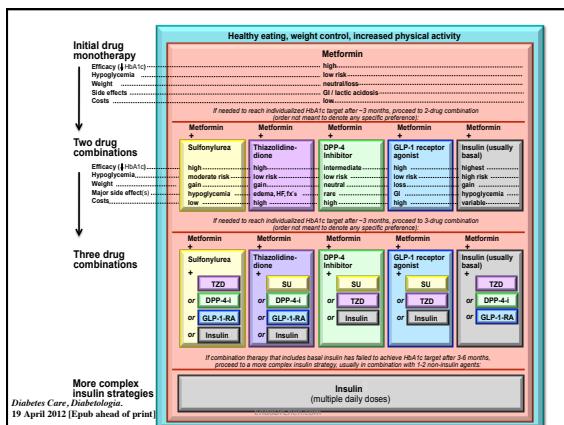


Figure 1

Pregunta #1

- Cuándo empezarían insulinoterapia en el paciente ambulatorio ASINTOMÁTICO?
 - Después de falla de 1 agente oral?
 - Después de falla de 2 agentes orales?
 - Después de falla de 3 agentes orales?
 - Después de falla de 4 agentes orales?

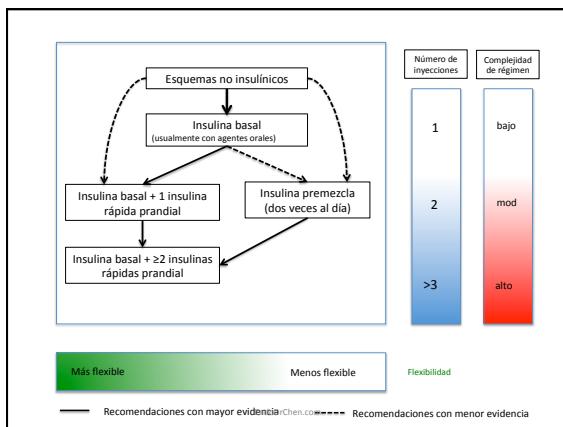
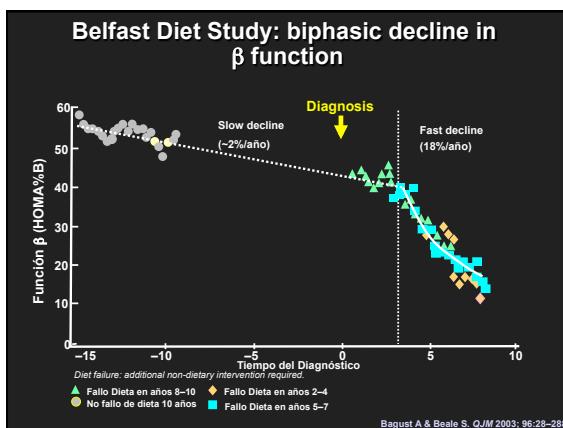
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Pregunta #2

- En la evolución natural de la diabetes, la mayoría de los pacientes van a terminar requiriendo insulina?
 - No
 - Si
- En caso de requerirlo, se va poder mantener bien controlado con sólo una insulina basal?
 - No
 - Si

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HAY ALGUNA VENTAJA EN INSULINIZAR
MUY TEMPRANAMENTE?

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ESTUDIOS INICIALES: SUECIA

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Introducción

- Glicemia entre 126 y 200 mg/dl
- Glibenclamida vs insulina NPH por 2 años
- Dosis promedio NPH 20 u al día

Endo: Alvarsson M. Diabetes Care. 2003;26:2231-2237

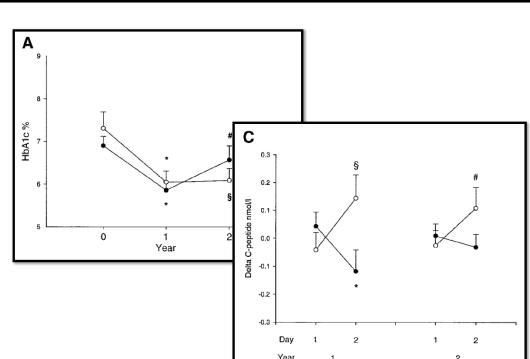
Insulina vs glibenclamida

Table 1—Clinical characteristics at baseline in the two treatment groups

	Glibenclamide	Insulin
n	21	18
Age (years)	55.6 ± 1.6	51.1 ± 1.7
Sex (M/F)	15/6	11/7
BMI (kg/m ²)	27.8 ± 0.8	27.3 ± 0.7
HbA _{1c} (%)	6.9 ± 0.2	7.3 ± 0.4
AER (mg/l)	9.7 ± 3.5	8.8 ± 2.1
Systolic blood pressure (mmHg)	139 ± 3 (18)	144 ± 7 (16)
Diastolic blood pressure (mmHg)	85 ± 2	83 ± 2
Retinopathy	3/19	3/16
Total cholesterol (mmol/l)	5.39 ± 0.16	5.47 ± 0.24
LDL cholesterol (mmol/l)	3.39 ± 0.13	3.40 ± 0.20
HDL cholesterol (mmol/l)	1.06 ± 0.06	1.09 ± 0.04
Triglycerides (mmol/l)	2.25 ± 0.26	2.06 ± 0.16

Data are mean ± SEM or mean ± SEM (n).

