

Inhaled insulin is *not*
an expensive waste of breath

ABCD Spring Meeting 2007
Chester

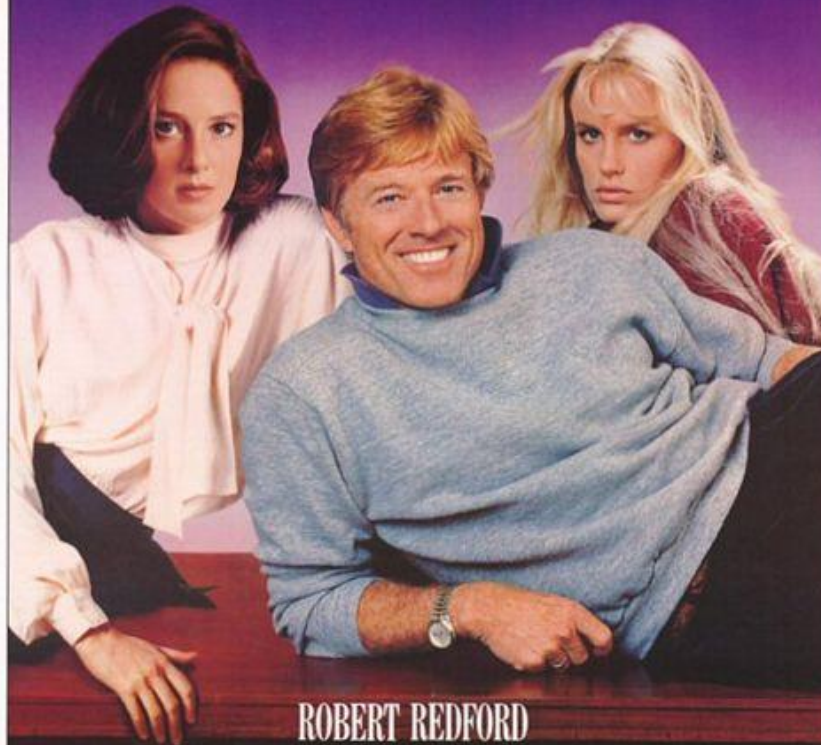
Stephen Gough

University of Birmingham

University Hospital Birmingham

NHS Foundation Trust

Tom Logan has a law partner who put a dog on the witness stand.
A client who can't enter a room without a crime being committed.
And a case that could turn out to be the murder of the year. His.



ROBERT REDFORD
DEBRA WINGER DARYL HANNAH

An IVAN REITMAN Film

LEGAL EAGLES

A NEW COMEDY FROM THE DIRECTOR OF GHOSTBUSTERS.

"LEGAL EAGLES" BRIAN DENNEHY TERENCE STAMP STEVEN HILL
Screenplay by JIM CASH & JACK EPPS, JR. Story by IVAN REITMAN & JIM CASH & JACK EPPS, JR. Production Design by JOHN DE CUIR
Director of Photography LASZLO ROVANS, A.S.C. Music by ELMER BERNSTEIN Executive Producers JOE MEDJUCK and MICHAEL C. GROSS
Produced and Directed by IVAN REITMAN "Love Youth" performed by Rod Stewart A UNIVERSAL PICTURES PRESENTATION

What I will demonstrate is that:

- **Inhaled insulin is another therapeutic option**
- **It will allow some patients to improve glycaemic control**
- **Improved glycaemic control will lead to reduced long term complications.**
- **Avoiding long term complications is better for the patient and is cost effective**
- **We owe it to our patients and ourselves to oppose the motion**

