ueg week
VIRTUAL 2020

Disclosure of Conflicts of Interest

I herewith declare the following paid or unpaid consultancies, business interests or sources of honoraria payments for the past three years, and anything else which could potentially be viewed as a conflict of interest:

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Duodenal mucosal resurfacing combined with GLP-1RA may eliminate insulin treatment in type 2 diabetes while improving glycaemic control and metabolic health

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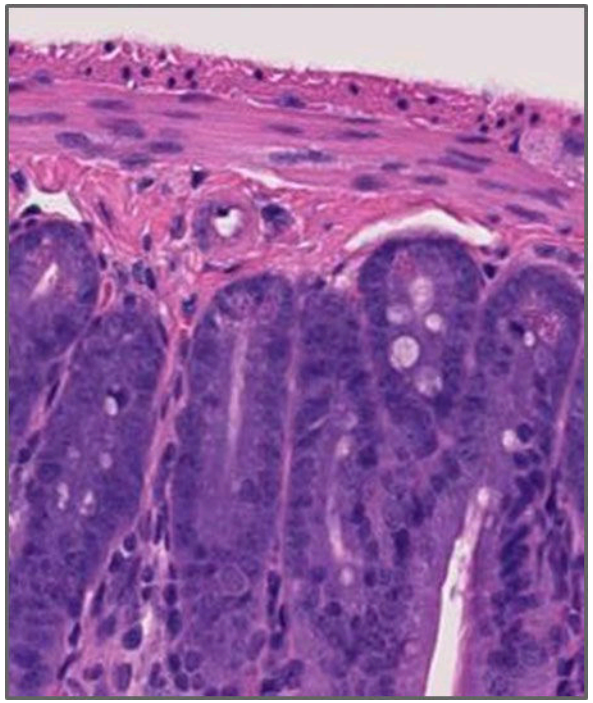
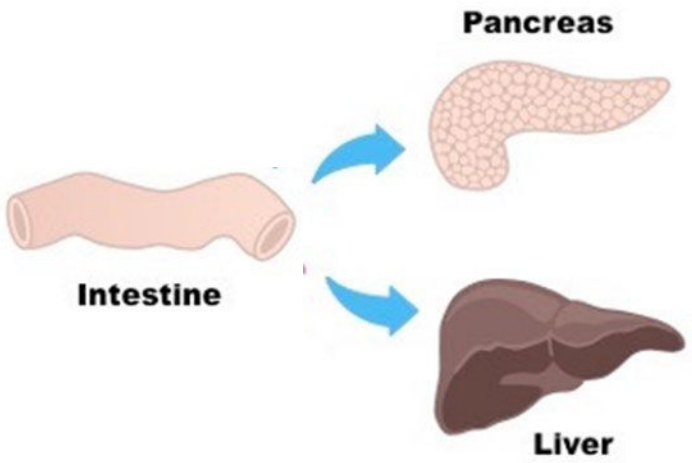
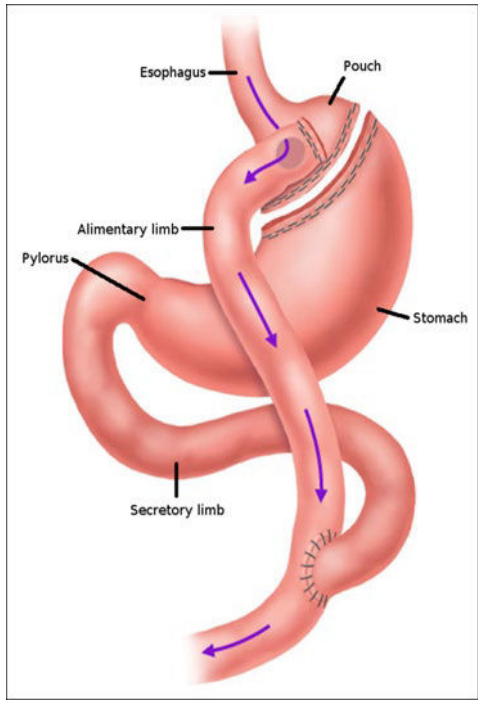
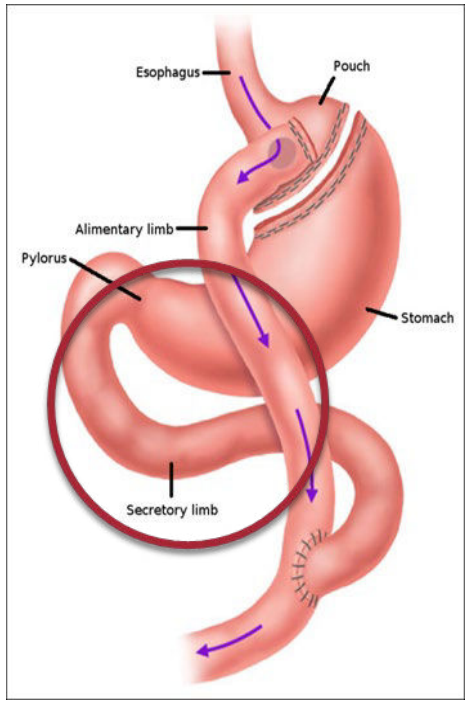
Target the duodenum for treatment of T2D