Endocrinol Alvarsson M. Diabetes Care. 2003;26:2231-2237



Endocrinol Alvarsson M. Diabetes Care. 2003;26:2231-2237

INSULINA VS GLIBENCLAMIDA EN TAIWAN

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Introducción

- Glicemias >300 mg/dl en ayunas o >400 mg/dl al azar
- Ingreso hospitalario, tratamiento con insulina por 2 semanas y luego se aleatorizan
 - Continuar con insulina vs orales (metformin, glicazida o ambas)

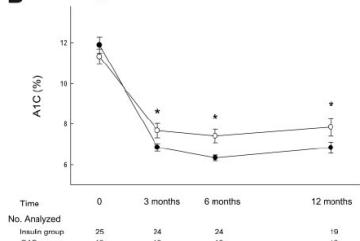
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Chen HS. Diabetes Care. 2008;31:1927-1932

Pacientes con glicemia >300 mg/dl

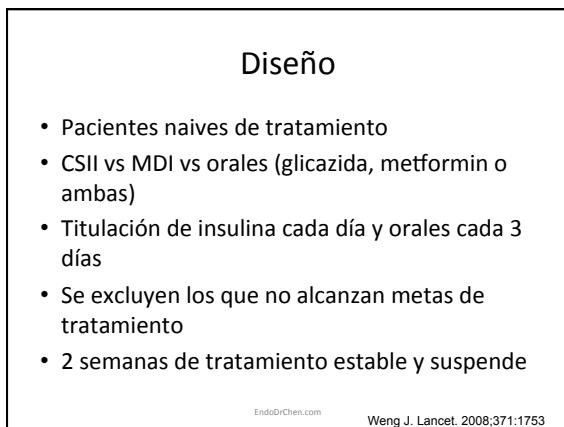
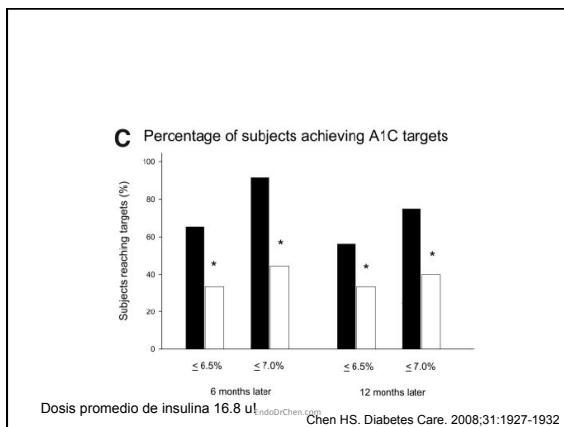
	Insulin group (intention to treat)	OAD group (intention to treat)
n	25	19
Age (years)	57.9 ± 8.5	59.6 ± 12.6
Sex (male-female)	19:6	13:6
Body weight (kg)	71.4 ± 10.6	71.7 ± 21.3
BMI (kg/m ²)	27.55 ± 4.20	28.31 ± 6.20
Peak FPG (mg/dl)*	345.0 ± 82.2	329.2 ± 24.0
Peak plasma glucose (mg/dl)*	527.3 ± 163.8	483.7 ± 217.2
A1C (%)	11.89 ± 1.91	11.33 ± 1.57
Systolic blood pressure (mmHg)	125.4 ± 13.4	130.7 ± 12.9
Diastolic blood pressure (mmHg)	74.2 ± 10.6	78.5 ± 8.1
Total cholesterol (mg/dl)	193.1 ± 54.8	184.7 ± 39.5
HDL cholesterol (mg/dl)	45.9 ± 15.1	45.7 ± 12.7
Triglycerides (mg/dl)	135 (52-1,234)	131 (34-1,074)
Urine albumin-to-creatinine ratio (mg/g)	14.1 (3.2-293.9)	17.3 (4.2-626.2)

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Chen HS. Diabetes Care. 2008;31:1927-1932

B Changes in A1C Levels



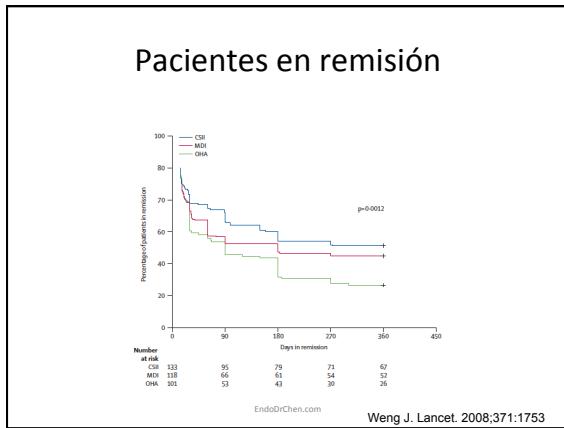
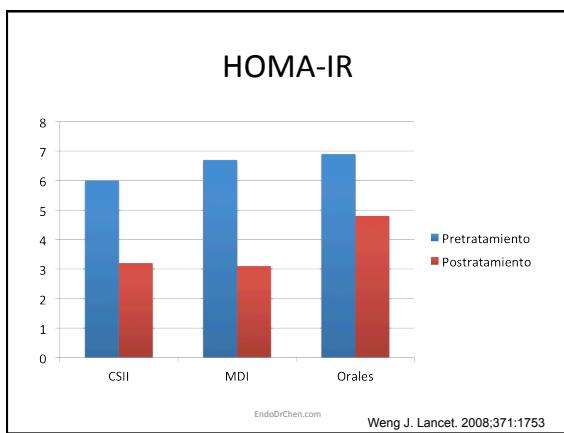
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Chen HS. Diabetes Care. 2008;31:1927-1932

