Introduction: A serious problem with genetic case control studies is population stratification, which refers to allele frequencies differences between cases and controls from ancestry differences rather than association of genes with disease. Population stratification results in association bias, resulting in erroneous inferences about these associations. This is a particular concern in genetic studies involving admixed populations such as African Americans, Latinos, and also European Americans populations. Genetic ancestry estimates utilizing ancestry informative markers (AIMs) is one method to detect and correct population stratification. But the use of AIMs and genetic ancestry estimates involves study design considerations. The purpose of this review is to provide an overview of study design considerations in genetic association studies of complex disease among bi- or tri-continental populations.

Method(s): The search strategy included a search of CINAHL, Medline, and Pubmed databases with specific aims of determining study design issues genetic ancestry estimates in genetic association studies. Inclusion criteria included genetic association studies based on admixed populations and detection methods of population structure during the years 2000-2009. Exclusion criteria included non-English studies. The identified studies were analyzed by design, sampling, and outcome measures. The studies were analyzed by domain and categorized by main findings by domain.

Results: Three systematic reviews and 20 quantitative studies met the inclusion criteria. Four major study design issues were identified.
Discussion & Conclusions: To maximize the potential for meaningful, reproducible genetic association studies, careful consideration to study design issues surrounding population stratification should be conducted. Study design considerations include: 1) knowledge of the immigration and migration patterns of the study population, 2) the informativeness and number of AIMs, 3) genetic estimates computation methods, and 4) adequate sample size for sufficient power. Generic AIM panels are now available and if appropriate for the study population, can also be effectively utilized in future genetic research of complex diseases.

Abstract History:
This abstract has not been presented or accepted for presentation in whole or in part at the SNRS or other scientific meeting.

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