Inhaled insulin systems

Eli Lilly/Alkermes
System



Pfizer Exubera



Novo Nordisk AERx
System



Technosphere Mannkind



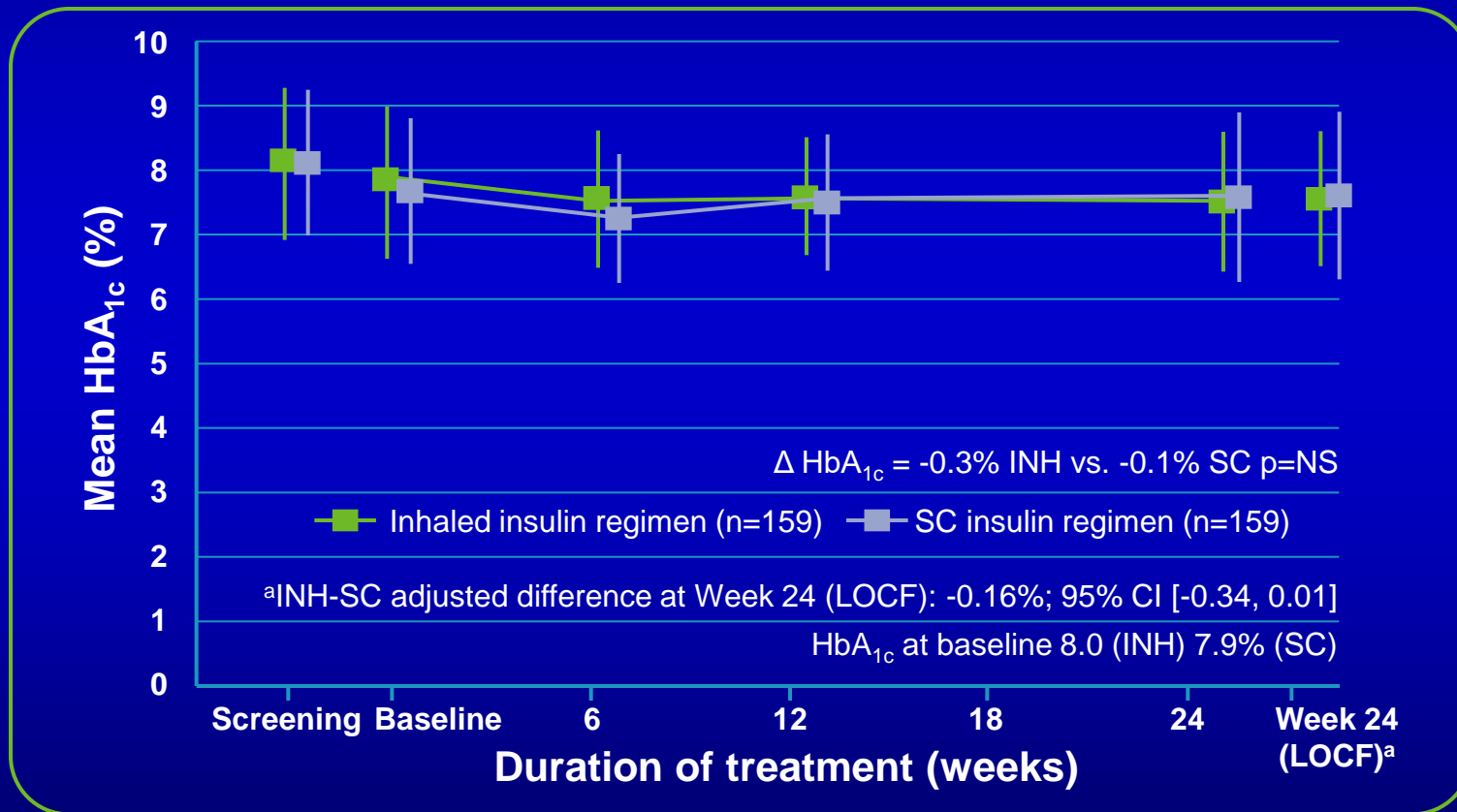
Exubera license

- **Exubera is indicated for:**
 - **The treatment of adult patients with type 2 diabetes mellitus not adequately controlled with oral anti-diabetic agents and requiring insulin therapy**
 - **The treatment of adult patients with type 1 diabetes mellitus, in addition to long or intermediate acting subcutaneous insulin, for whom the potential benefits of adding inhaled insulin outweigh the potential safety concerns**

NICE: TA 113

Exubera as effective as SC short-acting insulin

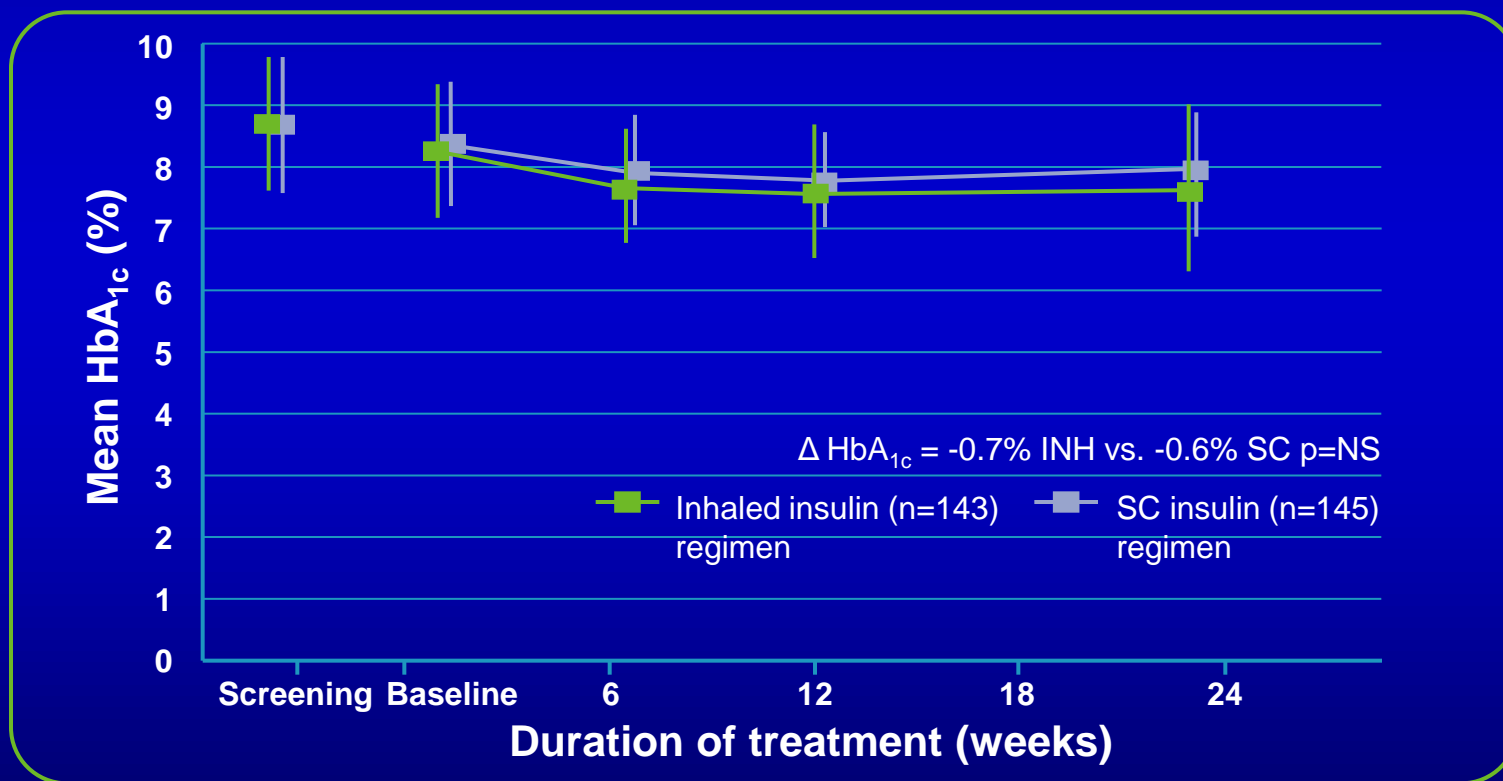
HbA_{1c} during 6 months' treatment with INH vs SC Insulin (mean \pm SD)



