New Insulin Injection Technique & Smart Insulin Pump Therapy in children

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Highlights

- Insulin Injections techniques
  - Syringe
  - Pens
  - I-Port
- Insulin Pump
  - Evolution of insulin pump
  - Advantage/ disadvantage of CSII
  - Smart pumps
- Future of pumps
- Artificial Pancreas

The Miracle of Insulin

Patient J.L., December 15, 1922

February 15, 1923

With Out Insulin

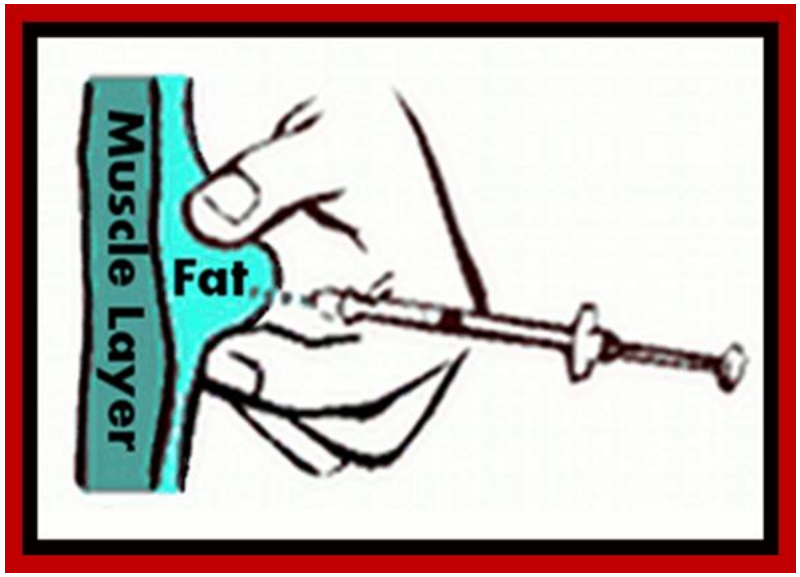
With Treatment of Insulin

Insulin Syringes

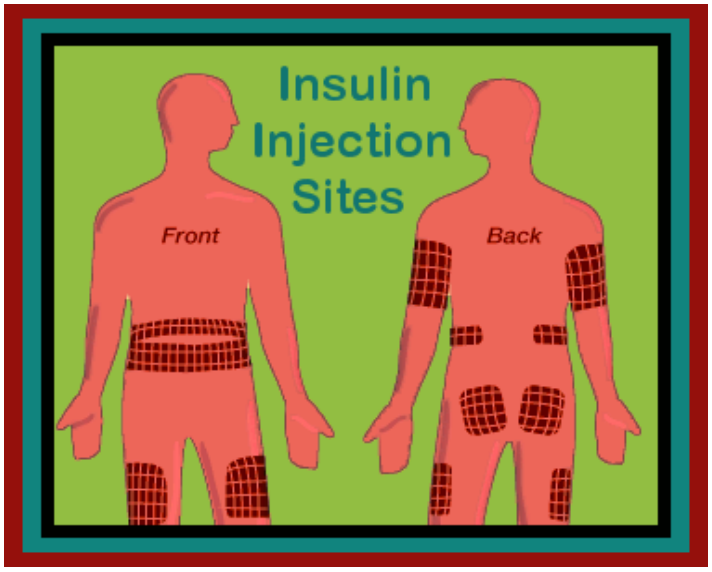
- U-30
- U-50
- U-100
- **One time, one person use only!**

Needle size does matter…

Where to Give Insulin: On Target!

