Efficacy of GLP-1 Analogues at Different Baseline Levels of HbA1c in T2DM A Systematic Review and Meta-Analysis

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Introduction:

peptide-1 Glucagon-like receptor analogues (GLP-1a) are a group of medications used in treating type 2 diabetes mellitus (T2DM) with added beneficial effect on weight and blood pressure since 2005. In this systematic review and meta-analysis, we gathered evidence to show whether baseline level of glycosylated haemoglobin (HbA1c) predicts the efficacy of GLP-1a in T2DM.

Aim:

Baseline levels HbA1c predict the efficacy of GLP-1a in T2DM. The aim of this systematic review and meta-analysis is to assess the efficacy of GLP-1a at different levels of baseline HbA1c in T2DM.

Methods:

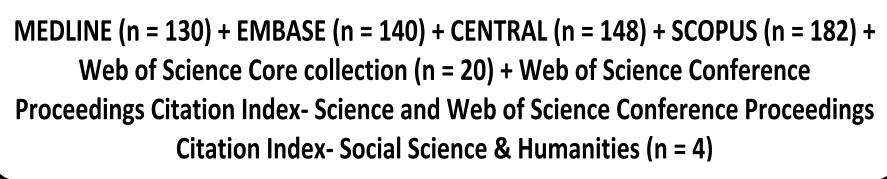
Five electronic databases were searched: MEDLINE (1990 - July 2014), EMBASE (1990 – July 2014), Cochrane Central Register of Controlled Trials (Issue 6 of 12, June 2014), SCOPUS (1990 - 2014) and Web of Science Core Collection (1990 – 2014) and abstracts proceedings. Trials were included if they were randomised, controlled and involved one or more of the GLP-1a in clinically-relevant doses compared to placebo and/or other glucose-lowering agents except GLP-1a. The identified trials were stratified according to level of baseline HbA1c.

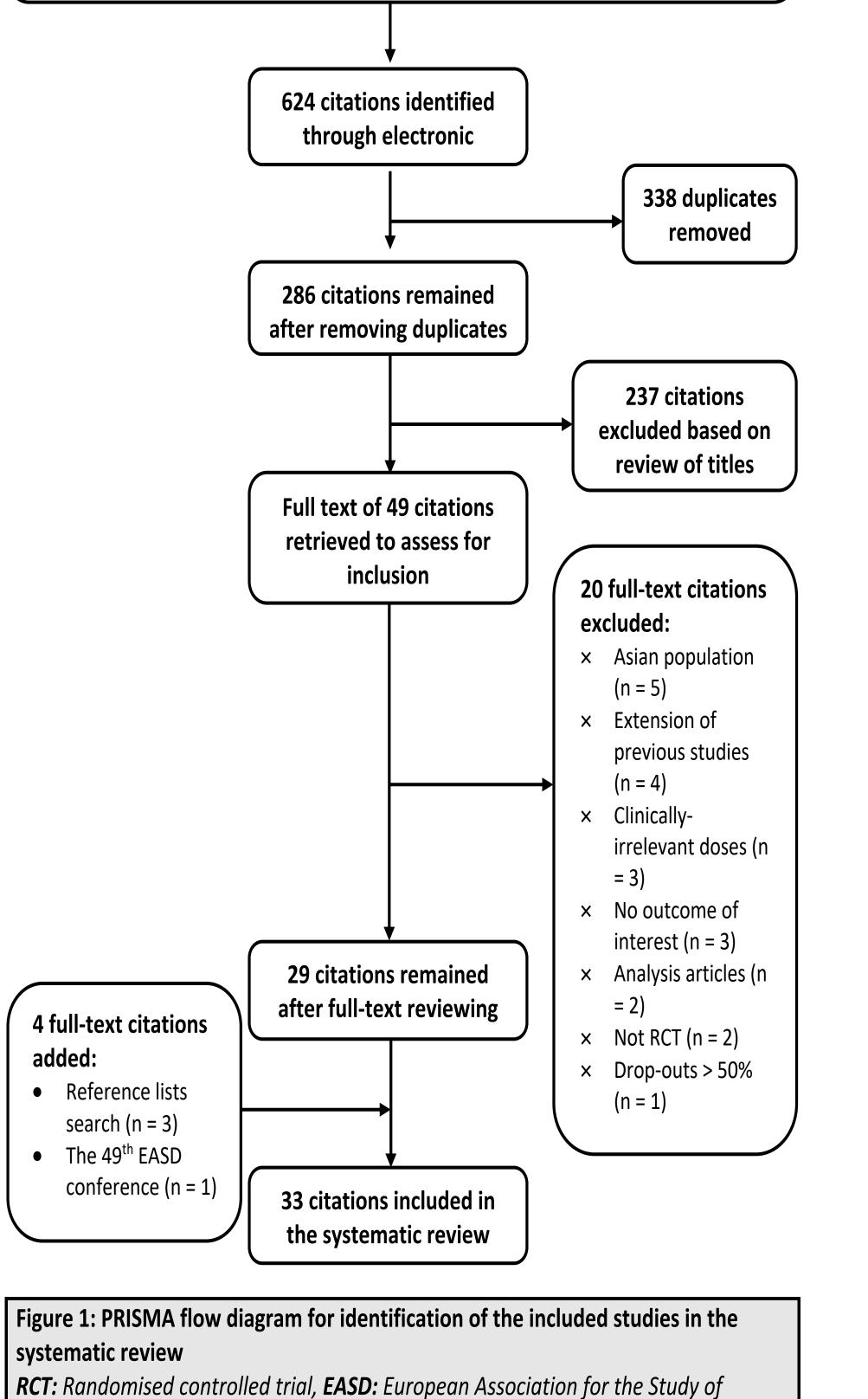
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Results:

Diabetes

Thirty-three trials met inclusion criteria (Figure 1) . RCTs were stratified into the predefined groups of baseline levels HbA1c.





