Dear editor

Thank you for the opportunity to send our paper on to *World Journal of Gastrointestinal Pharmacology and Therapeutics* (*WJGPT*). We have incorporated the reviewers' comments into our manuscript and believe that the revised paper has been significantly improved in the process. Please consider the manuscript in the revised version for publication. All comments have been responded to point by point as outlined below.

Best wishes

Christian Selinger

Reviewer 1

Good paper, would like to see an opinion or current advances in regards to technology platforms aiming to increase patient adherence. It can provide an optimistic view on an external factor to help assist patients to stay compliant due to the main rank determined as forgetfulness. A table of the questionnaire sent to the clinical care team would also be intriguing to read in the supplemental material.

We thank the reviewer for the kind comment. We have added a comment on technology platforms and the challenges associated with them. We have supplied a copy of the study questionnaire as supplementary material.

Reviewer 2

This manuscript is well written and gives a clear overview of the perception of clinicians about medication non-adherence in IBD.

We thank the reviewer for the kind comment.

Abstract In the method section, please rephrase the 1st question: to a web based survey collecting data were collected on clinician…

We thank the reviewer for spotting this mistake. We have rectified it now.

Background & Aims The background is well illustrated with references that support the importance of adherence in IBD and the impact on outcomes. The research questions and objective are clear. Methods The data collected were outlined.

We thank the reviewer for the kind comments.

But some extra clarification can be necessary: 1. The survey was piloted with 8 specialists…What kind of specialists? 2. The questionnaire was amended based on their feedback. What feedback was given? Were there a lot of changes made?

We thank the reviewer for the point made and have clarified the manuscript accordingly: 'The survey was piloted with 8 IBD specialists and some clarifying minor amendments were based on their feedback.'

3. When the questionnaire was not completed, was a reminder sent?

No systematic reminders were sent as the BSG does not allow for repeated use of their email lists.

4. During what time period were the data of survey collected?

We have clarified the manuscript to show that data were collected over a 3 months period.

Results Results are clearly described. Some minor remarks: 1. The 98 participants that completed the survey, did they all fully completed the questionnaire?

Thank you. The survey system only allows for submission of complete questionnaires.

2. Please change the last question in 'managing non-adherence'. (rank 3) and. Patient counselling was ranked…

Thank you for finding this error, which has now been rectified.

3. Maybe table 6 can be added?

We thank the reviewer for suggesting a 6th table but are no sure which content the reviewer suggests for this additional table.

Discussion All findings are well discussed. Some minor remarks: 1. In the 5th paragraph, you refer to the similar study by Trindade et al who found 77% of participants (self)reporting screening for adherence. Where did you find this in their manuscript? Maybe I am mistaken, but can you please clarify this. In the manuscript is stated United States (23). Why is the 23 standing here?

We thank the reviewer for the comment made. The '23' is there in error (old reference number) and was removed. The 77% is taken form the relevant abstract: 'Of the 77% of physicians who screened for adherence, only 19% (n = 58) use accepted measures of screening for adherence (pill counts, prescription refill rates, or adherence surveys).'

2. In the paragraph mentioning interventions aiming at improving non-adherence, you can also mention the important role of the IBD nurse in this.

An excellent suggestion, which have incorporated into the manuscript.

3. Do you have an explanation for the low response rate? Where reminders sent?

Surveys of clinicians tend to have such low response rates unfortunately as also found by similar studies.

Tables Table 2: please add (%) after column A:…levels

Thank you for finding this error, which has now been rectified.

Table 3: you are always mentioning BIOL and in this table you write anti-TNF therapy, please change this.

Thank you for finding this error, which has now been rectified.

Reviewer 3

It is a manuscript on the non-adherence to IBD maintenance medication which occurs frequently and yet clinicians struggle to detect and address it. Authors have conducted a survey trying to ascertain physicians and other health care providers perceptions and to describe current practice. Authors found that non-adherence was seen as an infrequent problem by 57% of 98 respondents and levels of non-adherence were estimated lower than evidence suggests by 29% for mesalazine (5ASA), 26% for immunomodulators (IMM) and 21% for biologics (BIOL). Most respondents identified the main factors associated with non-adherence in line with evidence and often counselled patients accordingly. Authors concluded that clinicians treating IBD patients frequently underestimate non-adherence and use of validated screening tools is infrequent. Authors suggest

that professional education should focus more on non-adherence practice to avoid adverse treatment outcomes associated with non-adherence.

We thank the reviewer for the kind comments.

Major comments 1. Please make clear in your survey the questions you choosed to separate reasons forn non-adherence as patient-related, physician-related, drug related and other reasons-related (i,e financial, insurance etc)

We thank the reviewer for this point. To clarify this we have added the study questionnaire as supplementary material.

2. Please inform how final questions were chosen and if there was a pilot study to check consistency or if your questionnaire was previously validated in a separate population.

We thank the reviewer for raising this point. The final questionnaire was decided upon by the authors after the initial 8 expert pilot. The questionnaire was not formally validated.

3. Please comment why you did not choose to investigate adherence to oral steroids or/and to enemas and/or number of pills

We thank the reviewer for raising this point. The main aim of the study was to look adherence to maintenance therapy. We chose to include maintenance medication only as adherence to flare and maintenance medication often differs. We have therefore excluded steroids and topical therapy. Data on pill burden are contradictory and were therefor not included.

4. Please explain your low response rates 98/775 and how this could have affect your results.

Surveys of clinicians tend to have such low response rates unfortunately as also found by similar studies. We have highlighted this in the limitations section.

5. Please comment on how different proportions of different health care providers (not balanced for age, sex and years of previous caring experience) who have answered your questionnaire could have affect your results.

We thank the reviewer for raising this point. As we have no data on non-responders, any influence on the data can only be speculated on. We have highlighted this in the updated manuscript.

6. Please comment if you found any relationship or prognostic factors regarding intentional vs non-intentional non-adherence

We thank the reviewer for the comment, but found no such relationship.

7. Discussion is long, please restrict it to your major findings and focus only on them.

We thank the reviewer for the comment, but feel as highlighted by the other reviewers that this level of detail is wanted and warranted.

Minor comments 1. Please amend references to the journal style

Thank you.

2. Please combine Tables 2 and 3 3.

We feel that separate tables reflect the content better.

Please omit Table 4 and incorporate results in the text.

We feel that the table offers additional data.

Reviewer 4

This is an interesting paper regarding to the important issue of IBD patients' non-adherence. Despite this well-known phenomenon most of physicians forget about it. In the discussion, could you please conclude what to do to improve this situation.

We thank the reviewer for the kind comment. We have further added more discussion to the paragraph on improving adherence.

In the list of causes for non-adherence there are not any financial reasons… Why?

We haven't included financial reasons as in the UK these do not apply because of the nature of the National Health Service.

Please, incorporate results of Table 4 in the text.

Thank you. The results are already included in the results section: ‘However, a higher level of interest in IBD was found to significantly correlate with estimating level of non-adherence for biologics therapy in line with evidence (p=0.012, table 4).’