**MEMORANDUM**

Project: Balanced energy protein (BEP) on maternal and child health outcomes

FROM: Nicole Young

DATE: 27 April 2020

RE: DAGs for maternal BMI and balanced energy protein and their effect sizes

**Background**: This memo outlines what are the possible relationships among balanced-energy protein (our intervention of interest), maternal BMI, birthweight, and child growth failure (specifically only weight-for-length z= WLZ scores and length-for-age z= LAZ scores), the effect sizes we need and how we apply them in our model.

-Correlation is represented by *italicized* small letter.

-Adjusted causal effects are represented by block small letter.

-Crude causal effects are represented by block small letter starred (\*).

-small block letter prime (‘) represents direct causal effect if there is an alternate mediated pathway

-Total effects are represented by capital letter

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| Full causal relationships: | |
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|  | D is the total effect of maternal BMI on LAZ/WLZ with birthweight as mediator (assume linear effect)  D =/~ bc + d’ |
|  | E is the total effect of maternal BEP on LAZ/WLZ with birthweight as mediator (assume linear effect)  E =/~ ac + e’ |

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| Current evidence implementation relationships: |
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| * Under the current evidence scenario, our intervention, BEP, affects only birthweight. It does so differentially by maternal BMI status (Ota 2015 (1)) * Current evidence does not show an effect between BEP and LAZ/WLZ scores (Ota, 2015). But there is reason to believe it should affect child growth. * While the literature has strong evidence there is some causal effect size between birthweight LAZ/WLZ (Harding 2017), the effect from BEP through birthweight might not be big enough to show an effect in LAZ/WLZ through birthweight?? Or the studies might not be powerful enough to detect a difference? This is probably why Gates believe BEP should have a causal effect on LAZ/WLZ scores which we will model in our hopes and dreams scenario. (this should be our justification for doing hopes and dreams scenario) * Following up to child-growth failure outcomes require a long follow-up period, hence this outcome might not be measured accurately in current studies. * BEP is only affecting maternal weight- gain during pregnancy and not pre-pregnancy BMI * BMI should have an effect on LAZ/WLZ scores suggested by the literature (and Gates) but we are not intervening on BMI, and so simply correlatng birthweight and LAZ / WLZ will capture the relationship between BMI and LAZ/WLZ.   + OR alternatively, we correlate BMI and LAZ/WLZ scores and not correlate birthweight and LAZ/WLZ * b\* use crude effect cuz we are not intervening (ideally crude mean shift birthweight by maternal BMI) * OR if there is only crude OR/RR, then we can try to back-calculate a correlation coefficient to model a correlation instead (second choice) |
| Hopes and dreams implementation: |
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| * Gates wanted us to model the same effect size (b adjusted) for BMI on LAZ/WLZ. However, since we are not intervening on BMI, we don’t need the causal effect d. We only want the baseline LAZ/WLZ by BMI strata. b\* and correlation c should capture this relationship between BMI and LAZ/WLZ * alternatively, as above, we can model the correlation between BMI and LAZ/WLZ instead of correlation c.   + note: we want to avoid modelling correlation of one variable with two variables as this will be too complicated to get right * We are using the effect size Gates gave us as the total effect of BEP on LAZ/WLZ, so we do not need to model the   indirect and direct effect sizes |

**Effect sizes and their evidence:**

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| **Effect** | **Evidence from** | **Confounding, effect modification** | **Size** | **Reference** |
| a | Current evidence from literature | Effect modification from maternal BMI | undernourished women:  - 66.96g (13.13,120.78)  adequately nourished women:  - 40.96g (4.66,77.26) | Ota (2015) Cochrane review |
| b | Current evidence from literature |  | Adjusted RR 1.64 (95% CI 1.38–1.94) | Han (2011) meta-analysis |
| b\* | Current evidence from literature | Crude |  |  |
| c | Current evidence from literature *(we are not modelling this)* | -adjusting for child's age, sex,  and preceding birth interval, as well as maternal age, education,  BMI and stature, household wealth, urban/rural residence and country,  and accounting for the random effect of survey clusters.  -Effect modification on the co-occurrence of wasting & stunting by age, stronger in younger age groups; wealth quintile | Wasted adjusted odds ratios:  -1.60 [1.45, 1.76] (0-59 months)  (*also has data broken down by age bands*) | Harding (2017)  6 multi-asian-country cohort data |
| *c* | Spearman correlation from Chris’ analysis of the MAL-ED study |  |  |  |
| D or d’ or  *d* | *Need more investigation (we do not model this)* We are modelling correlation *c* instead |  | Gates wanted us to use a causal effect size of 2 |  |
| e’ and E | None under current evidence but Gates wants to model an effect size of +0.3 (±0.1). We will apply it as the total effect for E. | None |  |  |

**\*** For maternal BMI status, we might want to stratify by 3 groups of pre-pregnancy BMI: low, normal, overweight (if the studies report it). This might be helped if we use effect sizes from similar demographic settings because they will have similar distribution of BMI in the population. The reason we want these three stratas is that each of these three groups will have an effect on bw- low BMI mothers have low bw babies, normal BMI mothers have normal bw babies and overweight mothers have high bw babies. The bw difference between low and not low BMI will be larger if the population has a higher proportion of overweight women and might not be accurate if we apply this difference to a population with low proportion of overweight women. *ALTERNATIVELY*, we can get a correlation co-efficient between birthweight and maternal pre-pregnancy BMI.

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| **Task** | **Researcher task** | **Source** |
| Effect size of a | Nicole | Literature |
| b\* | Nicole/Yaqi | Dig through Han 2011 meta-analysis + literature |
| Correlation *c* | Chris | Primary MAL-ED data analysis by Chris  Yaqi also pulled some data |

**References**

1. Ota E, Hori H, Mori R, Tobe‐Gai R, Farrar D. Antenatal dietary education and supplementation to increase energy and protein intake. Cochrane Database Syst Rev [Internet]. 2015 [cited 2020 Apr 15];(6). Available from: http://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD000032.pub3/full