Author's response to reviews

Title: Achievement of individualized treatment targets in patients with comorbid type-2 diabetes and hypertension: 6 months results of the DIALOGUE registry

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Author's response to reviews: see over
Dear Dr. Shipley,

Thank you for kindly considering our article for publication in *BMC Endocrine Disorders*. We have carefully revised the manuscript point-by-point and you will find the response to each of the reviewers’ comments attached.

We would be happy to publish our work in *BMC Endocrine Disorders*. We look forward to a favourable final decision on our manuscript.

Yours sincerely,

Peter Bramlage, MD, PhD
Review of the manuscript “Schmieder et al. Achievement of individualized treatment targets in patients with comorbid type-2 diabetes and hypertension: 6 months results of the DIALOGUE registry”

Reviewer: Georgios Valsamakis

Dear Dr. Valsamakis,

Thank you for your kind consideration of our article and the important comments you made that helped us to improve our manuscript. Pls find the response to each of your comments in line:

1) authors claim mean HbA1c (SD) of 7.8 (2.1) as a poor glycemic control in their cohort but it will be useful to know how many had HbA1c of less than 6.0 , which is considered as acceptable.

Response: This is indeed a valid question although we slightly disagree with the threshold you are suggesting. None of the guidelines asks for HbA1c control less than 6.0 percent and all, although pursuing individualized treatment targets, consider an HbA1c less than 6.5% to be perfect. For this reason we have added the information on actual HbA1c in table 1 and actual SBP in table 2.

2) Why the authors chose to limit their study into a six months period, as in some aspects this makes their observations weak

Response: Although the registry has an overall follow-up of 12 months we intentionally limited this analysis to 6 months because we learned that control rates and efforts to reach treatment targets stops at 6 months and values are not different at 12 months. We have thus added this information to the first paragraph of the discussion: “Although individualized therapy led to substantial reductions in HbA1c and BP after 6-months of follow-up, treatment goals were often unmet and no further effort was made to improve the situation thereafter.”
4) page 5 line 20 in the exclusion criteria it is stated that physicians were allowed to add only anti-diabetic oral tablets and no injectable drugs such as insulin or GLP 1 agonists, furthermore authors state that patients were excluded from the study if they were on insulin prior to enrollment. But in page 9, line 1 the authors refer to insulin users. Please explain.

Response: Patients were only registered for this observation if they received any oral antidiabetic drugs but no GLP-1A or insulin prior to enrolment. Physicians were allowed, however, to adjust treatment including the initiation of GLP-1A and insulin at/after baseline. See inclusion criteria for further information.

5) please explain into more detail: what were the criteria used to include patients into a strict or loose or medium target group?

Response: The decision to assign a patient to the strict, medium or loose treatment target group was solely based on the decision of the treating physician – in accordance with the guidance for individualized treatment targets. They were, however, not asked why they chose a specific treatment target and how to justify this decision in a particular case.

6) please describe which groups out of the three it’s targets were mostly unmet

Response: We added the description for HbA1c and BP target achievement as requested in the respective text.

7) it is useful in the discussion to be explained as to the reasons why even strict targets often fail

Response: We agree and added a comment on that particular question to the discussion of individualized treatment targets: “The failure to achieve pre-defined treatment has been associated
with inertia of physicians to make effort after an initial failure [11]. On the other hand multiple concomitant medications as well as treatment associated side-effects that become apparent after the defining the treatment target frequently require a reconsideration of these targets in an effort to balance benefits and risks of treatment [12].”

8) please discuss why the presence of comorbidities led to loose targets and results

Response: This is an important aspect and we browsed the literature for respective data. There actually is a recommendation of the ADA to loosen treatment targets in this patient group based on their higher propensity to develop treatment associated complications. Therefore we added the following to the respective part of the discussion: “This is in line with the guidance of the American Diabetes Association on the management of hyperglycemia [17], suggesting the loosening of glycemic targets in patients with important comorbidities, established vascular disease and limited life expectancy.”

Yours sincerely, Peter Bramlage

Reviewer: Farah McCrate

Dear Dr. McCrate,

Thank you for your kind assessment and consideration for its suitability for publication in BMC Endocrine Disorders. Pls find the response to each of your suggestions attached:

1) From a stylistic perspective, the expressions ‘notably’ and ‘in this regard’ are utilized quite heavily

Response: You are right and we have reduced their used throughout.
2) Pg. 7, line 21 - < 140% should read < 140mmHg

Response: Sorry for missing this. We have corrected this on page 7 as suggested and on page 2 where we found the same mistake in the abstract.

3) The figures as they are currently formatted in print are missing overall titles as well as labels for the x and y axes.

Response: We have carefully revised the figures to make sure x and y axes are correctly labelled. The title and the legend of figures is found on page 21 of the manuscript, straight after the list of references. The journal requires to separate these from the text.

Yours sincerely, Peter Bramlage