Thank you for the opportunity to review this revised version of the manuscript.

I am happy to see the efforts taken by the authors to provide detailed responses to our comments. However, I see that they not substantively addressed comments from all three reviewers.

This is especially the case for four main features

1. The framing or the rationale for the exposure setting
2. Sensor validation
3. Sample size calculations
4. Exposure Modelling

I am listing what the investigators could do strengthen their protocol description but unfortunately, I am not able approve the submission in its current form.

1. Framing of the exposure setting- Authors Response

Thank you for your valuable inputs on this. We have not defined the solid fuel as indoor air pollution in our study. Our objective is to see the total effect of individual's exposure to air pollutants mainly PM2.5, PM10, and CO inside the house as well as their levels in the ambient air during the second and third trimester of pregnancy. The exposure of interest in our study is the levels of PM2.5, PM10, and CO, not solid fuel use. Solid fuel use is a contributing factor for these pollutants. Not only cooking fuel but several other contributing factors like incense sticks, frankincense, mosquito repellents (solid/liquid) are also leading to a higher amount of exposure. Your study has provided a detailed note of all these sources. We have obtained information regarding all these sources and not just solid fuels. However, we are treating only the pollutants (as a result of all these sources) as exposure. Pregnant women are vulnerable to inhalation of a higher level of pollutants, due to the poor housing structure and inadequate ventilation in the urban slums. Our focus is not only on solid fuel use, there are several other activities done at the household level which contribute to the emission of higher level of PM2.5, PM10 and CO. We are recording each of these activities at the household occurring at regular basis. Prospective assessment at early pregnancy is the best design to prove the independent association between exposure to pollution and birth outcomes. We are recording the level of personal exposure to air pollutants during pregnancy, prospectively following them up until delivery to see the effect on birth weight of the baby. We are not here to address the air pollution from solid fuel use. Our findings may provide the contributing factors for higher level of PM2.5, PM10, and CO at the individual level. It is unfortunate that most of your comments are based on the incorrect assumption that we are assessing only solid fuel use. We request you to please see the questionnaire and be assured that this is not what we are doing.

We agree that the study design and methods cannot examine the independent association of indoor vs. ambient air pollution, but it is designed to examine the total effect of all pollutants (irrespective of indoor v/s outdoor) with birth weight in this setting. Accordingly, we have made changes in the manuscript. We did not intend to address estimate household air pollution from solid fuel use.
Response from Dr. Kalpana Balakrishnan

The author seems to agree with earlier comments on this issue of lack of clarity in defining the exposure of interest and sources that, I and the other two reviewers Dr. Julian Marshall (JM) and Dr. Ryan Allen (RA) have raised. But the current version of the text does not support this and does not reflect the corrections needed.

See for example the opening line in the abstract

“Exposure to air pollution (IAP) from the combustion of solid fuels is a significant cause of morbidity and mortality in developing countries. Pregnant women exposed to higher pollutant levels are at higher risk of delivering a low-birth-weight (LBW) baby. There is a lack of standardized data regarding the levels and types of specific pollutants and how they impact LBW. We aim to prospectively assess the association between ambient and indoor air pollution levels in pregnancy and low birth weight and understand the subsequent risk of adiposity in these infants”.

The authors explicitly say that household air pollution from solid fuels is not their primary concern in their response, but yet there is no mention of any other source anywhere else in the abstract or the main body (See below).

“Globally, nearly three billion people use traditional biomass fuels as their primary source of energy comprising of wood, charcoal and agricultural wastes. In India, nearly 67% of the population use biomass fuel as the primary source for cooking. As a result, exposure to indoor air pollution (IAP) from the combustion of these fuels has emerged as an important cause of morbidity and mortality”. Air pollution is contributing to the second-highest associated risk factor for mortality and morbidity.

I feel quite strongly that this section needs to be re-framed so that the reader knows what exposures are of relevance for the study population of interest.

A rationale based on (i) limited knowledge regarding exposures of slum populations/vulnerable subgroups in LMICs (ii) the importance of addressing exposure attributions of household and ambient sources through personal sampling (ii) the availability of indigenous novel sensors and (iv) the need for longitudinal measurements should be adequately framed to set the context.

Without these additions, it is hard to agree with the authors when they say “we are not here to address air pollution from household solid fuel use” (See comment on sample size as well).

Also loosely worded terms such as “total level of air pollutants”, “total effect of individual’s exposure to air pollutants” cause considerable confusion on what exactly is being proposed here.

