



# Clinical outcomes at 24 months

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On behalf of the DiRECT team

# Overview: DiRECT Study Design

## Tyneside & Scotland



Cluster randomisation  
(by GP Practice n=49)

**Control**  
(n = 26 practices)  
Usual diabetes care  
(Best Practice Guidelines)

**Intervention**  
(n = 23 practices)  
+ Structured weight  
management programme  
'Counterweight Plus<sup>®</sup>'

**28%** agreed to participate

### Main Inclusion Criteria

|                          |       |
|--------------------------|-------|
| Age (years)              | 20-65 |
| BMI (kg/m <sup>2</sup> ) | 27-45 |
| T2DM duration (years)    | ≤ 6   |

### Main Exclusion Criteria

Not on insulin

# DiRECT population is representative of type 2 diabetes

| Recruited population (n=298)   |      |
|--------------------------------|------|
| Male (%)                       | 59   |
| Most deprived SMS Quintile (%) | 21   |
| BMI (kg/m <sup>2</sup> )       | 34.6 |
| Age (years)                    | 54.4 |
| Duration T2DM (years)          | 3.0  |

| Baseline                  | Intervention | Control |
|---------------------------|--------------|---------|
| % on diabetes medications | 75           | 77      |
| HbA1c (mmol/mol)          | 60.4         | 58.2    |

# Structured Programme in Primary Care Setting



Practice nurse/dietitian programme delivery



During year 2, average number of 'monthly' appointments was 7.7

# 24 month analysis

## Data analysed by intention to treat

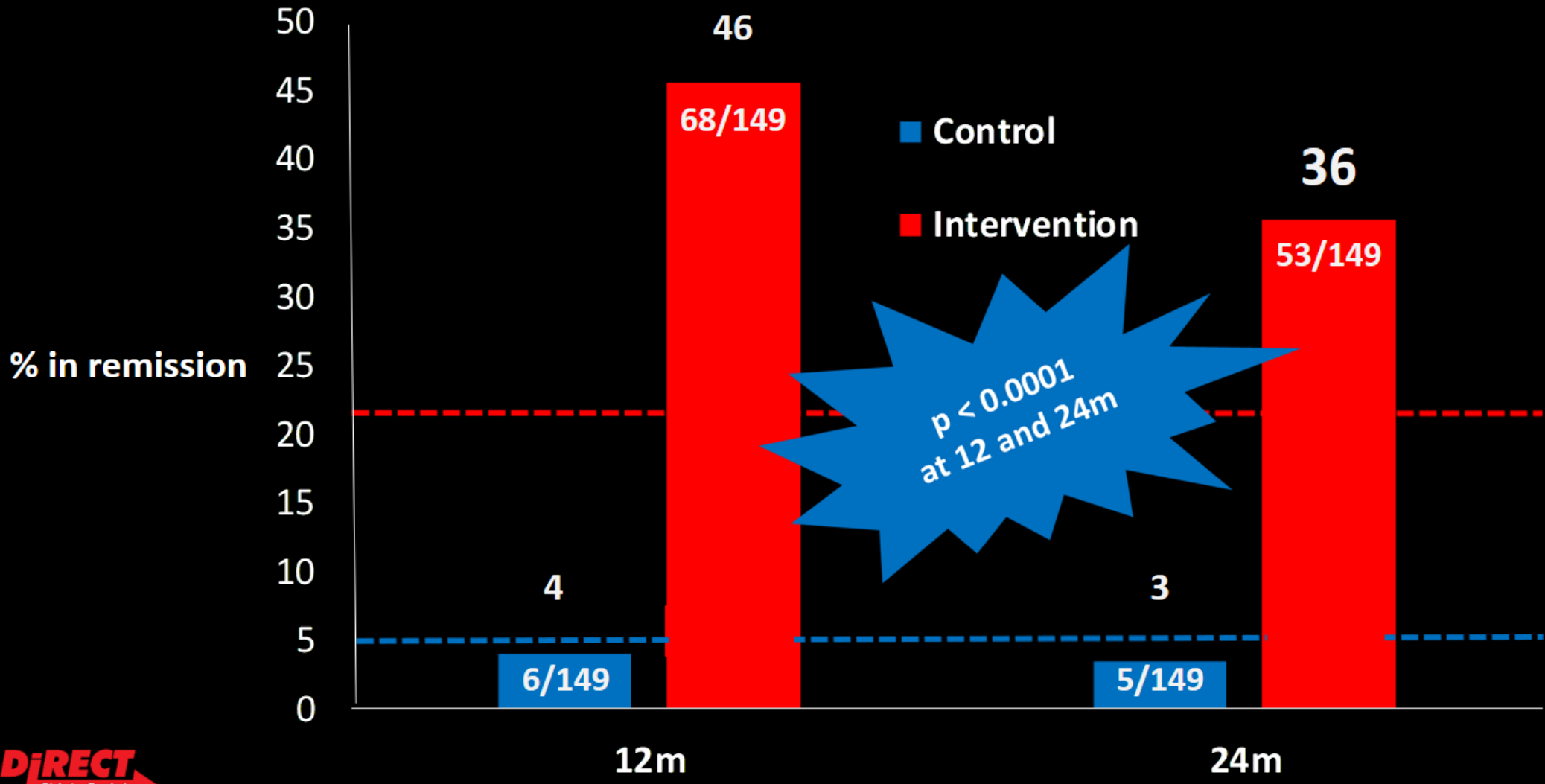
- 16 withdrew from intervention during year 2
- 86% attended 24 month review (n=256)
- Data from GP records for non-attenders at 24m review (n=16)
- 91% had data available
- No data available: assumed primary outcomes not met (n=26)
- Therefore analysis includes all 149 participants per group

