



hs-CRP Predicts Improvement in Depression in Patients With Type 1 Diabetes and Major Depression Undergoing Depression Treatment: Results From the Diabetes and Depression (DAD) Study

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hs-CRP is elevated in depression (1), but evidence on decreases of hs-CRP during depression treatment or the role of hs-CRP in the prediction of response to depression treatment is still controversial (2,3). To date, no study has examined this association in patients with diabetes. As elevated hs-CRP increases the risk of diabetes complications in diabetes (4), we aimed to explore hs-CRP in patients with diabetes and major depression undergoing depression treatment based on the data of the Diabetes and Depression (DAD) study (5).

Participants were randomized to 12 weeks (short-term phase) of diabetes-specific group cognitive behavioral therapy or sertraline treatment and followed up for 15 months (long-term phase). hs-CRP was assessed at baseline and at the end of the long-term phase with a latex-enhanced immunoturbidimetric method. Ethics approval and written informed consent were obtained (5). Information on baseline hs-CRP was available in 219 patients (mean age 48.1 ± 12.0 years, 62%

female, mean HbA_{1c} $9.25 \pm 1.4\%$ [78 ± 16.2 mmol/mol], 51.6% type 2 diabetes, median hs-CRP 0.33 mg/dL [interquartile range 0.10, 0.84]). Depression outcomes included short-term treatment response ($\geq 50\%$ reduction of the Hamilton Depression Rating Scale [HAMD-17] baseline score or HAMD-17 posttreatment score ≤ 7), remission of depression at the end of the long-term phase (HAMD-17 scores ≤ 7 and no current diagnosis of major depression according to the Structured Clinical Interview for DSM-IV), and short- and long-term improvement (HAMD-17 change scores after 12 weeks and 15 months).

Multiple linear and logistic regression analyses on depression outcomes did not reveal associations for log-transformed baseline hs-CRP or for interactions between hs-CRP and treatment over all participants (results not displayed). However, we detected significant interactions between baseline hs-CRP and diabetes type for short-term improvement ($B = 3.43$ [95% CI 0.51, 6.33], $P = 0.022$) and long-term improvement (3.60 [95% CI 0.56,

6.63], $P = 0.021$) in depression even after adjustment for confounders (age, sex, BMI, baseline HbA_{1c}, baseline HAMD-17 score, treatment). In type 1 diabetes, higher baseline hs-CRP was associated with less improvement, whereas in type 2 diabetes no significant association could be detected (Fig. 1). Logistic regressions on treatment response and remission stratified by diabetes type showed a similar pattern, although we did not find significant interactions between hs-CRP and diabetes type in the full sample (results not displayed). hs-CRP did not change during the study and changes in depression and type of treatment were not associated with changes in hs-CRP in both groups (results not displayed).

In sum, in a large sample of patients with poorly controlled diabetes, we found evidence that higher baseline hs-CRP predicts poorer outcomes of depression treatment in type 1 diabetes, which highlights the need for a closer examination of inflammatory processes in patients with type 1 diabetes with depression. Although hs-CRP appeared to