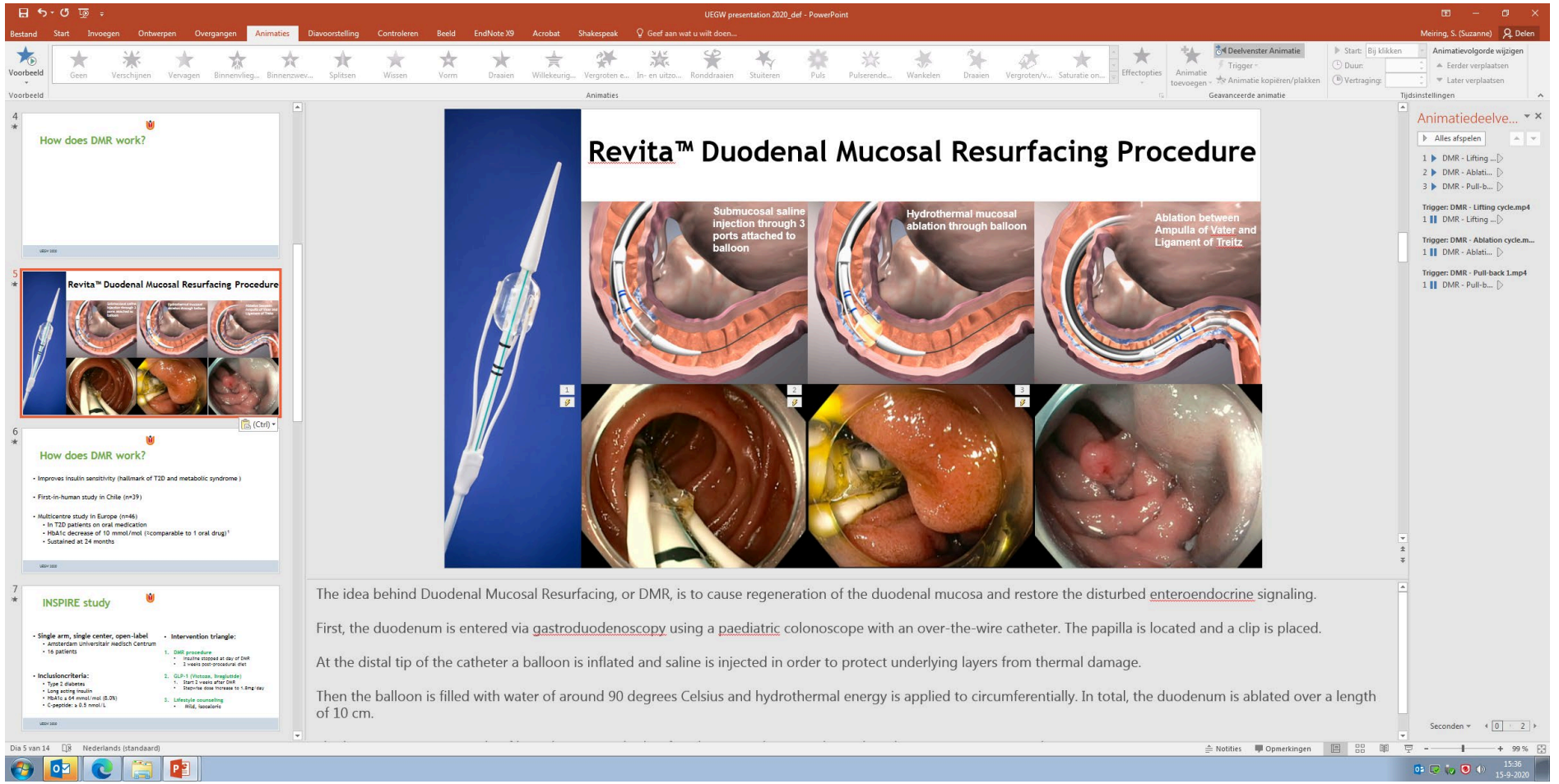








Duodenal mucosa changes due to 'Western diet' → **Changes in hormonal signaling causes insulin resistance** → **Bariatric Surgery effective treatment T2D** → **Bypassing duodenum improves insulin resistance**


UEGW presentation 2020_def - PowerPoint
Revita™ Duodenal Mucosal Resurfacing Procedure
Submucosal saline injection through 3 ports attached to balloon
Hydrothermal mucosal ablation through balloon
Ablation between Ampulla of Vater and Ligament of Treitz
The idea behind Duodenal Mucosal Resurfacing, or DMR, is to cause regeneration of the duodenal mucosa and restore the disturbed enteroendocrine signaling.
First, the duodenum is entered via gastroduodenoscopy using a paediatric colonoscope with an over-the-wire catheter. The papilla is located and a clip is placed.
At the distal tip of the catheter a balloon is inflated and saline is injected in order to protect underlying layers from thermal damage.
Then the balloon is filled with water of around 90 degrees Celsius and hydrothermal energy is applied to circumferentially. In total, the duodenum is ablated over a length of 10 cm.

How does DMR work?

- Improves insulin sensitivity (hallmark of T2D and metabolic syndrome)
- First-in-human study in Chile (n=39)
- Multicentre study in Europe (n=46)
  - In T2D patients on oral medication
  - HbA1c decrease of 10 mmol/mol (≈comparable to 1 oral drug)[1]
  - Sustained at 24 months

INSPIRE study

- **Single arm, single center, open-label**
  - Amsterdam Universitair Medisch Centrum
  - 16 patients

- **Inclusioncriteria:**
  - Type 2 diabetes
  - Long acting insulin
  - HbA1c ≤ 64 mmol/mol (8.0%)
  - C-peptide: ≥ 0.5 nmol/L

- **Intervention triangle:**

1. **DMR procedure**
   - Insuline stopped at day of DMR
   - 2 weeks post-procedural diet

