Liraglutide Induced WeiGHt Loss in Type 2 Diabetes (LIGHT2D)

Cindy San, B.Sc. (Pharm); Anar Dossa, B.Sc. (Pharm), Pharm D., CDE; David Thompson, M.D.; Sharon Leung, R.D.

Background

- One of the most well-established modifiable risk factors for type 2 diabetes mellitus (T2DM) is excess weight.
- Glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) are incretins, which are endogenous gastrointestinal hormones secreted following meal ingestion.
  - Stimulate insulin synthesis and secretion while preventing glucagon secretion.
  - It is proposed that up to 70% of the insulin response to a meal is mediated through the release of incretin hormones.
- Liraglutide is a novel GLP-1 receptor agonist for treatment of T2DM.
- In addition, it has been shown to promote weight loss by delaying gastric emptying and enhancing satiety.
- A series of studies showed decrease mean weight ranging from 1 to 3.2 kg over a course of 26 or 52 weeks with liraglutide in different diabetic regimens.
- Weight loss in patients with liraglutide at the outpatient diabetes centre is observed to be of greater magnitude, with approximately 4.5 kg to 7 kg weight loss over the course of 8 to 16 weeks.

Objectives

- Primary
  - To determine the extent of weight loss associated with liraglutide in patients at the Diabetes Education Centre of Vancouver General Hospital in comparison to what is reported in the literature.
- Secondary
  - To determine the safety and tolerability of liraglutide.
  - To determine the effect of liraglutide on other parameters including blood pressure, hemoglobin A1C and lipids.

Methods

- Design: A retrospective chart review of diabetes patients at Vancouver General Hospital Diamond Center Diabetes Education Centre.
- Population: Type 2 diabetes patients who have been started on liraglutide were identified through the clinic databases and chart review.
- Inclusion Criteria:
  - All patients aged greater than 18 years of age prescribed liraglutide between May 27th, 2010 and Sept 30th, 2011.
- Exclusion Criteria:
  - Use of approved weight-lowering therapy within the previous 3 months
  - Participation in a clinical weight control study within the previous 3 months
  - Previous surgical obesity treatment
  - Use of liraglutide for less than 3 months
  - No follow-up visits after liraglutide initiation
  - No baseline weight measurement
- Analysis:
  - Primary outcome: Spearman's rho correlation statistics between time, dose and percentage of weight reduction
  - Secondary outcome:
    - HbA1C, cholesterol, blood pressure: descriptive statistics
    - Adverse effects: qualitative descriptive reporting
  - Included trials in pooled analysis (PubMed, Medline, Embase)
    - MESH terms: Liraglutide; weight loss; type 2 diabetes
    - Limits: Randomized controlled trials; English; adults; liraglutide use > 24 weeks

Table 1: Demographic Characteristics of Study Participants (n=71)

Age (years, mean ±SD)	57 ± 10
Sex (%) (men/women)	62/38
Average weight (kg ± SD)	108 ± 21
Duration of diabetes (years, mean ±SD) (n=56)	14 ± 6
A1C (%, mean ±SD) (n=70)	9 ± 1.7
SBP (mmHg, mean ± SD) (n=53)	128 ± 15
DBP (mmHg, mean ± SD) (n=53)	73 ± 10
Total cholesterol/HDL (mean ± SD) (n=50)	4.08 ± 1.06
LDL cholesterol (mmol/L, mean ± SD) (n=50)	2.34 ± 0.77
HDL cholesterol (mmol/L, mean ± SD) (n=50)	1.10 ± 0.32
Triglycerides (mmol/L, mean ± SD) (n=50)	2.26 ± 1.38
Concomitant Therapies:	
Antihypertensive(s) (%)	79
Antiplatelet(s) (%)	37
Antilipemic(s) (%)	68
Antidepressant(s) (%)	18
Anticonvulsant(s) (%)	4
Concomitant Diabetes Therapies(%):	97
Metformin (%)	77
Gliclazide (%)	24
Glyburide (%)	34
Acarbose (%)	1
Rosiglitazone (%)	1
Pioglitazone (%)	13
Repaglinide (%)	0
Sitagliptin (%)	4
Exentinide (%)	1
Insulin (%)	46