GLP-1a showed more efficacy against placebo at higher baseline level of HbA1c (absolute reductions of HbA1c were -1.06, -0.79 and -0.63% at baseline levels of - 8.99% (69.4 – HbA1c 8.5 74.8mmol/mol), 8.0 – 8.49% (63.9 – 69.3mmol/mol) and 7.5 - 7.99% (58.5 -63.8mmol/mol), respectively) (Figure 2).

Group by	Study name	Statistics for each study			Difference in means and 95% Cl				
Baseline HbA1c		Difference in means	Lower limit	Upper limit					
7.50 - 7.99%		-0.629	-0.934	-0.324					
8.00 - 8.49%		-0.789	-0.987	-0.591					
8.50 - 8.99%		-1.059	-1.206	-0.913					
					-2.00	-1.00	0.00	1.00	2.00
CI: confiden			group				•	•	1.
When (GLP-1a	wer	e c	om					
When (and/or	GLP-1a insulin	wer	re c reta	om gogi	ues	, th	ne e	effic	cac
When (and/or of GLP	GLP-1a insulin -1a w	wer secr /as	re c reta out	om gogi weiį	ues ghe	, th d	ne e by	effic th	
When (and/or of GLP compara	GLP-1a insulin -1a w	wer secr at hig	e c eta out ghe	om gogi weig r le	ues ghe vels	, th d s o	nee by fb	effic th ase	cac los lin
When (and/or of GLP	GLP-1a insulin -1a w ators a 2 9.0%	wer secr at hig $(\geq 74$	re c reta outr ghe .9m	om gogi weig r le mo	ues ghe vels I/m	, th d s o ol)	ne e by f b (Fig	effic th ase gure	cac los lin e 3



Conclusion:

GLP-1a are highly efficacious glucoselowering agents at any level of baseline HbA1c. The pooled data showed that efficacy of GLP-1a increase at higher baseline levels of HbA1c in T2DM.

Group by Baseline HbA1c
9.00 - 9.00 -

Figure 3: Forest plot of efficacy of GLP-1 versus active comparator (insulin and/or SUs) at different baseline HbA1c

CI: confidence interval

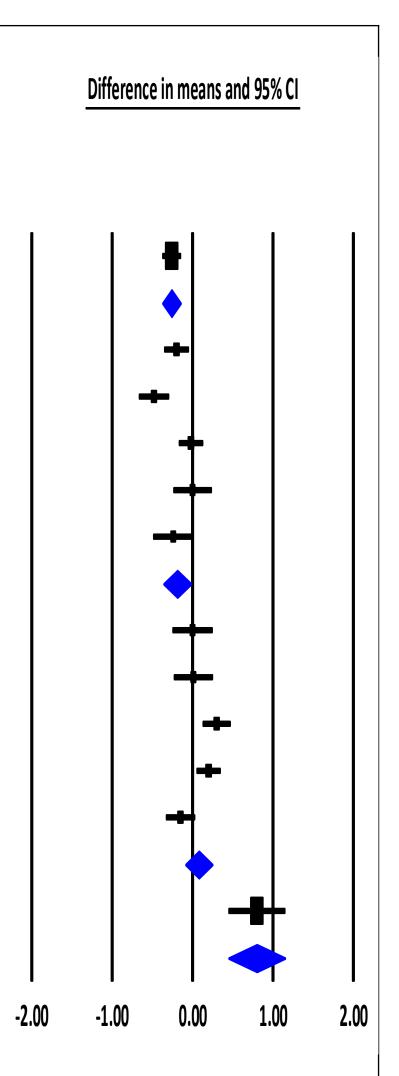
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Study name	Statistics for each study						
	Difference in means	Lower limit	Upper limit				
Lane 2014	-0.260	-0.376	-0.144				
	-0.260	-0.376	-0.144				
Diamant 2010	-0.200	-0.353	-0.047				
Garber 2009	-0.480	-0.667	-0.293				
Heine 2005	-0.020	-0.170	0.130				
Nauck 2009 (B)	0.000	-0.239	0.239				
Russell-Jones 2009 (B)	-0.240	-0.489	0.009				
	-0.188	-0.361	-0.016				
Barnett 2007	0.000	-0.249	0.249				
Davies 2009	0.010	-0.232	0.252				
Derosa 2010	0.300	0.126	0.474				
Derosa 2011	0.200	0.050	0.350				
Nauck 2007	-0.150	-0.331	0.031				
	0.080	-0.089	0.249				
Bergenstal 2009	0.800	0.448	1.152				
	0.800	0.448	1.152				



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