....and in Type 2 diabetes

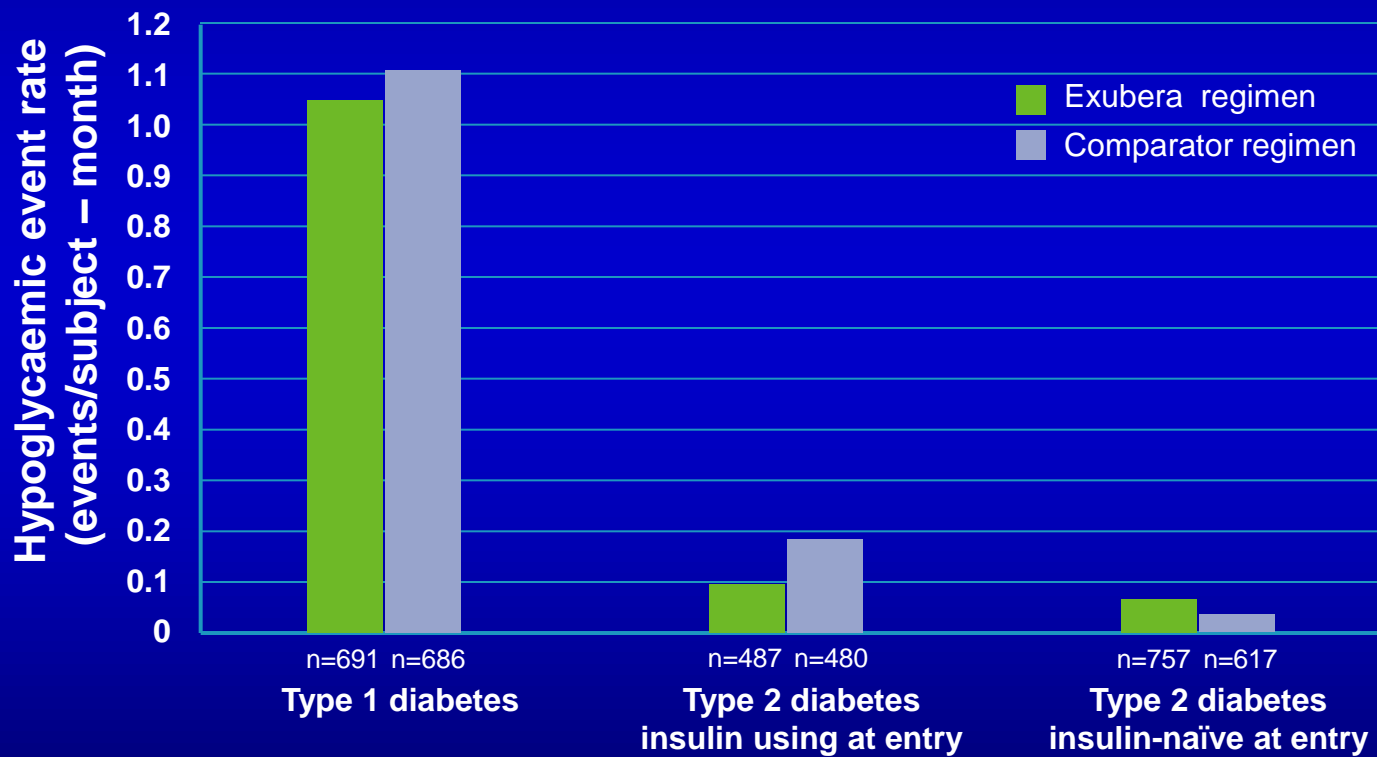
Exubera plus basal insulin compared to conventional SC insulin therapy

HbA_{1c} during 6 months' treatment with inhaled insulin vs SC insulin (mean \pm SD)



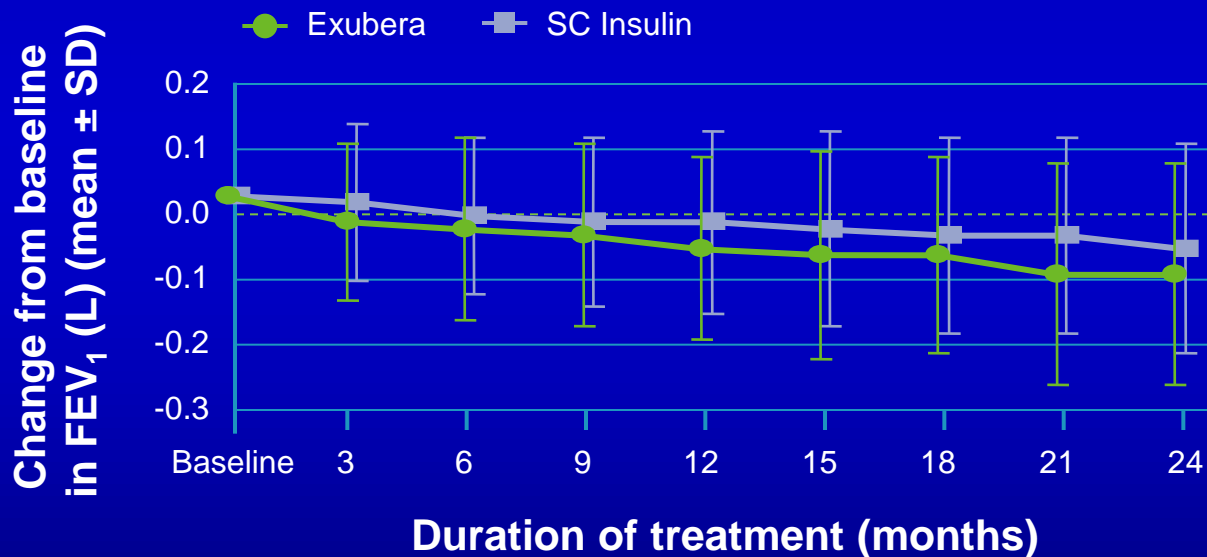
The basal insulins were once daily ultralente in the Exubera arm and twice daily NPH in the SC insulin arm

Hypoglycaemic events similar to short-acting SC insulin



FEV₁ 24 month extension data: Type 1 diabetes

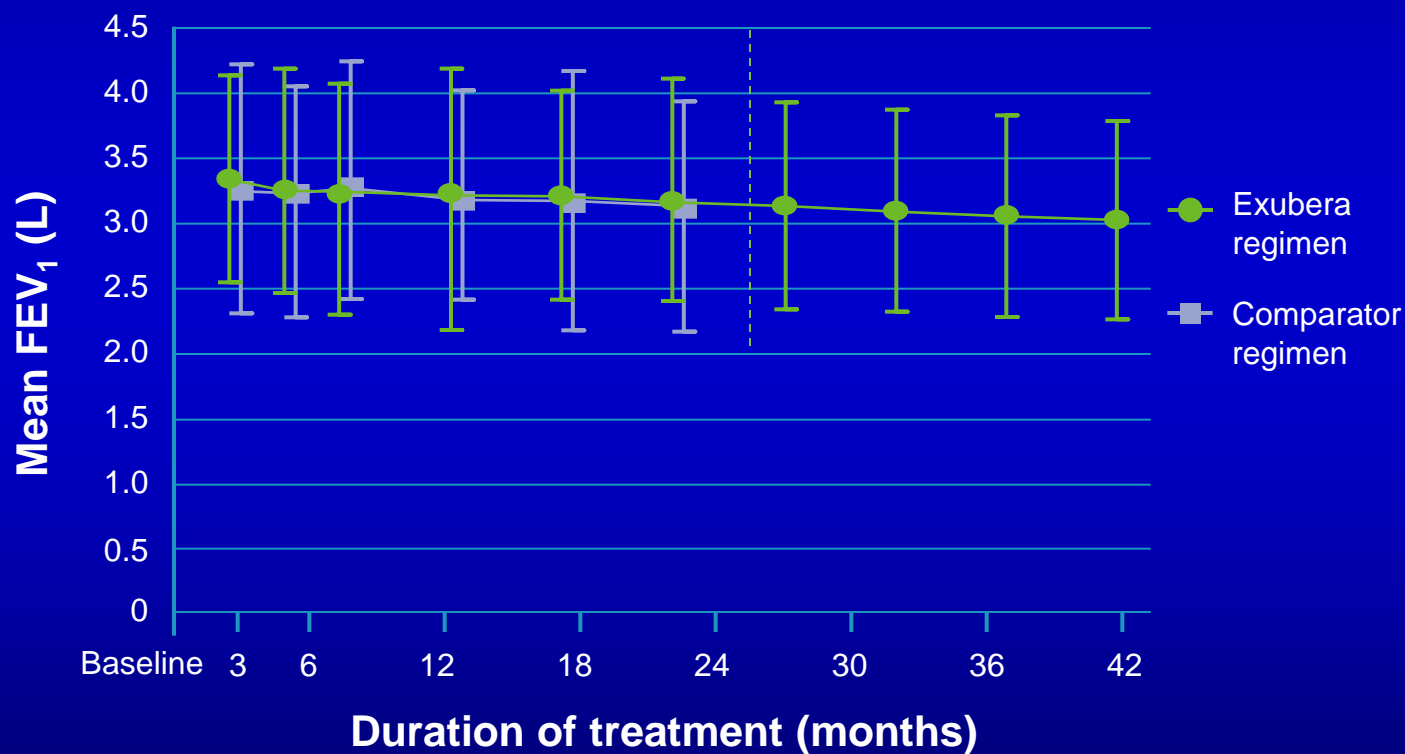
Exubera 3-24 months: - 0.041 L/y
SC insulin 3-24 months: - 0.031 L/y
Exubera-SC (90% CI): - 0.011 L/y (-0.023 to 0.002)