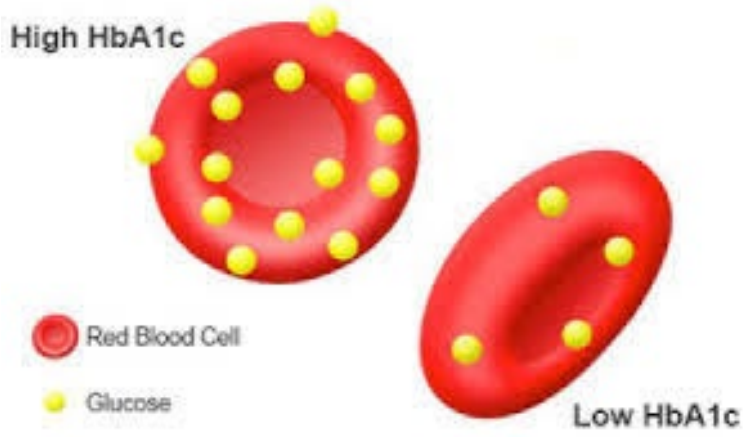
2. **GLP-1 (Victoza, liraglutide)**
   1. Start 2 weeks after DMR
   - Stepwise dose increase to 1.8mg/day

3. **Lifestyle counseling**
   - Mild, isocaloric

INSPIRE study

Follow-up: Every 4-12 weeks

- Lifestyle counseling
- Blood collection:
  - HbA1c ≤ 58 mmol/mol => Continue GLP-1RA
  - HbA1c > 58 mmol/mol => Stop GLP-1RA and restart insulin



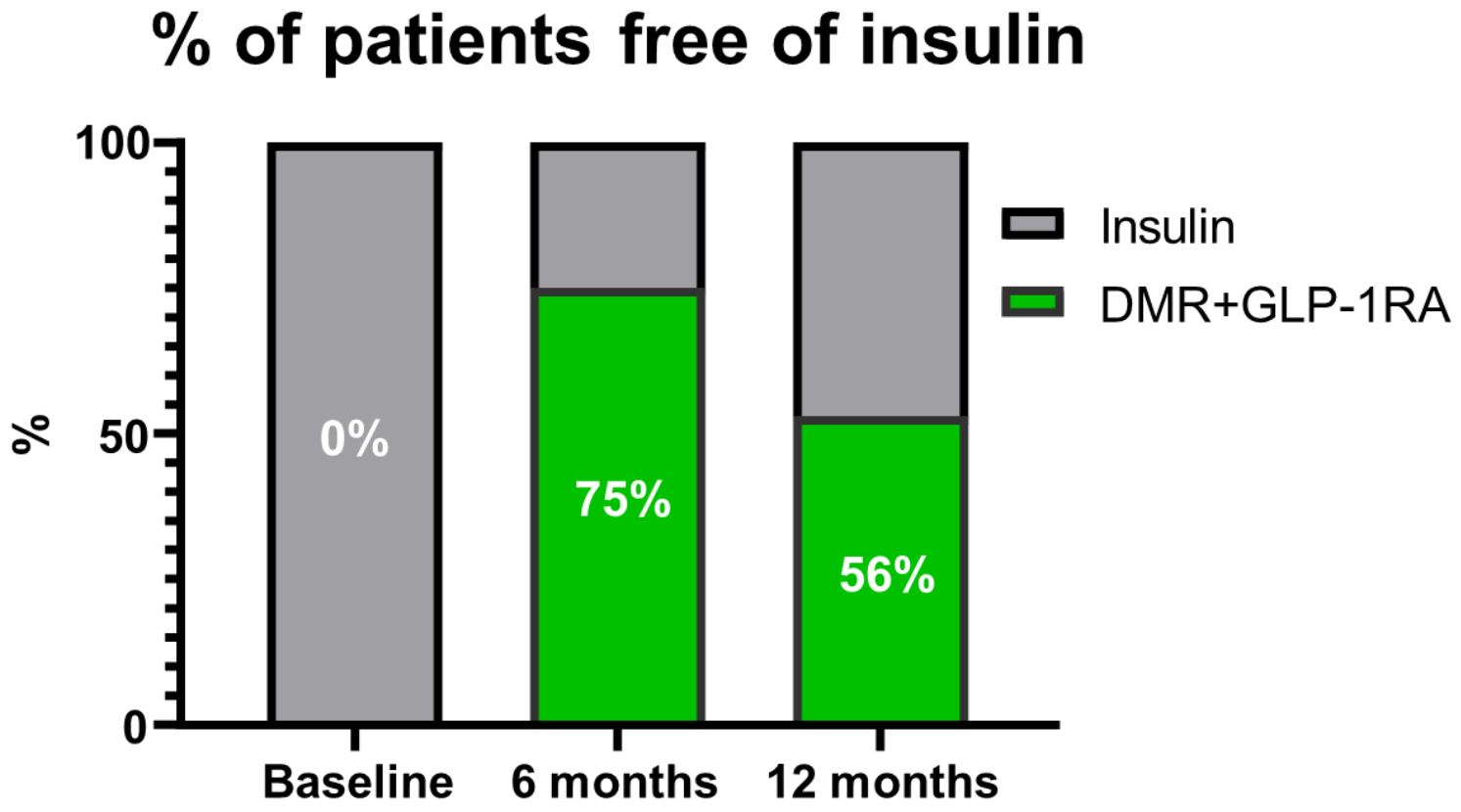
- **Primary endpoint:**
  - % of patients off insulin at 6 months with adequate glycaemic control (HbA1c ≤ 58 mmol/mol)
- **Secondary endpoints:**
  - Glycaemic and metabolic parameters
  - % of patients off insulin at 12 months