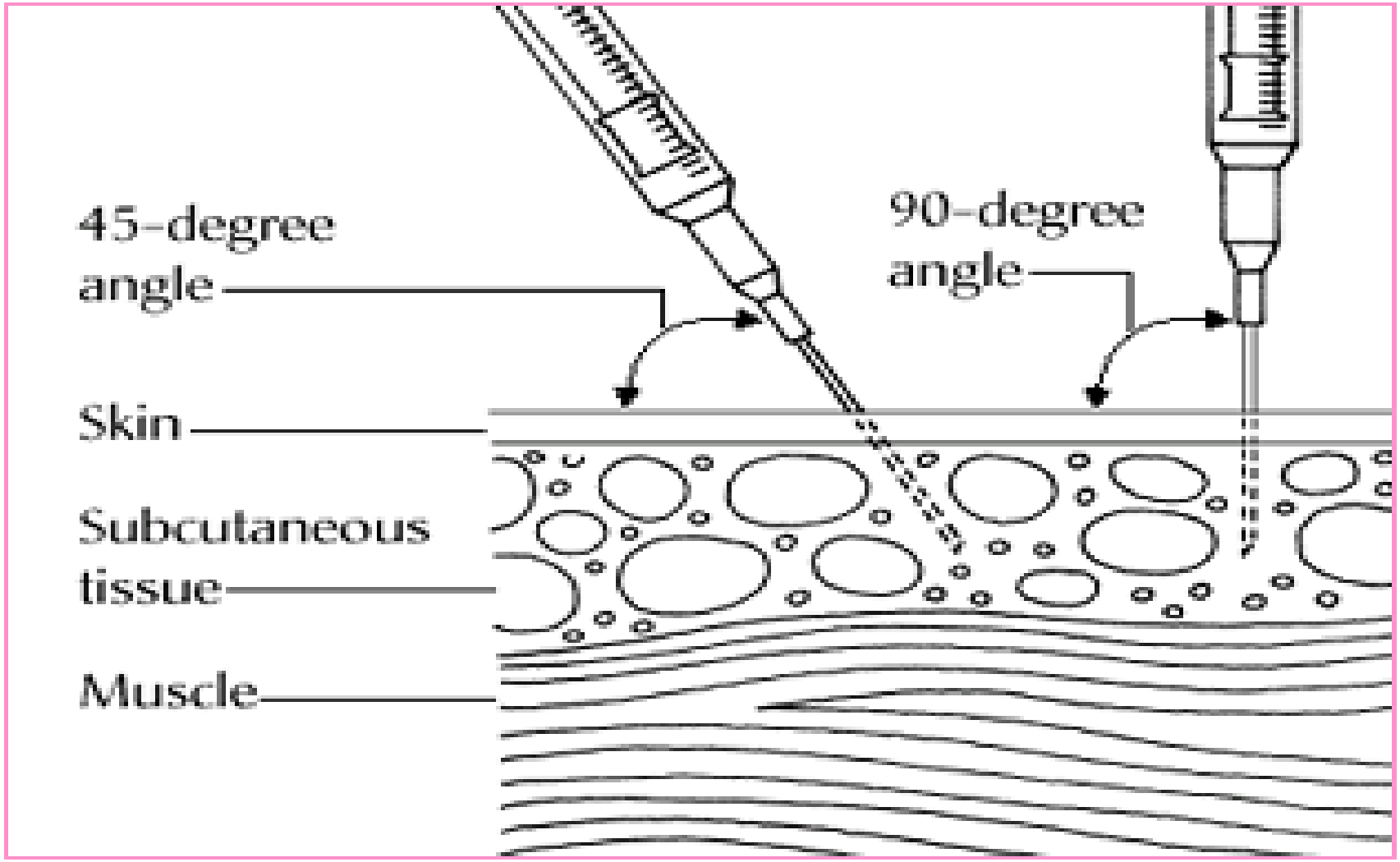


- Inject into fat layer under skin
- Rotate sites



- Common sites: abdomen, thigh buttocks, upper arms

Insulin Injection Technique

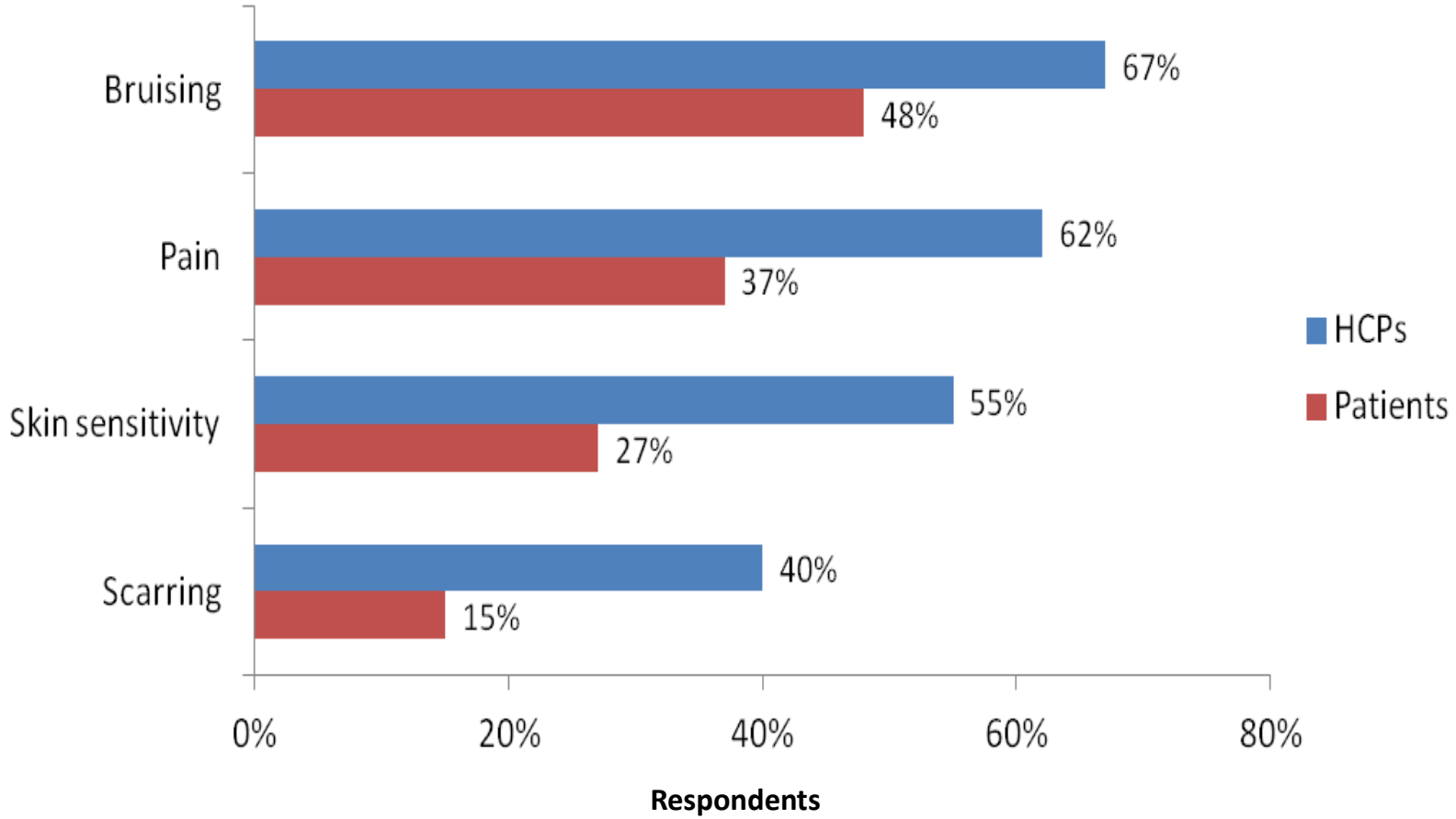


Insulin Delivery Devices

- Syringe
- Pump
- Pen Device

Unmet Need in Patients Requiring Daily Subcutaneous Injections

Physical consequences of daily insulin injections, as reported by patients and their HCPs*[1]

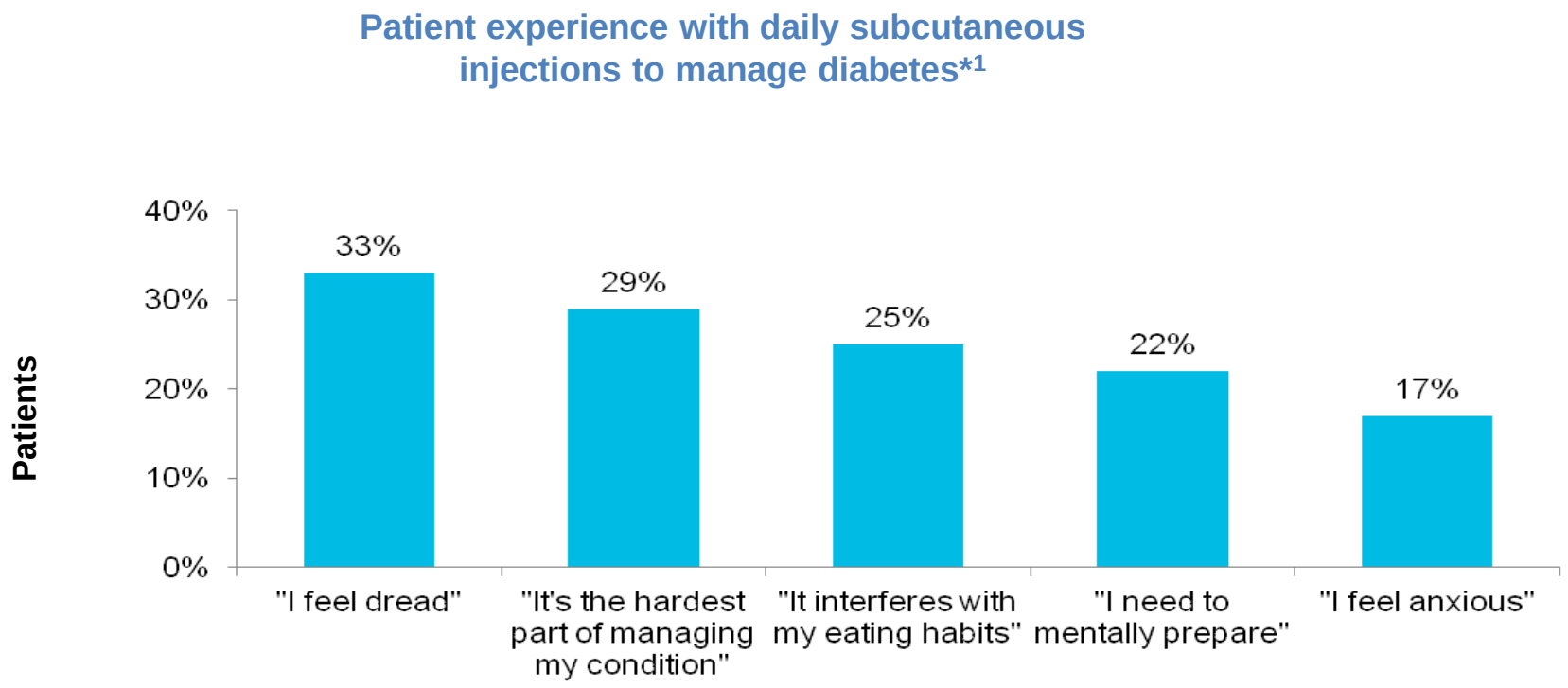


- Nearly half of all patients requiring daily injections report bruising – and more than one third report pain – as a result of daily subcutaneous injections*[1]

*Survey of 502 patients and 301 HCPs in the US in 2008, in which the impact of daily insulin injections was investigated
HCP=healthcare professional

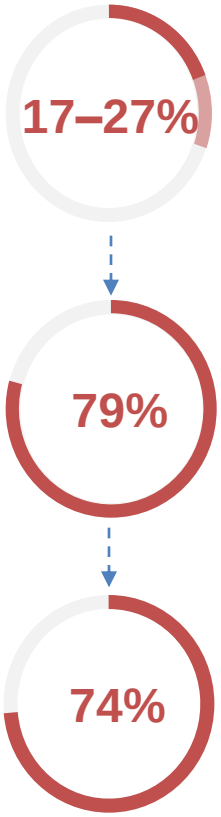
1. American Association of Diabetes Educators. Injection impact report. http://www.injectionimpact.com/index.html. Published 2008. Accessed May 1, 2015