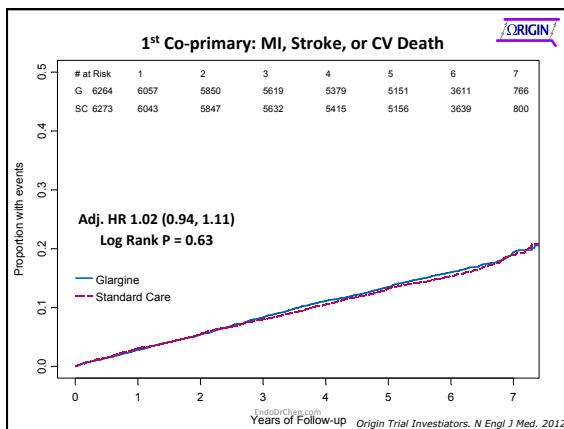
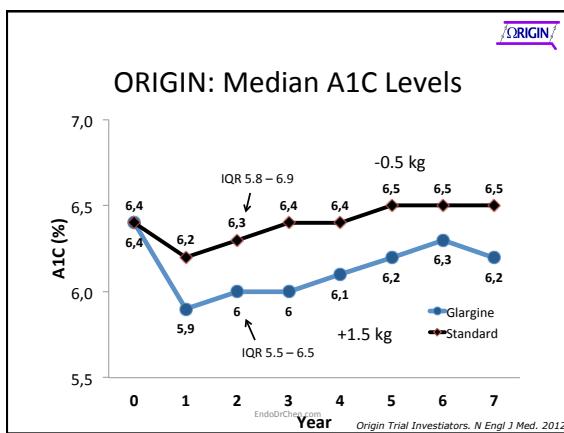
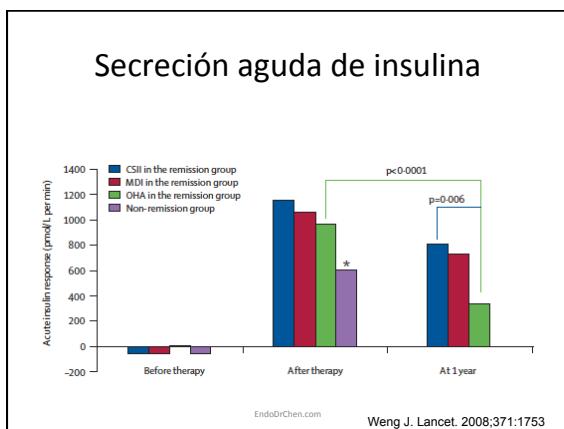


Características

	CSII	MDI	Oral hypoglycaemic agents
Number	133	118	101
Men (n)	88	81	58
Age (years)	50 (11)	51 (10)	52 (9)
Body-mass Index (kg/m ²)	25.1 (3.0)	24.4 (2.7)	25.1 (3.3)
Fasting plasma glucose (mmol/L)			
Before therapy	11.3 (3.3)	11.5 (3.2)	10.8 (2.9)
After therapy*	6.6 (1.5)	6.8 (1.6)	6.5 (1.6)
2-h postprandial plasma glucose (mmol/L)			
Before therapy	16.1 (5.5)	17.5 (5.5)	16.6 (5.0)
After therapy*	7.5 (2.2) (n=113)	8.1 (2.9) (n=111)	8.2 (2.7) (n=90)
HbA _{1c} (%)			
Before therapy	9.8 (2.3)	9.7 (2.3)	9.5 (2.5)
After therapy*	8.0 (1.5)	8.0 (1.6)	7.9 (1.7)

EndoDrChen.com Weng J. Lancet. 2008;371:1753





Factores predictores para alcanzar Hba1c <6.5%

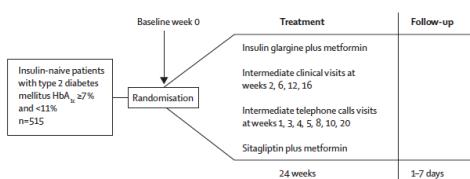
Factor	OR para alcanzar Hba1c <6.5%
Mayor edad	1.014 (1.008-1.019)
Uso de alcohol (>2 veces por semana)	1.727 (1.561-1.911)
A1c (por %)	0.191 (0.179-0.205)
Depresión	1.457 (1.256-1.691)
Relación cintura cadera (por unidad)	0.371 (0.244-0.565)
Diabetes	0.102 (0.081-0.128)

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Origin Trial Investigators. Diabetes Care. 2013. Online May 8.

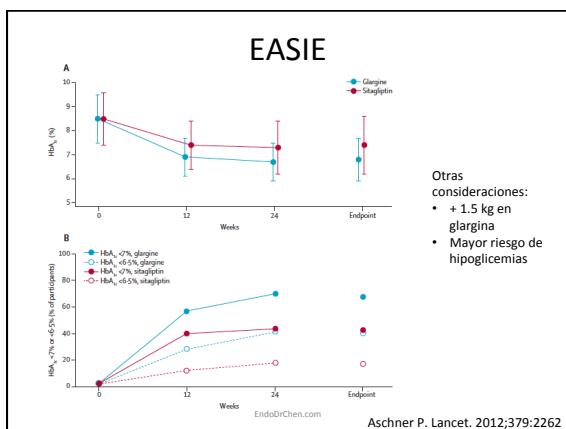
QUÉ SIGUE DESPUÉS DE MONOTERAPIA CON METFORMIN, INSULINA O UN SEGUNDO AGENTE ORAL?