# Co-Primary Outcomes

Weight loss  $\geq$  15kg

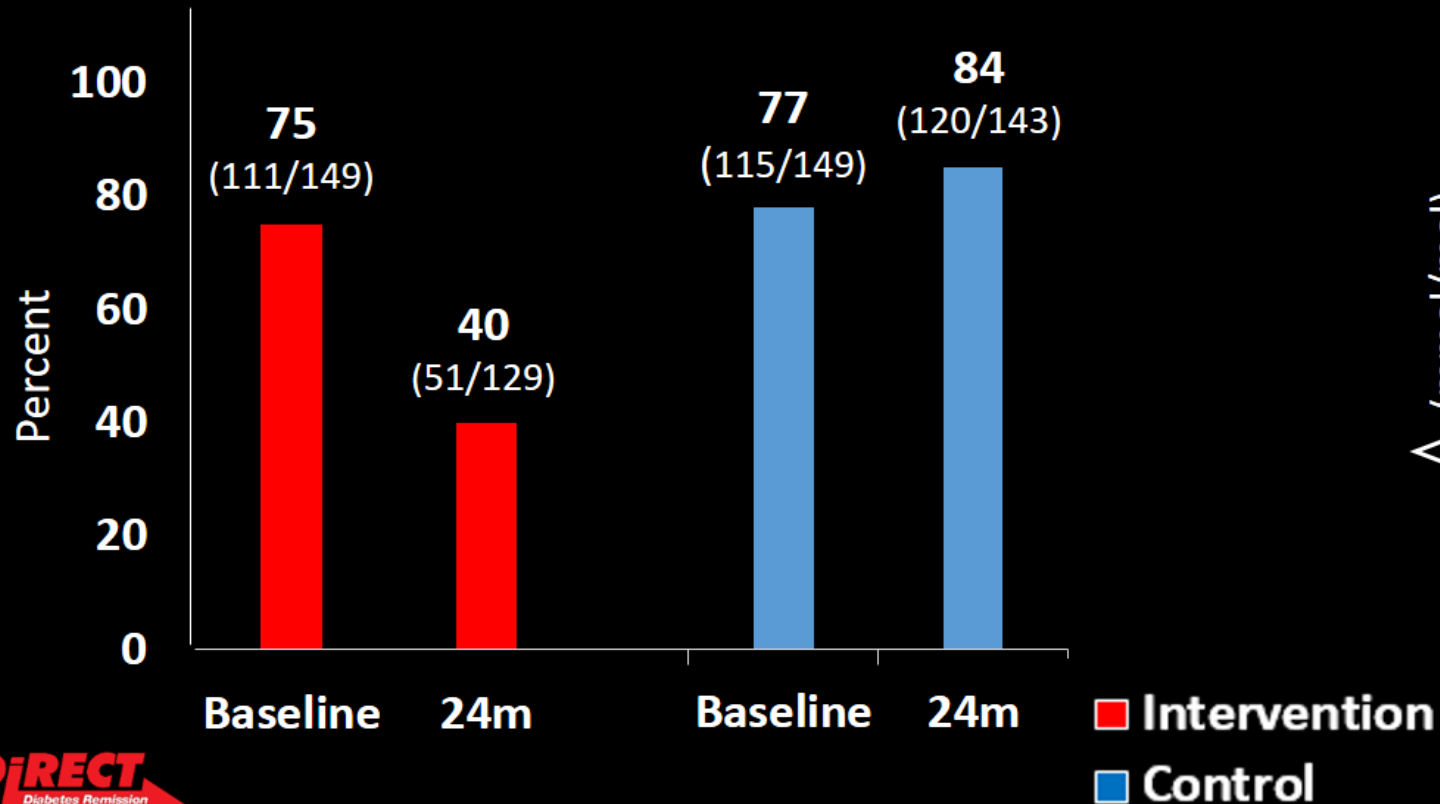
Remission T2DM  
HbA1c  $<$  48mmol/mol on no diabetes medications

