Diabetologia (2007) 50:1111
DOI 10.1007/s00125-007-0632-1

LETTER

Response to comment on: Evans JMM, Ogston SA, Emslie-Smith A, Morris AD (2006) Risk of mortality and adverse cardiovascular outcomes in type 2 diabetes: a comparison of patients treated with sulphonylureas and metformin. Diabetologia 49:930–936

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Received: 24 January 2007 / Accepted: 24 January 2007 / Published online: 10 March 2007

To the Editor: In a recent letter to *Diabetologia* [1], D. Raccah questions the value of several recent observational studies, discussed by J. A. Tayek [2], that have identified increased cardiovascular mortality among type 2 diabetic patients treated with sulphonylureas compared with patients prescribed other therapies (such as metformin). He argues that prospective, randomised clinical trials are necessary to establish whether sulphonylureas are linked with excess mortality.

We would like to clarify some of his misunderstandings surrounding our own observational study [3]. We used the databases of the Diabetes Audit and Research in Tayside, Scotland (DARTS)/the Medicines Monitoring Unit (MEMO) Collaboration, which contain comprehensive clinical data for all patients with type 2 diabetes in this region. Our study was retrospective only in the sense that it used 'historical' data collected (at the time) for patients from 1993 onwards. In fact, our study was a prospective cohort study that was specifically designed to evaluate cardiovascular risk (in contrast to Raccah's assertion).

We acknowledge that, in observational research, the distribution of confounding factors may vary between different comparison groups. In our study, patients in the sulphonylurea cohort did appear to have an increased cardiovascular risk at baseline compared with the other patients. However, there are statistical techniques that deal with such issues of confounding. We found increased cardiovascular risks associated with sulphonylurea use even after adjusting for confounding (as did others). We feel that Raccah has not made this sufficiently clear in his letter.

Observational research can be difficult to interpret, particularly where there is concern as to whether these differences have been sufficiently adjusted for. However, it is essential that we do not disregard the signals generated by the observational studies that Raccah has described. Unfortunately, it would now be difficult to conduct further clinical trials in high-risk patient groups on a drug that is so widely used. This is why well-conducted observational studies (like our own) are essential to keep the debate alive.

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