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EASIE: sitagliptin vs glargin en pacientes no controlados con metformin en monoterapia

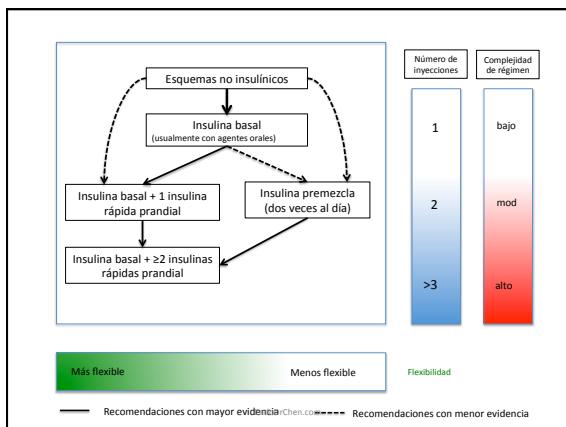


EndoDrChen.com Aschner P. Lancet. 2012;379:2262



SIN EMBARGO, LA SITUACIÓN ES USUAL ES INSULINIZAR LUEGO DE FALLA A 2 AGENTES ORALES

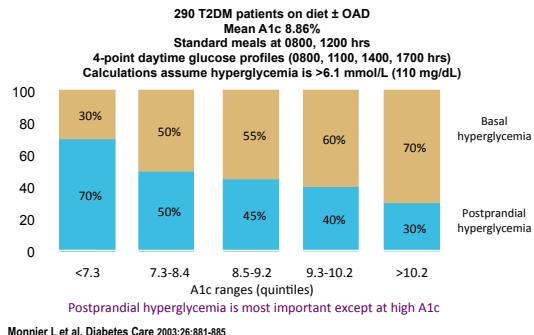
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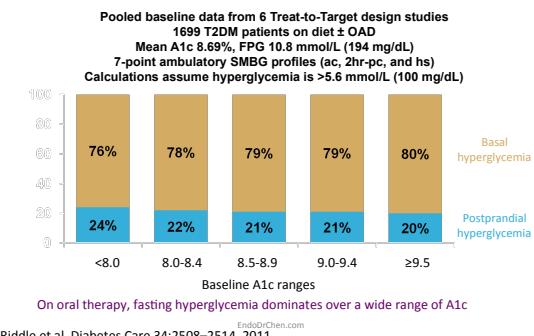
POR QUÉ INICIAR CON INSULINAS BASALES?

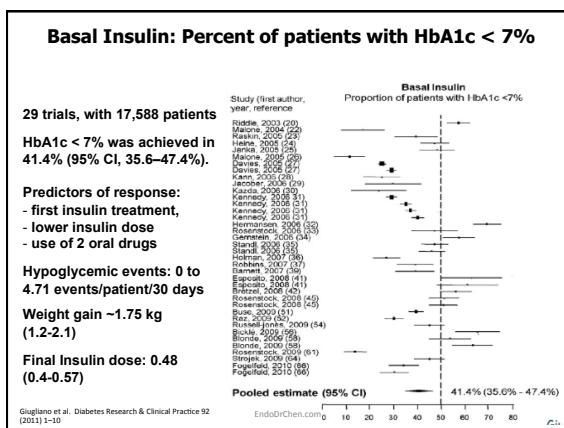
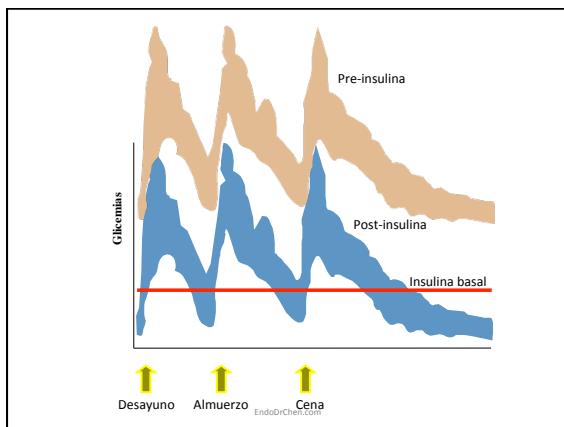
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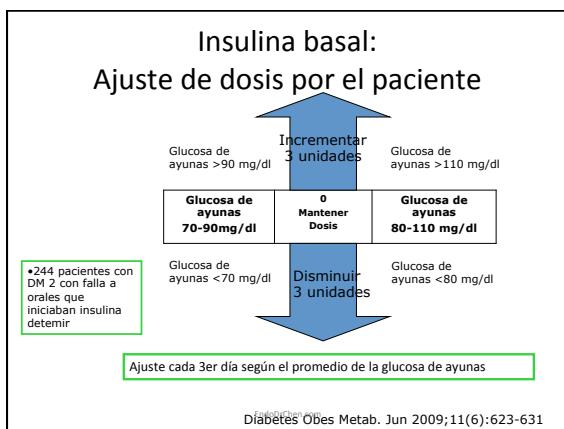
Basal and postprandial contributions to hyperglycemia by A1c range



