1144-62-234 **Li Zhang*** (li.zhang@ucsf.edu), 550 16th Street, UCSF Box 3211, San Francisco, CA 94158, **Iryna Lobach** (ryna.lobach@ucsf.edu), 550 16th Street, San Francisco, CA 94158, **Joshua Sampson**, Bethesda, MD, **Alexander Alekseyenko**, Charleston, SC , and **Siarhei Lobach**, Minsk, Belarus. *Case-control studies of gene-environment interactions: when a case might not be the case or a control might be a silent disease.*

Case-control Genome-Wide Association Studies (GWAS) provide a rich resource for studying the genetic architecture of complex diseases. A key is to elucidate how the genetic effects vary by the environment, i.e., Gene-Environment interactions (GxE). Two major overlooked complication are that 1) distinct pathophysiologic mechanisms may lead to the same clinical diagnosis and often these mechanisms have distinct genetic bases; and 2) a subset of the controls have silent, or undiagnosed, disease. These complications are not trivial mainly because the frequency of the pathologic disease of interest within the set of clinically diagnosed cases and the frequency of the silent disease vary by the environmental variable. We first show that using case–control status without accounting for misdiagnosis can lead to severely biased estimates of GxE interactions. We further propose a pseudolikelihood approach to correct the bias and accurately estimate how the relationship between the genetic variant and the true disease status varies by the environmental variable. Finally, we demonstrate our methods with a GWAS of Alzheimer's disease and a GWAS of prostate cancer. (Received August 26, 2018)