# Remissions at 24 months

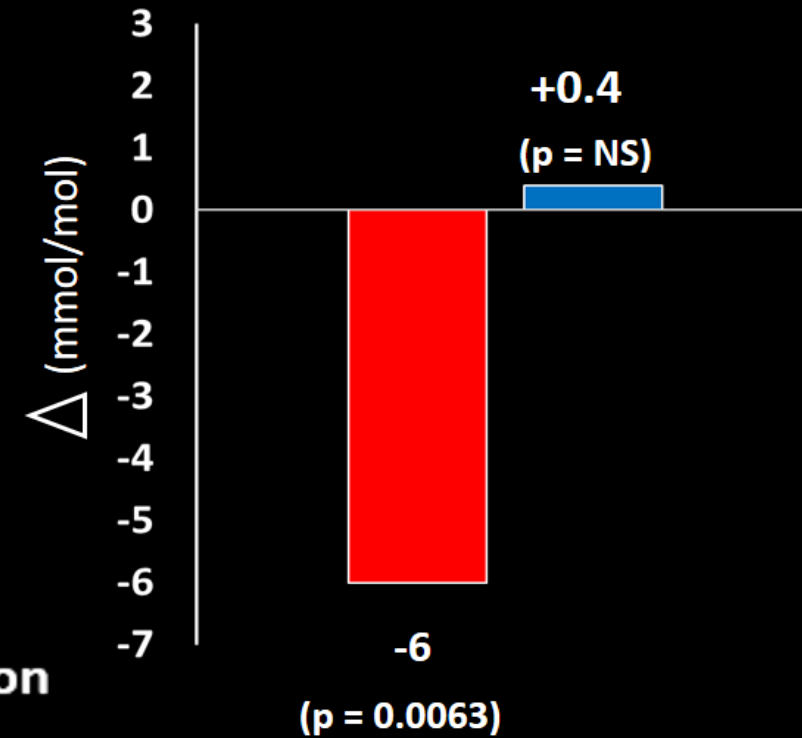


# Change in Diabetes Medications & HbA1c (Post-hoc analyses)

## Numbers on diabetes meds



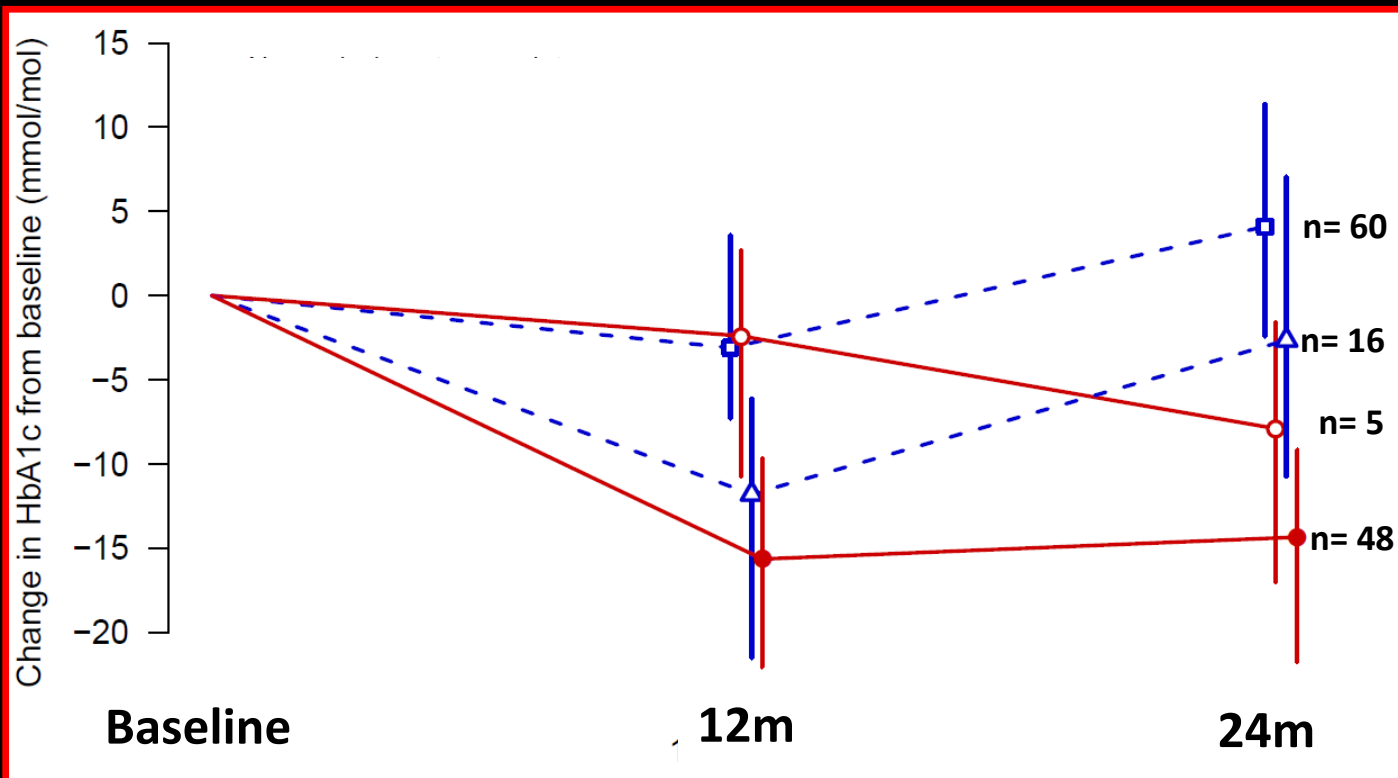
## HbA1c (baseline – 24m)





# HbA1c by remission group

p Intervention group: post-hoc analyses:



No remission at any time



Remission at 12m but not 24m



Remission achieved during year 2



Remission at both 12 & 24m

# Who achieves durable remission? (entire study population)

- Remission at 24 months was more likely with
  - Greater weight loss from baseline (aOR 1.2 per kg loss)
  - Greater weight loss from 12-24m (aOR 1.11 per kg loss)
- Remission did not vary with baseline BMI or duration of diabetes
- Remission was slightly more likely with
  - Older age (aOR 1.08 per year)
  - Male sex (aOR 0.44 female v male)

# Remissions Summary

1. **36% of intervention participants had sustained remission at 24 months**
2. **HbA1c was significantly reduced in the intervention group, with 50% reduction in use of diabetes medications**
3. **Durable remission of short duration T2DM is attainable in a Primary Care setting**

