



Starting and intensifying with insulin analogues: how and when?

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Conflicts of interest

- I have received payment as speaker, member of advisory board and/or investigator in clinical trials from:
 - Astra Zeneca
 - Novartis Pharma Logistics Inc
 - Novartis Oncology
 - Novo Nordisk
 - Merck Sharp & Dohme
 - Roche
 - Glaxo SmithKline
 - Sanofi Aventis
 - Boehringer
 - Organon
 - Abbott Nutrition

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Agenda

- When should we start insulin?
- Which are the different available strategies?
- Is there any difference between basal insulins?
- Which is the best strategy when we need to intensify insulin treatment?

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Clinical case

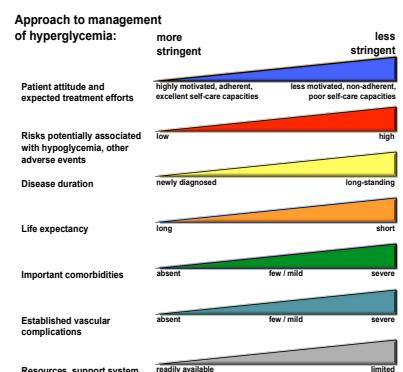
- 55 years old female patient with T2D diagnosed en 2005, hypertension. No coronary disease and no end organ damage
- Current treatment metformin 850 mg bid and glimepiride 4 mg per day
- PE: weight 90 kg, height 164 cm. BMI 33.46 kg/m²
- Hba1c 8.0%. FPG 160 (8.9 mmol) mg/dl

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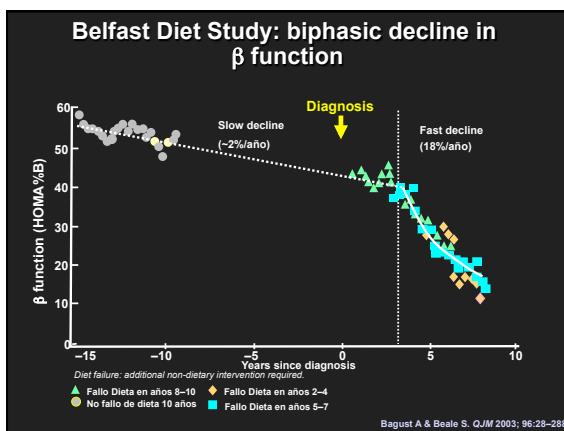
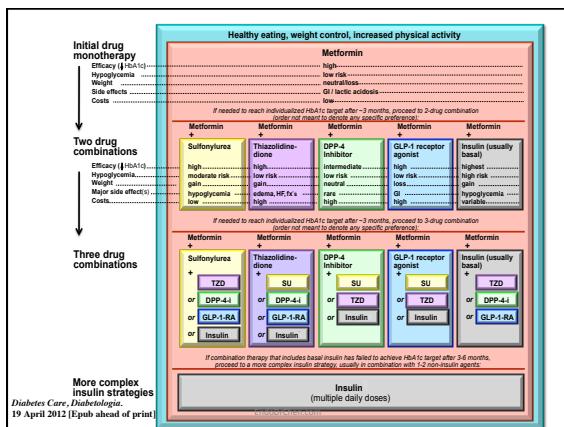
Clinical case

- What should be her Hba1c target?

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**Figure 1**

EndoDrChen. *Diabetes Care, Diabetologia*, 19 April 2012 [Epub ahead of print]
(Adapted with permission from: Ismail-Begi F, et al. *Ann Intern Med* 2011;154:554)



Clinical case

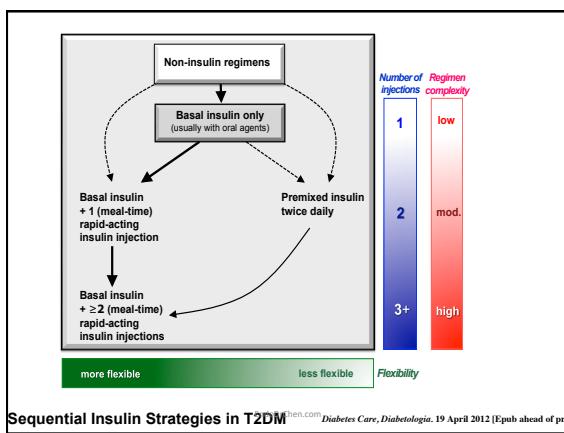
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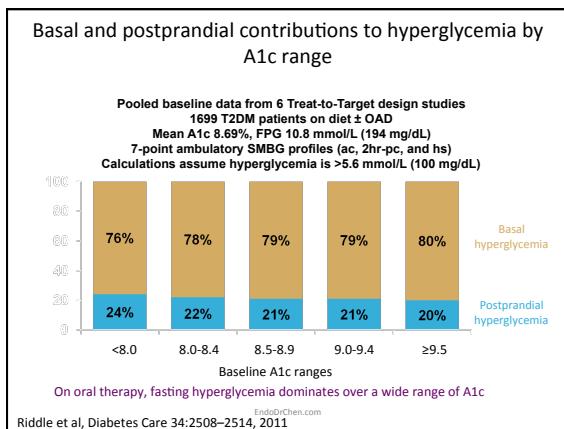
Endocrinology

