

Commentary

Beyond Soil Selenium: Agroindustrial Exposure Pathways and Diabetes Risk Assessment in Contemporary China

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ABSTRACT

A recent multicenter Chinese cohort study reported a prospective association between high serum selenium (Se) status and incident type 2 diabetes (T2D), while interpreting regional serum Se variation largely through local soil geochemistry. Although the correlation between soil and serum Se is robust at the regional scale, the inferential leap from geochemistry to dietary exposure may underestimate contemporary food system inputs. Two structural features of modern China, institutionalized Se supplementation in compound feed since 2009 and large-scale importation of soybean meal from geochemically heterogeneous origins, have introduced agroindustrial Se pathways that may partially decouple animal-source dietary Se from local soils. Risk mapping based solely on geochemical proxies may misclassify exposure burden in regions where these pathways dominate. Future Se exposure assessments should integrate geochemical, dietary, food supply chain, environmental, and biomarker data, particularly for populations with serum Se levels comparable to the highest tertile in that cohort.

Given the country's heterogeneous soil chemistry and rapidly evolving food system, the question of whether environmental geography shapes the burden of metabolic diseases in China is of mounting public health importance. Wang et al. (1) reported that residents in the highest serum Se tertile (107.2–162.8 µg/L) face a 35% greater risk of incident T2D, with a stronger association in men (relative risk=1.96), in a prospective multicenter Chinese cohort in which exposure was characterized through serum Se as an internal-dose biomarker rather than dietary recall alone. This design substantially strengthens exposure characterization and supports the prospective interpretation of the Se–T2D association in a Chinese

population.

However, one interpretive step warrants reconsideration, namely, the attribution of regional serum Se variation to local soil geochemistry. The authors' own stepwise model retained three predictors, that is, soil Se, aquatic product consumption, and PM_{2.5}, which together accounted for 82% of the regional variance in mean serum Se. Soil Se alone explained 67% of the variance. The retention of aquatic product consumption and PM_{2.5}, along with soil Se, indicated that non-soil predictors added explanatory information at the city level. However, this ecological model could not identify the specific exposure pathways involved. The simplification to a soil-Se-only prediction model was adopted explicitly for interpretability and applicability outside China, a transparent and pragmatic modeling choice. However, this methodological convenience should not be interpreted as evidence that local soil Se is the primary determinant of serum Se levels in contemporary China. The authors note that actual serum Se "may deviate in areas with substantial non-local food sourcing, high seafood intake, Se-fortified products or feed supplementation." These caveats likely capture the important determinants of dietary Se exposure in many regions of contemporary China, rather than marginal exceptions.

The two structural features of China's modern food system complicate the importance of local soil geochemistry as a governing exposure pathway (Figure 1). Since the promulgation of China's Regulation on the Safe Use of Feed Additives in 2009 (2), selenium supplementation in compound feed and total mixed rations has been institutionalized under mandatory maximum inclusion limits. In the extensive Se-deficient zones of China, which encompass more than half of the country's land area (3), locally produced feed ingredients are similarly constrained by low environmental Se availability. This makes livestock Se requirements unattainable from local crops alone. Therefore, routine Se supplementation of poultry and swine diets, increasingly with organic sources such as



FIGURE 1. Multi-source selenium exposure pathways in contemporary China.

Note: Imported soybean meal and regulated selenium feed additives, including selenium yeast, sodium selenite, and nano-selenium, enter compound animal feed and reach consumers through animal-source foods. Seafood and locally produced plant foods, including those from localized high-selenium areas, such as Ziyang and Enshi, provide additional dietary sources. These pathways shape human selenium status. Here, higher serum selenium was prospectively associated with incident type 2 diabetes risk.