# DiRECT Intervention used Counterweight-Plus

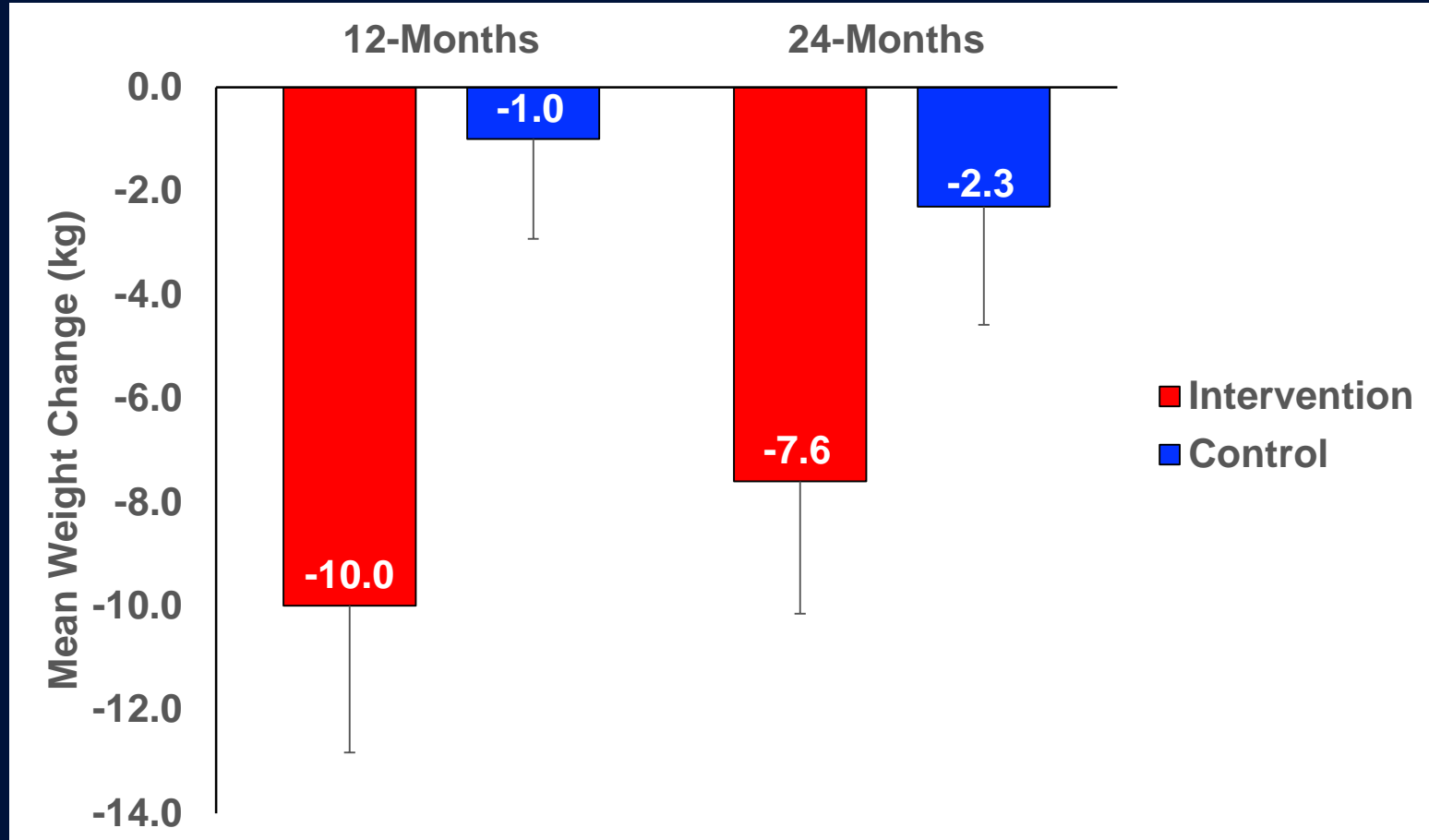


## Weight Loss Maintenance

- Principles integrated from day-1 of TDR
- Monthly appointments with practice nurse or dietitian
  - Review BP, BG, weight
  - Review of weight and remission expectations
  - Behavioural strategies to limit weight regain
- Access to DiRECT RA support

*Lean et al, Br J General Practice (2013),  
Leslie et al, BMC Family Practice (2016)*

