NORTH CAROLINA DIABETES ADVISORY COUNCIL MEETING
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DISCLOSURE

- Consultant for Johnson & Johnson

- Advisory board for Rhythm pharmaceuticals

- Investigator on clinical trials with Novo-Nordisk

DIABETES REMISSION CLINICAL TRIAL (DIRECT)

Participant eligibility

- **DM diagnosed within 6 yr**

- BMI 27-45 kg/m^2

- Age 20-65 yr

- HbA1c **6.0** to 12.0

- If HbA1c 6.0 to 6.5, they should be receiving anti-obesity medications

Lean M et al, The Lancet 2017

STUDY DESIGN

Exclusion

- **<u>Insulin use</u>**
- **<u>HbA1c >12%</u>**
- **Weight loss > 5 kg in past 6 months**
- eGFR <30 ml/min/1.732 m^2
- Heart failure
- Anti-obesity medications, antipsychotic drugs
- Hospitalization for depression
- Substance abuse
- Pregnancy or consideration of pregnancy
- Bulemia

STUDY INTERVENTIONS

- Randomization of practices to weight management commercial program Counterweight –Plus or control

- Nurse of dietitian with 8 hrs of training

- 15 kg weight loss

- Low calorie diet 825-853 Kcal a day for 3 months

- Reintroduction phase of 2-8 weeks

- Maintenance program with monthly visits

- All the diabetes and hypertension drugs stopped on day one.

STUDY OUTCOME MEASURES

Primary Measures

- % of individuals who lost 15 kg weight
- **% of individuals with HbA1c <6.5 off meds (Remission rate)**

Secondary measures

- Quality of life (EQ-5D)
- Serum lipids
- Physical activity
- Program acceptability
- Sleep quality
- Blood pressure

STUDY RESULTS

- 49 primary care centers

- Intervention in 150, control in 149.

- 33 withdrew from the intervention group **(20%)**

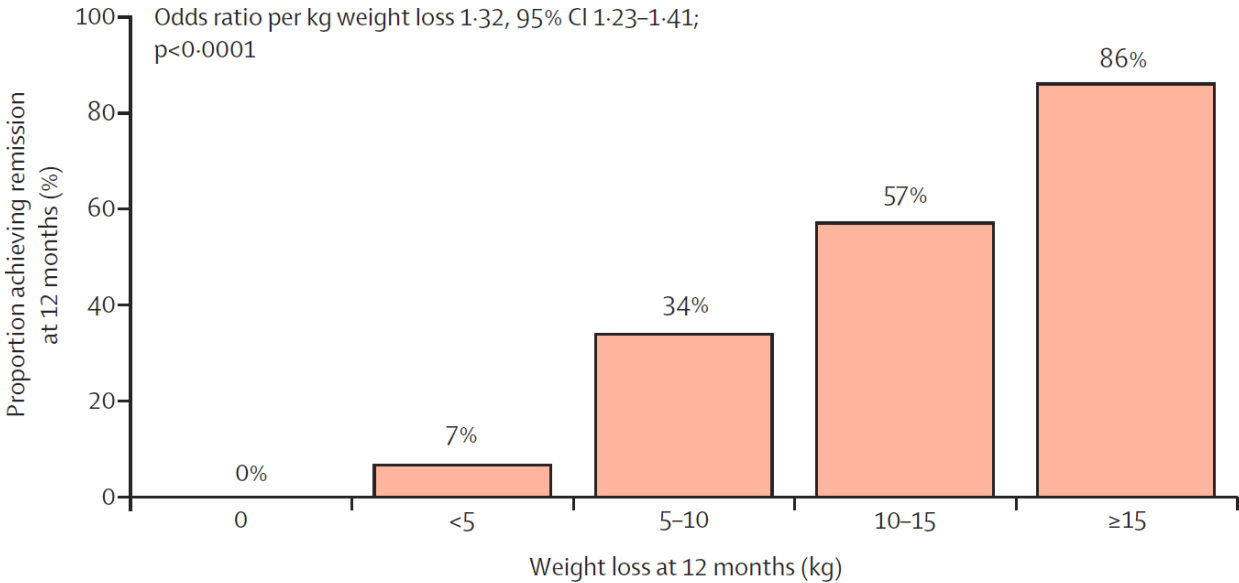- **149 from intervention group included in the analysis**

OUTCOME RESULTS

	Weight loss group	Control group	P value
% with 15 Kg wt loss	24%	0%	<0.001
Mean weight loss	10 kg	1 kg	<0.001
Remission of diabetes	46%	4%	<0.001
Mean HbA1c change	-0.9%	+ 0.1%	<0.001

	Weight loss group	Control group	P value
EQ- 5D	↑7.2 points	↓2.9 points	P<0.0012
Triglycerides	↓0.31 mmol/L	↑0.09 mmol/L	P<0.001

Although average BP was the same reduced use of BP meds.

DIABETES REMISSION RATE PROPORTIONAL TO WEIGHT LOSS

Odds ratio per kg weight loss 1·32, 95% CI 1·23–1·41; p<0·0001

Proportion achieving remission at 12 months (%)

0% — 0
7% — <5
34% — 5–10
57% — 10–15
86% — ≥15

Weight loss at 12 months (kg)

HOW DO THE RESULTS COMPARE ?

Look AHEAD Study

- N=4503,
- Specialized setting and intensive follow up in intervention group.
- Average weight loss over control - 7.9% vs 8.7%
- Weight loss of >10% - 38% vs 61%
- Average HbA1c lowering 0.7% vs 0.9%
- Remission of diabetes at 1 yr 11.5% vs 46%

Look AHEAD remission criteria more stringent.

More uniform weight loss distribution in Look Ahead versus responders and non responders in DiRECT

Is it something special about the 800 Kcal diet ?

HOW DO THE RESULTS COMPARE ?

- Clinical experience of the Wake Forest Baptist Medical Center using Optifast program (comparable to Counterweight-plus).

- Average follow up 280 ± 160 days

- HbA1c reduced by 0.9% same as DiRECT

- Remission of Diabetes 48.7% vs 46%

- Mean weight loss 13.5 kg vs 10 kg

HOW DO THE RESULTS COMPARE ?

- Bariatric surgery in the STAMPEDE trial

- Sleeve Gastrectomy remission 27% vs 46% !

- Gastric bypass remission 42% vs 46% !

Is 800 Kcal diet as good as surgery ?

- Diabetes was more advanced in STAMPEDE (44% on insulin).

- Average duration of diabetes much longer

- Average HBA1c in STAMPEDE was 9.4 vs 7.6

- Remission criteria for STAMPEDE much more stringent.

- Using the <6.5 criteria- 39% and 36% at 5 yrs for bypass and sleeve respectively

Schauer P. , et al. NEJM 2012

FINAL THOUGHTS

- Shows a scalable option which can be administered from primary care offices with minimal training 8 hrs.

- A significant number of patients will not tolerate this intervention 20-25% even if motivated.

- 800 Kcal diets appear to have unique effects on diabetes- fantastic results in the SHORT term.

- Need to look at 2 yr and 5 yrs outcomes.

- Data very supportive of aggressive weight management solutions as **primary treatment** for diabetes type 2

THANK YOU