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Author's reply

To the Editor: While it is interesting to note that Beyan et al. have found yet another variable that correlates (albeit negatively) with the incidence of Type 1 diabetes, I think it is a mistake to confuse the hygiene hypothesis with "personal hygiene" as judged by the use of deodorants, aftershave, etc. The hygiene hypothesis is based on the concept that early exposure to infectious agents is important for education of the immune system, and I am not aware that airborne infection (or for that matter infestation with *Enterobius*) is related in any way to the number of personal care items in a shopping basket.

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–to: M. Koopmanschap: Coping with Type 2 diabetes: the patient's perspective. Diabetologia 45:S18–S22

To the Editor: In a recent issue, Koopmanschap [1] reported very interesting and relevant results, confirming the idea that health-related quality of life (HRQoL) is an important issue in Type 2 diabetes. The data of this study was collected in five European countries, within the framework of the Costs of Diabetes in Europe – Type II (CODE-2) study. The core measure was the Euroqol 5 dimensions (EQ-5D) questionnaire. This tool involves patient self-reporting of their health status in five dimensions: mobility, self-care, usual activities, pain and discomfort, anxiety and depression. It is a widely used instrument that was also utilised in the United Kingdom Prospective Diabetes Study (UKPDS) for assessing generic HRQoL.

In the final analyses of this manuscript regarding the results of the CODE-2 study, HRQoL is analysed by treatment type (diet and exercise, oral drugs or insulin). It seemed that those who used insulin had a lower mean level of HRQoL when compared to those who did not use insulin. Furthermore, it was described that treatment type was a predictor of quality of life after adjusting for age, sex and any complications. Based on these findings, the author concludes: "... the CODE-2 study shows that progression to insulin treatment is independently associated with a reduction in quality of life as is poor glycaemic control and a BMI of more than 27." and "... the implication for policy makers is that an avoidance of insulin therapy and the reduction or prevention of complications is the key to improving patients' HRQoL."

We feel that the data of the CODE-2 study do not permit this conclusion and implications, as the cross-sectional design of this study does not allow for causal inferences. The author states that treatment with insulin is a cause of impaired HRQoL, but different dimensions of HRQoL could also have contributed to the start of insulin therapy. For example, depression (with anxiety one of the five dimensions that is assessed by the EQ-5D) was found to be associated with poor glycaemic control in many studies, probably partly as a result of impaired self-care behaviour [2, 3, 4]. Furthermore, poor glycaemic control is one of the main reasons for physicians to start insulin therapy. Thus, poor HRQoL could also be causally linked to initiation of treatment with insulin.

Moreover, previous studies investigating the relationship between insulin therapy and quality of life in Type 2 diabetes have produced conflicting results. Some prospective studies suggest that the shift from a treatment consisting of exercise and/or tablets to insulin therapy can improve the glycaemic control of patients with Type 2 diabetes, without influencing their quality of life [5, 6] or with even improving it [7]. In contrast, another study [8] has found that introduction of insulin therapy, initially had no effect on the quality of life of patients with Type 2 diabetes. But, they also found that a substantial number of subjects experienced a steady deterioration in glycaemic control during the first few years after insulin therapy,

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and these subjects also reported a progressive reduction in quality of life. These authors therefore concluded that initiation of insulin therapy in Type 2 diabetes should be associated with sustained education, monitoring and support for which the UKPDS intensive policy could be used as a model [5, 8].

More knowledge about the associations between insulin therapy and quality of life in people with Type 2 diabetes is of crucial importance. Therefore, we fully agree with Koopmanschap's initiative to study this topic in a large European sample using a validated measure of HRQoL. However, we regret that the author used only one overall score for HRQoL. This overall-score for HRQoL is calculated from five health status dimensions. These five dimensions are related, but for example, an extreme limitation in mobility does not necessarily mean that one also experiences extreme limitations in pain and discomfort. In our opinion, it would be most interesting to publish the associations between insulin therapy and all five dimensions. In the large sample of the CODE-2 study, this should preferably be done separately for each of the five countries, in order to study whether the associations are consistent across countries.

We believe that there is evidence from prospective studies to suggest that a substantial number of patients with Type 2 diabetes could use insulin therapy to achieve good or acceptable glycaemic control, without influencing their HRQoL. This should be accompanied by continuous support from the diabetes team. The recent results of the CODE-2 study regarding the impact of Type 2 diabetes on HRQoL are limited, due to the cross-sectional design of the study and the use of only one overall measure of health-related quality of life. We therefore consider the advice to avoid insulin therapy, in order to improve the patients' HRQoL, as premature and not based on convincing evidence.

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–to: Hales CN, Barker DJP (1992) Type 2 (non-insulin-dependent) diabetes mellitus: the thrifty phenotype hypothesis. Diabetologia 35:595–601

To the Editor: One of the key concepts underlying discussions of the pathogenesis of Type 2 diabetes is that of the 'thrifty' organism, whether speaking of its genes [1] or its phenotypes [2]. But what's the evidence for thrift?

To block one diversion, we are considering 'usual' Type 2 diabetes in which patients are obese or over-weight at diagnosis or at least, if diagnosed very late, have been so previously. No one knows whether any group of 100 diabetic patients consists of ten groups of ten patients, with a different pathogenesis for each group; or whether 90 patients have the same pathogenesis, while the other ten each have a different pathogenesis from one another. The Type 2 diabetic patients with normal weight could be particularly well represented among these latter ten, who perhaps have ten different genetic modifications. Subjective impression favours the latter type of distribution, but it could be the result of many different abnormalities in a single biochemical or physiological pathways.

Neel's postulate [1] was an attempt to describe the nature of a constitution beneficial in 'lean' years but disadvantageous in 'fat' ones, and to explain its evolutionary origin and possible current disadvantage. However, there is no sustained evidence of alterations in metabolic rate certain enough to fulfil a 'thrifty' hypothesis [3], among either of those with Type 2 diabetes, those at very high risk of developing it in the future or even among obese non-diabetic subjects. But perhaps the search hasn't been made under the necessary circumstances to evoke the necessary difference.

A different explanation of the basic postulated ability to maintain weight in the face of famine would be success in obtaining resources when they're scarce. Many characteristics could underlie this but, given the importance of 'motivation' or 'drive', increased hunger could be an important component. Increasing knowledge of the multiple and complex pathways involved in hunger, satiety and reward offers ample sites for important alterations in levels of hunger. Such factors, or the

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