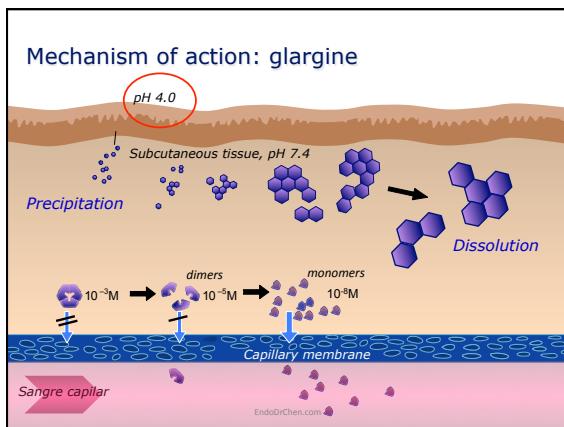
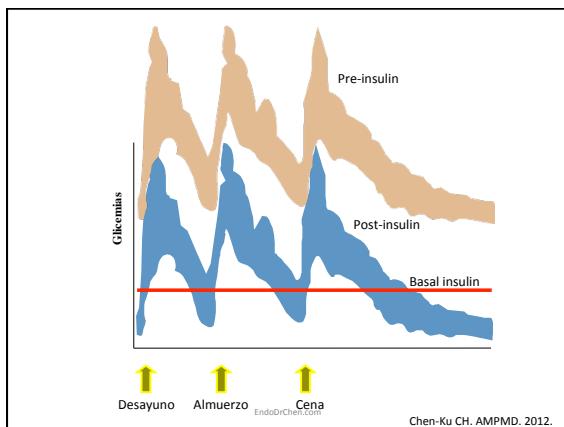
Clinical case

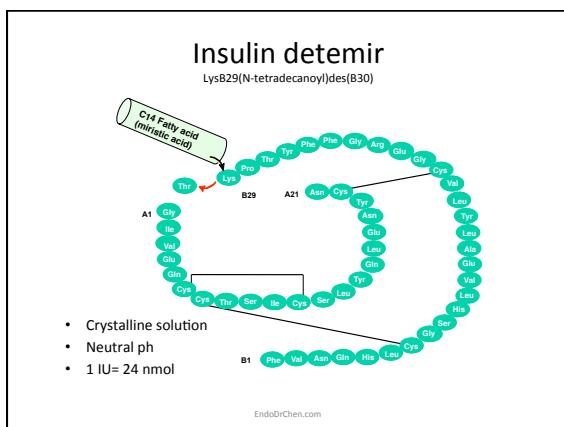
- What should be her Hba1c target?
- How should we start insulin treatment?

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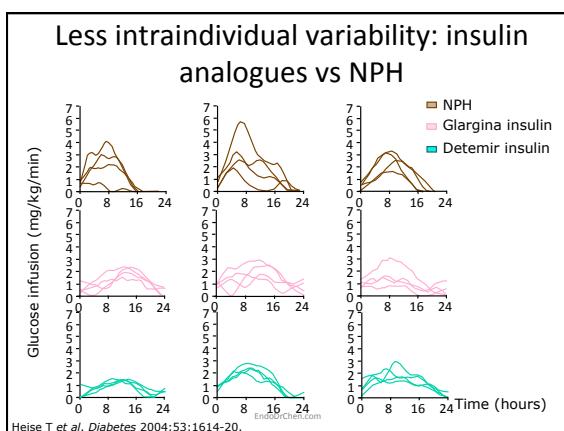






DIFFERENCES BETWEEN BASAL INSULINS: VARIABILITY, WEIGHT AND HYPOGLCEMIAS

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Glycemic variability: DM-1

Study	NPH	Detemir	P
Bartley	0	2	<0.001
Home	0	2	<0.001
Rusell-Jones	0	2	<0.001
Pieber	0	2	<0.001
Vague	0	2	0.001
De Leeuw	-	-	-
Standl	-	-	-
Kolendorf	0	2	<0.001
Hermansen	0	2	<0.001

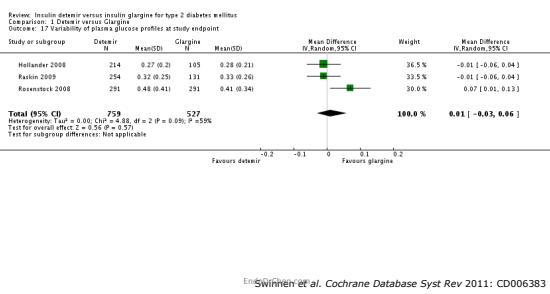
EndoDrChen.com Frier BM, Diab Obes Metab. 2013: online april 3.

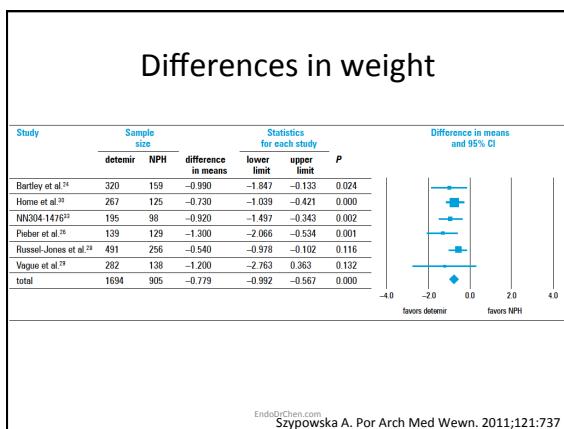
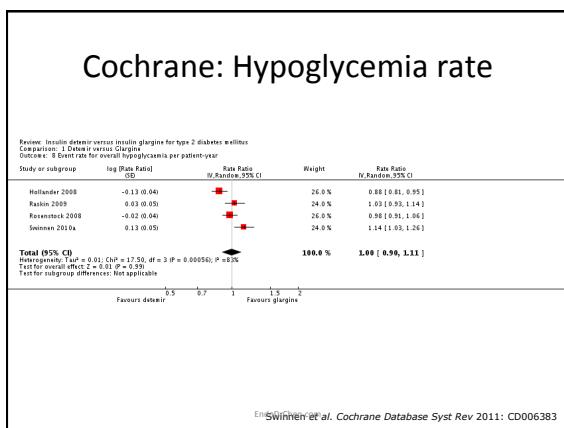
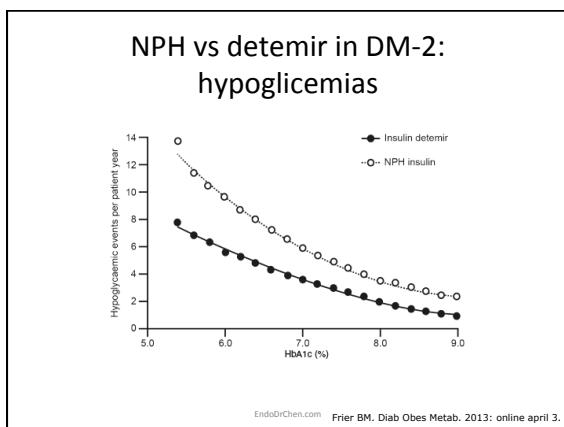
Glycemic variability: DM-2

