Are insulin analogs worth their cost in type 2 diabetes?

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Chair, Technology Appraisal Committee, National Institute of Clinical Health and Excellent (NICE), London
We cannot afford everything that is effective

"The NHS, just like every other healthcare system in the world—public or private—has to set priorities and make choices. The issue is not whether there are choices to be made, but how those choices are made. There is not a service in the world, defence, education or health, where this is not the case."

Rt Hon Alan Milburn MP, Secretary of State for Health, 1999
Parliamentary Select Committee on Health
NICE provides guidance to the NHS

Does this drug lower blood glucose?

Does this drug lower blood glucose better than what we already have?

Regulators tell Britain whether it CAN use a drug
NICE tell Britain whether it SHOULD use a drug
Adding a agent 3\textsuperscript{rd} in type 2 diabetes - UK

Generally:
• After metformin and sulphonylurea
• HbA1c $\geq 7.5\%$
• Preferably add basal NPH insulin at bedtime
• Continue with oral drugs
• Review use of sulfonylurea if hypoglycaemia occurs
• Consider biphasic insulin if HbA1c $>9.0\%$

Newer Drugs:
• Long-acting insulin analogues: glargine and levemir
• Incretins

Clinical effectiveness
“relevant comparator”
How do glargine and detemir compare to (human) NPH insulin?
Fixed budgets and ‘opportunity costs’

New diabetes drug

Other diabetes drug?
Diabetes education?
Diabetes nurses?
Alzheimer’s drugs?
Cancer drugs?
Hospice?

Willett, BMJ
Measure of effectiveness common to all diseases

Length of Life \times \text{Quality of Life} = \text{Quality-adjusted Life Years}

Adler 2012
Most trials don’t measure ‘QALYs’

\[ \Delta = \text{Difference between new and comparison therapy} \]

Requires modelling

\[ \Delta \text{ Quality Adjusted Life Year (QALY)} \]

\[ \Delta \text{ Length of Life} \]

\[ \Delta \text{ Diabetic complications} \]

\[ \Delta \text{ Risk factors for complications e.g. HbA1c} \]

\[ \Delta \text{ Quality of Life} \]

\[ \Delta \text{ Measure Quality of Life} \]

\[ \Delta \text{ Quality of life resulting from complications or from side effects} \]
UKPDS Outcomes Model

Uses utility equations estimated from UKPDS quality of life data to calculate Quality-Adjusted Life Years (QALYs)

- Age
- Sex
- Ethnicity
- Duration of diabetes
- HbA1c
- SBP
- Lipids
- Smoking

1: Angina (IHD)
2: CHD
3: Heart failure (CHF)
4: Stroke
5: Amputation
6: Blindness
7: Renal failure
8: MI death
9: Stroke death
10: Other death diabetes
11: Other death – non diabetes

Source: P Clarke and A Gray
A Adler Keystone 2012
# Results Effectiveness

## Long Acting Insulin Analogues vs. NPH Insulin

<table>
<thead>
<tr>
<th></th>
<th>Glargine vs NPH</th>
<th>Determir vs NPH</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glycemia ∆ HbA1c</strong></td>
<td>0.00%</td>
<td>0.08% (favours NPH)</td>
</tr>
<tr>
<td><strong>Weight ∆</strong></td>
<td>- 0.28 kg (not significant)</td>
<td>- 1.2 kg (significant)</td>
</tr>
<tr>
<td><strong>Severe hypoglycemia</strong></td>
<td>No difference</td>
<td>No difference</td>
</tr>
<tr>
<td><strong>Any hypoglycemia</strong></td>
<td>Odds ratio 0.74, 95% CI 0.63 to 0.89</td>
<td>Odds ratio 0.51, 95% CI 0.35 to 0.76</td>
</tr>
<tr>
<td><strong>Quality of Life from studies</strong></td>
<td>Not enough information in trials</td>
<td>Not enough information in trials</td>
</tr>
<tr>
<td><strong>Summary</strong></td>
<td>Glargine and detemir equivalent to NPH (and to each other) for glycemic control, but have modest advantages in terms of hypoglycemia</td>
<td></td>
</tr>
</tbody>
</table>
Levemir and slightly less weight gain

What is it worth?
Is it important to health?

What is it worth?