Patients and HCPs report a variety of psychological issues with daily subcutaneous injections



Children and their parents fear injections

8% of children and adolescents with type 1 diabetes, and 17% of their parents, have pronounced needle phobia



Initiation

diabetes patients are **reluctant to initiate** insulin therapy*

Adherence

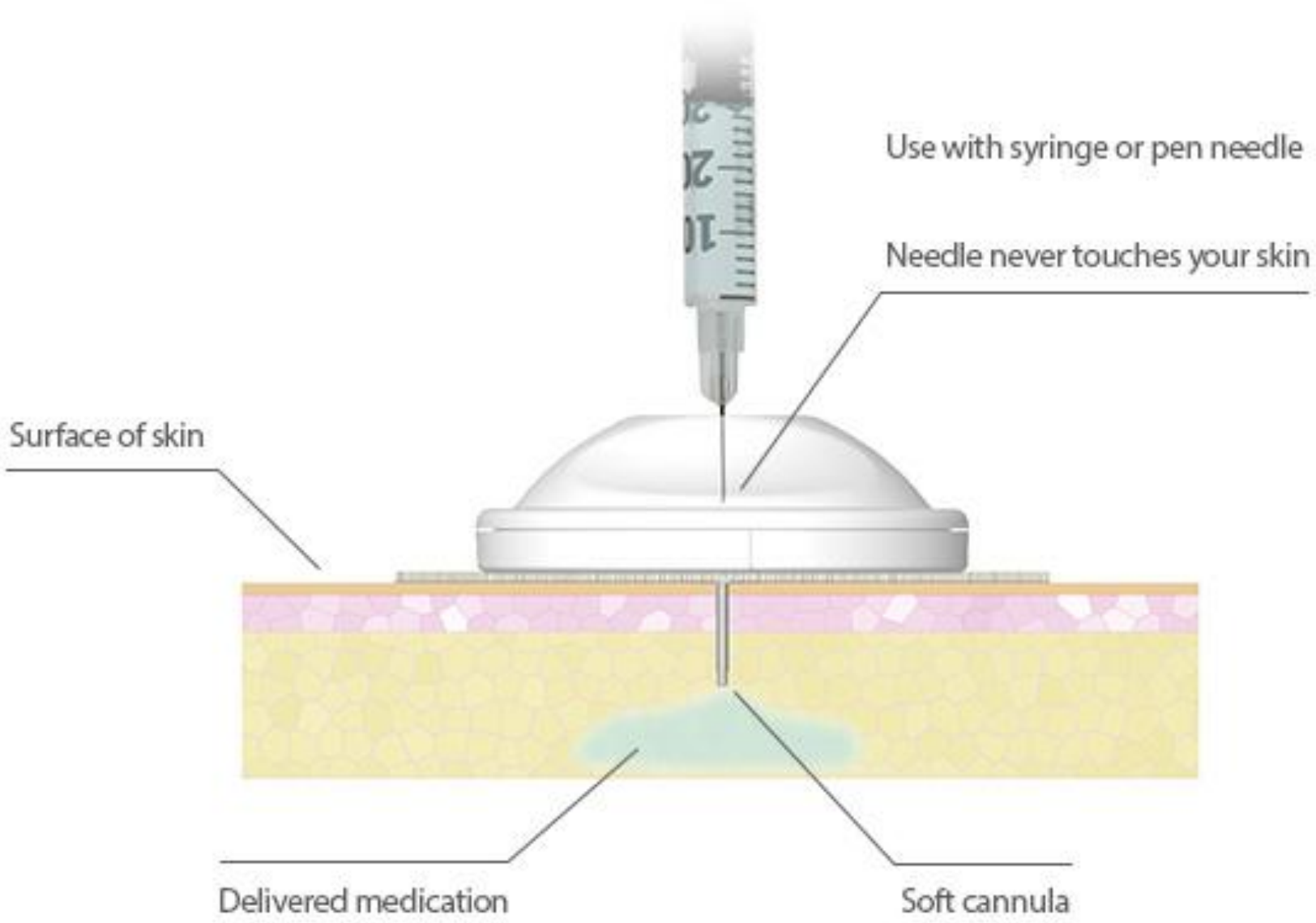
of physicians state that diabetes patients **skip injections** “at least sometimes

Continuation

Children who **discontinue** insulin therapy do so for reasons relating to the insulin injection itself

Value summary

The value of i-Port Advance® in patients requiring daily subcutaneous injections



No needle remains under the skin

Unmet need with insulin injections/ Pens

- There is a need for new injection technologies to reduce the pain, stress and adherence issues associated with daily subcutaneous injections

Technological advancements with i-Port Advance

- i-Port Advance – an FDA-approved subcutaneous injection port – is inserted with a single skin puncture, after which no more punctures are required for 72 hours

Clinical benefit of i-Port Advance

- In patients requiring daily subcutaneous injections, injection ports – such as i-Port Advance – significantly improve disease control, and quality of life, compared with standard injections

Economics of daily subcutaneous injections

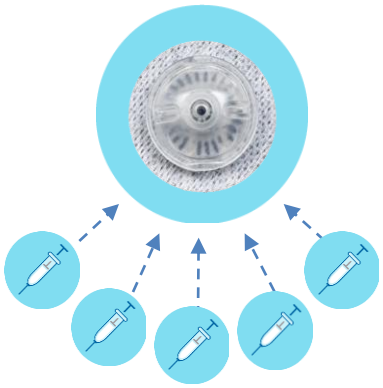
- Injection ports – such as i-Port Advance – may improve adherence and disease control compared with standard injections, leading to substantial reductions in healthcare resource use and costs

Technological Advancements with i-Port Advance

i-Port Advance®

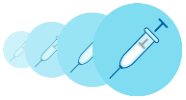
FDA cleared*

For use in patients who receive **multiple daily subcutaneous injections** of physician-prescribed medications



Practical

Can be used for up to **72 hours** to accommodate up to **75 injections**[1]



75 injections

Versatile

Can be worn

- at **home**
- while **exercising**
- while **sleeping**
- when **washing**

*FDA clearance is granted when the FDA has determined that the medical device is substantially equivalent to another legally marketed device

FDA=Food and Drug Administration

1. Medtronic MiniMed, Inc. i-Port Advance. http://www.medtronicdiabetes.com/treatment-and-products/i-Port Advance. Published: 2015. Accessed: May 1, 2015

i-Port Advance®

Number of skin punctures required in thirty days using i-Port Advance versus standard injection*[1]

Month **without i-Port Advance**

S	M	T	W	TH	F	S
4	8	12	16	20	24	28
32	36	40	44	48	52	56
60	64	68	72	76	80	84
88	92	96	100	104	108	112
116	120					

120 skin punctures

Month **with i-Port Advance**

S	M	T	W	TH	F	S
1			2			3
		4			5	
	6			7		
8			9			10

10 skin punctures

*Assuming four injections per day

1. i-Port Advance. i-Port injection port mitigates problems identified by injection impact report. Medtronic MiniMed, Inc. 2014