CI = confidence interval.

INH = inhaled insulin regimen SC = subcutaneous insulin regimen

FEV₁ extension data over 4 years



Open-label extension studies from 3 RCTs

NICE guidance

- **Poor glycaemic control despite other interventions and unable to initiate or intensify pre-prandial SC insulin therapy due to:**
 - 1. Persistent fear of needles/phobia**
 - 2. Severe/persistent problems with injection sites**
- **Type 1 and type 2 diabetes**
- **Not recommended for routine treatment**
- **Initiation by specialist**

How much does inhaled cost?

1mg (3U) with each meal	£25.19/month
3mg (8U) with each meal	£62.28/month
Insulin release units (IRU) box of 6	£3.04/month

Based on average weight (76.5kg, T1D and 83.7kg, T2D) and dose 13mg/day at unit cost £0.23/mg
annual cost of Exubera = £1102

Comparative Costs

- **Competact (Pio+Met)** £36.96/month
- **Avandamet (Rosi+Met)** £52.45/month
- **Rosiglitazone** £50.78/month
- **Exenatide** £68.24/month
- **Sitagliptin** £33.36/month

- **Novomix 5 x 3ml Flexpen** £32.00
- **Humalog 5 x 3 ml** £30.98

“A cynic is a man who knows the price of everything and the value of nothing”

Oscar Wilde



Why do we need inhaled insulin?