# Greater weight loss 0-24months in intervention group

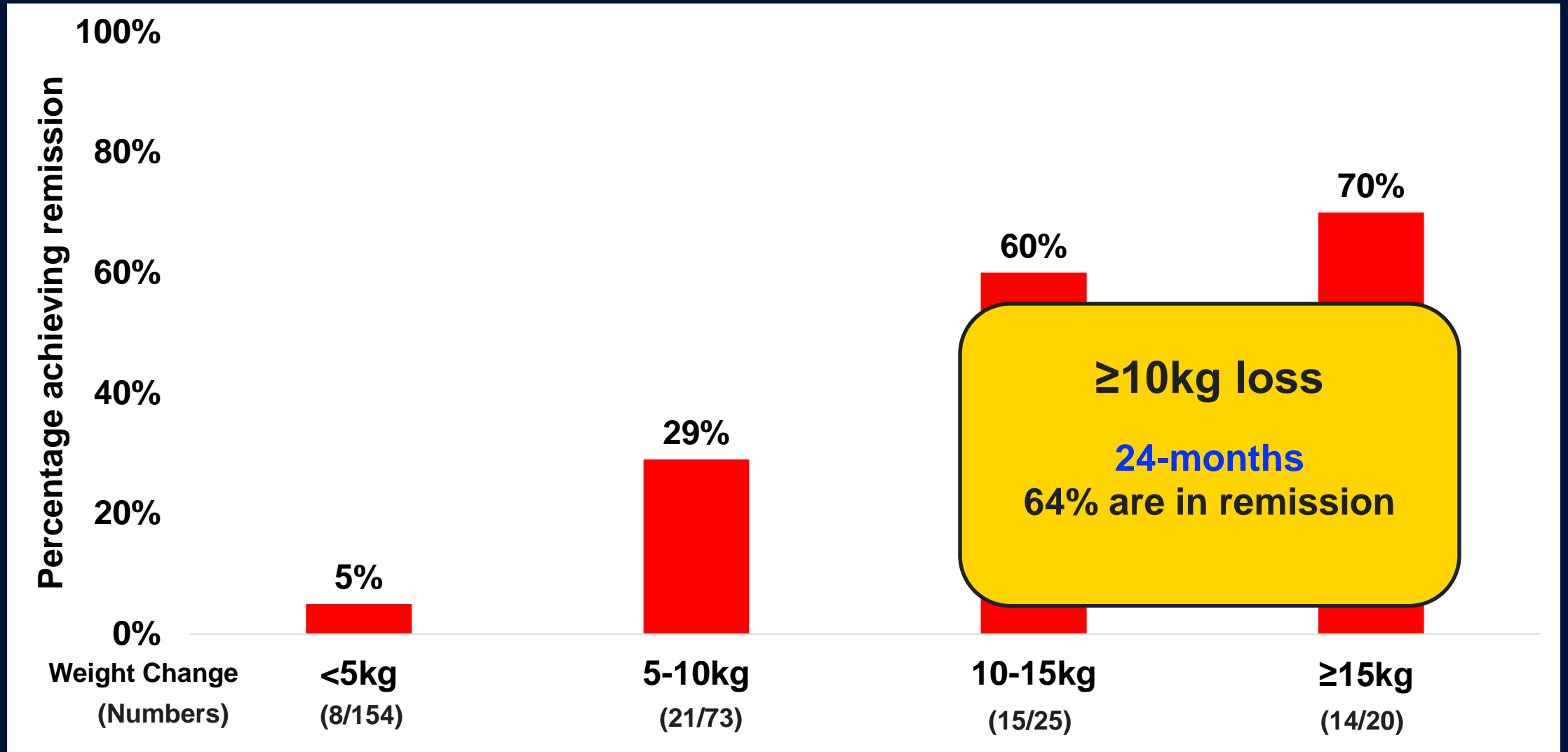


# ITT 24-Month Primary Outcome Results

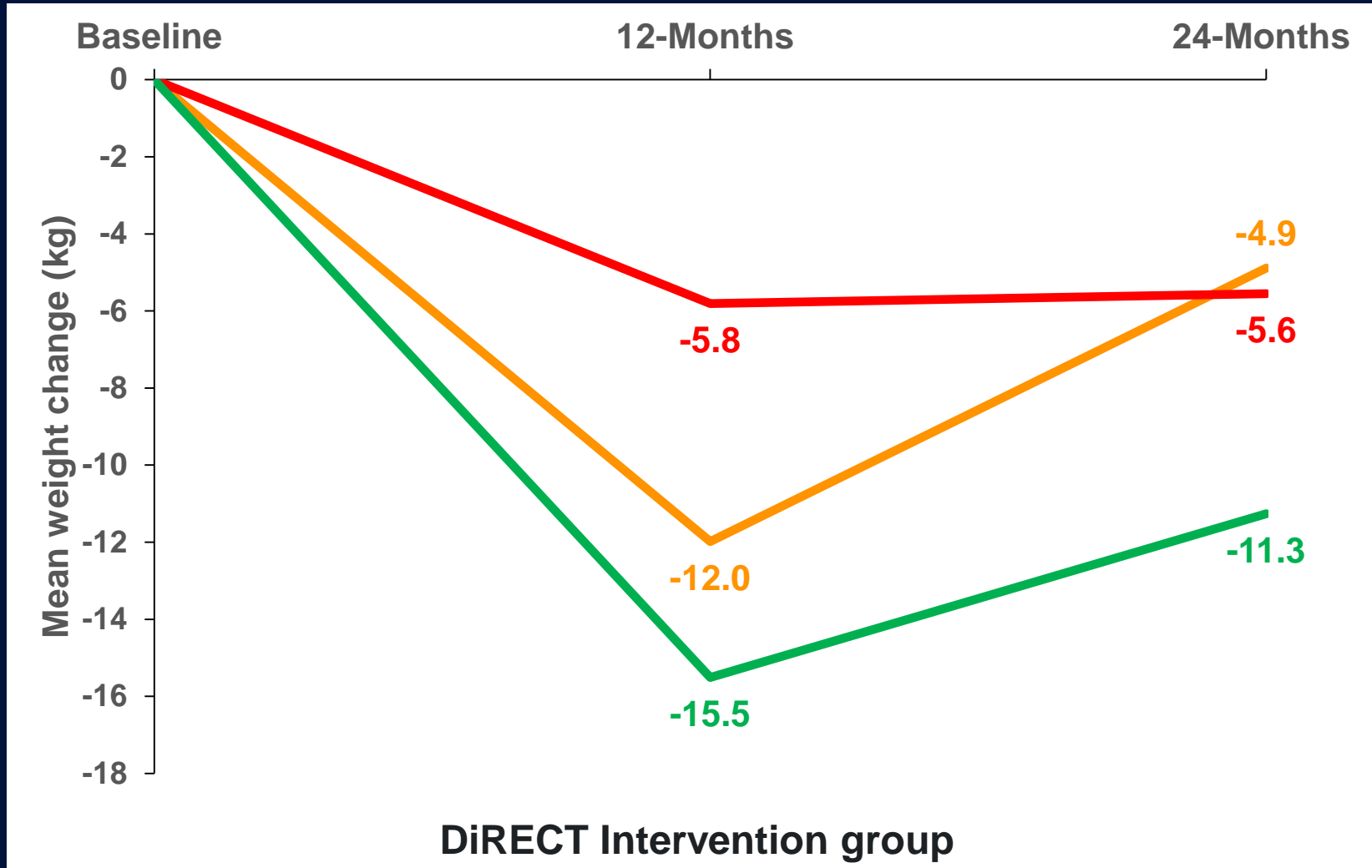
## Co-Primary Outcome: $\geq 15$ kg weight loss

|              |        |       |              |
|--------------|--------|-------|--------------|
| Intervention | 17/149 | (11%) | $p < 0.0001$ |
| Control      | 3/149  | (2%)  |              |

# Remissions by 24-month weight loss: entire study population



# Weight management is critical for T2D remission



No Remission at  
12 or 24-months  
n = 62 (42%)

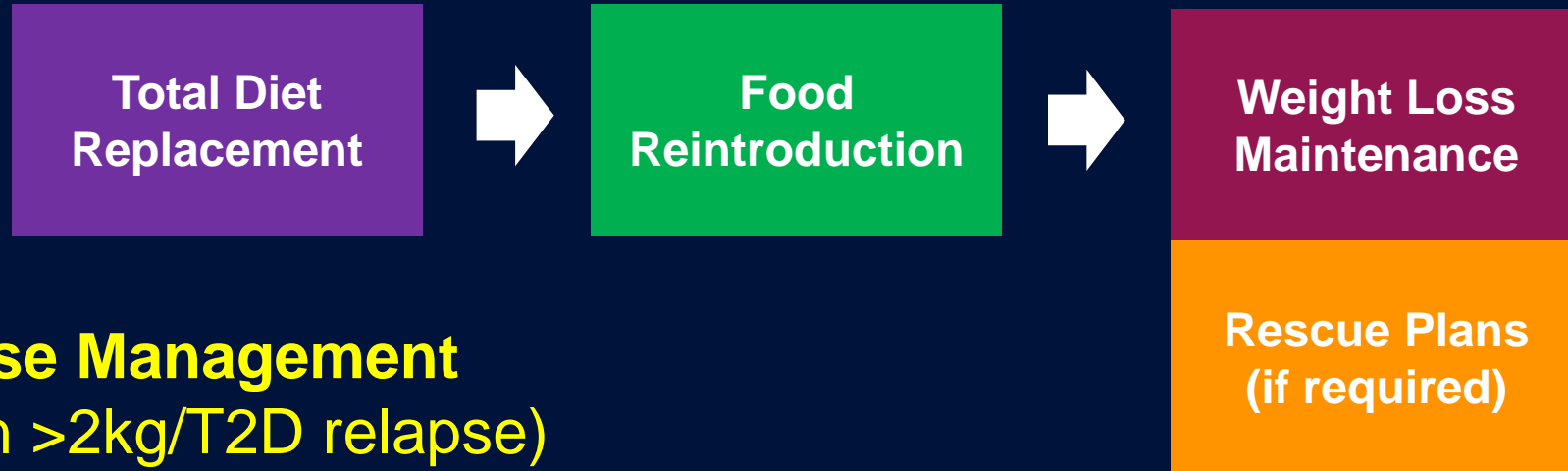
Remission at  
12 but not 24-months  
n = 15 (10%)

Remission at  
12 and 24-Months  
n = 48 (32%)

No data  
n = 24 (16%)



