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Should survey weights be taken into account to come up with beta coefficients?

Either approach may be used. We suggest using unweighted regression estimates (e.g., using proc reg instead of proc surveyreg or any weighted linear regression model with design effects) since the intent of the regression correction is to account for the biological association between inflammation and given nutrition biomarker among the sampled individuals, not to produce a regression coefficient with an exact variance estimation and/or to be representative of an external population. Once the regression coefficient is calculated, we suggest accounting for complex survey design in later applications of data.

What do I do with a negative or 0 value for any biomarker of nutrition or inflammation (e.g., ferritin, CRP)?

We recommend replacing the 0 with a nominal value (0.001) as logarithm of 0 is undefined. Thus, in order to Log transform (normalization) the variable, a very low number is added to the zero values to facilitate this numeric operation. The low number can be too low because it may automatically turn to zero in the software procedures. We recommend recoding negative biomarker values with missing.

Which β coefficients should we use? The ones from the internal regression correction (IRC) or those from the BRINDA regression correction (BRC)?

We suggest using the IRC approach to calculate your own β coefficients.

How many decimal places should be used for estimates in the regression equation?

We recommend using 4 decimal places when calculating regression coefficients (i.e. nutrition biomarker-inflammation) as well as CRP and AGP reference decile values. Different statistical programs may automatically produce more or less decimal places, so this should be checked. *In SPSS: Download and double click "spss output decimals tool". Click Utilities -> Set Decimal Places for Output Tables. Some Stata versions may need to install "Python essentials" first. However, if you are not cross-comparing with others, then the use of more or less than 4 decimal places would not hinder your work.

When do you use the BRINDA external deciles for CRP and AGP vs individual survey deciles?

If assay's limit of detection for CRP is $\leq$ 0.1 mg/L and AGP and is $\leq$ 0.5 g/L, then use the BRINDA external decile; If not, use individual survey decile (10^{th} percentile).

When calculating the external decile, what was the rationale for excluding surveys?

Lab data quality (limit of detection). If assay's limit of detection for CRP was > 0.1 mg/L or > 0.5 g/L for AGP, then that survey was excluded from the calculation of the BRINDA external decile.

Can I add additional covariates in the BRINDA regression correction approach?

At this point we are NOT recommending this, as the intent is to adjust for the biological confounding effects of the acute phase response on nutrition biomarkers. We have also explored malaria as a confounder. The implications of other covariates in regression correction needs further exploration.

Do I still apply the BRINDA regression correction if there is no correlation between CRP and/or AGP and the selected nutritional biomarker?

Generally speaking, regression correction should be done if both the biological relation between CRP and/or AGP and the selected nutritional biomarker has been warranted in previous literature, and there is also an evident correlation in the individual survey dataset.

What if I only have CRP or AGP?

The BRINDA regression correction can be applied for CRP or AGP only or both. Single inflammatory biomarker macro is provided on the BRINDA website.

What do I do with the model intercept in the BRINDA regression correction for inflammation approach?

Ignore the intercept, just use the beta coefficient. But do not specify a ”no intercept model”, as that would artificially influence your beta estimate. It is essential that a model with linear model with intercept is fitted.

What if I have a different inflammatory biomarker other than CRP or AGP (e.g., IL-1, calcitonin)?

There is literature that have published ways to account for inflammation when assessing micronutrient not using CRP and AGP, specifically. For the BRINDA approach, however, the relationships between other inflammatory biomarkers and nutritional biomarkers has not been conducted. Therefore, we don't have formal recommendations. CRP and AGP are most commonly measured inflammatory proteins in nutrition surveys, so BRINDA analyses have focused on these biomarkers.

Can the BRINDA approach be used for populations other than preschool children, school-aged children, or women of reproductive age? For example, newborns, men pregnant women?

Unclear. Interrogation of these target groups is warranted in future studies. However, the BRINDA approach has been applied to other populations groups and that decision is at the discretion of the researchers.

Can BRINDA approach be used in clinical settings?

At the current time, the BRINDA approach cannot be used in clinical settings. It is intended to improve the accurate estimation of population micronutrient deficiencies. The validity of the BRINDA approach in clinical settings is warranted in future studies.

Does BRINDA exclude outliers?

No, we don't exclude outliers. We have a flag variable for hemoglobin based on biological plausible values - “hbbivflag”. We don't have any flag variables for other biomarkers. The rationale is that we don't know the extreme value is due to error or due to inflammation.