- **Alternative to injections**

 - Needle aversion/phobia**

 - Injection site problems**

- **Delay in insulin initiation**

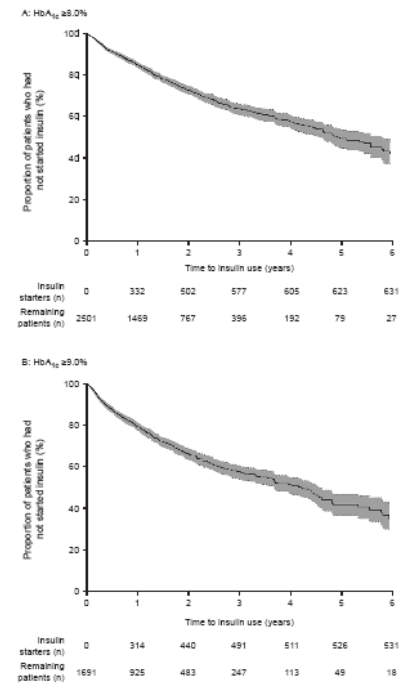
 - Increased risk of complications**

Delayed insulin initiation in type 2 diabetes in the UK

Health Improvement
Network (THIN) database
2501 T2DM OAD failure

25% patients insulin
delayed 1.8 years
50% patients insulin
delayed 5 years

Even in patients with
complications



Kaplan-Meier survival curves

Inertia to start insulin

- **Health Maintenance Organisation Study, USA**

Brown JB et al Diabetes Care 2004

- **GPRD study (HbA1c >7% 1988-2002, 79-76%)**

