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# Genetic Susceptibility to Type 2 Diabetes and Implications for Therapy

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## Abstract

Since 2000, we have witnessed an explosion of known genetic determinants of type 2 diabetes risk. These findings have seeded the expectation that our ability to make personalized, predictive, therapeutic clinical decisions is imminent. However, the loci discovered to date explain only a small fraction of overall inheritable risk for this disease. In many cases, the reported associations merely signal regions of the genome that are overrepresented in disease versus health but do not identify the causal variants. Well-powered cohort studies have shown that the set of markers detected thus far does not significantly improve individual risk prediction or stratification over common clinical variables, with the possible exception of younger subjects. On the other hand, risk genotypes may help target subgroups for more intensive surveillance or prevention efforts, although whether such a strategy improves patient outcomes and/or is cost-effective should be examined. Similarly, whether genetic information will help guide therapeutic decisions must be tested in adequately designed and rigorously conducted clinical trials.

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**Abbreviations:** (A1C) glycated hemoglobin A1c, (DPP) Diabetes Prevention Program, (SNP) single nucleotide polymorphismt

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