Clinical Benefit of I-Port Advance

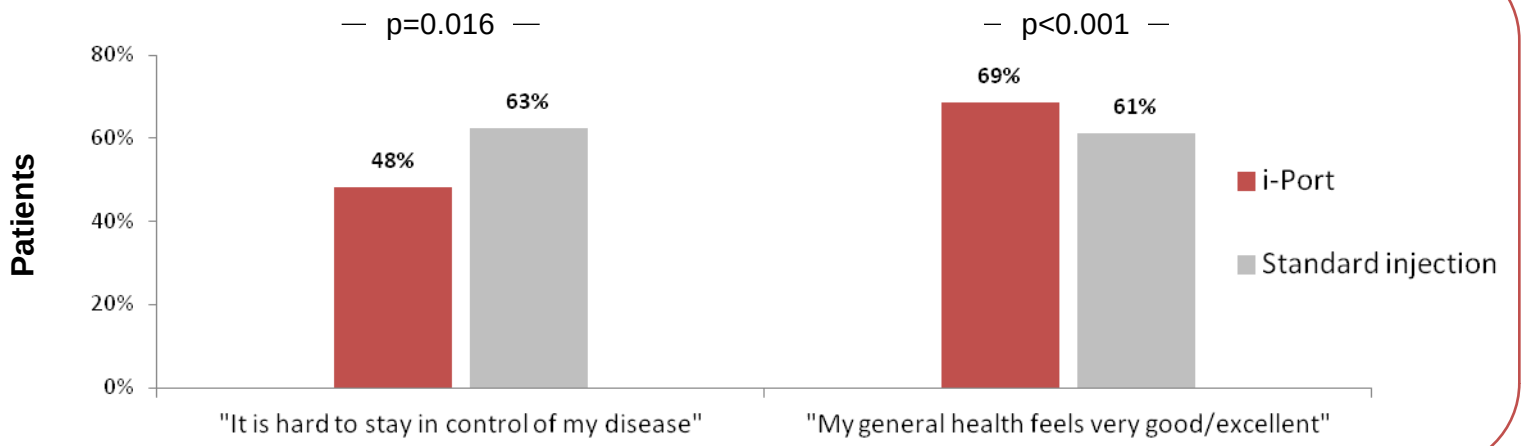
69% of patients felt **i-Port was useful and helped manage their condition**

68% of patients **forgot they were wearing i-Port**

71% of patients thought **using i-Port was not difficult**

- Using i-Port significantly improved patient-reported disease control and general health versus standard injection*[1]:

User experience with i-Port versus standard injection[1]



*Multicenter, randomized, prospective, controlled, open-label, two-period crossover study investigating the function of i-Port versus standard injections in 74 patients with diabetes

1. Blevins T, Shwartz SL, Bode B et al. A study assessing an injection port for administration of insulin. *Diabetes Spectr.* 2008;21(3):197–202

Significantly lower perception of pain

when using injection ports versus standard injections, as reported by patients, their parents and their provider*[1]

Lower anxiety

in parents of children using injection ports versus standard injections*[1]

Improved QoL

as reported by the parents of children using injection ports versus standard injections**[2]

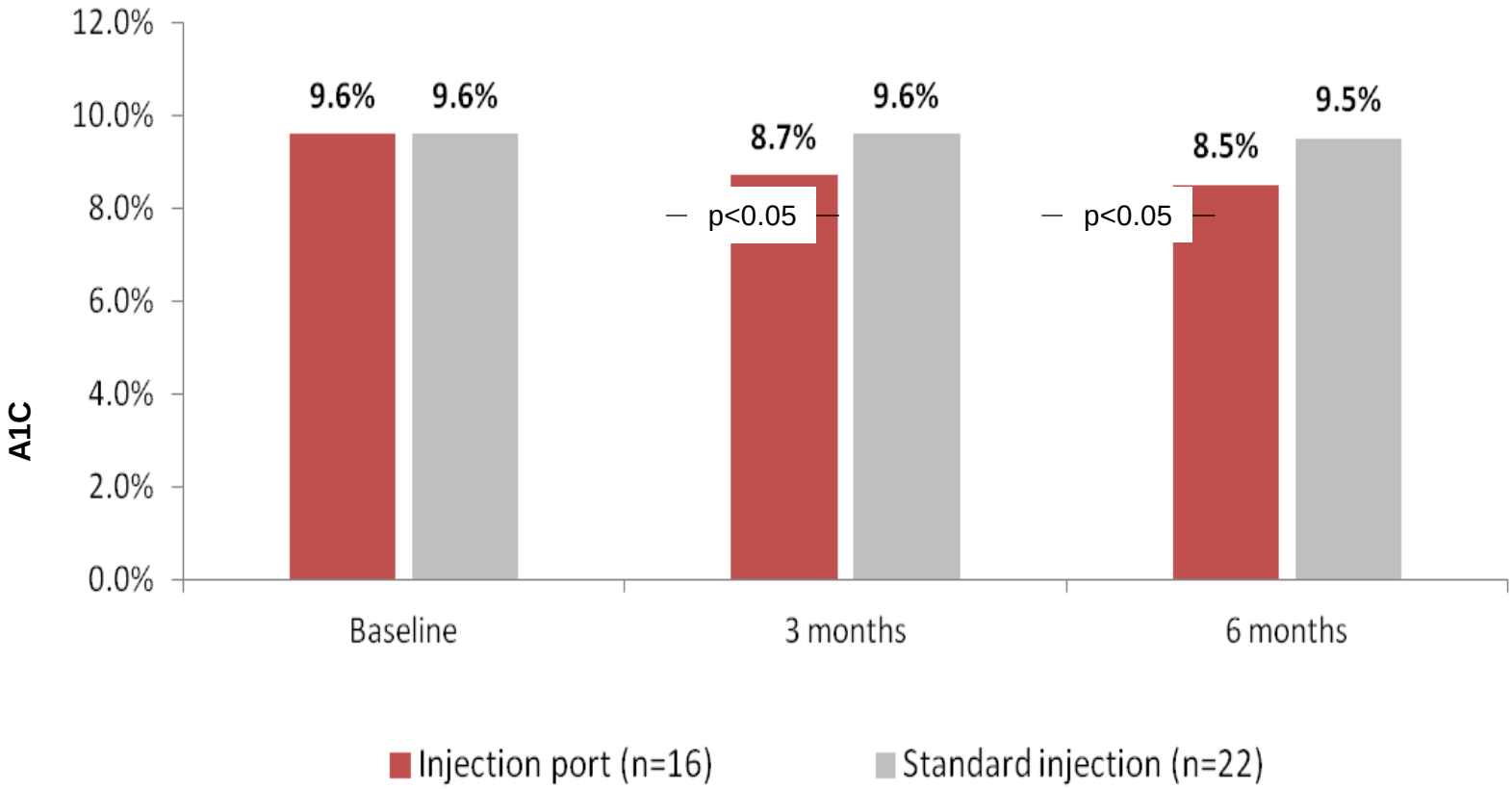
*Open label, randomized, controlled trial of 41 young patients (aged 3–15 years) with diabetes, investigating patient anxiety and pain when using an injection port versus standard injection to deliver insulin

**Study of 40 young patients (aged 1–5 years) with diabetes, investigating glycemic control and QoL when using an injection port versus standard injection to deliver insulin

HCP=healthcare professional; QoL=quality of life

1. Hanas R, Adolfsson P, Elfvin-Åkesson K et al. Indwelling catheters used from the onset of diabetes decrease injection pain and pre-injection anxiety. *J Pediatr.* 2002;140(3):315–320; 2. Rabbone I, Bobbio A, Di Gianni V, Sacchetti C, Cerutti F. Intensive insulin therapy in preschool-aged diabetic children: from multiple daily injections to continuous subcutaneous insulin infusion through indwelling catheters. *J Endocrinol Invest.* 2008;31(3):193–195

A1C control with injection port versus standard injections*[1]



*Randomized controlled trial of 66 young patients with diabetes, investigating A1C control when using an injection port versus standard injection ± alarm to administer insulin

