Author's response to reviews

Title: A pattern of unspecific somatic symptoms as long-term premonitory signs of type 2 diabetes: Findings from the population-based MONICA/KORA Cohort Study, 1984-2009

Authors:

Jens Baumert (baumert@helmholtz-muenchen.de)
Christa Meisinger (c.meisinger@helmholtz-muenchen.de)
Karoline Lukaschek (karoline.lukaschek@helmholtz-muenchen.de)
Rebecca T Emeny (rebecca.emeny@helmholtz-muenchen.de)
Ina-Maria Rückert (ina-maria.rueckert@helmholtz-muenchen.de)
Johannes Kruse (Johannes.Kruse@psycho.med.uni-giessen.de)
Karl-Heinz Ladwig (ladwig@helmholtz-muenchen.de)

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Author's response to reviews: see over
To
Dr. Timothy Shipley
Executive Editor of *BMC Endocrine Disorders*

Neuherberg, 24/09/2014

Dear Dr. Shipley,

Please find attached our manuscript entitled “A pattern of unspecific somatic symptoms as long-term premonitory signs of type 2 diabetes: Findings from the population-based MONICA/KORA Cohort Study, 1984-2009” to be considered for publication in *BMC Endocrine Disorders*.

The present manuscript is a revision of a former manuscript which we had previously submitted to *BMC Medicine* (MS 1912592905135372). This manuscript was rejected after a re-submission (MS 6984515514066006) but a submission to *BMC Endocrine Disorders* was suggested. We appreciate this opportunity very much. We also are deeply grateful for the constructive and extended work of the two invited reviewers which we tried to follow in detail. We believe that the modifications proposed by the reviewers have considerably improved our manuscript.

In internal medicine, unspecific symptom patterns are often seen as prodromal signs of a serious chronic disease condition long before the onset of the disease and may largely be unrelated to the underlying disease condition itself. A good example of this is the phenomenon of *vital exhaustion* which precedes an acute myocardial infarction in about one third of all cases although it appears to be unrelated to pathological changes of the heart condition.

To the best of our knowledge, for type 2 diabetes mellitus (T2DM), early symptoms of hyperglycaemic states are well established, however, the existence of a pre-monitory unspecific symptom patterns before the onset of T2DM has not been described so far. The aim of the present study was therefore to identify participants who suffer from unspecific symptoms and to investigate whether these symptoms were prospectively associated with the onset of Type 2 diabetes mellitus. Based on data from the large MONICA/KORA study drawn from the general population of southern Germany and followed up to 16 years on average, the present study found a substantial relationship of an elevated burden of unspecific premonitory symptoms and subsequent T2DM manifestation independent of established cardio-metabolic risk factors.

All authors substantially contributed to the conception and design of the study, the acquisition, analysis or interpretation of data, drafting of the article or revising it critically for important intellectual content. All authors have read and approved the final manuscript. The results of this paper have not been published elsewhere nor are they under consideration at any other journal. We would be honoured if you consider our manuscript eligible for publication in the *BMC Endocrine Disorders*.

Yours sincerely,

Prof. Karl-Heinz Ladwig

(Senior lecturer in psychosomatic medicine)