Basal and postprandial contributions to hyperglycemia by A1c range



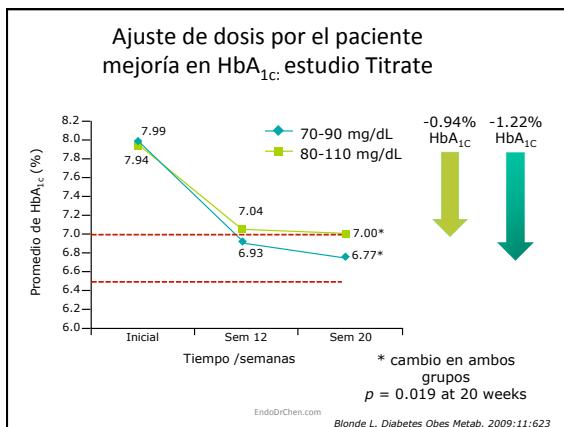


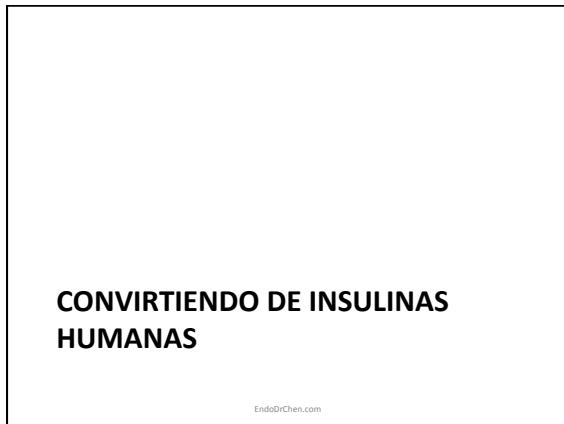


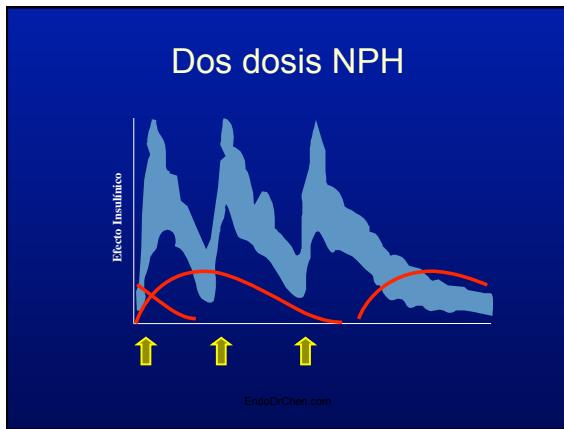
Metas de tratamiento

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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Pregunta #3

- Masculino de 55 años, en tratamiento con insulina glargina 38 u al día, metformin 500 mg tid y glimepiride 4 mg por día. Tiene glicemia ayunas 114 mg/dl y Hba1c en 8.2%.
- Quién es la responsable de la Hba1c alta?
 - Hiperglicemia en ayunas?
 - Hiperglicemia postprandial?

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Pregunta #4

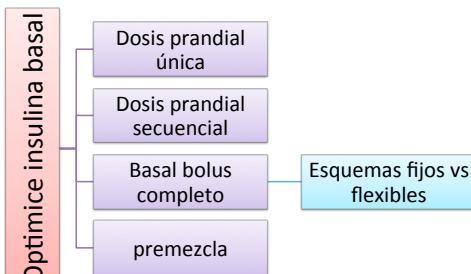
- En este paciente, si queremos tratar la hiperglicemia postprandial, la mejor estrategia sería...
 - Suspender glimepiride y cambiar por sitagliptina?
 - Suspender glimepiride y aumentar dosis de metformin?
 - Suspender glimepiride e iniciar una insulina prandial?
 - Dejar glimepiride y agregar una insulina prandial

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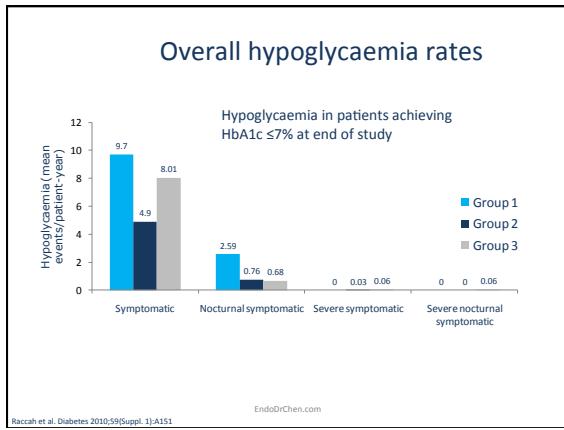
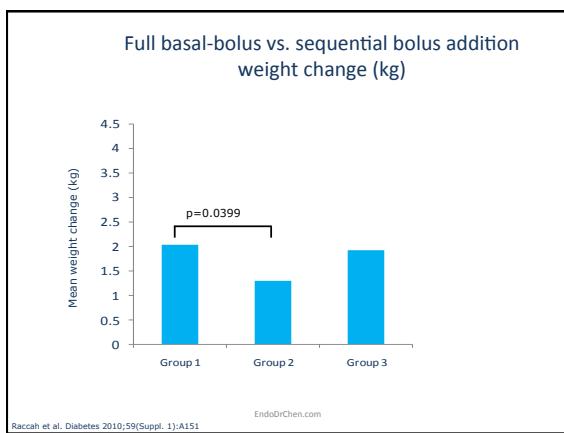
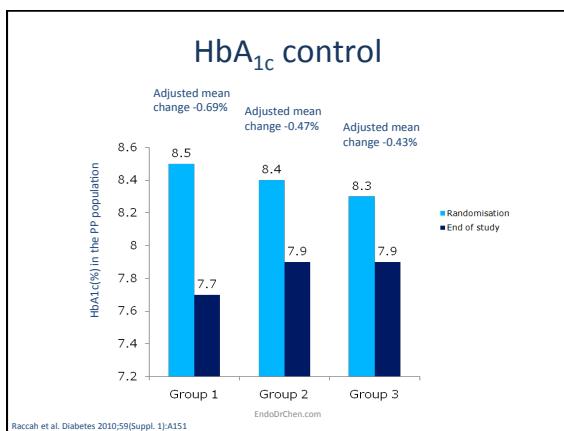
CÓMO PROGRESAR EN LA INSULINIZACIÓN?