Figure 1: Histogram Model of the Duration of Therapy
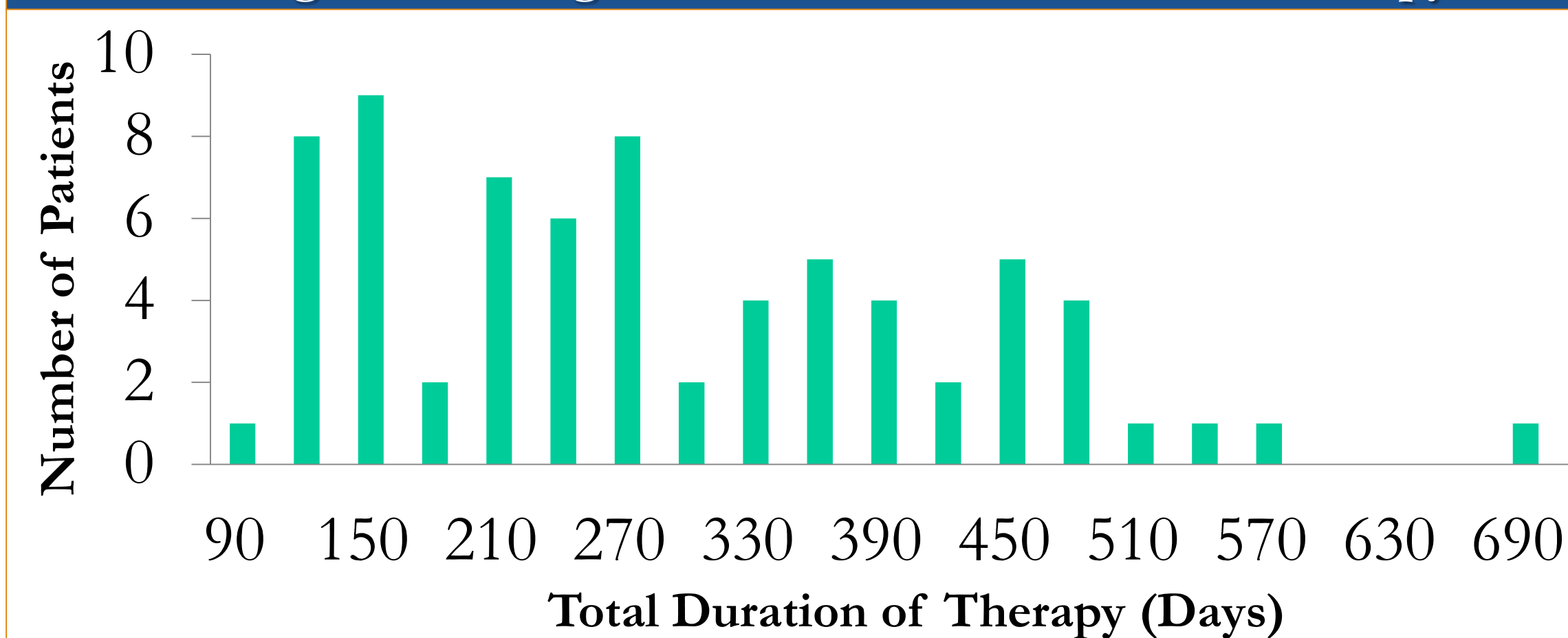
