Response to: 'Is non-industrial society undergoing an energy balance transition predisposed to accumulate abdominal adipose tissue and susceptible to knee osteoarthritis?' by Yu *et al*

Many thanks to Yu and colleagues¹ for their interest in our recent paper on knee osteoarthritis (OA) susceptibility among the Tarahumara, an indigenous population of subsistence farmers in Mexico undergoing rapid lifestyle changes that promote positive energy balance.² We welcome their constructive comments and are happy to respond.

As Yu *et al* point out, a key prediction of the model we proposed for knee OA risk among non-industrial societies is that people born under conditions of limited energy availability are prone to accumulate and maintain excess abdominal adipose tissue if they later experience chronic positive energy balance.^{3,4} As a result, such people are vulnerable to developing a relatively low body mass index (BMI) but high abdominal adiposity,⁵ which we hypothesised puts them at greater risk of knee OA for a given BMI.

Yu *et al* do not disagree that the Tarahumara men we studied had significantly lower BMIs, on average, than the individuals in our comparative sample, urban American men from Framingham, Massachusetts. However, they question whether the Tarahumara had relatively larger abdomens and were prone to accumulating and maintaining abdominal adipose tissue. Average overall body size among the Tarahumara was much smaller than among Framingham individuals, which we needed to account for when comparing abdomen sizes between the two groups. In our paper, we showed that after controlling statistically for body weight and age, Tarahumara's abdomen circumferences were significantly larger than those of Framingham individuals. If both body weight and stature are accounted for, a similar result is obtained: After controlling for body weight, stature and age, Tarahumara abdomen circumferences (adjusted mean, 107.0 cm; 95% CI 105.2 to 108.2 cm) were, on average, larger ($p < 0.0001$) than those of Framingham individuals (adjusted mean, 100.2 cm; 95% CI 99.7 to 100.8 cm). Thus, for their body size, the Tarahumara indeed tended to have larger abdomens compared with Framingham individuals.

Two additional lines of evidence further illustrate the propensity of the Tarahumara to accumulate and maintain abdominal adipose tissue under conditions of chronic positive energy balance. First, adipose tissue distribution can be compared among the Tarahumara and Framingham individuals by assessing the ratio of abdomen circumference to hip circumference (figure 1A). After controlling for age, Tarahumara abdomen-to-hip ratios (adjusted mean, 1.01; 95% CI 1.00 to 1.02) were, on average, 2.7% higher (95% CI 1.6% to 3.8%; $p < 0.0001$) than those of Framingham individuals (adjusted mean, 0.99; 95% CI 0.98 to 0.99). Controlling for age as well as stature, average Tarahumara abdomen-to-hip ratios (adjusted mean, 1.02; 95% CI 1.00 to 1.04) were 3.4% higher (95% CI 1.2% to 5.7%; $p = 0.0030$) than those of Framingham individuals (adjusted mean, 0.99; 95% CI 0.98 to 0.99). The Tarahumara thus had a greater concentration of adipose tissue in their abdomens. Second, anthropometric data we collected from the Tarahumara can be compared with measurements reported by researchers of the Tarahumara working roughly a half century ago, prior to the lifestyle changes that are currently promoting positive energy balance.^{6,7} Compared with the Tarahumara in our

Figure 1 Evidence of the Tarahumara's propensity to accumulate and maintain abdominal adipose tissue under conditions of chronic positive energy balance. (A) Density plot of the ratio of abdomen circumference to hip circumference among the Tarahumara and Framingham individuals in our study. (B) Abdomen size among the Tarahumara in our study compared with a sample of Tarahumara men ($n=77$) studied in the 1970s.⁶ (C) Triceps skin fold thickness among the Tarahumara in our study compared with a sample of Tarahumara men ($n=108$) studied in the 1970s.⁷ Bars in (B) and (C) are group means and whiskers are 95% CIs.

study, Tarahumara men living in the 1970s had abdomens that were, on average, 13 cm thinner (t test: $p < 0.0001$) (figure 1B). However, triceps skin fold thickness was not markedly different among Tarahumara men in the 1970s compared with the Tarahumara in our study (t test: $p = 0.76$) (figure 1C), indicating that recent shifts toward chronic positive energy balance have led to greater increases in abdominal than peripheral adiposity.

The second issue raised by Yu *et al* concerns our finding that the probability of knee OA increased more markedly with greater abdomen size among the Tarahumara than Framingham individuals, after controlling for body weight and age. Specifically, Yu *et al* consider it unexpected that knee OA probability was not more positively related to abdomen size among the Framingham individuals. This should not be surprising, however, since it has been reported previously that, after adjustment for body weight, abdomen size is not associated with knee OA among Framingham individuals.⁸ Studies of other populations have yielded similar findings.^{9,10} This is almost certainly because abdomen size and body weight are typically highly correlated and, among some populations, potentially measures of the same risk factor.

Figure 2 Tarahumara subsistence farmer working in a field. Photo by David Ramos and used here with permission.

Intriguingly, however, this is evidently not true for the Tarahumara, for whom abdomen size was a strong risk factor for knee OA independent of body weight. In our paper, we hypothesised that this is because, under conditions of energetic abundance, the adipocytes of people whose metabolic phenotype is adapted to energetic scarcity secrete higher concentrations of proinflammatory adipokines, which has been suggested by experimental studies.^{11 12} However, this hypothesis requires further testing.

Finally, Yu *et al* wonder whether the Tarahumara's physically active lifestyles may have been a stronger determinant of knee OA than abdominal adiposity. Lacking good data on physical activity from the Tarahumara, it is difficult to assess this hypothesis rigorously. In our paper, we provided evidence that the Tarahumara are not more prone to either injury-related knee OA or generally greater joint tissue degeneration throughout life compared with Framingham individuals. Conceivably, the postures that the Tarahumara adopt during farming could cause harmful loading of their knees. For example, frequent squatting, kneeling and lifting have been shown to be associated with increased knee OA risk in post-industrial societies,¹³ and such behaviours are not uncommon among the Tarahumara (figure 2) or other non-industrial societies.^{14 15} Yet, in a previous study in which knee OA levels were compared between prehistoric subsistence farmers in North America and those of modern urban Americans, prevalence of knee OA was found to be half as high among the prehistoric individuals as the modern individuals.¹⁶ Thus, it is unclear whether the activities involved in subsistence farming are inherently bad for knees. Ultimately, as we stated in our paper, we suspect that if Tarahumara activity patterns affected knee OA risk, it was not primarily because their knees sustained loads that were excessively high, frequent or abnormal, but that due to lifestyle changes that promote positive energy balance, knee loading in many individuals occurred in the context of chronic low-grade systemic inflammation that weakened their joint tissues. But this hypothesis remains to be tested.

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