# DiRECT Intervention: 'Rescue Plans'

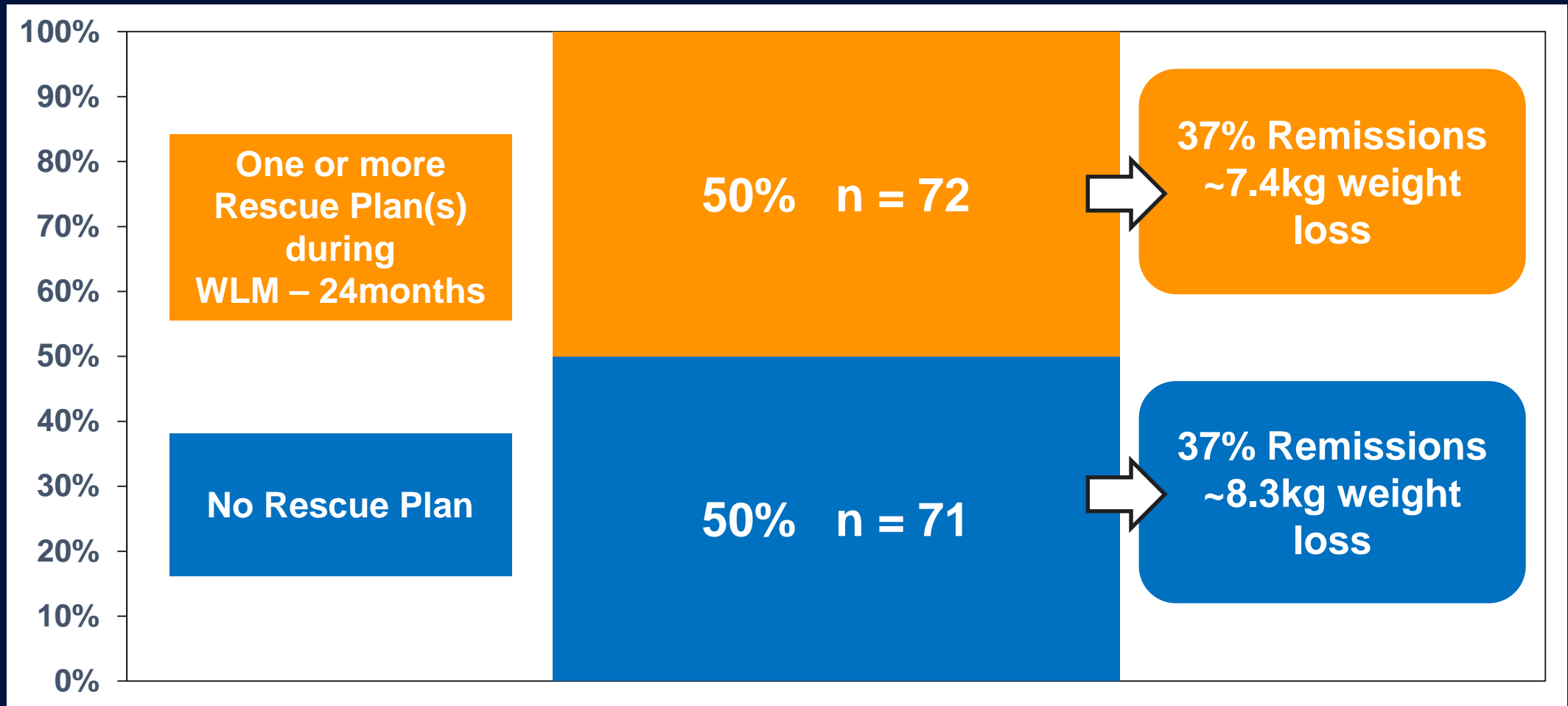


**Relapse Management**  
(regain >2kg/T2D relapse)

Tool-kit approach:

- Review causes of weight regain
- Review of behavioural strategies
- Brief Total Diet Replacement and/ or Food Reintroduction
- Offer of orlistat

# 'Rescue Plans' helped maintain weight and T2D remission



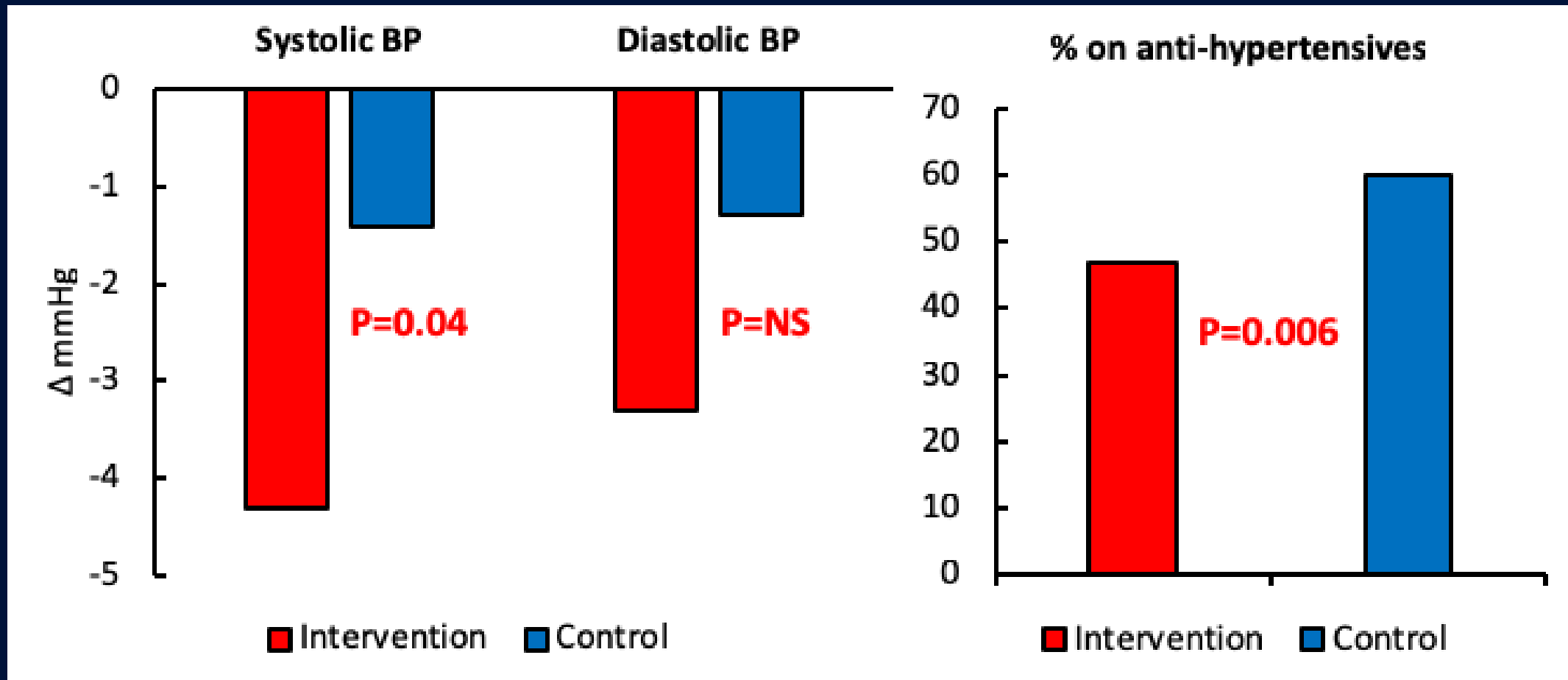
## Summary at 24-Months

- One third with early T2D achieve remission, -64% if  $\geq 10$ kg loss
- Achieving and maintaining weight loss are critical for success
- Weight loss at 24-months remains greater than most lifestyle interventions, despite modest regain

