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**Patient characteristics are associated with treatment response to second line glucose lowering therapy: a MASTERMIND study**

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**Background and aims:** The most common second-line glucose-lowering agent in type 2 diabetes is a sulfonylurea (SU). Draft NICE (UK) guidelines, currently out for consultation, propose using a thiazolidinedione (TZD), pioglitazone, as second-line. There is no guidance regarding which treatment is most effective in which patients. We assessed whether patient clinical characteristics could be used to predict response and aid treatment decisions.
**Materials and methods:** 12-month glycaemic response (HbA1c change from baseline) was calculated for patients in the CPRD (UK primary care) dataset treated with SUs (n=8748) or TZDs (n=8876). Relationships between clinical phenotype and glycaemic response were assessed using linear regression, with adjustment for baseline HbA1c. This analysis was repeated for the ADOPT randomised controlled trial (SUs n=1441; TZDs n=1456).
**Results:** In CPRD, patients diagnosed younger had a smaller glycaemic response to both SUs and TZDs (~2mmol/mol greater response per 10-year increase in age at diagnosis, $p<0.0001$). Female patients responded better to TZDs (1.9mmol/mol greater HbA1c reduction compared with males, $p<0.0001$), but worse to SUs (2.4mmol/mol smaller response, $p<0.0001$). Obese patients (BMI≥30kg/m2) responded better to TZDs (2.1mmol/mol greater HbA1c reduction compared with non-obese patients, $p<0.0001$), but non-obese patients responded better to SUs (1.9mmol/mol greater HbA1c response, $p<0.0001$). Combining categories led to greater differences (obese females: 4.4mmol/mol greater response to TZDs; non-obese males: 3.3mmol/mol greater response to SUs). Effect sizes were similar in ADOPT.
**Conclusion:** Clinical phenotype helps determine likely initial response to second-line glucose lowering therapies, and could influence therapeutic choices. Obese females have the greatest HbA1c reduction with TZDs, and non-obese males with SUs.
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