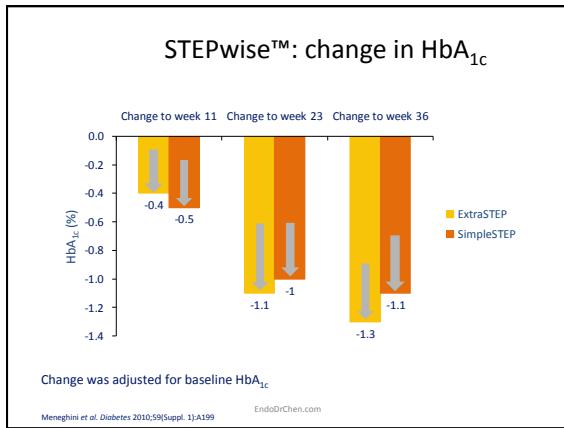
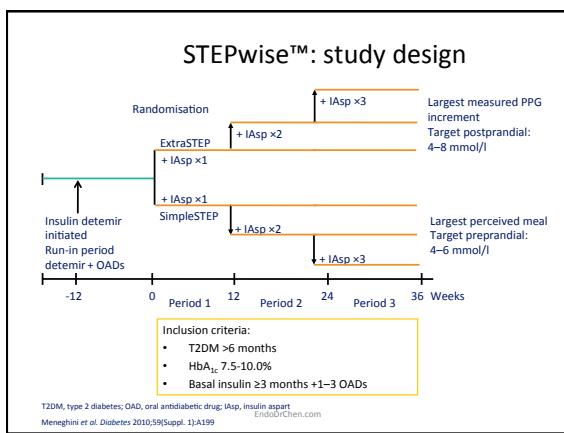
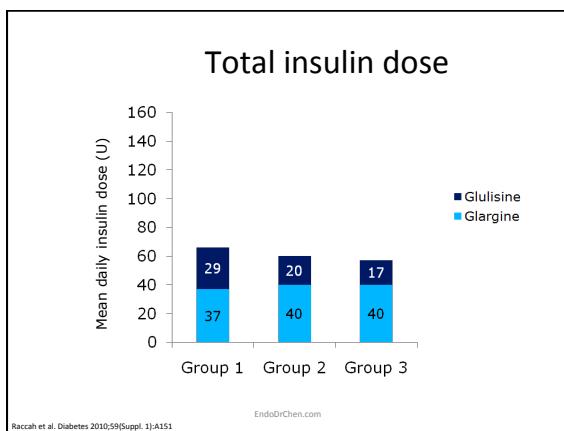
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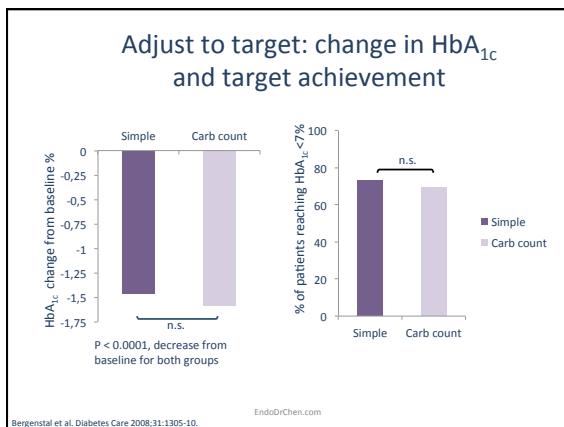
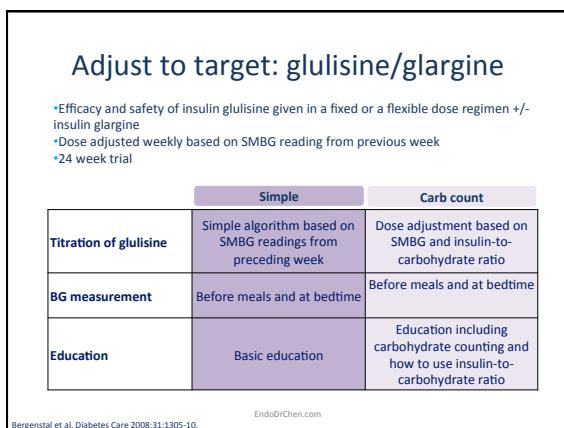
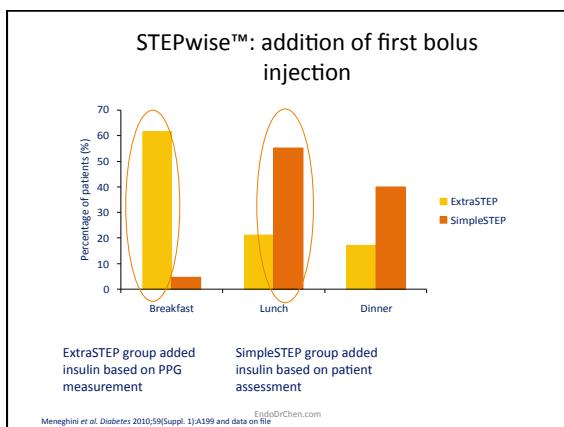
Cómo intensificar?

