
Reply to SA Lederman

Dear Sir:

We thank Lederman for her critical appraisal of our article. A broader discussion of the possible implications of our findings would have gone beyond the scope of the original article, but we are pleased to be given the opportunity to discuss some further points here.

We agree with Lederman that the restriction to term pregnancies limits the generalizability of our results. The rationale for this approach was that total gestational weight gain (GWG) in term and preterm deliveries is not directly comparable, because women who deliver earlier do not have the chance to gain as much weight as women who deliver at term. Assessing GWG per week of gestation is also critical, because the amount of GWG is not constant over the whole course of pregnancy (1). Our approach is in accordance with several other studies in this field that also excluded preterm deliveries (2–5).

Lederman emphasizes that being born small-for-gestational-age (SGA) is probably more harmful to child’s health than is being born large-for-gestational-age (LGA). The actual discussions regarding the obesity epidemic (6) prompted us to give equal weight to SGA and LGA. We agree with Lederman that the focus on cardiovascular risks might have accounted for an overestimation of the clinical relevance of LGA in our analyses.

SGA may be related to adverse perinatal outcomes, such as fetal or neonatal deaths, but we found no evidence for elevated perinatal mortality in the optimal GWG ranges determined in our study compared with those recommended by the Institute of Medicine. Furthermore, as we stated in our article, 2 other studies had reported that those GWG ranges with the lowest proportion of SGA and LGA were associated with low risks of a number of other poor pregnancy outcomes (2, 3). However, potentially increased risks of lower IQ and mental health problems in later life or of postnatal hospitalizations due to serious diseases certainly provide an important argument for the avoidance of low birth weight.

In principle, it is possible to integrate a specific threshold for SGA into our approach—eg, by defining “optimal” GWG ranges in which the estimated risk of SGA does not exceed 10%. As an example, we reran the analyses with the addition of the condition SGA ≤10% to the original one of a joint predicted risk of ≤20%. In this case, the lower limits of the optimal GWG ranges in the overall analyses were shifted to the right, as expected (Table 1).

Similar effects occurred in the subgroups defined by parity and smoking in pregnancy (data not shown). These additional analyses indicate that the definition of optimal GWG is dependent on the choice of the outcome parameters (and/or their benchmarks). Different outcome parameters are also likely to explain the differing ranges for optimal GWG identified in other studies (3, 4, 7, 8).

The main purpose of our study was to introduce a new approach to define optimal GWG with respect to “optimal” birth weight. This approach can be adapted to different benchmarks, as shown in the additional analyses presented here. A further objective was to point to the need to consider parity and smoking status in assessing optimal GWG. The importance of these results is supported by a contemporary study that was also published in the Journal (5).

We further detected that the effect of GWG on birth weight is limited, as we also stated in the Discussion, suggesting that it may be more important to enter pregnancy with a healthy body mass index and to avoid smoking during pregnancy than to follow strict GWG recommendations. In the light of these considerations, it may appear debatable whether optimal GWG ranges can be determined without consensus on the relative importance of different adverse outcomes and their benchmarks.

Neither author had a conflict of interest.

Andreas Beyerlein
Rüdiger von Kries

TABLE 1

<table>
<thead>
<tr>
<th>Institute of Medicine</th>
<th>Underweight</th>
<th>Normal weight</th>
<th>Overweight</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original analysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>JPR ≤20%</td>
<td>8 to 25</td>
<td>2 to 18</td>
<td>−7 to 12</td>
<td>−15 to 2</td>
</tr>
<tr>
<td>Current analysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>JPR ≤20% and SGA ≤10%</td>
<td>14 to 25</td>
<td>8 to 18</td>
<td>0 to 12</td>
<td>−7 to 2</td>
</tr>
</tbody>
</table>

*These analyses pertain to term infants only.*
Although the authors tried to explain this discrepancy, an important flaw of the study design that was not mentioned in the article should be highlighted. This pertains to the fact that the participants were overfed at the time during which appetite was assessed, and blood samples were collected for the analysis of appetite-related hormones. Indeed, on the whole, the subjects ingested a rather high amount of energy that on average exceeded their estimated daily energy demand by \( \approx 60\% \) in both study conditions. We believe that such an excess caloric intake alone may explain the absence of difference in leptin and ghrelin concentrations and consequently in appetite sensations. The pattern of response in these 2 hormones (leptin was increased and ghrelin was suppressed without showing the typical diurnal variations) is also concordant with this state of overfeeding. This collection of data contrasts with the study of Spiegel et al (2), in which men were subjected to mild caloric restriction in the form of intravenous glucose infusion. Accordingly, these results must be interpreted with caution, and the effects of sleep restriction on appetite control cannot be adequately determined on the basis of this study.

The study results also emphasize the difficulty of assessing in an experimental context the influence of short sleep duration on energy balance. The mismatch between energy input and output as a result of short sleeping will probably be more accurately determined under free-living conditions and chronic short sleep duration (as opposed to an acute manipulation in a laboratory setting). The propensity of many individuals to overeat in the setting of sedentary living with unlimited food availability also suggests that the nonhomeostatic feeding behavior—ie, eating in the absence of hunger—could play a more important role. This concept is supported by recent data showing that recurrent bedtime restriction under free-living conditions did not down-regulate the satiety hormone leptin nor up-regulate the appetite-stimulating hormone ghrelin but increased intake of calories from snacks (9). Likewise, a study carried out in 1985 observed that habitual short-sleepers (average of 6 h/night) ate proportionally more often (ie, >3 meals/d with more frequent nibbling) than did long-sleepers (10).

Future studies will thus have to differentiate the variations in energy intake associated with short sleep duration between 1) the increased time and opportunities to eat (due to extra waking hours) as well as eating as a result of cues other than those that are appetite related and 2) the homeostatic regulation of feeding (hormonal signals that increase appetite). With the advent of functional magnetic resonance imaging, the documentation of food-related reward activation in the brain after sleep restriction will open new research avenues. Moreover, future experimental studies that examine the influence of objectively measured restricted sleep on both sides of the energy balance equation should focus more on children and adolescents to build up the cause-and-effect evidence between short sleep duration and obesity. No interventional study to date has tested the effects of sleep loss on energy balance in children/adolescents despite the fact that the relation between short sleep duration and obesity is more robust in this population. Future studies should also address the question of whether increasing sleep time in sleep-deprived obese individuals will reduce the amount of body fat or influence the concentration of hormones that help to control appetite. Whether people can voluntarily change their sleeping hours is also unknown; therefore, the causes of sleep curtailment should be investigated. If most of the extra waking hours take place at the end of the day, future studies should document late-night snacking. This will be especially important if most of wakefulness is spent in sedentary activities, such as watching television, in which snacking is common.