Reviewer 1

The authors of the manuscript presented very interesting information on the specific diagnosis of bronchial asthma. The manuscript is written in the format of a mini-review. A diagnostic method for GAS CHROMATOGRAPHY and MASS SPECTROMETRY is presented. The manuscript contains a description of the detection of bronchial asthma markers, volatile organic compounds using electronic noses. This is a very promising, highly specific and highly sensitive method. The method can be used for screening studies for the mass detection of asymptomatic patients with bronchial asthma and preclinical stages of bronchial asthma. This scientific topic needs to be continued of clinical assau. The manuscript is recommended for publication in WJCC.

R- We thank the reviewer for his/her highly appreciated comments.

Reviewer 2

The authors have performed an in depth review of two methods for the diagnosis and follow-up of asthma based on the detection of volatile compounds. While there is still a long way to consider the analyzed technologies for routine clinical applications, the strengths and drawbacks of each approach have been thoroughly debated.

R- We thank the reviewer for his/her comments, for the questions and for the attention to detail.
The answers to the questions follow.

1. From the different studies the authors extract a number of compounds that might have value for the stratification of the patients according to the application of diverse regression methods. The degree of feature overlapping across studies is not clear. Is there a consensus across GC-MS or e-nose analyses? Considerations on overlapping between GC-MS and e-nose studies is mentioned. Perhaps a table with the most relevant compounds detected and their potential application could be included.

R - Both techniques, GC-MS and e-nose, aim to discriminate asthma patients and the various characteristics of the disease as accurately as possible. In our review, we have collected a series of studies where both GC-MS and e-nose are integrated into the natural history of the disease and its therapies in different ways: these two techniques seem to be able to discriminate asthmatic patients from healthy controls, recognize various inflammatory subtypes of the disease, predict exacerbations and therapy responses and perform differential diagnosis with other diseases such as transient wheezing, cystic fibrosis or COPD. In this sense, the two techniques are potentially overlapping. However, their purposes are extremely different, making them complementary and non-interchangeable tools: GC-MS represents the gold standard test for exhaled breath analysis as it has the ability to perform precise structural analysis of individual molecules within the VOCs mixture present in the exhaled breath; on the other hand, e-nose is not intended to identify individual molecules but rather to recognize patterns given by different fractions of the VOC mixture, which are then compared to a breath print database. It is able to give quantitative response to a comprehensive VOCs profile, but in this case individual VOCs remain unidentified. Therefore, it is only possible to compare the two techniques if it is clear that they have different purposes. Indeed, in our text, we have cited two studies (Dragonieri 2007 and Brinkman 2017) in which the examination of exhaled breath using e-nose was combined with GC-MS to conduct an exploratory analysis of individual components. That's why, based on the literature, we propose two possible different uses: research purposes for GC-MS and clinical practice and screening purposes for e-nose.
We appreciate your feedback and have added further clarification in the introductory part.
Regarding the table, we found the proposal very interesting. Therefore, we have added six tables in which the identified VOCs have been categorized into thematic areas (diagnosis, inflammatory substrates, exacerbations, therapies, differential diagnosis with transient wheezing, comorbidities). However, for the aforementioned reasons, it summarized the studies based on GC-MS rather than the e-nose.

2. Intro first paragraph: "Not surprisingly, only the measurement of exhaled nitric has become part of international guidelines". Do the authors mean nitric oxide?

R - Thank you, it was a sight. The sentence has been corrected as follows: "Not surprisingly, only the measurement of exhaled nitric oxide has become part of international guidelines".

3. Page 5. revise the sentence "Here, the separation of molecules, the "stationary phase," the critical component of the system, occurs" 4. Page 6. m/c should be m/z. Page 6 and 7. references are needed to support the observations in the sentence "(Mass spectrometry (MS) is commonly used to rapidly and accurately identify chemical compounds for a wide range of applications such as drug detection, pollution monitoring, petrochemical processing, and disease diagnosis through biomarkers.)"

R - Page 5. We have revised the sentence as follows: "Within the chromatographic column, the so called "stationary phase" occurs, during which the molecules are separated. This phase represents the critical

component of the system." Page 6. Correction applied in m/z. Page 6 and 7. The bibliographic references supporting the sentence "(Mass spectrometry (MS) is commonly used to rapidly and accurately identify chemical compounds for a wide range of applications such as drug detection, pollution monitoring, petrochemical processing, and disease diagnosis through biomarkers.)" have been included.