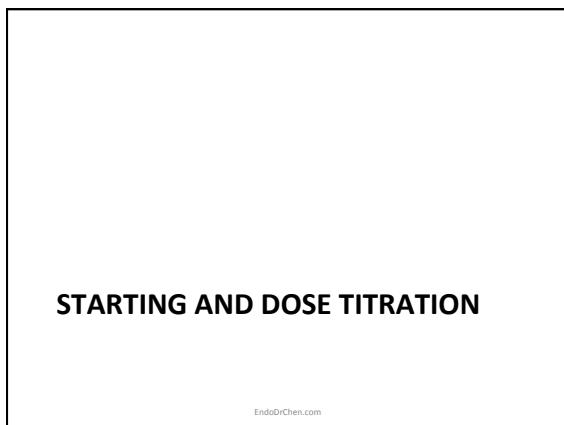
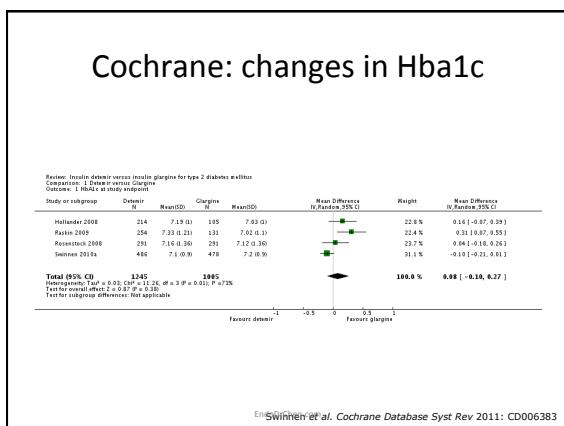
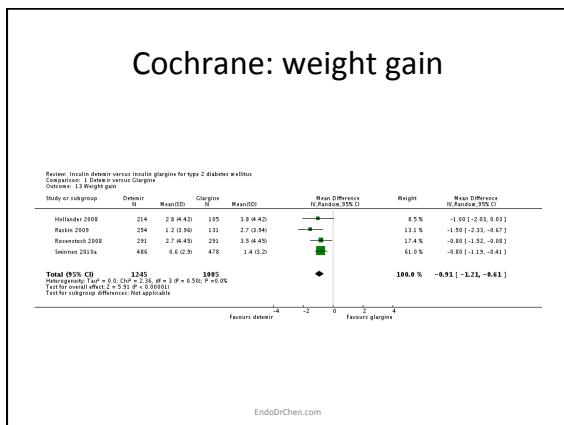
Study	NPH	Detemir	P
Raslova	0	2	<0.001
Hermansen	0	2	0.008
Haak	0	2	0.021
Fajardo Montaña 2008	0	2	<0.001
Philis-Tsimikas	1	1	NS

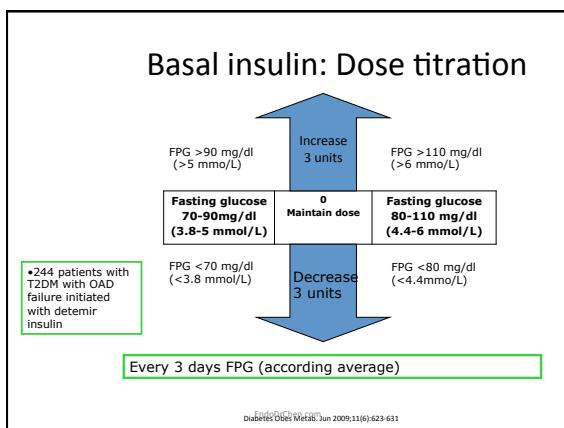
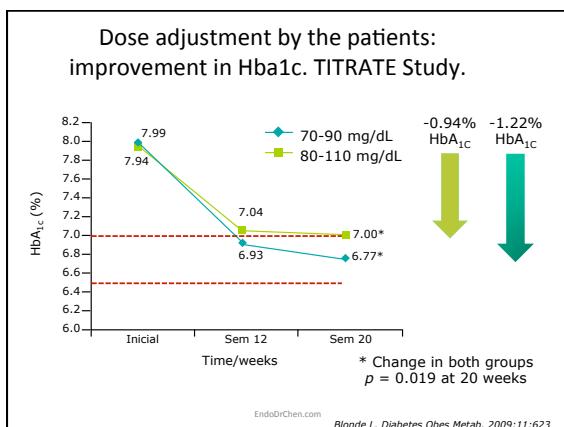
EndoDrChen.com Frier BM, Diab Obes Metab. 2013: online april 3.