Fox KM et al Clin Ther 2006

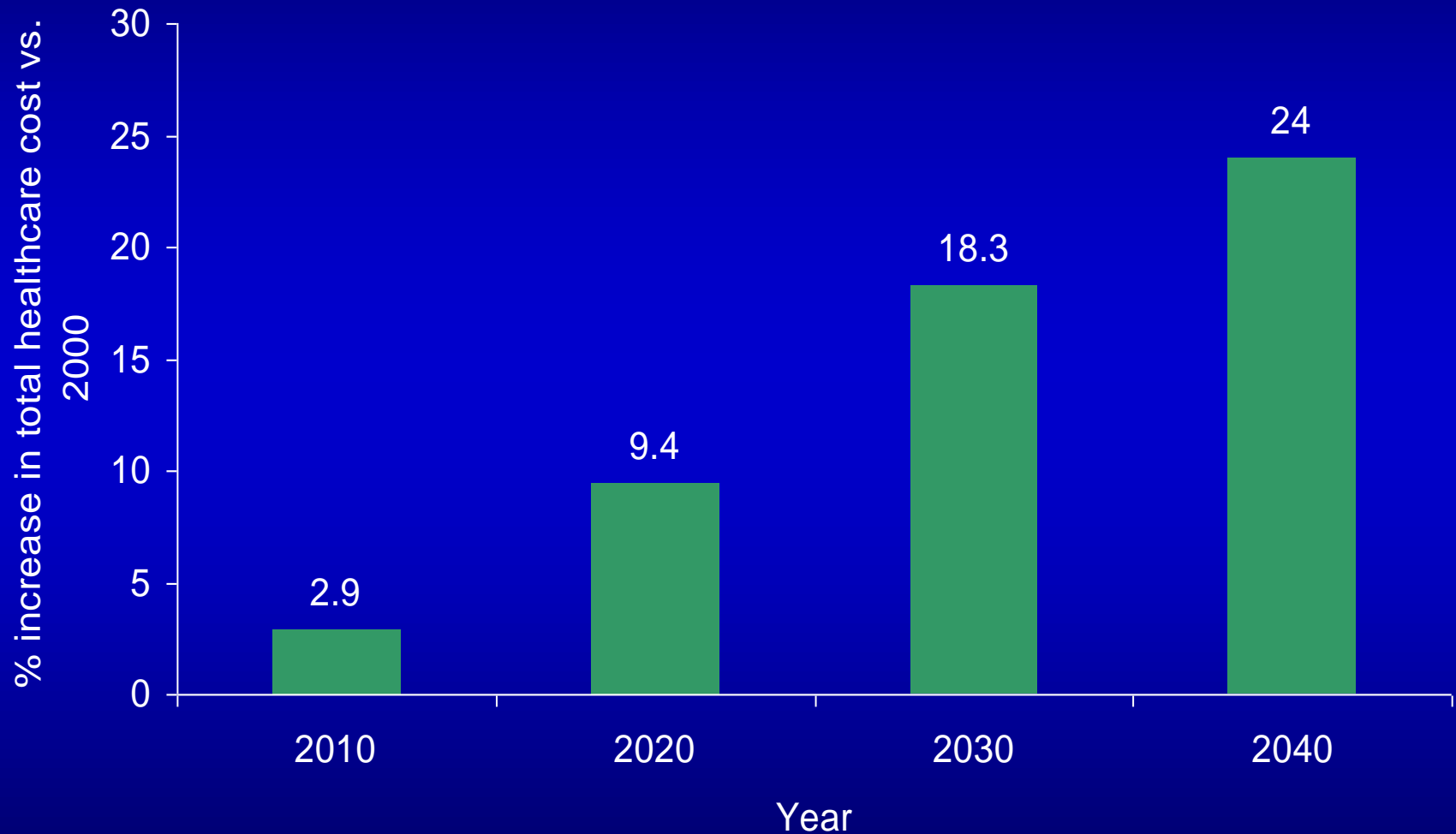
- **Psychological Insulin Resistance**

- Hypoglycaemia
- Weight gain
- Patient failure
- Needle anxiety

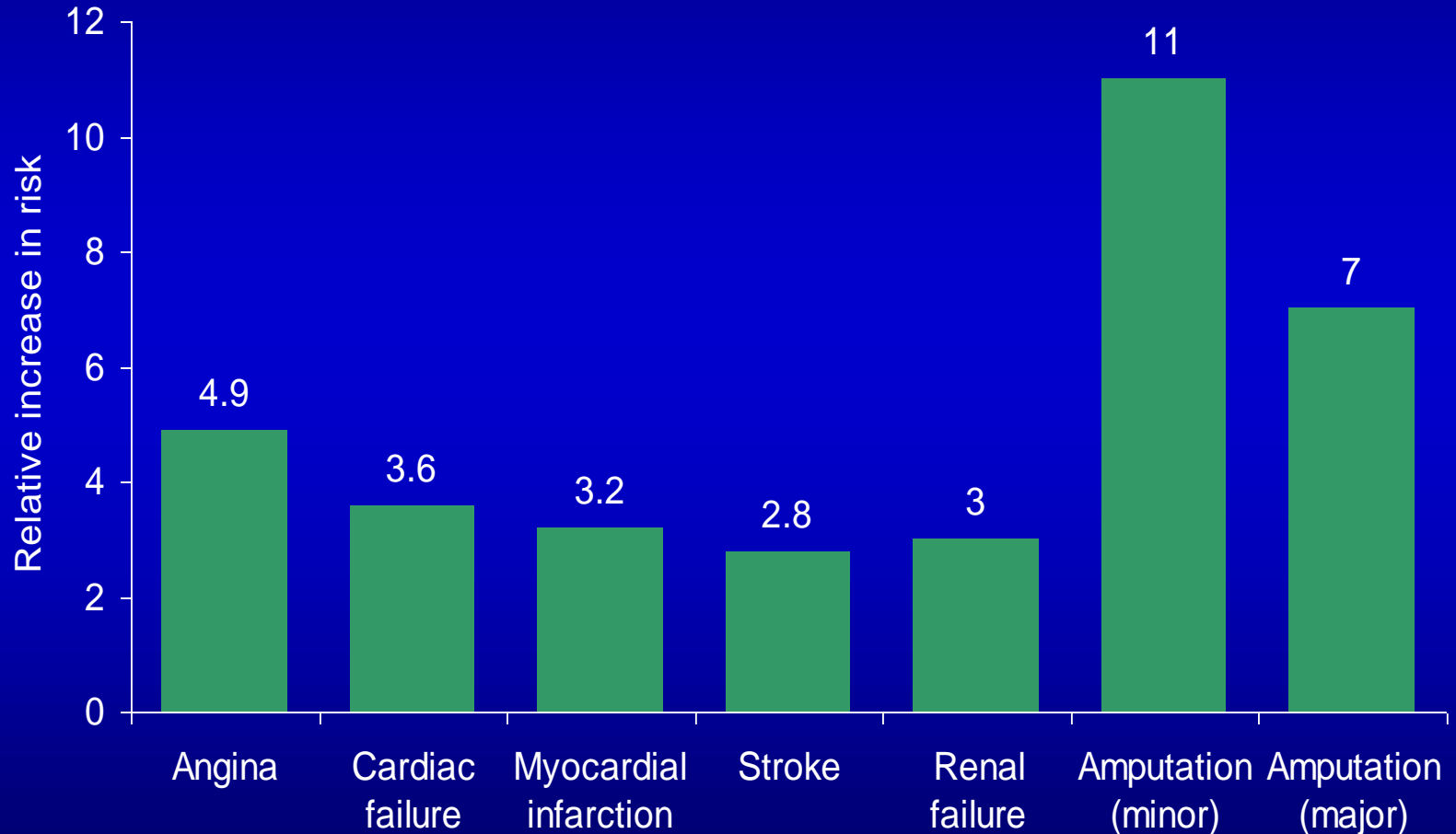
Hunt LM Diabetes Care 1997

Peyot M et al Diabetes Care 2005

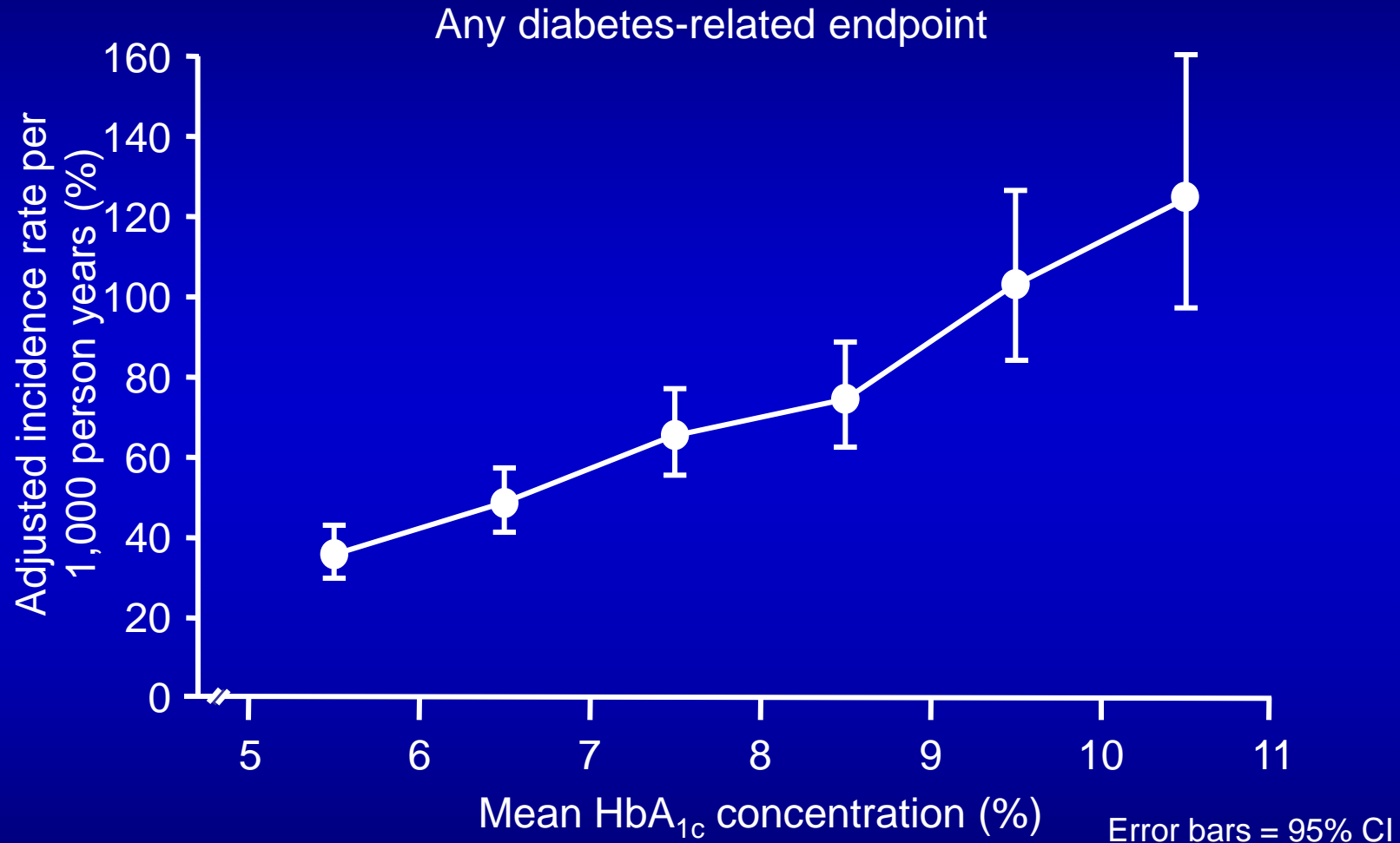
In the UK, the predicted healthcare costs of Type 2 diabetes will increase



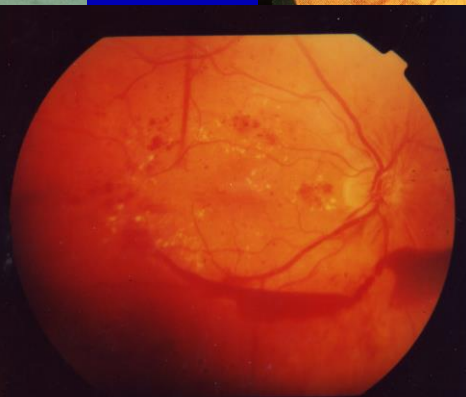
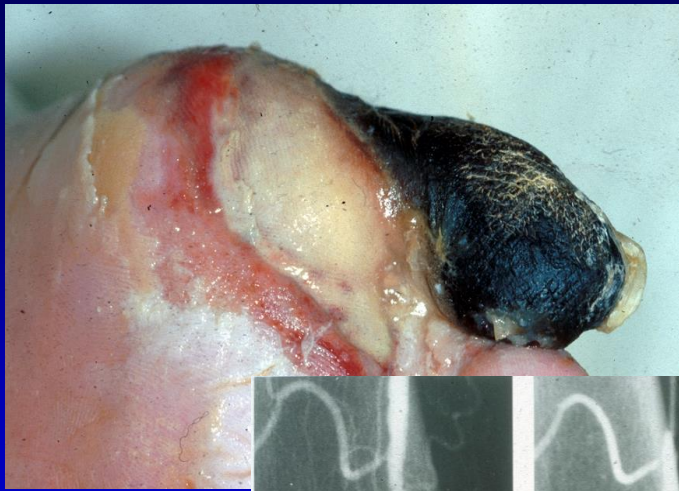
Type 2 diabetes increases the risk of serious morbidity



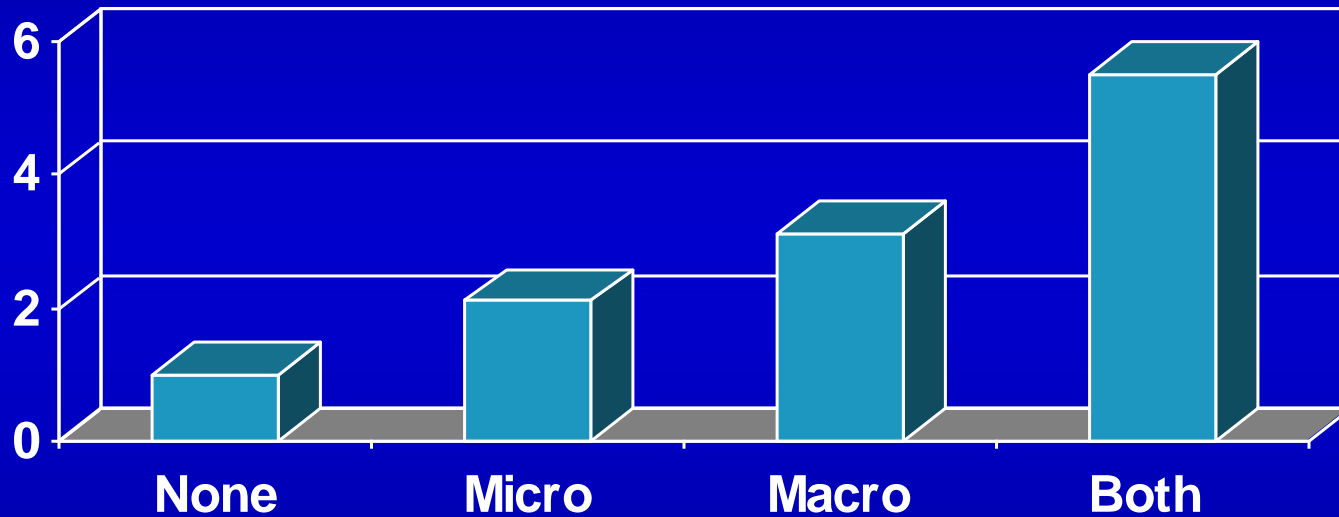
UKPDS: Correlation of HbA_{1c} with rates of complications



