The role of inorganic arsenic exposure in chronic diseases, including type 2 diabetes, is a major public health research question. This has been underscored by recent epidemiologic1-4 and experimental5-8 evidence supporting increased risks at low exposure levels. In this context, it is critical to understand the biology and the technical limitations of biomarkers of inorganic arsenic exposure, usually measured in urine.9-11 Total urine arsenic integrates exposure from multiple sources including inorganic (arsenite, arsenate) and organic (mainly arsenobetaine, arsenosugars, and arsenolipids) arsenic compounds and their metabolites (Fig. 1). In population-based studies, arsenic speciation in urine is important to differentiate inorganic from organic exposure because organic arsenicals, mostly found in seafood, have little toxicity relative to inorganic arsenic and its metabolites. Despite analytic advances in the measurement of arsenosugars, arsenolipids, and their metabolites,9 their determination remains technically challenging in epidemiologic studies. For example, those compounds were not measured in the 2003-2004 National Health Nutrition Examination Survey (NHANES). Moreover, because arsenite, arsenate, and methylarsonate—species that directly reflect inorganic arsenic exposure and metabolism (Fig. 1)—were measured in NHANES 2003-2004 with high limits of detection,9,12-14 only total arsenic, dimethylarsinate, arsenobetaine and arsenocholine (a minor seafood arsenical) were available for analyses of arsenic and health endpoints.

To evaluate the association of inorganic arsenic exposure with the prevalence of type 2 diabetes in NHANES 2003-2004,2 we reported 2 main strategies to remove the contribution of organic arsenicals of marine origin to total urine arsenic. First, we conducted analyses of the association between total urine arsenic and the prevalence of type 2 diabetes adjusted for sociodemographic factors, diabetes risk factors, and 2 markers of seafood intake (urine arsenobetaine and blood mercury). More importantly, we reported analyses of the association between total urine arsenic and the prevalence of type 2 diabetes adjusted only for sociodemographic and diabetes risk factors but restricted to participants with low arsenobetaine levels (i.e., participants with unlikely seafood intake, in whom urine arsenic would be derived mainly from inorganic arsenic). The magnitude of the association in this subgroup was similar to the analysis...