Cochrane: variability in plasma glucose profiles









Glycaemic Goals

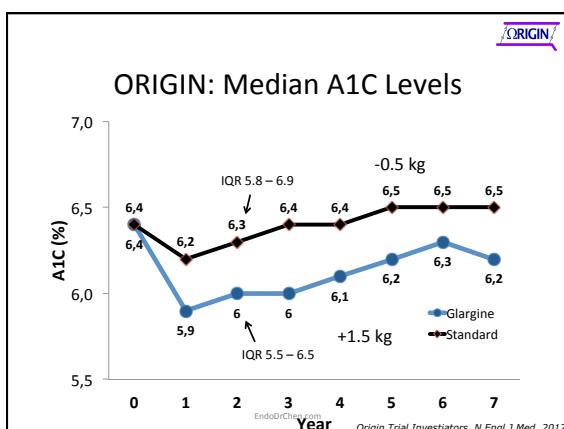
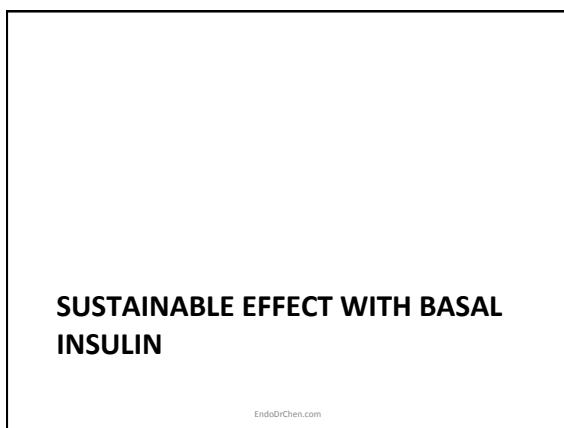
	ACE	ADA
HbA _{1c}	<6.5%	<7.0%
Fasting plasmatic glucose (FPG)	<110 mg/dL (6 mmol/L)	70-130 mg/dL (4-7 mmol/L)
PPG	<140 mg/dL (<8 mmol/L)	<180 mg/dL (<10 mmol/L)

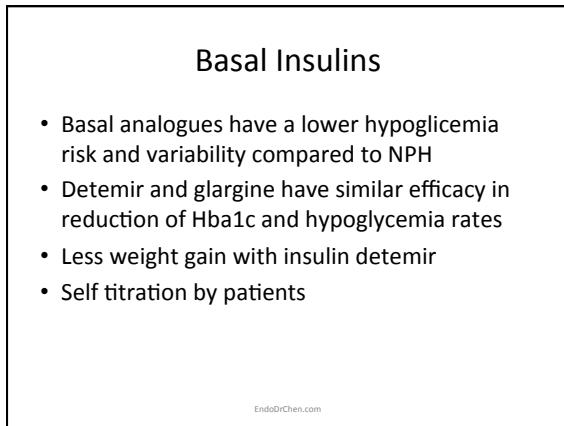
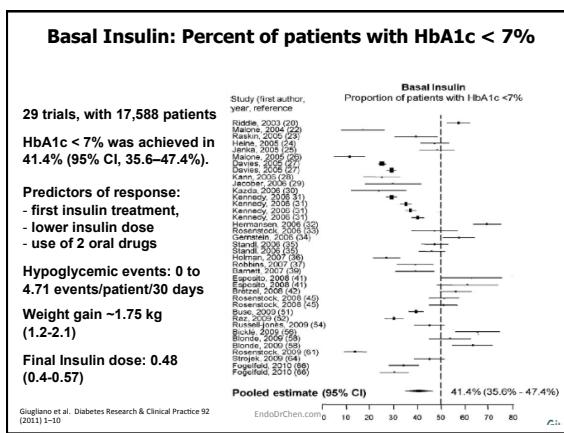
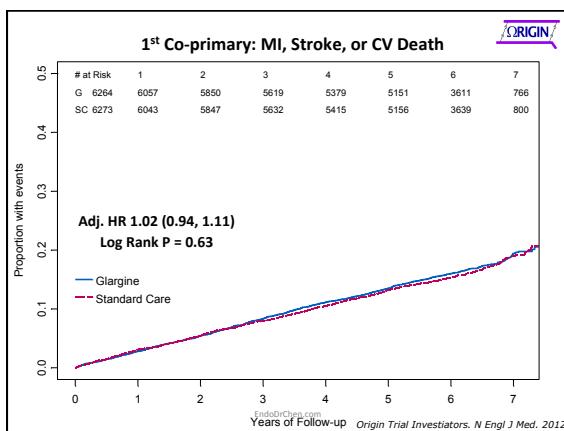
Adapted from Diabetes Care 2013;36(suppl 1):pp S11-S66

Treatment goals

Goal	Fasting glucose	Postprandial glucose
<6.5%	70 (4 mmol)-110 (6 mmol) mg/dl	<140 (8 mmol) mg/dl
<7%	80 (4.4 mmol)-140 (7.7 mmol) mg/dl	<180 (10 mmol) mg/dl

