

In adolescents with poorly controlled type 1 diabetes mellitus, could a bionic, bihormonal pancreas provide better blood glucose control than continuous subcutaneous insulin infusion therapy?

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# The Question

Miss E. is a 14 year old girl with poorly controlled type 1 diabetes mellitus. She is currently using the insulin infusion pump but has had frequent hypoglycaemic events, particularly at night.

Could the introduction of the automated pancreas improve her blood glucose control and would this provide more long term benefit, compared to her current treatment?

<b>P</b>	Adolescents with poorly controlled type 1 diabetes mellitus (T1DM)
<b>I</b>	Bionic, bihormonal pancreas
<b>C</b>	Continuous subcutaneous insulin infusion (Insulin pump therapy)
<b>O</b>	<ul style="list-style-type: none"><li>• Mean blood glucose level</li><li>• Incidence of hypo- or hyperglycaemic events</li></ul>

# The search and search results

- **Pubmed (with clinical trial filters)**

**SEARCH:** bionic pancreas OR artificial pancreas OR automated pancreas AND type 1 diabetes mellitus AND adolescents

- 59 Therapy (Clinical Study Categories)

- 1 Systematic review

We chose:

**[Outpatient glycaemic control with a bionic pancreas in type 1 diabetes – Russell, NEJM, 2014](#)**

Qu: *How effective is glycaemic control using a bionic bihormal pancreas compared to insulin-pump therapy in adolescents with T1DM over 5 days in a outpatient setting?*

(#1 on: Pubmed and Scopus and Cochrane with same search terms)

**SEARCH:** Continuous subcutaneous insulin infusion therapy AND ... as above.

- 305 therapy (Clinical Study Categories)

- 15 Systematic reviews

- **Cochrane Library**

**SEARCH:** Type 1 Diabetes Mellitus AND Glucose Control

- 8686 Cochrane reviews

We chose:

**[Intensive glucose control versus conventional glucose control for type 1 diabetes mellitus – Fullerton et al, 2014](#)**

Qu: *Does Intensive glucose control in T1DM have any effect on long term complications compared to conventional glycaemic targets, and does aiming for normoglycaemia provide additional benefit?*



# We also looked at...

## **A prior paper by the same group:**

Autonomous and continuous adaptation of a bihormonal **bionic pancreas** in adults and adolescents with type 1 diabetes.

*Is a bihormonal system beneficial in T1DM compared to an insulin only model? (Does a system able to respond to a carbohydrate load have a better outcome re plasma glucose control?)*

## **A different group's perspective:**

The "Glucositter" overnight **automated** closed loop system for type 1 diabetes: a randomized crossover trial.- Nimri et al, 2013

*Is a "closed loop" artificial pancreas able to control nocturnal glucose levels in T1DM patients better than insulin-pump therapy?*

## **Background (setting the scene for the use of an artificial pancreas):**

Fully integrated artificial **pancreas** in type 1 diabetes: modular closed-loop glucose control maintains near normoglycemia. – Breton et al, 2012

*Can combining Continuous Glucose Monitoring with an insulin pump, to form a closed-loop control artificial pancreas, optimise glycaemic control better than insulin-pump therapy over a 22 hour period of simulated "normal" life?*



# The Study Appraisal

## Recruitment:

- 1 year history of T1DM on insulin pump therapy.
- Age 12-21
- Attending Diabetes Summer Camp (NB. Likely to be more aware of diabetes control etc)
- Excluded individuals unaware of hypoglycaemia episodes (NB excluding potential target group)

## Randomisation:

- In blocks of two

## Measurement:

- Unblinded
- Plasma glucose and finger-prick glucose, plus number of hypoglycaemic events and carbohydrate interventions.



# The Study Appraisal

Study	Good Points	Bad Points
Russell et al, NEJM, 2014	Adolescent age group	Paracetamol interferes with glucose monitoring
Study	Good Points	Bad Points
Nimri et al, 2013	Randomised, multicentre,	Small sample size
Study	Good Points	Bad Points
Breton et al, 2012	Randomised cross-over trial	Small sample size
	Monitoring included over meals, overnight and with 30 mins	Inpatient setting
Study	Good Points	Bad Points
Fullerton et al, 2014	Systematic review of 12 trials	Very different patient groups included
	Majority of evidence from younger patients in early T1DM stages	
	Multiple databases searched	

# The Results

## Russel et al

- Not much difference in blood glucose control during the day
- Statistically and clinically significantly fewer carbohydrate interventions to prevent hyperglycaemia:

**97 carbohydrate interventions versus 210**

- The bionic pancreas was much better than infusion-pump therapy overnight for both glucose average and % time in normal range:

**mean glucose level on continuous monitoring**

**$6.9 \pm 0.6$  vs.  $8.7 \pm 2.0$**

**time within normal range for plasma glucose**

**$86.9 \pm 8.1$  % vs.  $66.7 \pm 19.9$  %**

- Bionic pancreas was also clinically significantly better at keeping glucose below 9.3mmol/L, which is needed to keep glycated Hb below 7%:

**31/32 versus 23/32**

- Likely to have more benefits to adolescents who are less aware of hypoglycaemic episodes or those with less diligent glucose monitoring.



# This is backed up by:

## Nimri et al results:

- “closed loop MD-logic artificial pancreas” was better than insulin-pump therapy for preventing nocturnal hypoglycaemia
- Statistically and clinically significantly more time spent in normal glucose range
- Less glucose variability using the artificial pancreas.

## Breton et al results:

- Increased % of time in normoglycaemia
- Statistically and clinically significantly reduced incidence of hypoglycaemia 2.7 fold

## Fullerton et al results:

- Intensively controlling glucose significantly reduced the risks of retinopathy, nephropathy and neuropathy
- but had little effect once these were manifest.



# The Implications for Miss E.

The bionic pancreas is likely to improve blood glucose level and range, particularly at night, and is very likely to improve glycated haemoglobin level.

This will reduce her relative risk of complications associated with T1DM.

If the bionic pancreas becomes available, we would recommend this in Miss E.'s case.