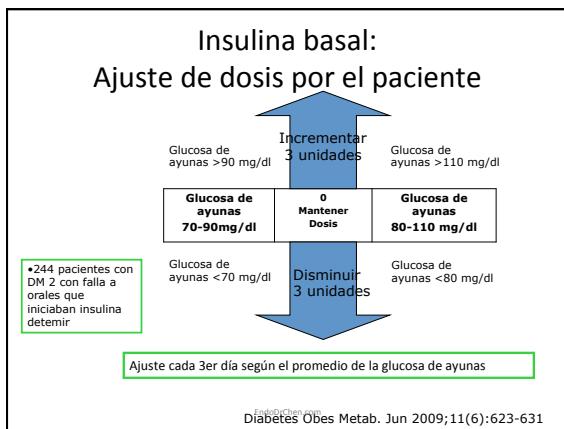
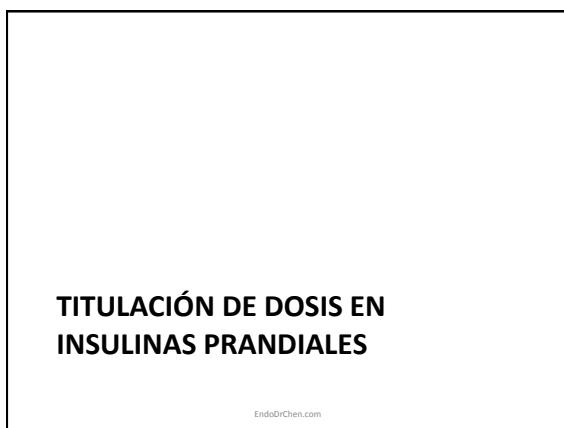
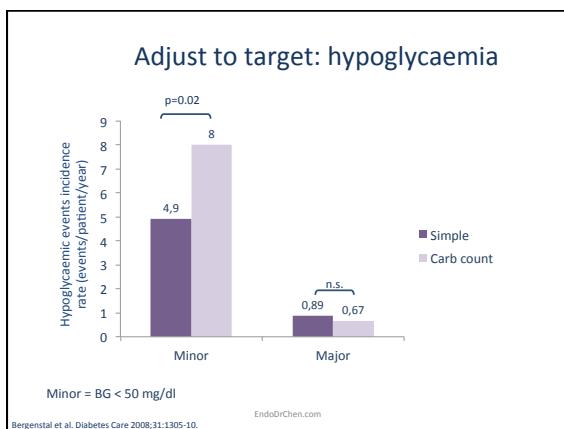


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Metas de tratamiento

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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Basal Bolus Insulin: Percent of patients with HbA1c < 7%

12 trials, with 2114 patients

HbA1c < 7% was achieved in 53.9% (95% CI, 43.5–64)

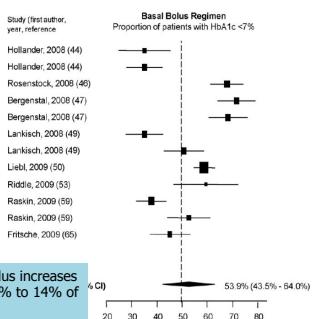
Hypoglycemic events (mean/patient/30 days): 0.88 (0.35-1.3)

Weight gain ~2.75 kg (1.8-3.7)

Final insulin dose: 0.89 U/kg (0.78-1.3)

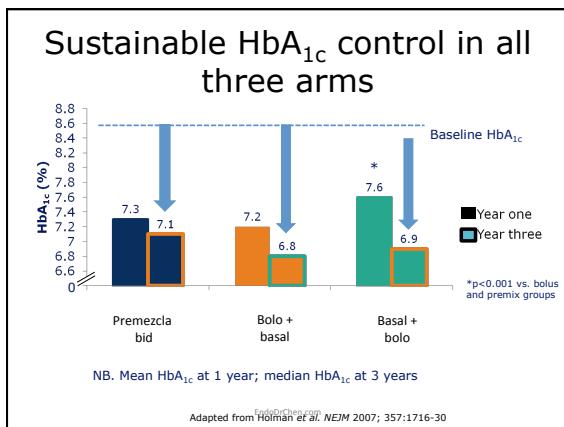
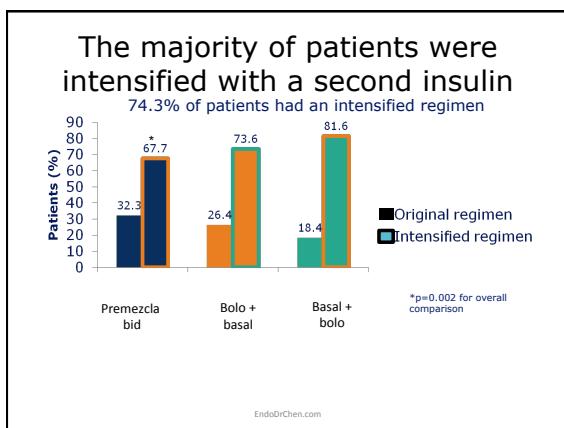
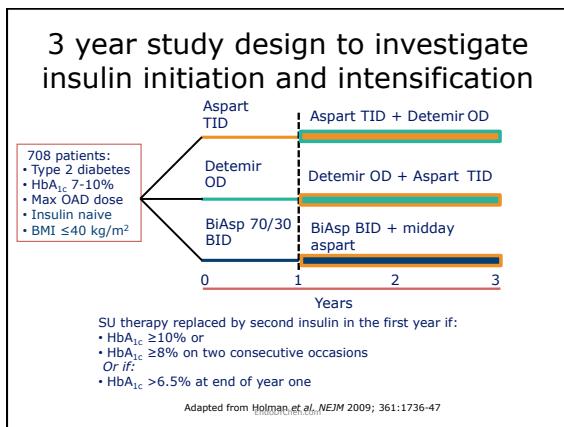
Escalation from basal to basal-bolus increases success rate in an additional ~12% to 14% of patients