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Clinical case

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- Current treatment metformin 850 mg bid and glimepiride 4 mg per day
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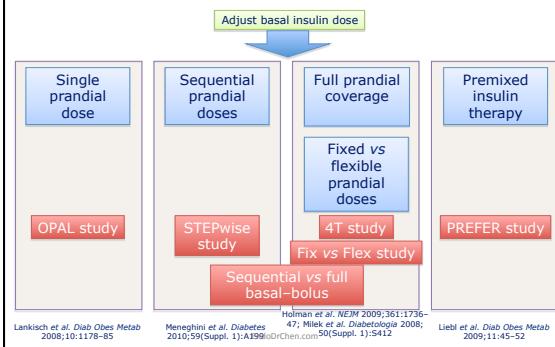
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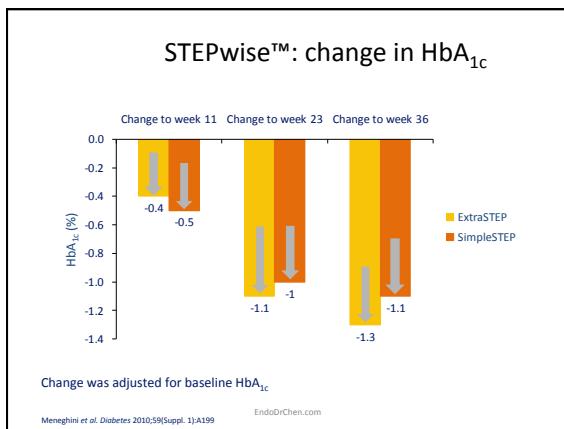
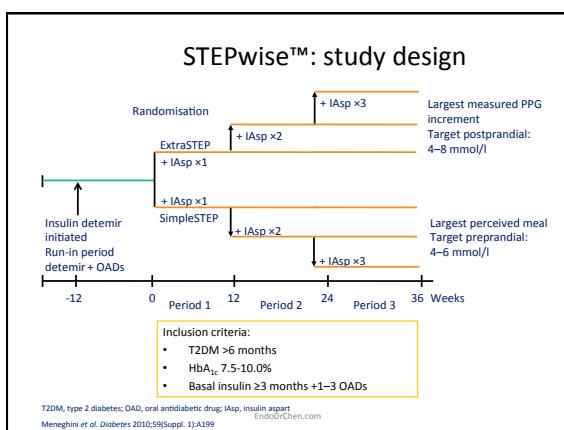
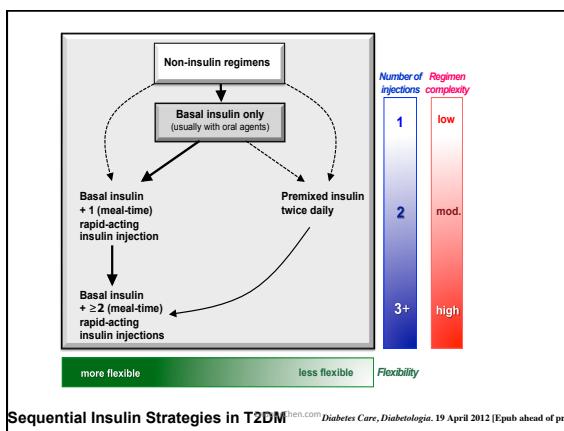
Clinical case

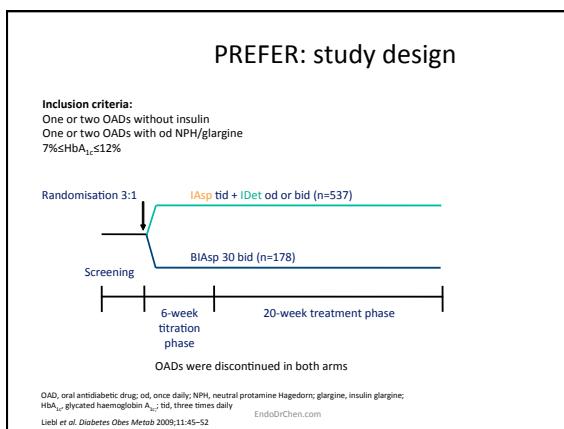
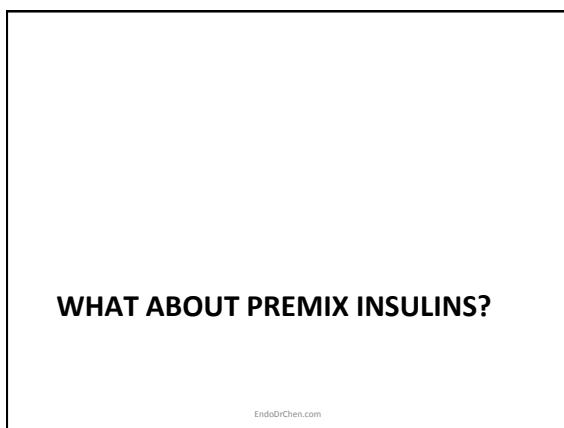
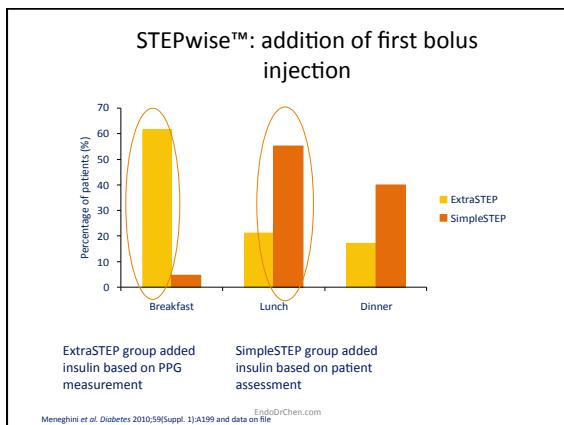
- What should be her Hba1c target?
- How should we start insulin treatment?
 - Patient was started with 10 u daily of insulin detemir and up titrated to 32 u daily
 - Fasting plasma glucose 106 (5.9 mmol) mg/dl
 - Hba1c 6.4%
 - 1 year later, her Hba1c increased to 7.5%. FPG 113 mg/dl (6.3 mmol)
- What should be the next step?