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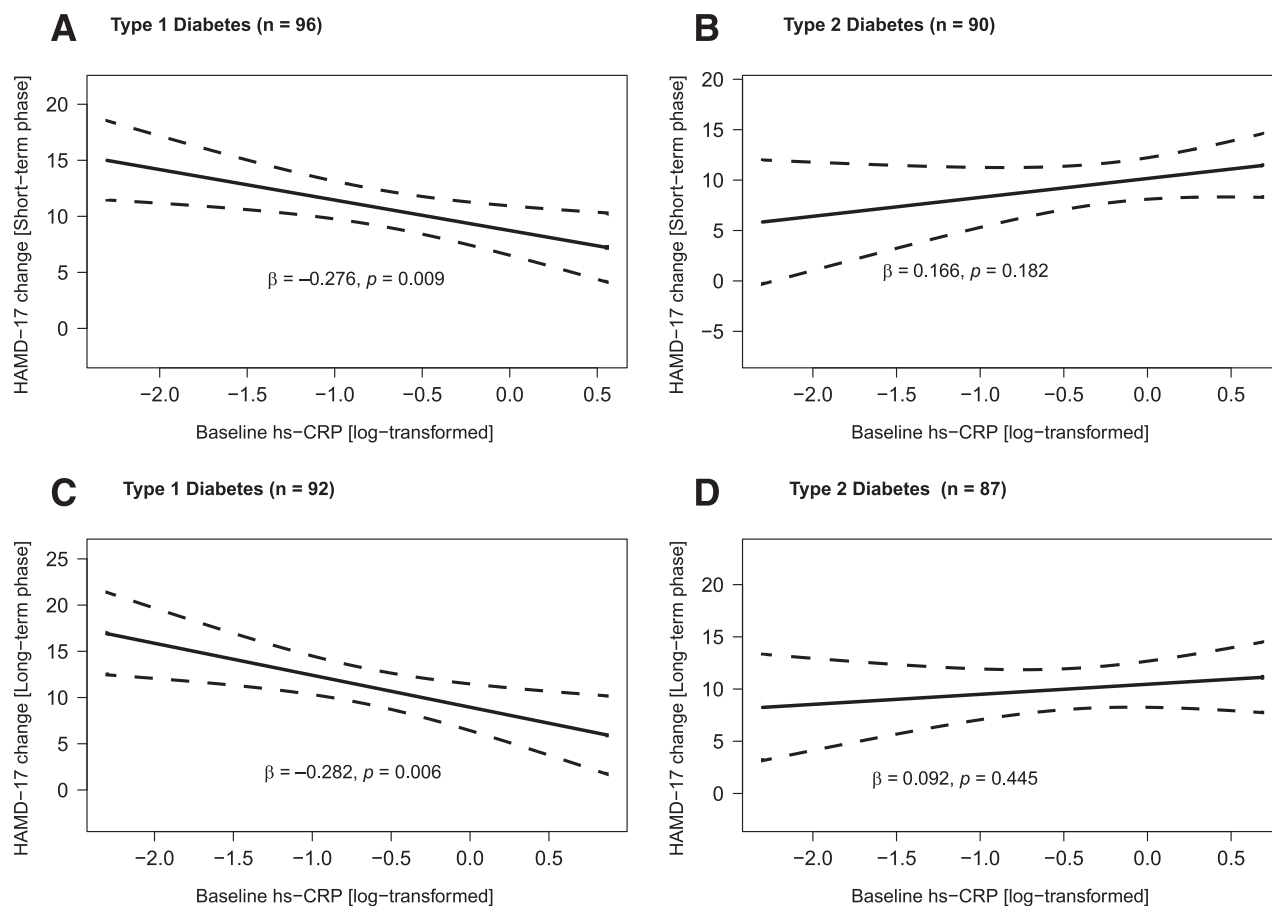


Figure 1—Regression lines (solid lines) (adjusted for age, sex, BMI, baseline HbA_{1c}, baseline HAMD-17, treatment) and 95% CIs (dashed lines) for the relationship between hs-CRP and improvement of depression (HAMD-17 change scores) during the short-term (A and B) and the long-term (C and D) phase by diabetes type.

be less relevant in type 2 diabetes, including other markers of inflammation as suggested by others (3) may be necessary to determine the role of inflammation and depression outcomes in this group.

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Germany and as a speaker for Novo Nordisk, Abbott, Berlin-Chemie, and Ypsomed. He is an advisory board member of Abbott Germany and Ypsomed Switzerland. He has received grants in support of investigator trials from Dexcom, Berlin-Chemie, and Roche Diagnostics. C.H. has served as a consultant for Sevier (Paris, France) and Janssen-Cilag (Beerse, Belgium) outside the submitted work. B.K. has received funding from Novo Nordisk for travel and accommodation to attend DAWN2 planning meetings but has not received any fee for this work. He has also acted as a national advisory board member of DAWN Germany and as a speaker for Novo Nordisk, Abbott, Berlin-Chemie, Roche Diagnostics, and Merck Sharp & Dohme. He is an advisory board member of Roche and Sanofi-Aventis. He has received grants in support of investigator trials from Dexcom, Berlin-Chemie, and Roche Diagnostics. No other potential conflicts of interest relevant to this article were reported.

Author Contributions. D.Z. analyzed the data, wrote the manuscript, had full access to all study data, and was responsible for the decision to submit the manuscript for publication. S.H. and C.H. designed the study, were responsible for its conduct, and contributed to the discussion and the introduction. C.A. was responsible for study conduct and contributed to the discussion, results, and introduction. N.H., W.H., J.K., B.K.,

and M.J.M. designed the study, were responsible for its conduct, and reviewed and edited the manuscript. K.K. designed the study, was responsible for study management and data collection, advised on the results, and reviewed and edited the manuscript. C.R. designed the study, was responsible for data management, advised on the statistical analyses, and reviewed and edited the manuscript. F.P. was the principle investigator of the DAD study, designed the study, was responsible for its conduct, and contributed to all parts of the manuscript. All authors approved the final version of the manuscript. F.P. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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