A1C=glycated hemoglobin

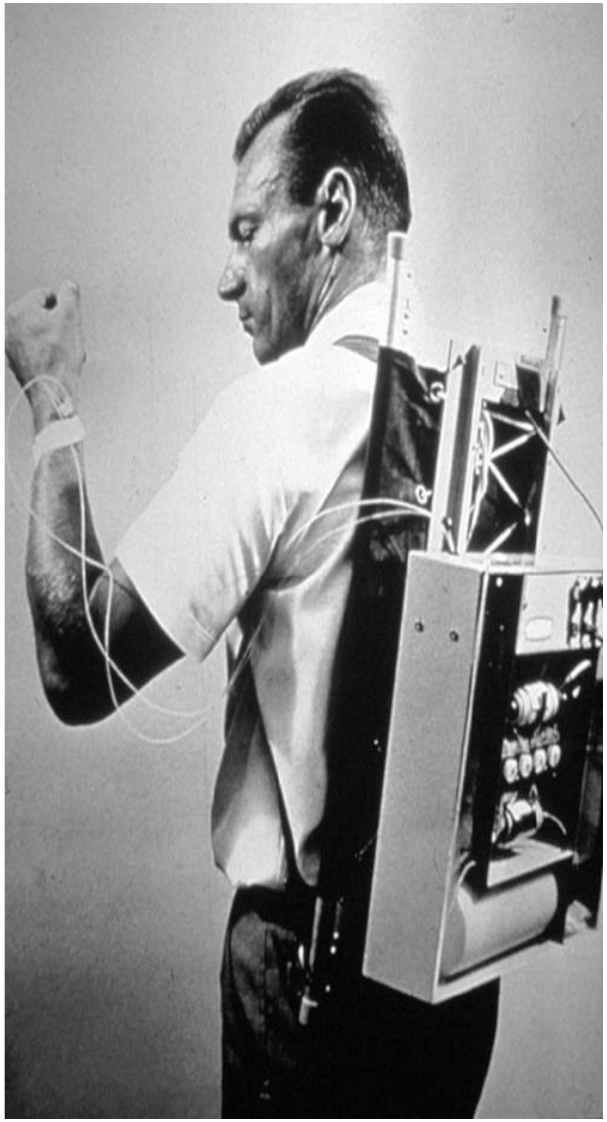
1. Burdick P, Cooper S, Horner B, Cobry E, McFann K, Chase HP. Use of a subcutaneous injection port to improve glycemic control in children with type 1 diabetes. *Pediatr Diabetes.* 2009;10:116–119

Smart Insulin Pump

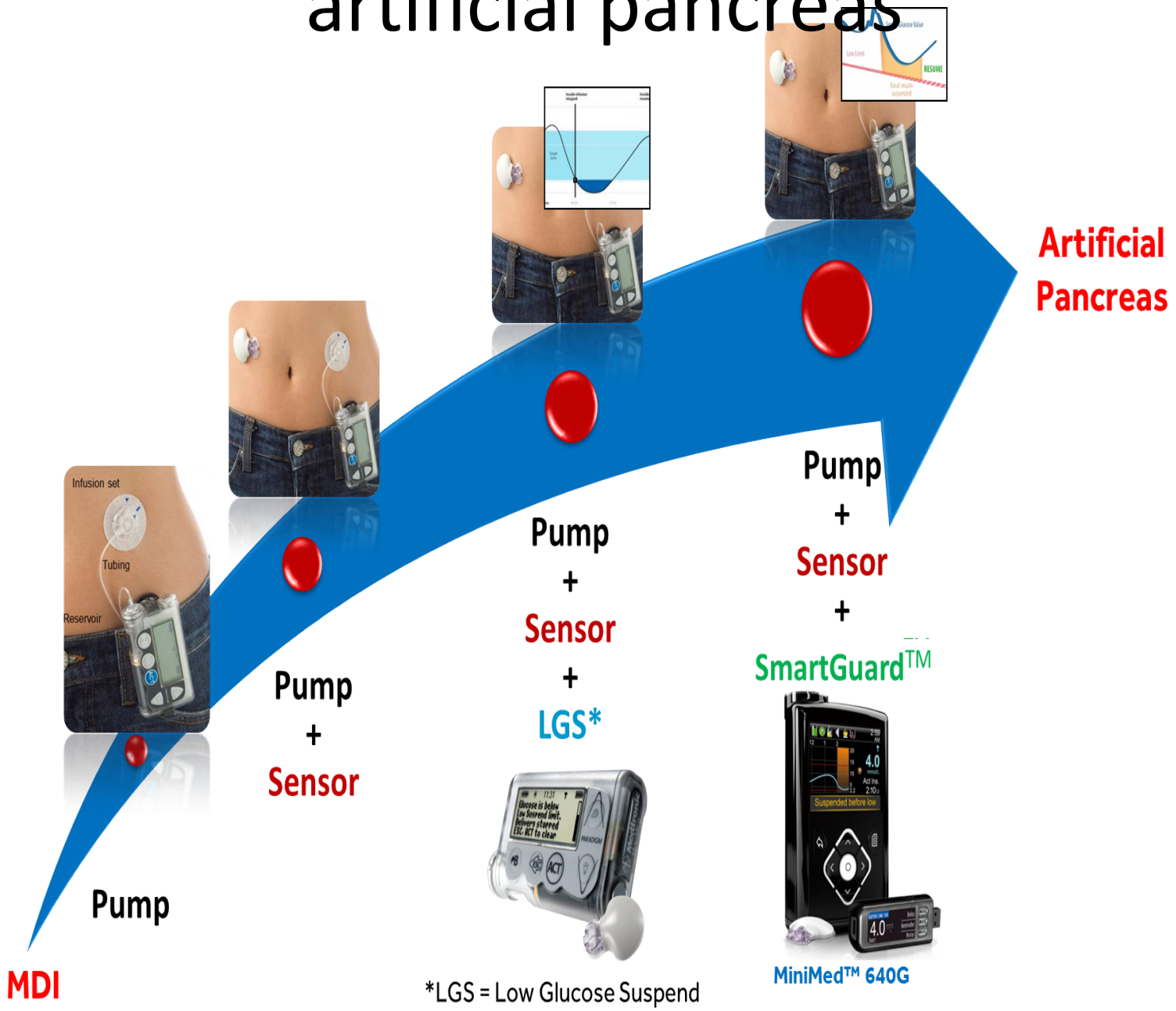
EVOLUTION OF INSULIN PUMP THERAPY

- The idea of continuous insulin delivery first emerged in the early 1960s when Dr Arnold Kadish from Los Angeles fashioned a device that would permit such insulin delivery
- This device was the size of an army backpack making it impractical for everyday use
- First pump employed continuous intravenous insulin delivery, and then by the more practical means of continuous subcutaneous insulin infusion (CSII)