Adjusted for age, sex and ethnic group; expressed for white males, aged 50–54 at diagnosis, mean duration of diabetes of 10 years



Effect of complications on hospitalisation costs



Complication status



Direct annual costs of treating complications

Year	Number of complications	Average cost/ complication (£)	Total annual cost (£)
2006	864,000	2900 (2000-4000)	2.5 billion (1.7-3.5 billion)
2026	993,600	2900 (2000-4000)	2.9 billion (2.0-4.0 billion)

Assumptions

48% will have complications

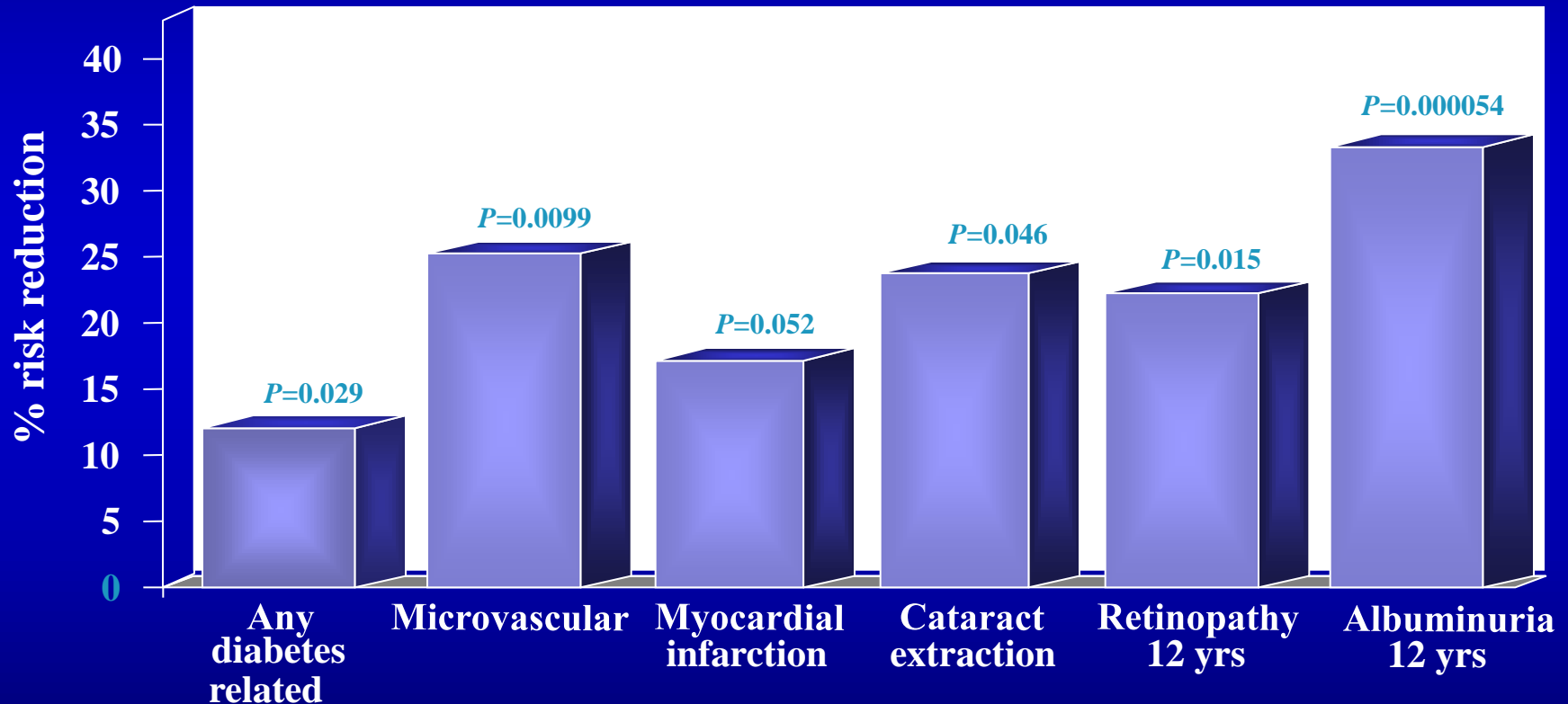
Diabetes prevalence increases by 15%

Costs in 2003, therefore underestimate

Overall costs of treating diabetes (2006)

- Number of NHS bed days 1.1 million
- Costs of complications £2.5 billion
- Average drug costs £592 million
- **Total health care costs £3.09 million**
- Social services £230 million
- Lost working days £418 million
- Premature death £113 million
- **Industry costs £531 million**
- **Total costs £3.851 billion**