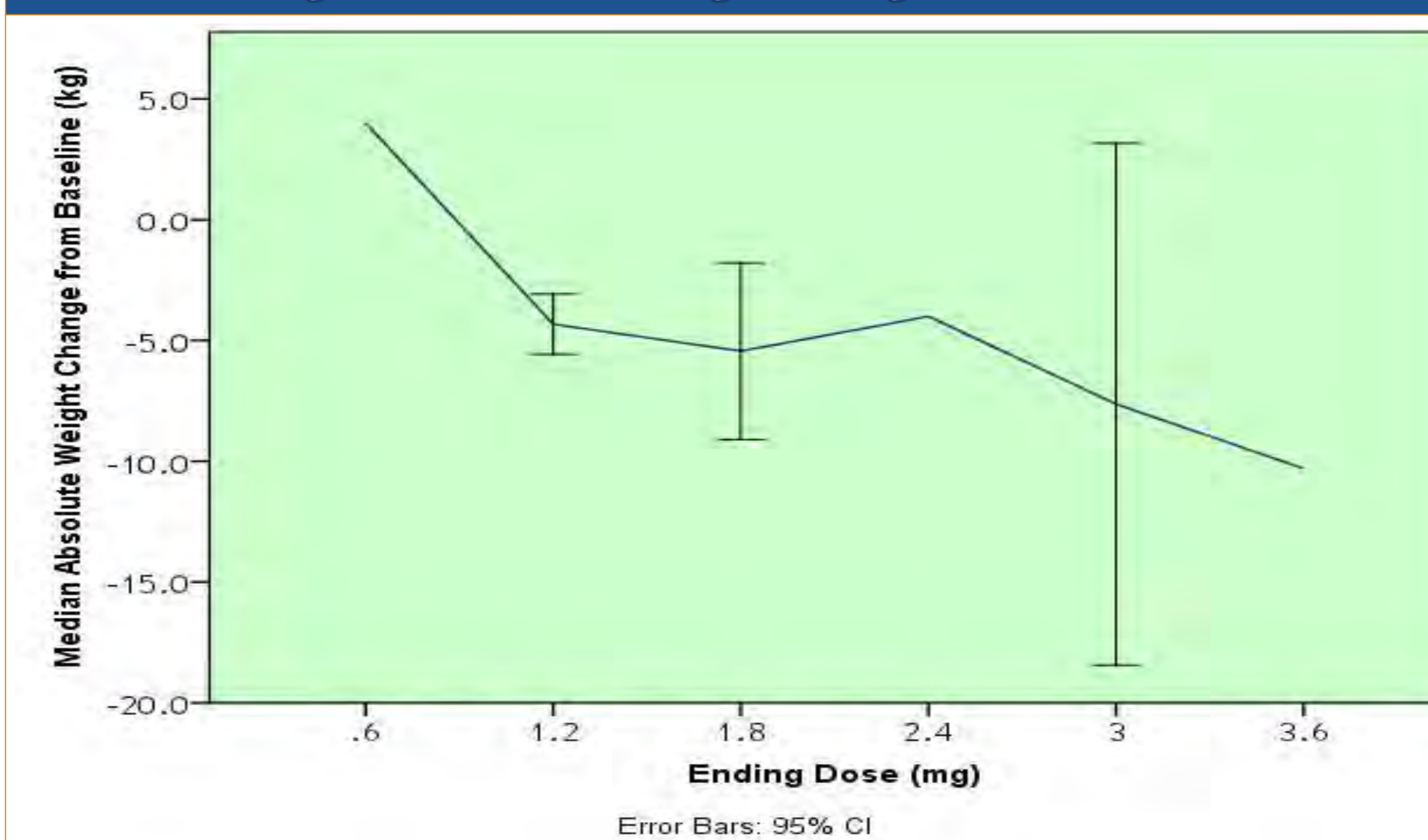### Figure 2: Absolute Weight Change From Baseline