Insulin Pump Therapy: Past



Evolution in diabetes technology towards artificial pancreas



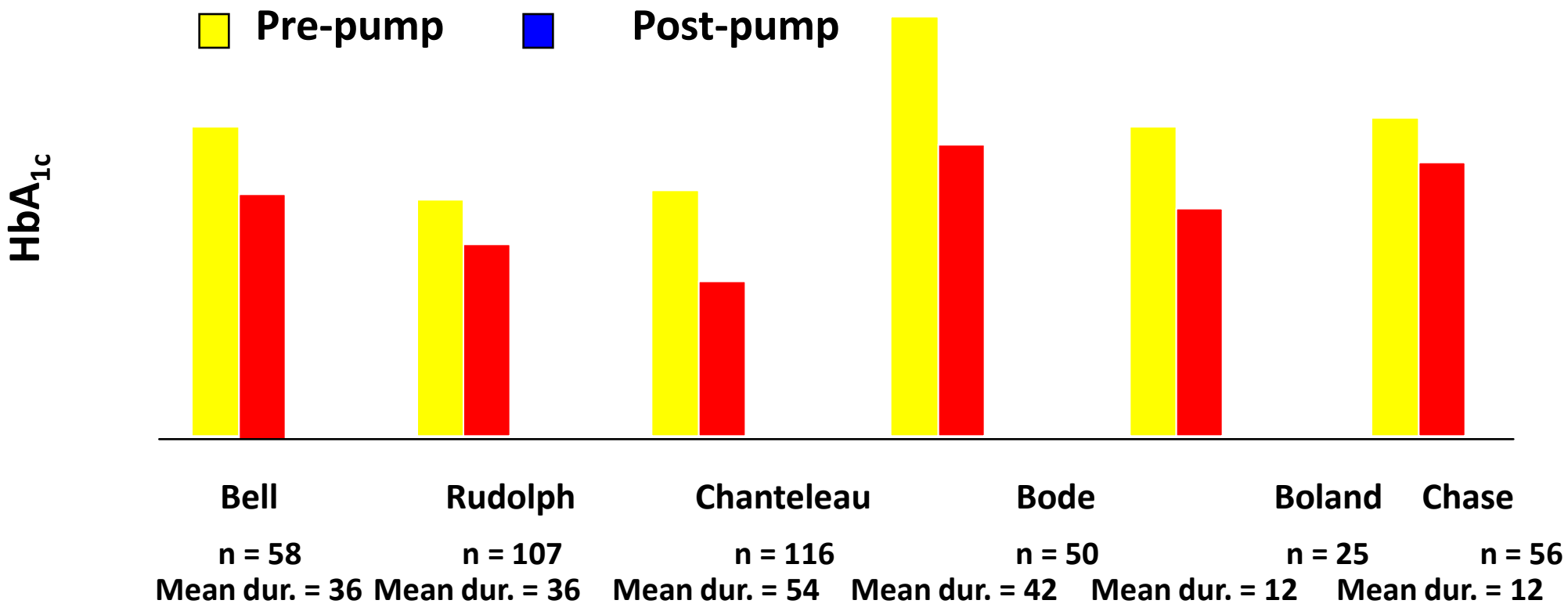
Insulin Pump Therapy: Present

Coming Soon


2:59
AM
12 1 2
20
15
10
5
2.2
4.0
mmol/L
Act Ins.
2.10 U
Suspended before low
0253 10/11
4.0
mmol
L
Sent
Bolus
Reminder
Notes

ADVANTAGES

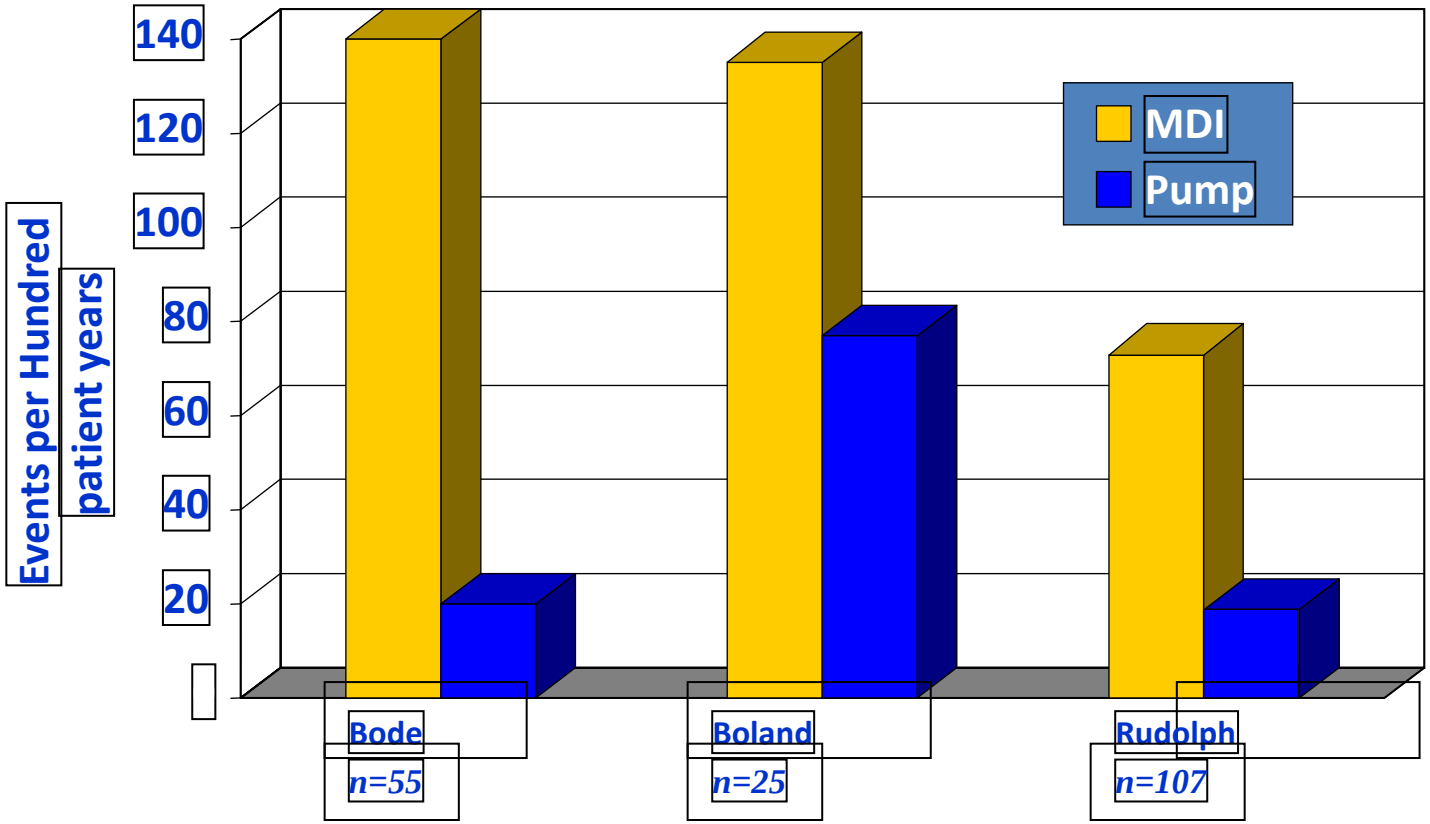
CSII Reduces HbA_{1c}



Chantelau E, et al. *Diabetologia*. 1989;32:421–426; Bode BW, et al. *Diabetes Care*. 1996;19:324–327; Boland EA, et al. *Diabetes Care*. 1999;22:1779–1784; Bell DSH, et al. *Endocrine Practice*. 2000;6:357–360; Chase HP, et al. *Pediatrics*. 2001;107:351–356.

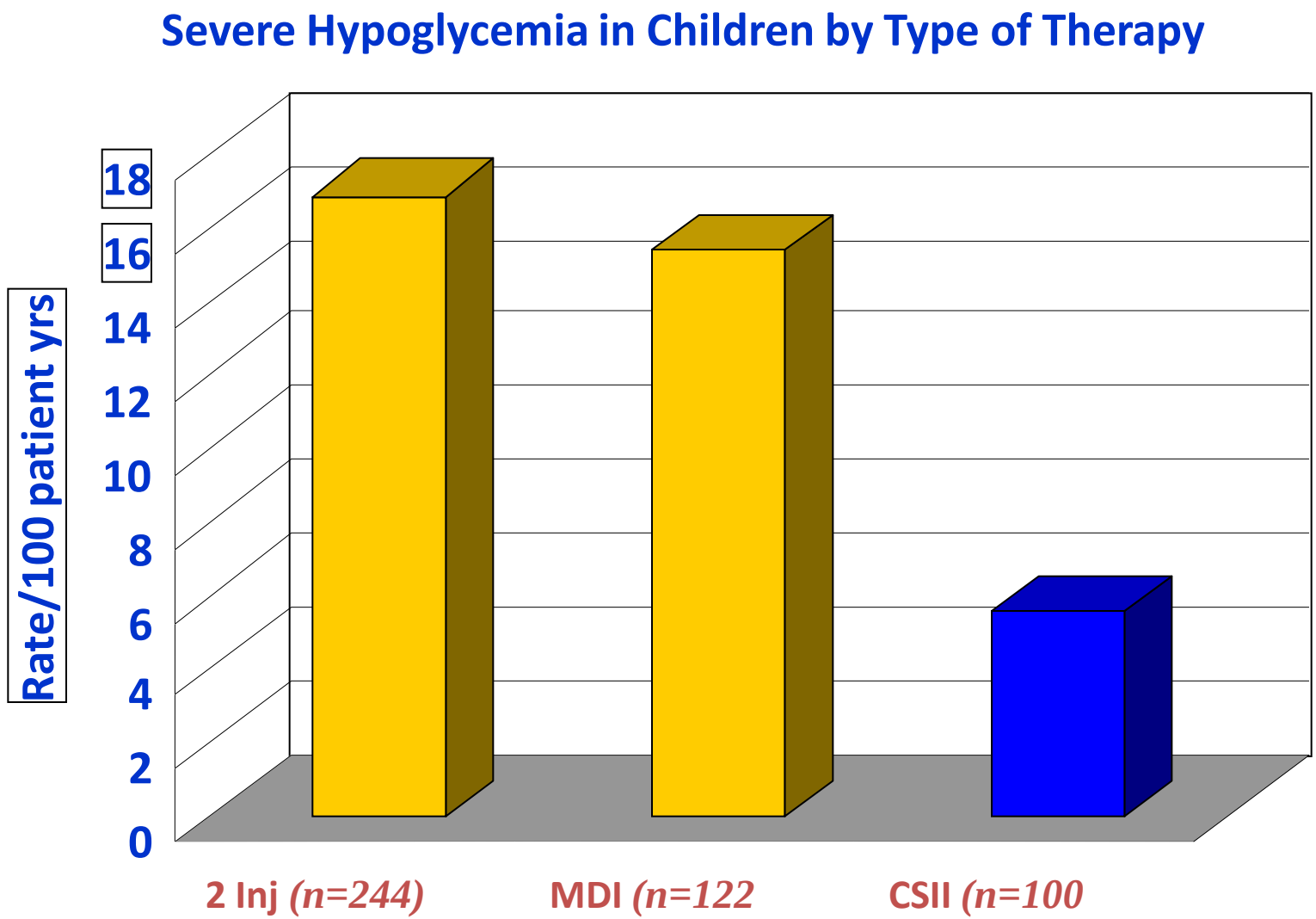
Pump Therapy Reduces Incidents of Severe Hypoglycemia