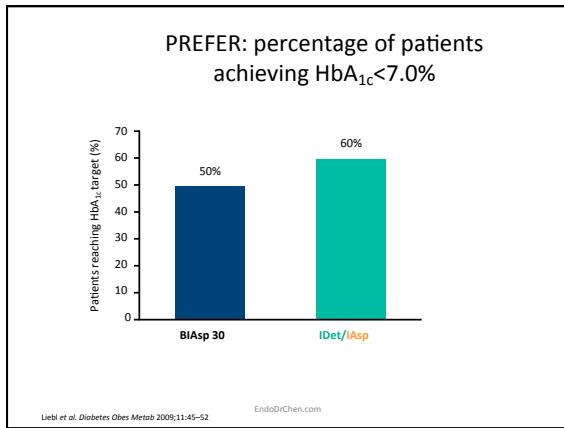
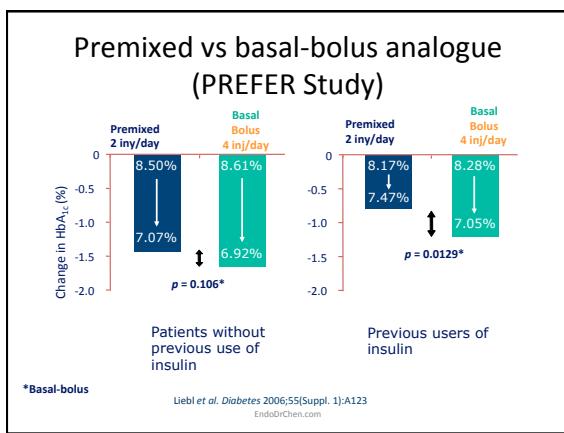
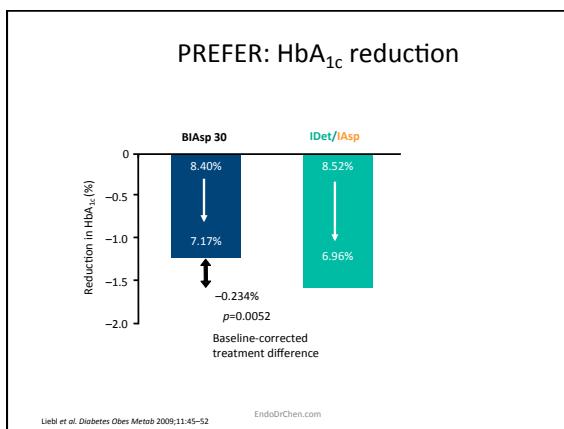
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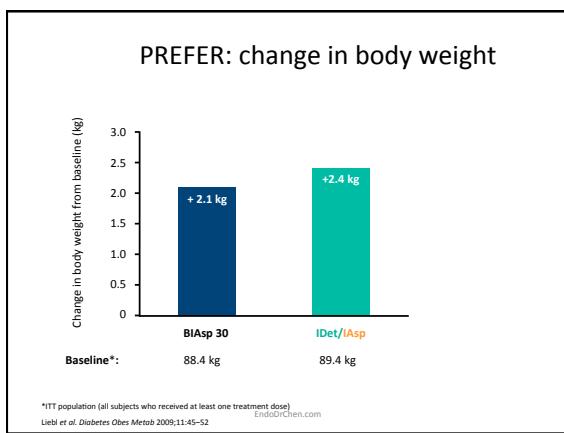
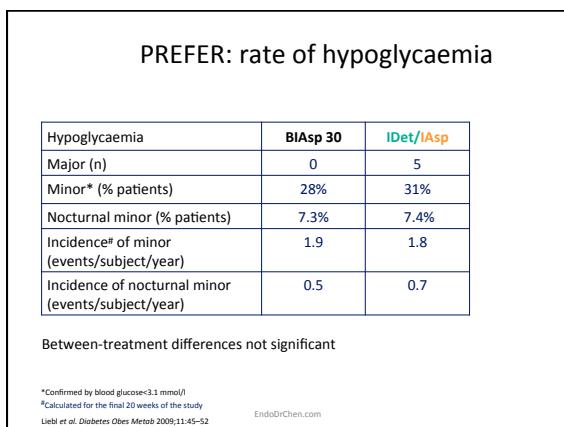
Optimizing and intensifying





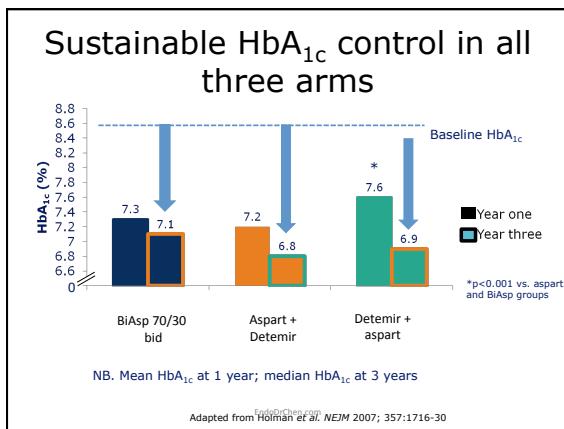
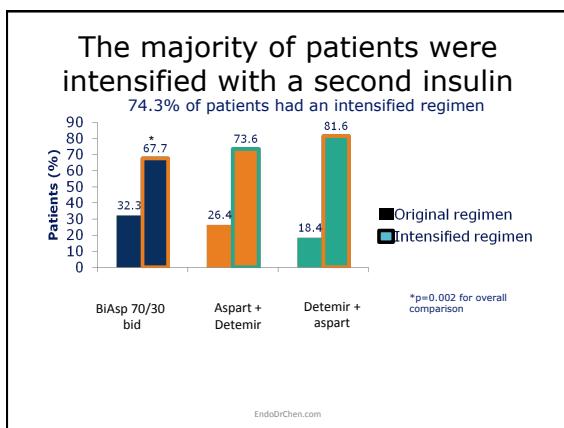
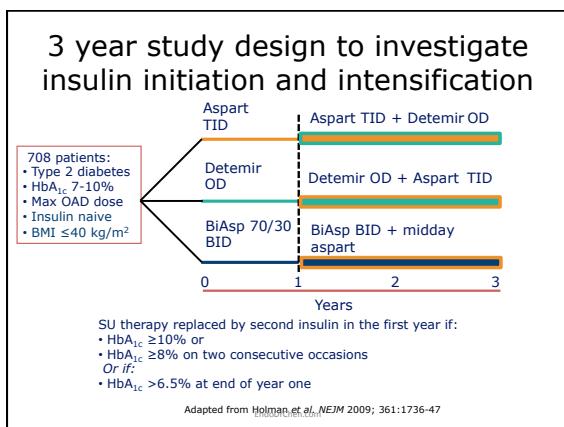