UKPDS showed intensive glycaemic control reduces risk of complications



**Intensive therapy with a sulphonylurea and insulin.
Benefits of a 0.9% reduction in median HbA_{1c} over 10 years**

Improving compliance and glycaemic control

Syringes to pens



Other devices



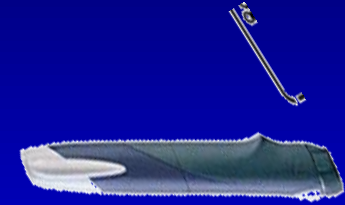
Some of the commonly used devices



NovoPen® 3



HumaPen® Luxura



HumaPen® Ergo



Autopen® 3 ml



Autopen® 24



Optipen® Pro

Re-usable

Prefilled



FlexPen®



Humalog® Pen



Optiset®

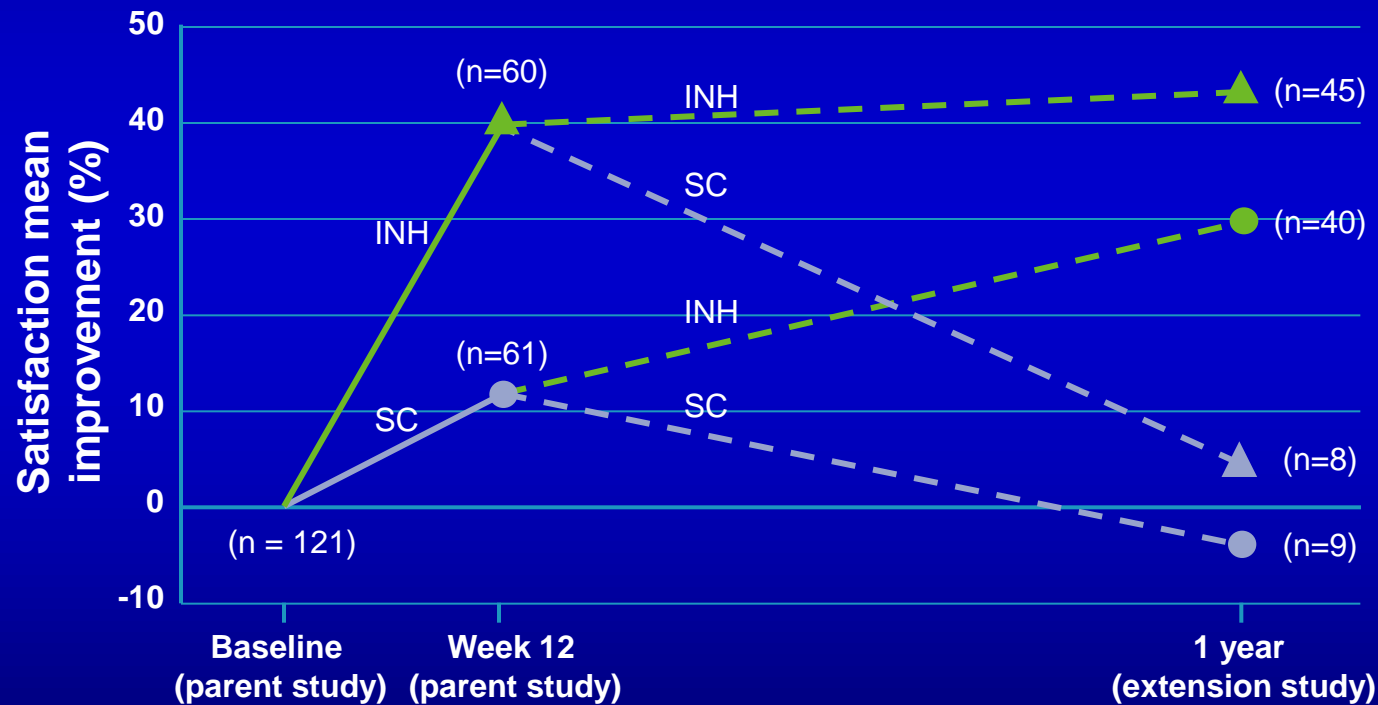
Advances lead to improvements and choice



Patients views

- **Greater patient satisfaction**
-
- **Patient preference for inhaled insulin**
- **Improved quality of life**

Patient satisfaction – 1-year data (convenience and social comfort)



INH = inhaled insulin regimen
SC = subcutaneous insulin regimen

So what are the real costs of treatment?

NICE appraisal (TA113): Cost effectiveness

- **Models**

“A probabilistic Monte Carlo simulation model using a modified Markov process with yearly intervals and a 20 year time horizon”

- **Utility gains**

- **Incremental cost effectiveness ratios (ICER)**

- **ICER/ Quality-Adjusted Life Year (QALY)**

- **Differences between Manufacturer and Assessment Group (based on sensitivity analyses and assumptions)**

Utility Gain: assessment

- **Generic measure of health status:EQ5D questionnaire**
 - **Mobility**
 - **Self care**
 - **Usual activities**
 - **Pain/discomfort**
 - **Anxiety/depression**
- **Time trade off method**
- **Utility decrements based on complications and 2 year insulin delay**

Utility Gain

- EQ5D questionnaire 0.02-0.04
- Time trade off method 0.04-0.08
- NICE used
no utility gain
0.02 and 0.04

QALY: quantification of cost effectiveness

- **>£30,000 proposed treatment unlikely to be cost effective**
- **£20,000-£30,000 a judgement needs to be made**
- **<£20,000 new treatment cost effective**

NICE Assessment Group Cost Effectiveness (ICER/QALY)

T2DM uncontrolled on basal insulin

Utility Gain 0.04

Utility Gain 0.02

£10,000 - £17,000

£21,000

T2DM OAD failure Met+SU+Glargine or Met+Premix

Utility Gain 0.04

£22,000 - £24,000

NICE Assessment Group Cost Effectiveness (ICER/QALY)

T1DM and T2DM unable to inject

Utility Gain 0.04

ICER <£25,000

Mr MG

- 76 years, T2DM 18 years
- HbA1c 9.5%, weight 92.8kg
- Gliclazide 160 mg bd
- Glargine 52 units OD (12 months)

- Hates needles, wife gives insulin

Mr MG continued

- **Started Exubera (5.2.07)**
- **4mg with each meal**
- **Reduced Gliclazide 80 mg bd**
- **Weekly telephone contact**

Mr MG continued

- Last seen: 16.4.07 (~10 weeks)
- Now on: Exubera 5mg, 4mg, 8mg
- HbA1c: 9.5 - 7.2%
- Weight: 92.8 – 94.6 kg
- Feeling: Happier!
(HBGM minor issue)

What is the cost of Exubera in Mr MG?

- Estimated mean cost of complications
- £1,498.71 v £1,810.22
- After 5 years ICER = £10,753.64

Well below £30,000!

What I have demonstrated

- **Inhaled insulin is another therapeutic option**
- **It will allow some patients to improve glycaemic control**
- **Improved glycaemic control will lead to reduced long term complications.**
- **Avoiding long term complications is better for the patient and is cost effective**

If we accept the motion

- **Stop innovation**
- **Reduce patient choice**
- **Deny a treatment option to reduce complications**

We owe it to our patients and ourselves to reject the motion

- **To provide the best possible treatment for our patients at all stages of the diabetes disease continuum**
- **We need choices**
- **We need specialists to help make choices**

What do we expect from inhaled insulin?

“Expectations were so high. Too high. Too high in a way for either of us.”

Tony Blair Thursday May 10th 2007

Inhaled insulin: a breath of fresh air!



Conclusions

- **Inhaled insulin, another option**
- **Exubera available, new systems soon**
- **As effective as SC prandial insulin**
- **Of benefit to certain type 1 and type 2 patients**
- **Patients like it**
- **Cost effective**