Severe Hypoglycemic Episodes MDI vs CSII



Adapted from Bode,BW et al., Diabettes Care *1996, 19:325-7. Boland, EA et al.,* Diabetes Care *1999, 22:1779 - 84. Rudolph JW, Hirsch IB. Assessment of Therapy with ContinuousSubcutaneous Insulin Infusion in an Academic Diabetes Clinic.* Endocrine Practice *2002: 8; 401 - 405*

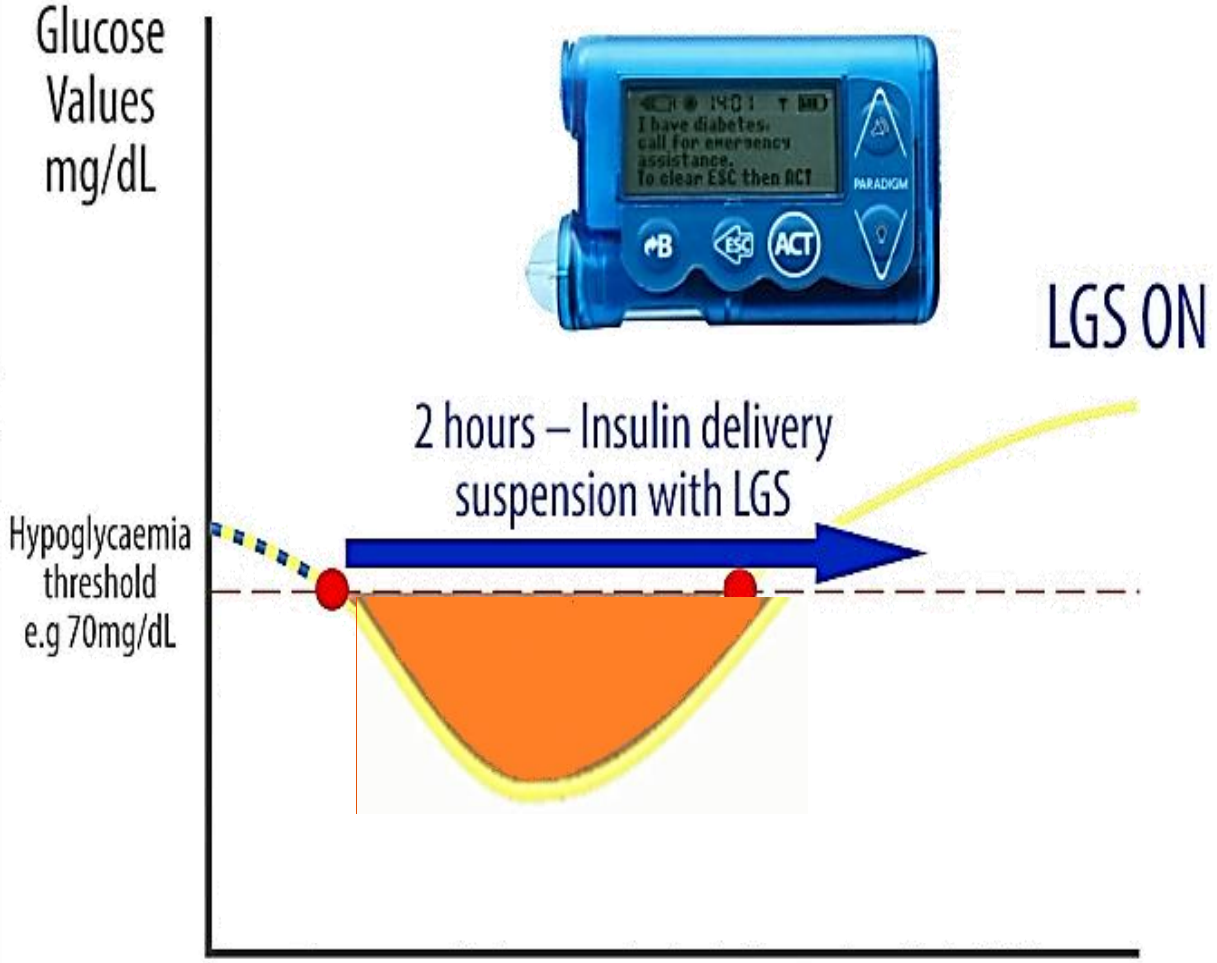
Decreased Risk of Severe Hypoglycemia

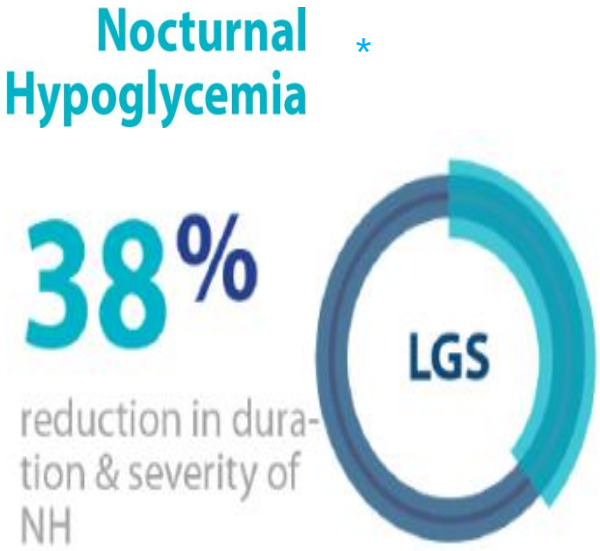


Adapted from Jones TW, Davis EA. Hypoglycemia in Children with Type 1 Diabetes: Current Issues and Controversies. Pediatric Diabetes *2003; 4: 143*

‘LOW GLUCOSE SUSPEND (LGS)’ MINIMIZES SEVERE HYPOGLYCEMIA

MiniMed® Paradigm Veo™ with LGS is the ONLY automated insulin delivery system clinically proven to significantly reduce hypoglycaemia