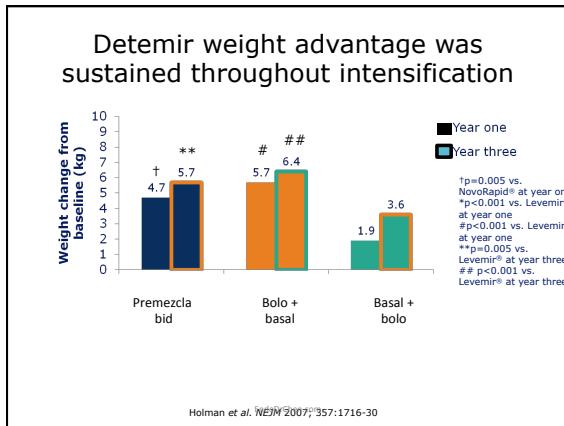
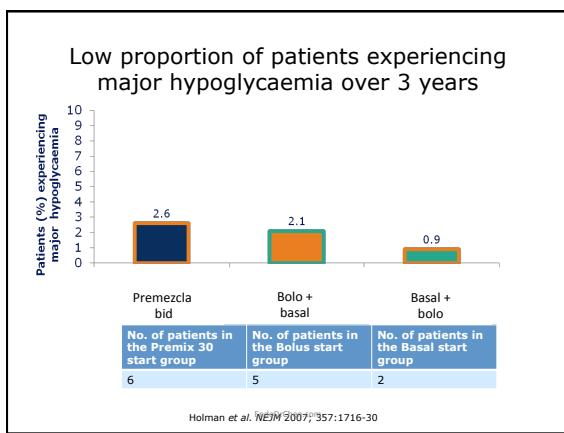
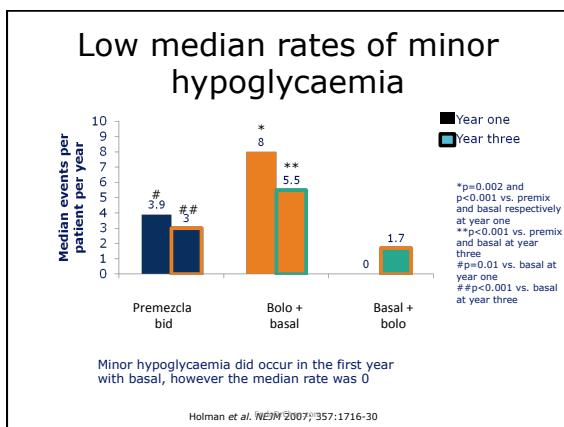
- HbA1c < 7% is achieve in ~54% of patients



ESTRATEGIAS PARA INSULINIZAR: MEDICINA BASADO EN LA EVIDENCIA

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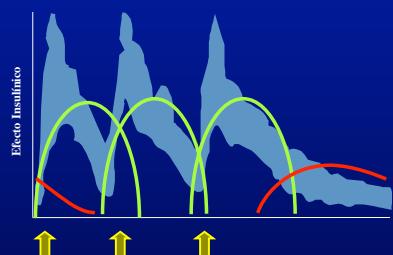




CÓMO PASAR A ANÁLOGOS EN UN ESQUEMA BASAL BOLUS?

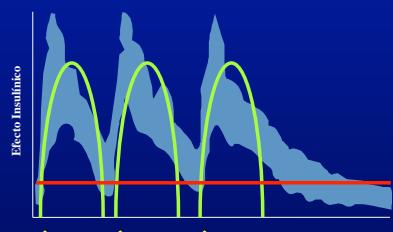
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3 dosis simple + 1 dosis NPH

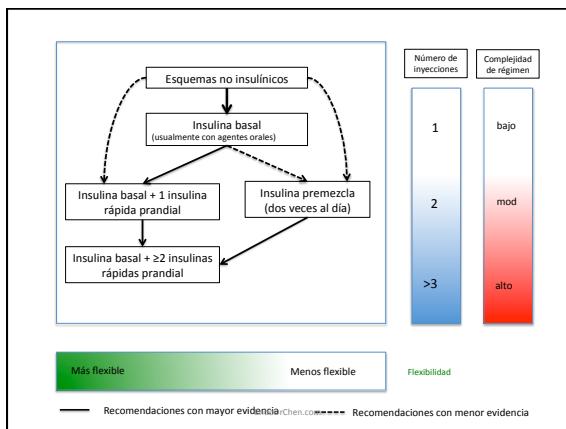


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3 dosis lispro/aspart + 1 glargin



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Actualización Médica Periódica



Conclusiones

- En la evolución natural de la DM, mayoría de pacientes requieren insulinizar
- La mejor estrategia es empezar con una insulina basal y progresar luego a basal plus
- Importancia de titulación de dosis
- Hacer insulinización lo más sencillo posible para pacientes y personal de salud



Preguntas...
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