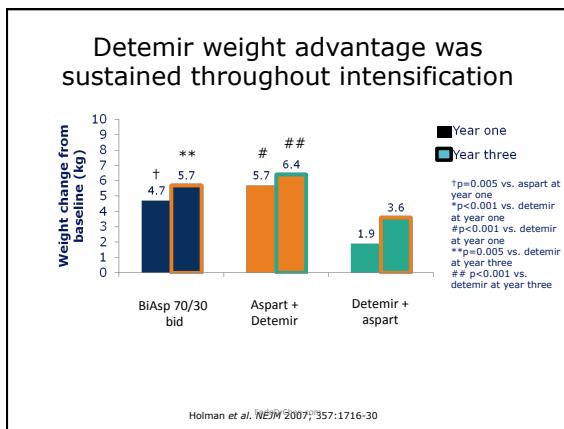
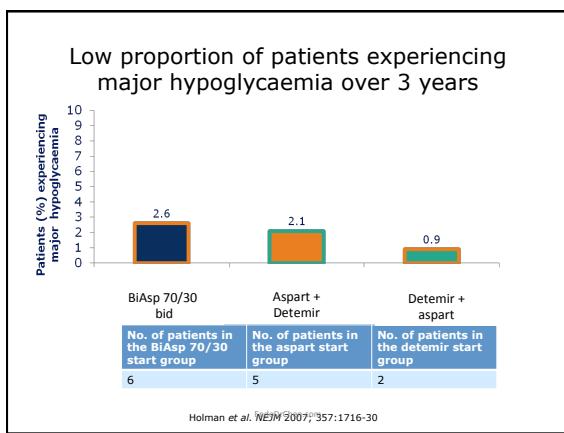
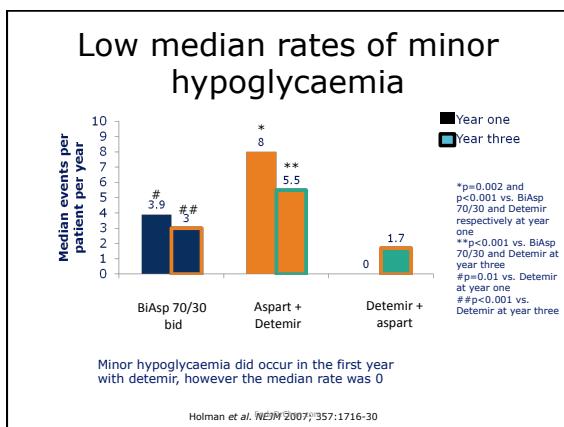


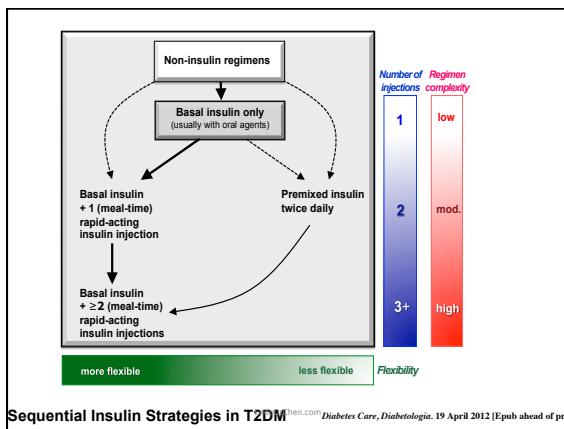


WHICH IS THE BEST STRATEGY?

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What are the benefits of pre-mixed insulin analogues?

- Good for patients moderately insulinopenic with: 1) not enough control with basal insulin and 2) does not require basal-bolus scheme
- Easier handling and less confusion for the patient
- Can be used as first insulinization instead of basal in type 2 diabetes
- Basal and Prandial coverage
- Mimics some insulin secretion phases (1st and 2nd)
- A second or third injection addition of biphasic aspart Mix 30 provides an additional benefit in terms of reduction in:
 - FPG, PPG and HbA_{1c}

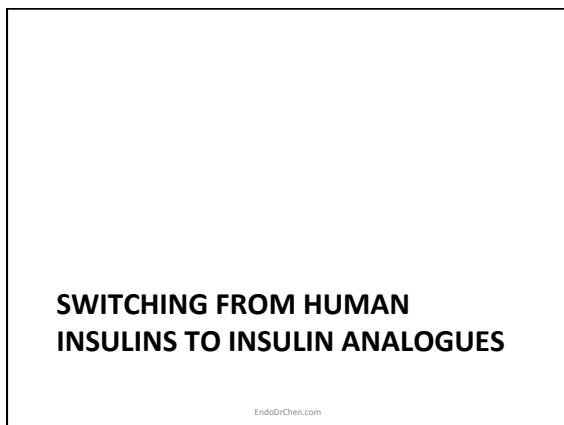
Garber et al. Diabetes Clin Res Metab 2006;8:58-66

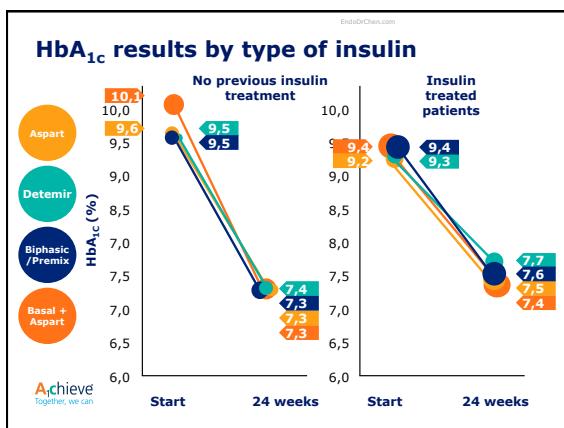
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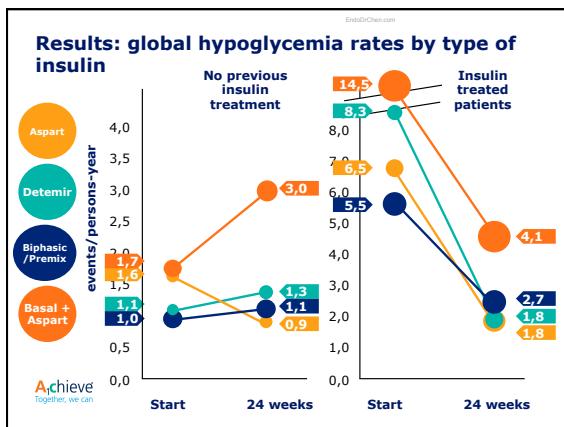
Basal-bolus: key advantage