I Stock Photo
Adler 2012
“The most common side effect with levemir is hypoglycaemia”

<table>
<thead>
<tr>
<th>From Summary of Product Characteristics</th>
<th>“Very Common”</th>
<th>“Common”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detemir</td>
<td>Hypoglycaemia</td>
<td>Injection site reactions</td>
</tr>
<tr>
<td>Glargine</td>
<td>Hypoglycaemia</td>
<td>Lipohypertrophy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Injection site reactions</td>
</tr>
</tbody>
</table>
Calculating Cost Effectiveness
Incremental Cost Effectiveness Ratio = ICER

Cost £
QALY

*Costs include insulin, nurse time, adverse events, complications, annual diabetes care
Results Cost Effectiveness

Male, body mass index 30 kg/m², with complications

<table>
<thead>
<tr>
<th></th>
<th>Glargine</th>
<th>NPH</th>
<th>Net</th>
<th>Detemir</th>
<th>NPH</th>
<th>Net</th>
</tr>
</thead>
<tbody>
<tr>
<td>QALYs</td>
<td>8.258</td>
<td>8.253</td>
<td>0.006</td>
<td>8.259</td>
<td>8.253</td>
<td>0.006</td>
</tr>
<tr>
<td>Drug Costs</td>
<td>£7727</td>
<td>£5946</td>
<td>£1780</td>
<td>£8585</td>
<td>£5946</td>
<td>£2638</td>
</tr>
<tr>
<td>Total Costs</td>
<td>£18,778</td>
<td>£16,980</td>
<td>£1798</td>
<td>£19,621</td>
<td>£16,980</td>
<td>£2,641</td>
</tr>
<tr>
<td>Cost per QALY</td>
<td>£320,029</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Health Technology Assessment 2010; Vol. 14: No. 36*
What is the “value” of a QALY?
What is Britain willing to pay?

Probability of rejecting drug; ‘not good value for money’

Cost per QALY £

1

0

10,000 20,000 30,000 40,000 50,000

Glargine £320,029 per QALY
Levemir £417,625 per QALY
Recommendations Basal Insulin

• **Begin** with human NPH
• **Start** long-acting insulin analogues if:
  – assistance from a carer
  – long-acting insulin analogue would reduce the frequency of injections from twice to once daily
  – lifestyle restricted by recurrent symptomatic hypoglycemia
• **Switch** to long-acting insulin analogues if:
  – target HbA$_{1c}$ not reached because of significant hypoglycemia
  – significant hypoglycemia on NPH irrespective of level of HbA1c achieved

Source: NICE Clinical Guidelines 87
Important aspects of NICE process

- Clear Question
- Consultative
- Minimises conflict of Interest
The results of this report was that insulin analogues have not shown superiority over human insulin; hence no higher price is justifiable.

Peter Sawicki, former head of IQWiG

Adler 2012
“Emergency patients in the German city of Stuttgart will be rushed to hospital with extra speed and style in a luxury custom made Porsche ambulance”
From 2000 to 2009, annual NHS spending on "designer" insulin increased from £18m (12% of total insulin cost) to £305m (85% of total insulin cost)

- No corresponding improvement in HbA1c
- If half of those taking analogue insulins had been put on human insulin instead the NHS would have saved £250m over five years
- As a rough estimate, this money could have been spent on over 400 hospital consultants or 1,000 diabetes nurses in the same time period

Adler 2012
Why do doctors prescribe insulin analogues against guidance?

- Withdrawing cheaper insulins (Mixtard 30 – 90,000 users in UK)
- Providing more attractive devices
- Supporting hiring diabetes specialist nurses within public hospitals
- Teaching primary care doctors and nurses to start insulin “Insulin for Life” – (Sanofi); MERIT (Novo Nordisk)
- Aggressive (and sometimes questionable) marketing

How small changes led to big profits for insulin manufacturers

In the first of a series of investigations by the BMI and Channel 4 News, Deborah Cohen and Philip Carter discover why more expensive analogue insulins are increasingly prescribed instead of cheaper human insulin despite lack of evidence of benefit for patients with type 2 diabetes
“It’s time for diabetes doctors and nurses to take a long hard look in the mirror”

Prof Ken Paterson, Diabetologist and former Chair, Scottish Medicine Consortium, 2012
Position Statement
Analogue insulin (2012)
Diabetes UK

“The decision of which insulin is most appropriate should be made in consultation between the person with diabetes and their healthcare team and should follow NICE guidance i.e. human insulins should, in general, be tried as first line treatment, with analogues being introduced if optimal control cannot be attained.”
In type 2 diabetes:

- Well performed review shows that long-acting insulin analogues do not control blood glucose better than do human insulins.
- Modest benefits related to hypoglycemia.
- Given the prices the manufacturers currently choose to charge, long-acting insulin analogues do not represent good value for money in type 2 diabetes.
- NICE guidance recommends starting most, but not all, people with type 2 diabetes on NPH insulin.
- Human insulin permits freeing up resources to make (greater) health gains elsewhere in diabetes or elsewhere.
Thank you