Baseline characteristics

Patient characteristics (N=16)	
Age [years]	61
Male gender, n (%)	10 (63%)
Duration of T2D [years]	11
Weight [kg]	87.5
BMI [kg/m^2]	29.2
HbA1c [mmol/mol]	58
Fasting plasma glucose [mmol/l]	10.1
C-peptide [nmol/l]	0.70
HOMA-IR	8.1
Antidiabetic medication	
Mean number of daily units of insulin	31

Primary endpoint;

Responders : HbA1c < 59 mmol/mol



Despite elimination of insulin, improved glycaemic parameters

Responders

		6 months (n=12)		12 months (n=9)	
	Baseline	6 months	p-value	12 months	p-value
HbA1c [%]	7.4 (7.1-7.6)	6.7 (6.6-7.3)	0.009	6.7 (6.5-7.2)	0.024
HOMA-IR	8.9 (4.5-13.3)	2.6 (1.4-4.1)	0.004	7.1 (6.7-7.7)	0.008
FPG [mmol/l]	10.5 (9.2-12.0)	7.6 (6.5-8.8)	0.003	3.6 (1.6-6.7)	0.015

Without daily median insulin dose of 31 units

Improved metabolic parameters

Responders

		6 months (n=12)		12 months (n=9)	
BMI [kg/m2]	29.8 (26.5-34.2)	27.2 (23.4-31.9)	0.002	25.5 (22.1-29.5)	0.008
Liver fat [%]	8.1 (5.1-13.2)	4.6 (2.4-11.0)	0.016	6.0 (2.7-10.9)	0.208

Complete study population

		6 months(N=16)		12 months(n=16)	
BMI [kg/m2]	29.2 (26.5-32.0)	27.6 (24.3-29.8)	<0.001	26.4 (22.7-29.8)	<0.001
Liver fat [%]	8.1 (4.0-13.5)	5.3 (3.9-11.4)	0.053	5.6 (2.8-10.9)	0.030

Conclusion

- Single endoscopic DMR, combined with GLP-1 and lifestyle counseling, can eliminate insulin therapy in a subset of T2D patients…
  - …while improving parameters of glycaemia
  - …while improving overall metabolic health
- The effect slightly fades after 12 months, but majority is off insulin
  - Effect of multiple DMRs is unknown, but could extend/enlarge effect
- May be a game changing approach in the treatment of metabolic syndrome
  - A large international RCT has been started, based on these results

Limitations

- Uncontrolled pilot study with limited sample size
- Contribution of each of the individual treatment components unknown
  - Data must be confirmed by new multicenter RCT
- Mechanism of DMR not yet completely clear
  - Results of mechanistic studies will follow soon