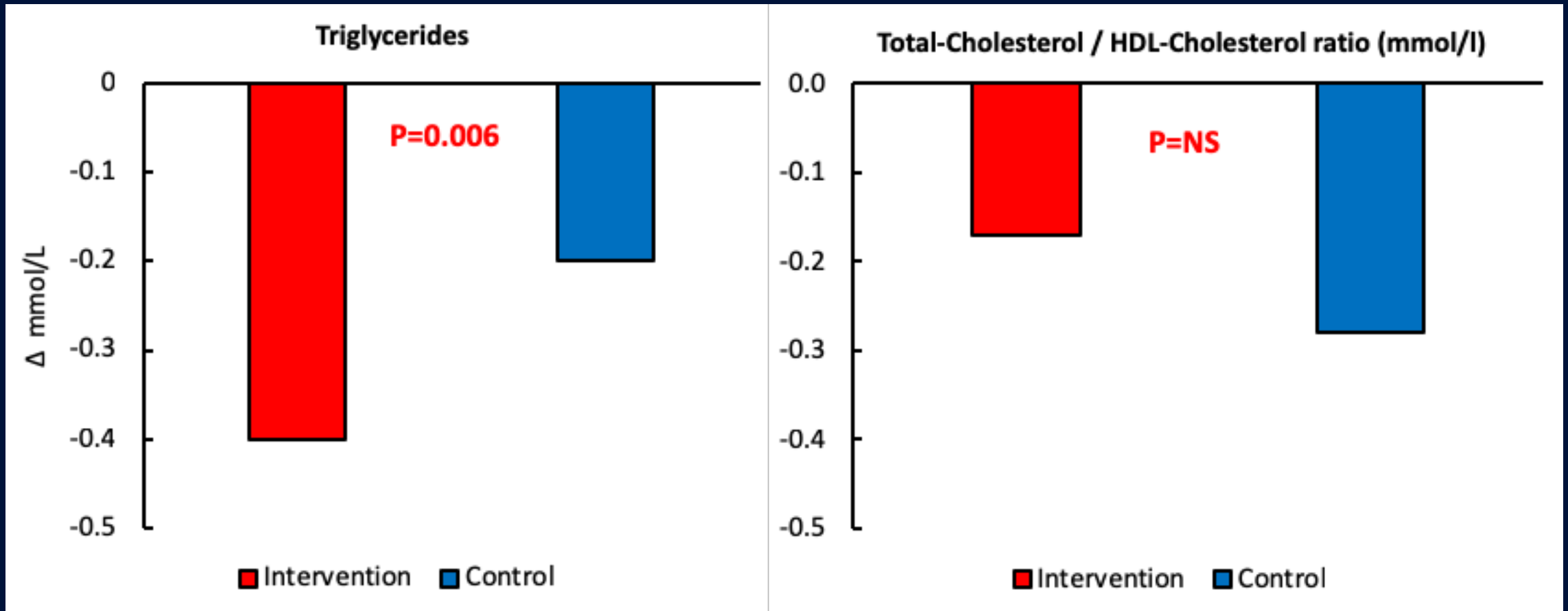
# Secondary outcomes at 24 months (ITT)

- Blood pressure
- Serum lipids
- Adverse events
- Quality of life

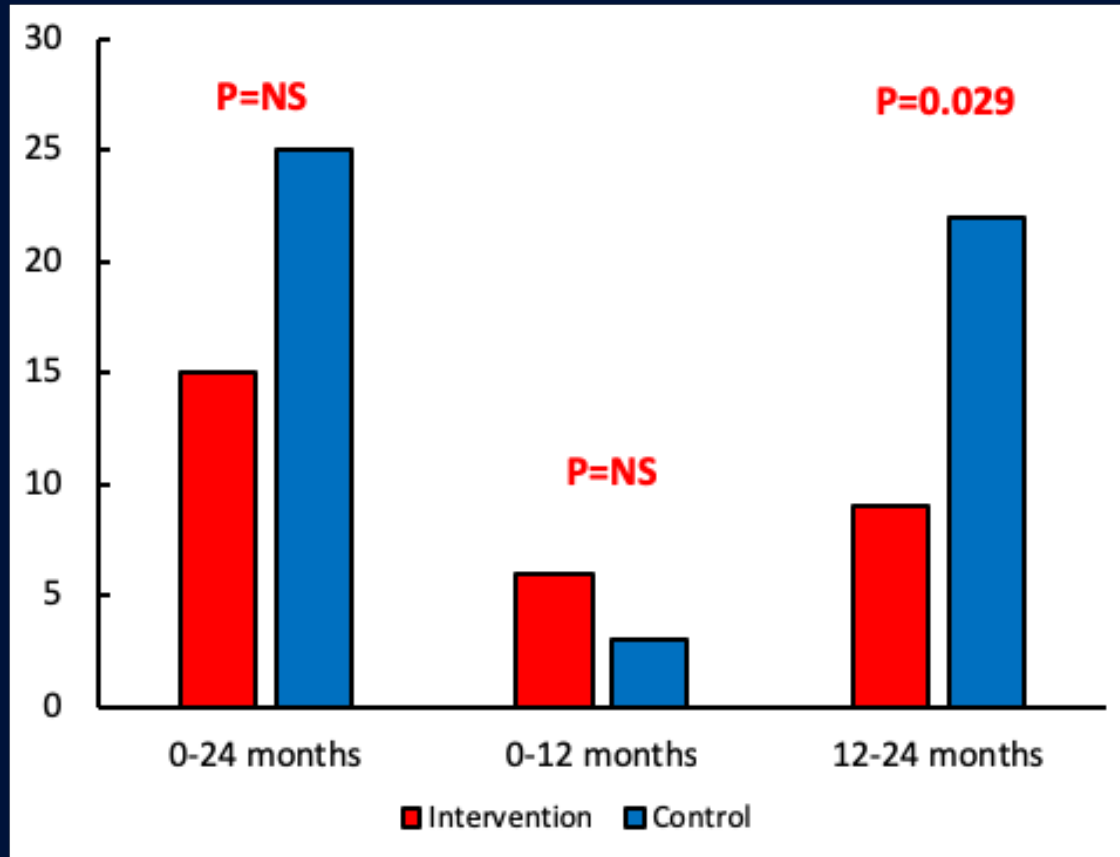
# DiRECT: BP falls, with fewer drugs



# DiRECT: Lipids improve



# DiRECT: Fewer serious adverse events 12-24m



CV & cancer events (post-hoc analysis):