2. Sample Size- Author Response

We have now re-calculated the sample size using a published systematic review report/ risk estimates reported by Tielsch et al, 2009. Risk of Low Birth Weight and Stillbirth Associated With Indoor Air Pollution From Solid Fuel Use in Developing Countries-2010: Increased risk of LBW of 38%
(OR ¼ 1.38, 95% CI: 1.25, 1.52) from exposure to IAP and an associated reduction in birth weight of 96.6 g\cite{1} Tielsch et al, 2009:Adjusted analysis: Risk of Low birth weight by exposure to solid biomass fuel [RR (term) ¼ 1.49, 95% CI: 1.25, 1.77; RR (preterm ) ¼ 1.70, 95% CI: 0.93, 3.10] A cohort study\cite{2}

Kalpana Balakrishnan response 2

The use of this reference is not appropriate for an exposure setting predominated by sources other than solid cook fuel emissions (as also noted by Dr. Allen). These ORs are based on exposure differentials as captured by categorical indicators of primary cook-fuel use among rural populations.

There are estimates available from continuous exposure-response assessments (For meta-analytical estimates see for e.g. Steib et al 2012 or use the only E-R study for birthweight from India Balakrishnan et al 2018) to get an estimate of the ORs or unit change in birthweight as a continuous variable.

Also there is enough information on the exposure gradients experienced in the specific zones of Bangalore.

Finally, the investigators may have access to secondary data from the study area to estimate the prevalence of low birth weight.

I strongly suggest they recalculate on the basis the revised effects estimate from previous studies and the expected exposure gradients/prevalence of low birth weight in the study population.

3. Sensor validation- Author Response

Please note that a manuscript describing validation is under the process of publication elsewhere. The device we are using is a low cost monitoring device which measures parameters PM2.5, PM10, and CO. The manufacturer is Ambience Monitoring India, New Delhi. It is a custom-built device. The scattered light is transformed into signals, that are amplified and processed.

Field calibration: the State Pollution Control Board of Karnataka (KSPCB) possesses several outdoor samplers, with some located in the city of Bangalore, to measure ambient CO and PM2.5 levels. For our calibration, we used the outdoor sampler located at the Indira Gandhi Institute of Child Health Hospital, Bangalore (device name: Ecotech Monitoring Solutions, NIMHANS). The board very frequently calibrates this device. During 6 hours, we placed our outdoor sampler and three of our indoor samplers directly next to the board's sampler. After that, we calibrated our devices against the board's sampler based on the outdoor readings. Correction factors were developed for all our devices.

Kalpana Balakrishnan Response 3

Dr. Julian Marshall has provided an elaborate response to the lacunae in this approach and I fully concur with him. Dr. Allen too notes a serious concern regarding the sensor validation.

Calibration of low cost sensors can be a very challenging exercise and strongly suggest that they take external help and document their ability to perform routine calibration. Further, validation of these sensors that is being published is not a substitute for routine calibration that would need to address
spatio-temporal gradients in particle size distribution and meteorological parameters in the study area.

The inter-monitor correlations for low cost sensors usually tends to be very poor and thus in the absence of an exhaustive co-location strategy with a gold standard instrument, the outputs from the sensors cannot be easily used (as also noted by JM)

Further, the value of performing CO monitoring in this setting is negligible. In addition, the BAM collocations will not obviously be applicable for gases and the authors need to identify another resource for the same. In any case it may be best to drop CO.

4. Model Specifications- Author response

We are using a multivariate linear regression model to examine the association between birth weight and pollution parameters (in continuous variables) separately adjusting for listed potential confounders.

We consider the long term exposure measurements of all three parameters at the ambient level using data extracted from the state pollution control board (annual average for that year).

Kalpana Balakrishnan Response 4

Perhaps I did not make this clear. Before examining the association between exposures and the birth weight, one would need a good sense of how well the 1-2 measurements done during pregnancy are going to be representative of pregnancy period exposures. This is echoed in comment provided by Dr. Allen.

Developing exposure models to provide reasonable estimates of pregnancy period exposures thus needs to precede the regression models. One way of doing this would be to do more than 2 measurements in a sub-set. A recent study that both I and Dr. Marshall were part of a study that developed such exposure models based on personal monitoring and ambient concentrations together with other co-variates (Sanchez et al 2019). Investigators could explore the applicability of this approach or provide details of an alternate approach for exposure modelling.

Given the uncertainties of the sensor performance and the limited number of valid personal measurements that may eventually be obtained, there is a need to define how exposure misclassification would be addressed and how alternative exposure metrics/ models will be used for exploring the association.