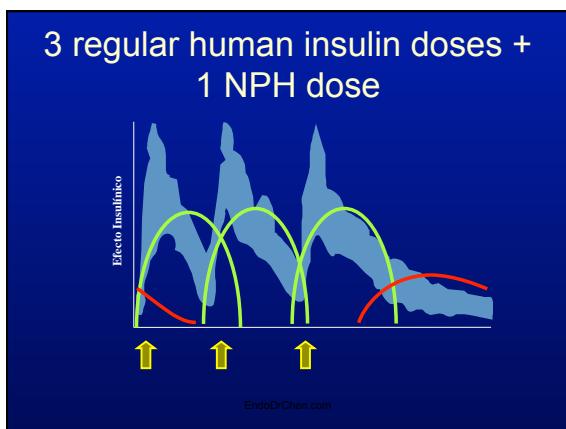
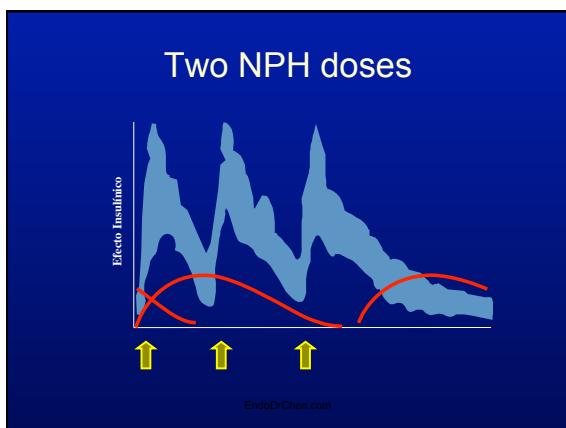
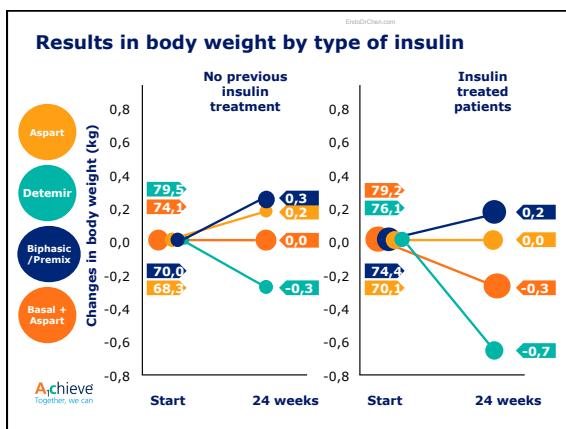
- Advantage:
 - Is more physiologic
 - Is the best for patients with type 1 diabetes or patients with type 2 with deep insulinopenia
- Consideration:
 - Requires motivation and care (patient)
 - Is a more complex treatment

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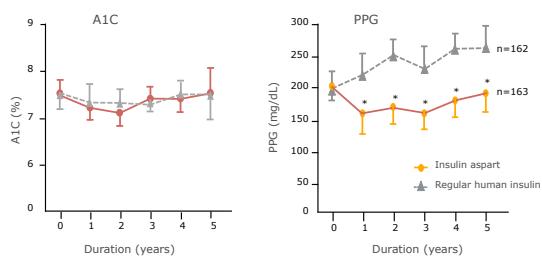




WHAT OTHER BENEFITS CAN WE EXPECT FROM ULTRARAPID INSULIN ANALOGUES?

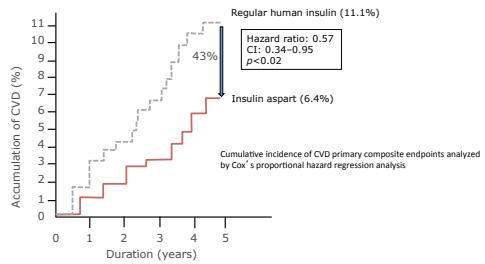
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A1C and postprandial glucose control



Nishimura et al. Diabetologia 2008;51(Suppl. 1):S543 (Poster 1349)

Long-term use of insulin aspart and effect on cardiovascular disease (CVD)



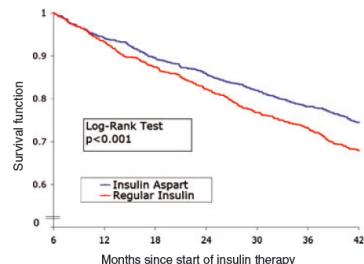
Nishimura et al. Diabetologia 2008;51(Suppl. 1):S543 (Poster 1349)

Lower incidence of recorded cardiovascular outcomes in patients with type 2 diabetes using insulin aspart vs. those on human regular insulin: observational evidence from general practices

Methods

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

Eventos cardiovasculares



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

Conclusions

- Natural history of type 2 diabetes will lead to insulinopenia so insulin treatment will be needed in most patients
- Treatment goals differ in each patient and this determines when is the right moment to start insulin
- Best strategy is to start with a basal insulin, then progress to a basal plus and then to a basal bolus

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Questions...
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