Error Bars: 95% CI

Figure 3: Number of Patients Receiving Liraglutide Doses at the End of the Study
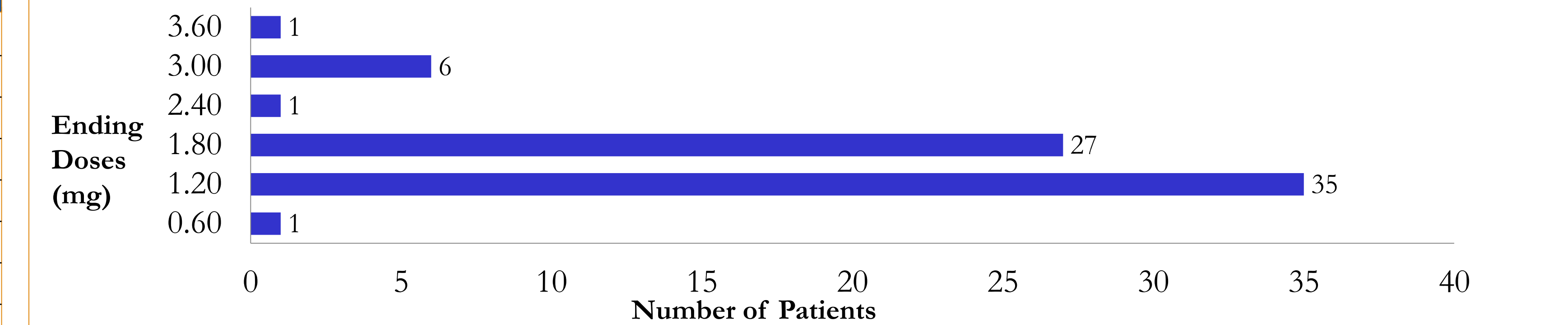

Table 2: Results

Primary:	
Liraglutide ending dose (mg, mean ± SD)	1.6 ± 0.59
Median duration of liraglutide treatment (weeks, range)	36 (13 to 95)
Patients with weight loss by the end of the study (%)	83
Median Change in Weight from Baseline (kg) (range)	-3.2 (-31 to 10.5)
Median Percentage Reduction in Weight from Baseline (%) (range)	3.2 (-10 to 27.3)
Correlation coefficient between dose versus % weight reduction (p value)	0.02 (p=0.87)
Correlation coefficient between 1.2 mg &1.8 mg versus % weight reduction (p value)	-0.16 (p=0.22)
Correlation coefficient between time versus % weight reduction (p value)	-0.42 (p=0.73)
Secondary:	
Absolute Change in A1C (%) (mean ± SD) (n=63)	-0.6 ± 1.4
Absolute Change in SBP (mmHg) (mean ± SD) (n=40)	-1.9 ± 10.3
Absolute Change in DBP (mmHg) (mean ± SD) (n=40)	-0.5 ± 8
Absolute Change in Total cholesterol/HDL (mean ± SD) (n=31)	-0.41 ± 1.19
Absolute Change in LDL cholesterol (mmol/L, mean ± SD) (n=31)	-0.39 ± 0.77
Absolute Change in HDL cholesterol (mmol/L, mean ± SD) (n=31)	-0.06 ± 0.27
Absolute Change in Triglycerides (mmol/L, mean ± SD) (n=31)	-0.53 ± 1.60
Majority of adverse events: Nausea, diarrhea and vomiting (%)	13

Figure 4: Pooled analysis of change in body weight (kg) in included trials for Liraglutide 1.8 mg versus placebo after at least 24 weeks of treatment, using random effects model

Study or Subgroup	Liraglutide Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Garber 2009	-2.45	7.8	246	1	7.8	248	18.0%	-3.45 [-4.83, -2.07]
Marre 2009	-0.2	0.5	234	-0.1	0.6	114	21.0%	-0.10 [-0.23, 0.03]
Nauck 2009	-2.8	0.2	242	-1.5	3	122	20.5%	-1.30 [-1.83, -0.77]
Russell-Jones 2009	-1.8	5	230	-0.4	4.1	114	19.4%	-1.40 [-2.39, -0.41]
Zinman 2009	-2	0.3	178	0.6	0.3	177	21.1%	-2.60 [-2.66, -2.54]
Total (95% CI)			1130			775	100.0%	-1.73 [-3.26, -0.19]

Conclusions

- Liraglutide appears to cause higher degree of weight loss in certain patients compared to the literature and is not correlated with the dose of the medication or the duration of use.
- Liraglutide 1.2mg may be more cost-effective for the indication of weight loss compared to 1.8mg in type 2 diabetic patients because there appears to be little therapeutic benefit with the 1.8mg dosage.
- Future analysis needed to determine the reason for the difference in the extent of weight loss in this study than what is reported in the literature.

Limitations

- Retrospective review design. No control group.
- Potential underreporting of adverse effects.
- Most patients on concomitant medications that may affect outcomes.
- Compliance to liraglutide not assessed.
- Only ending doses used for statistical analysis.