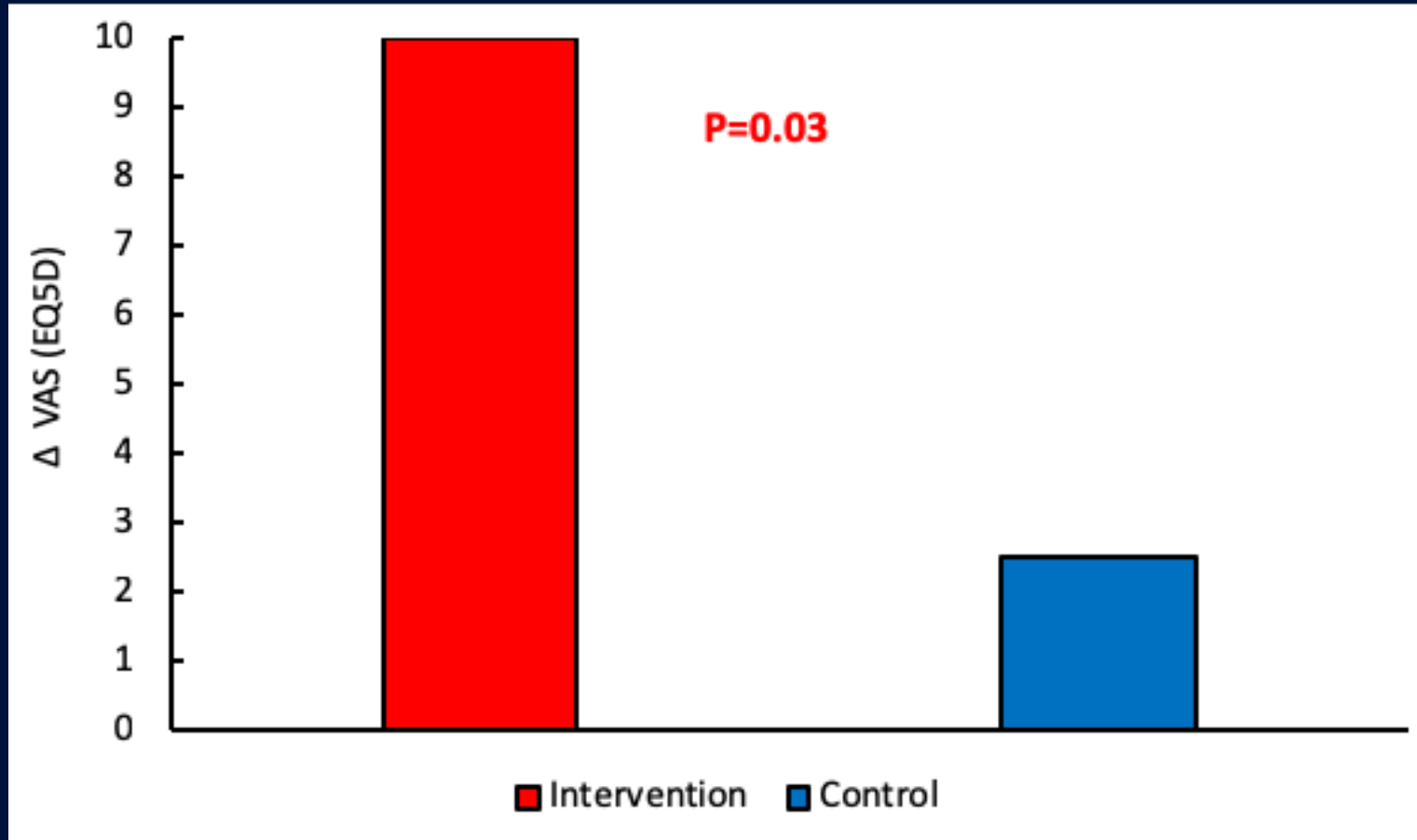
## Intervention

- 1 Non-fatal MI, 1 coronary artery disease

## Control

- 1 Sudden death, 2 CVA, 1 aortic aneurysm rupture, 1 toe amputation
- 5 cancers: 2 colon, 1 bladder, 1 renal, 1 prostate

# DiRECT: Quality of life improves 😊



Scale: 0 – 100

Worst imaginable  
to  
Best imaginable



## Summary:

### Intervention group secondary outcomes

- Blood pressure: ↓ Systolic BP, ↓ medications
- Serum lipids: ↓ Triglycerides
- Quality of life ↑ 😊
- Adverse events ↓ SAEs in 12-24 months

# DiRECT: 24 month conclusions

1. T2D is not necessarily a lifelong condition, & is reversible by weight loss
  - 36% in remission at 24 months
  - 70% in remission with >15kg loss
2. Maintaining weight loss is challenging
  - ≥10 kg weight loss achieved by 1/4 of intervention group
  - Ongoing support & relapse management limits weight regain
3. Fewer SAEs supports weight loss reducing complications of T2D
4. Early remission should be a primary management target for T2D

# Thank you

- GP practices and patients
- Academic & clinical colleagues
- Ethical and R&D committees
- Cambridge Weight Plan
- Diabetes UK, and funding donors



<http://www.directclinicaltrial.org.uk/>

# Declarations of Interests

MEJL reports research grants and personal fees for lecturing and consultancy from Novo Nordisk, consultancy fees from Counterweight Ltd, Novartis, and Eli Lilly.

RT reports educational lecture fees from Eli Lilly and Novartis and advisory board fees from Wilmington Healthcare.

ACB reports lecture fees from Novo Nordisk and Napp Pharmaceuticals.

LM was employed by Counterweight Ltd and reports research funding from Cambridge Weight Plan and consultancy fees from Counterweight Ltd.

GT reports PhD fees and conference expenses from Cambridge Weight Plan.

WSL reports conference expenses from Cambridge Weight Plan.

NS reports research grants and speaker's honoraria from Boehringer Ingelheim and speaker's honoraria from Amgen, AstraZeneca, Eli Lilly, Janssen, Napp Pharmaceuticals, Novo Nordisk, and Sanofi.


NB reports personal fees for freelance work and share holdings from Counterweight Ltd from Cambridge Weight Plan.

HMR was employed by Counterweight Ltd

All other authors declare no competing interests.

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Doctopic: Primary Research This version saved: 15:01, 01-Mar-19

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**Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial** 

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