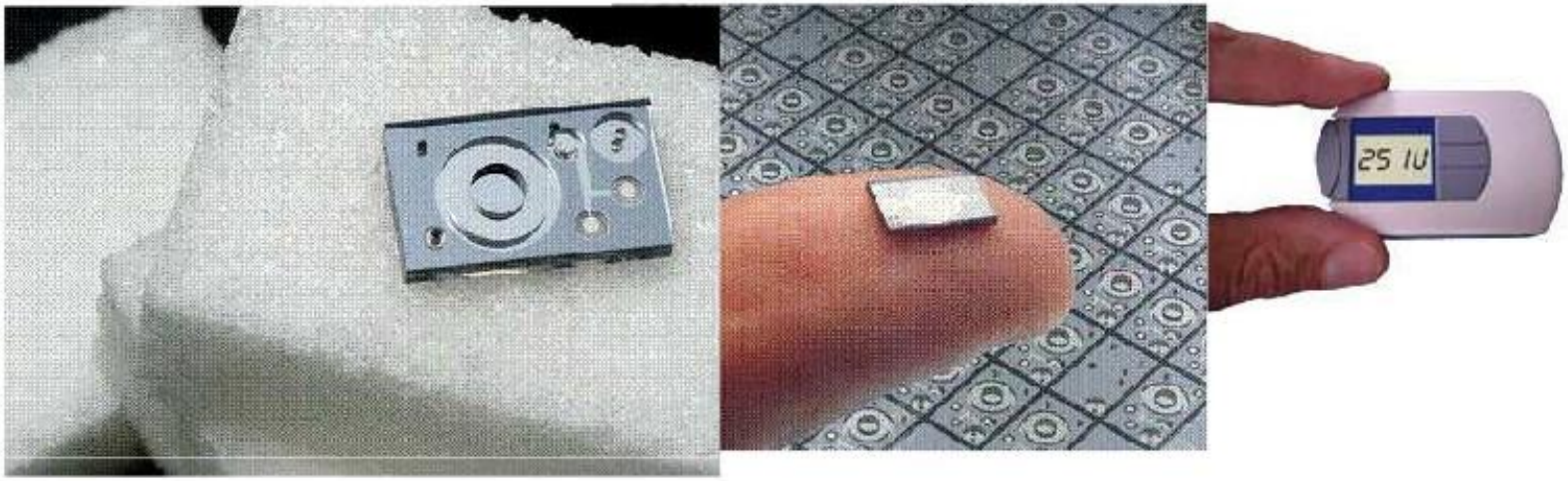




‘SMARTGUARD™ TECHNOLOGY PROVIDES ADVANCED PROTECTION AGAINST HYPOGLYCEMIA (AUTO SUSPENSION & AUTO-RESUME OF INSULIN)

Future Development

Micro-pump



Debiotech has been developing small pumps from Micro-Electro-Mechanical Systems or MEMS technology. These devices are made from silicon (not silicone!) and easily mass-produced to keep cost low.

Silicon is harmless, but it is not clear how insulin may interact with silicon surfaces.

Insulin pump technology is to combine with a continuous blood glucose monitoring system

“2 in 1 machine”

Clinical trials: implantable insulin pumps and continuous glucose sensors

Dual hormone insulin pumps that infuse either insulin or glucagon. In event of hypoglycemia, the glucagon could be triggered to increase the blood glucose.

It would be particularly valuable in a closed loop system under the control of a glucose sensor

Ultrafast insulin which are absorbed more quickly than the currently available rapid acting insulin which have a peak at about 60 minutes

It theoretically coordinate with meals better, and allow faster recovery from hyperglycemia if the insulin infusion is suspended.

They are in development by Biodel Halozyme, and Novo Nordisk

Future Pump Features

Automatic TDD adjustment

- Average blood sugar and standard deviation
- % TDD used for corrections
- Basal/bolus balance

Automatic basal testing

- Overnight
- Daytime, when meal is skipped

Automatic carb factor testing

- Premeal, 2 hr postmeal peak, normal in 4-5 hrs?

Automatic correction factor testing

- High-to-normal in 4-5 hours?

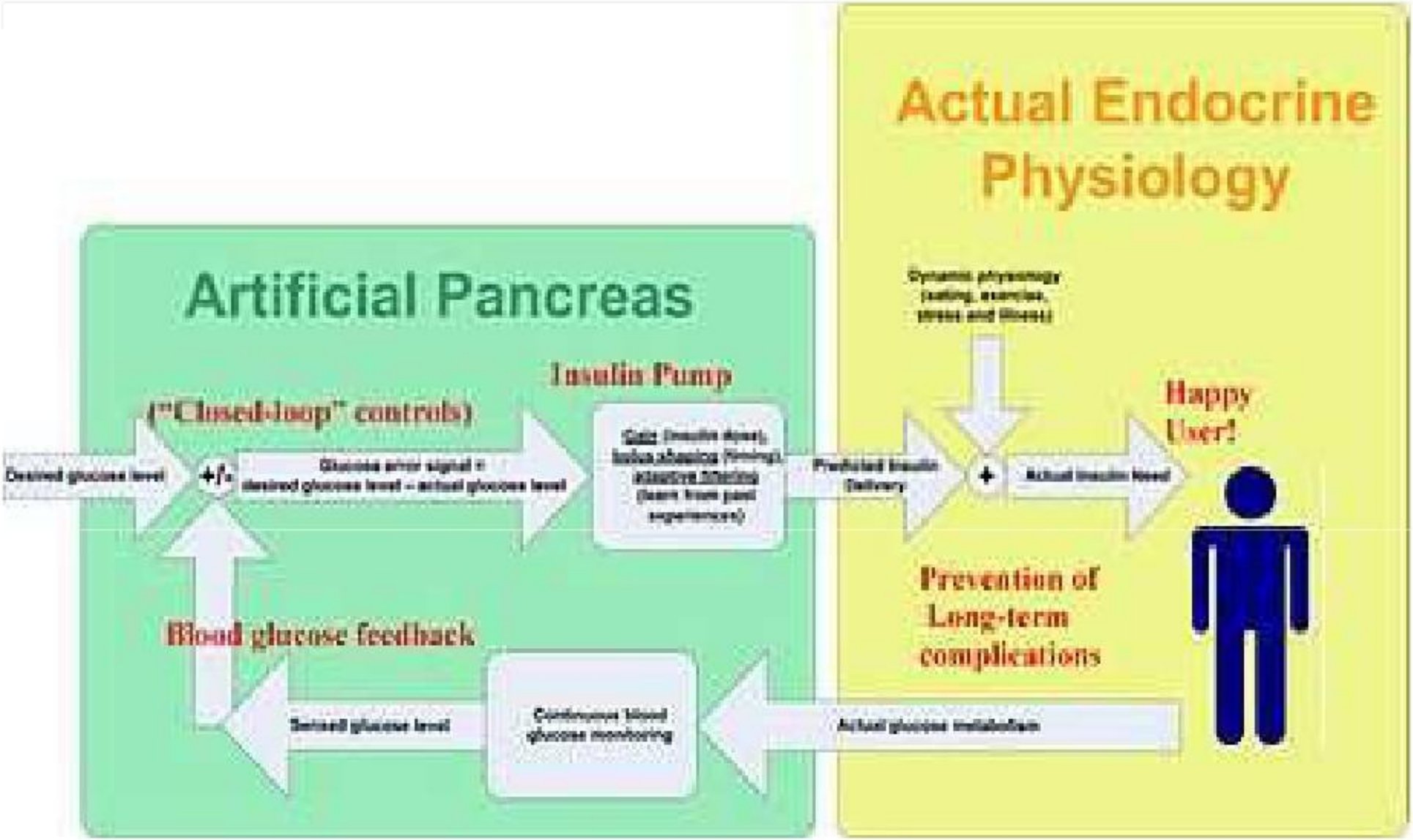
Our Dream !!

An Artificial Pancreas

“ Closed Loop System”

The artificial pancreas (AP)

- known as closed-loop control of blood glucose in diabetes, is a system combining;
  - glucose sensor
  - **smart" control algorithms**
  - insulin infusion device



Feedback of real-time blood glucose data to an insulin pump for basal & bolus control

Thanks