Abbreviation: Se=selenium; T2D=type 2 diabetes.

selenized yeast, has become standard industry practice. The resulting feed-to-food Se transfer partially decouples animal-source dietary Se from a local geochemical background. This means that residents of historically low-Se regions may obtain substantially more Se through animal-source foods than that predicted by soil maps. China's soybean meal supply chain, the primary protein source in compound feed, is heavily dependent on imports, approaching 100 million metric tons annually (4). It is sourced predominantly from Brazil, the United States, and Argentina. Given the pronounced geochemical heterogeneity among these major exporting regions, where US Midwest soils are among the most Se-replete globally, in contrast to the lower Se agricultural zones of Brazil and China (5), Se concentrations in imported soybean meal are likely to vary substantially by origin. This introduces a supply chain Se input that cannot be inferred from domestic soil maps alone. The soil-serum Se correlation reported by Wang et al. ($r=0.83$ at the city scale) is undeniably robust. However, the ecological model on which it rests was not constructed to distinguish geochemical from

agroindustrial exposure pathways, and the spatial signal it captures likely reflects both. These feed chain inputs may not be captured by local soil maps alone and should be assessed through measurements of feed, animal-source foods, and human biomarkers.

These considerations do not challenge the biological reality or public health significance of the Se-T2D association itself. Independent human evidence supports this association: selenium supplementation increased incident T2D in a large randomized trial (6). Higher serum Se has been positively associated with diabetes prevalence and with elevated fasting glucose and HbA1c in nationally representative US adults (7). In Chinese populations, the highest Se quartile in nail and serum measurements predicted a greater risk of incident diabetes and pre-diabetes (8). At the mechanistic level, selenoprotein overabundance, whether through GPX1 overexpression driving obesity and insulin resistance (9), or through the hepatokine action of selenoprotein P suppressing AMP-activated protein kinase signaling (10), impairs glucose homeostasis in experimental models. Another pathway, centered on the *de novo* serine synthesis pathway (SSP)

in high-Se mice, has been characterized, in which upregulation of phosphoglycerate dehydrogenase (PHGDH) is accompanied by impaired glucose and insulin tolerance (11). In selenomethionine-treated myotubes, SSP activation coincides with the suppression of PI3K–AKT–mTOR insulin signaling (12). Both pharmacological PHGDH inhibition and exogenous serine supplementation attenuate high-Se-induced insulin resistance in vivo (13), establishing the causal directionality and reversibility of this axis. These mechanistically distinct routes, selenoprotein-mediated redox dysregulation, and SSP-driven metabolic remodeling, have been reviewed comprehensively elsewhere (14) and lend robust biological support to the prospective risk signal reported by Wang et al. This pronounced male-specific risk pattern is consistent with the evidence that estrogen-mediated regulation of selenoprotein expression may buffer women against Se-related metabolic perturbation (15).

The most significant contribution by Wang et al. may be the identification of a clinically relevant high-serum Se phenotype that is prospectively associated with T2D risk. In contemporary China, this phenotype is likely shaped by the intersection of local geochemistry, institutionalized feed chain Se supplementation, and globalized agricultural commodity flows. Treating it as a purely geochemical signal misclassifies the exposure burden in regions where agroindustrial Se inputs are substantial. Meanwhile, selenium is an essential micronutrient, and its deficiency remains a concern in historically low-Se regions. Therefore, the prevention of deficiency and avoidance of excessive exposure are complementary rather than competing public health objectives. Future risk mapping should integrate multi-source exposure data spanning soil and water, crops, food circulation, feed supplementation, nutritional fortification, atmospheric co-exposures, and individual dietary patterns with internal-dose biomarkers rather than relying on geochemical proxies alone. Targeted and monitored Se interventions may be appropriate for Se-deficient populations, whereas routine additional enrichment should be avoided in Se-replete populations. Populations with a high internal Se status may require source tracing and continued biomarker surveillance. In populations with high serum Se levels, caution regarding further Se enrichment is warranted, regardless of the upstream source. Understanding where high-Se phenotypes arise and through which pathways is the next step toward geographically nuanced and effective prevention.

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