

# Do DPP-4 inhibitors differ in efficacy between patients of Asians and White ethnicity? A systematic review and meta-analysis

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## Introduction

One of the greatest threats of the century to the health of mankind is Type 2 diabetes mellitus(T2D). The pharmacodynamics and pharmacokinetics of specific oral hypoglycaemic agents (OHA)s can be different among different ethnic groups.

Dipeptidyl Peptidase 4 (DPP-4) inhibitors are commonly used OHAs to treat Type 2 diabetes. Previous reports have suggested contradictory findings in their efficacy, when comparing Asian with White populations. We aimed to evaluate the efficacy of Dipeptidyl Peptidase 4 (DPP-4) inhibitors in different ethnic groups.

## Methods

A literature search was conducted in PubMed for studies published from the period January 2006 to March 2019, by two independent investigators. Randomised controlled trials with atleast 50 patients in each arm and treatment duration nearest to 24 weeks were selected. These trials assessed the efficacy of a DPP-4 inhibitor versus placebo on HbA1c level in T2D patients. Studies which were focused on patients with adverse health conditions were rejected.



Outcome variable was the absolute change in HbA1c from baseline to the last available follow up measure. A systematic review and metaanalysis was conducted.

Figure 1 : Prisma Flowchart showing the study selection procedure

		Experimental				Control				
Study	Total	Mean	SD	Total	Mean	SD	Mean Difference	MD	95%-CI	Weight
Gantz I	102	-0.33 1	1.3910	101	-0.45	1.3840	: <u> </u>	0.12	[-0.26; 0.50]	4.2%
Tinahones FJ	122	-0.53 (	0.7820	125	-0.21	0.7820		-0.32	[-0.52; -0.12]	6.8%
Matthaei S	153	-0.51 (	0.7570	162	-0.16	0.7790		-0.35	[-0.52; -0.18]	7.2%
Barnett AH	160	-0.61 0	0.7590	78	0.04	0.6180		-0.65	[-0.83; -0.47]	7.0%
Karyekar CS	135	-0.78 1	1.6300	136	-0.17	1.0400	- <u>m</u> -	-0.61	[-0.94; -0.28]	4.9%
Derosa G	91	-0.60 (	0.6320	87	-0.40	0.5760		-0.20	[-0.38; -0.02]	7.1%
Taskinen MR	513	-0.49 (	0.9060	175	0.15	0.7940		-0.64	[-0.78; -0.50]	7.6%
Rosenstock J	102	-0.43 1	1.0480	95	0.19	1.0480		-0.62	[-0.91; -0.33]	5.3%
DeFronzo RA	186	-0.59 (	0.9550	175	0.13	0.9260		-0.72	[-0.91; -0.53]	6.8%
Nauck MA	213	-0.60 1	1.4590	104	-0.10	1.0200			[-0.78; -0.22]	5.5%
Garber AJ	146	-0.90 1	1.0540	158	-0.60	1.1690			[-0.55; -0.05]	6.0%
Bosi E	177	-0.50 1	1.3300	182	0.20	1.3490			[-0.98; -0.42]	5.5%
Rosenstock J	175	-0.85 (	0.8770	178	-0.15	0.8510			[-0.88; -0.52]	7.0%
Gomis	252	-1.06 0	0.9520	128	-0.56	1.0180		-0.50	[-0.71; -0.29]	6.6%
Bergenstal	177	-0.89 (	0.7980	90	-0.10	7.5890			[-2.36; 0.78]	0.4%

### Results

389 potentially relevant articles were identified through database searching in PubMed. Overall, 30 studies were included in the meta-analysis (Figure 1). 17 studies compared DPP-4 inhibitors to placebo therapy in the White population, and 13 other studies were in the Asian population. In the meta-analysis, the studies that included more than 70% White participants had an HbA1c change of (weighted mean difference[WMD]) -0.48% ; 95% CI -0.59, -0.38) (Figure2);



#### Figure 2 : Forest plot for Whites

		Experim	Experimental		Control					
Study	Total	Mean	SD	Total	Mean	SD	Mean Difference	MD	95%-CI	Weight
Dou J	210	-3.00 1.	.0140	207	-2.80	1.0070		-0.20	[-0.39; -0.01]	8.0%
Wang W	185	-0.76 1.	1800	180	-0.14	1.1980		-0.62	[-0.86; -0.38]	7.4%
Yang W	143	-0.70 1.	.1960	136	-0.20	1.1660		-0.50	[-0.78; -0.22]	7.0%
Lukashevich V	158	-1.01 1.	.9270	160	0.25	1.9270		-1.26	[-1.68; -0.84]	5.3%
Pan C	146	-1.05 0.	.9660	144	-0.54	0.9600		-0.51	[-0.73; -0.29]	7.7%
Pan CY	284	-0.84 0.	.9420	284	-0.34	0.9420		-0.50	[-0.65; -0.35]	8.4%
Yang W	283	-0.78 0.	7920	287	-0.37	0.7920		-0.41	[-0.54; -0.28]	8.6%
Yang	191	-1.00 1.	.0580	194	-0.10	1.0660		-0.90	[-1.11; -0.69]	7.8%
Forst	62	-0.50 0.	.8100	70	0.24	0.7400		-0.74	[-1.01; -0.47]	7.2%
Kaku	111	-0.91 0.	.4400	115	-0.19	0.5500	-	-0.72	[-0.85; -0.59]	8.6%
Hanefeld	107	-0.28 0.	7390	107	0.12	0.7390		-0.40	[-0.60; -0.20]	8.0%
Seino	76	-0.96 0.	.5500	75	0.04	0.4600		-1.00	[-1.16; -0.84]	8.3%
Kikuchi	71	-0.53 0.	.7010	72	0.28	0.7010		-0.81	[-1.04; -0.58]	7.6%
Random effects model	2027			2031			\$	-0.64	[-0.79; -0.49]	100.0%
Prediction interval									[-1.23: -0.06]	

whereas in those studies including more than 70% Asian participants, HbA1c changed by -0.64%; 95% CI -0.79, -0.49) (Figure 3).

### Conclusion

The glucose lowering efficacy of DPP-4 inhibitors showed no significant differences between Whites and Asians.

Further investigation is required to understand the underlying mechanism particularly in relation to BMI, duration of diabetes, treatment duration and baseline HbA1c.

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#### Prediction interval Heterogeneity: $I^2 = 85\%$ , $\tau^2 = 0.0645$ , p < 0.01



#### Figure 3 : Forest plot for Asians

**Disclamer:** The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.









