

STATISTICAL

SIGNIFICANCE

Complex diseases are caused by a combination of genetic, environmental, and lifestyle factors. Statisticians are critical to understanding the etiology of these diseases, helping researchers to plan studies and analyze results to identify which genes are associated with a disease, how behavioral and environmental factors influence one's risk, and finally piecing together the whole picture to better understand how these variables interact.

Type 1 Diabetes: A Complex Disease

Type 1 diabetes (T1D) is a complex disease in which the insulin-producing cells in the pancreas are destroyed by one's own immune system. This results in a lack of insulin in the body, leading to increased blood and urine glucose, which, if left untreated, can ultimately be fatal. Incidence of T1D is increasing worldwide, and scientists are working to understand how various genetic, environmental, and behavioral factors affect one's risk for developing this condition.

Inconsistent Risk Factors

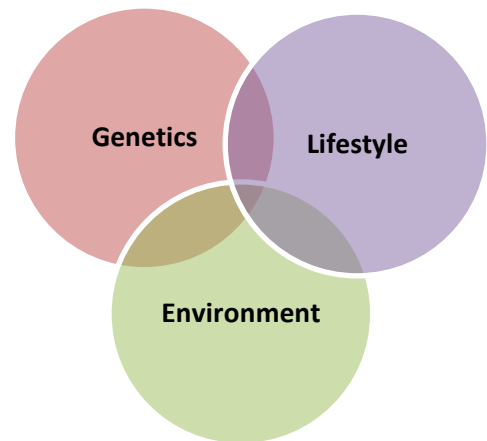
One difficulty in understanding T1D, as well as many other complex diseases, is that certain factors are inconsistently associated with its development. One example is height, wherein some studies have found that taller children are at higher risk of developing the disease, while other studies have indicated that shorter children are at higher risk. One explanation for these inconsistencies is that there

is an age-related effect, and consequently the association between height and T1D changes with age. Statisticians are now working to understand these inconsistencies between studies and determine whether heterogeneity exists in the association between certain risk factors, such as height, and T1D.

Better Analyses Improves Our Understanding

One common assumption in many statistical analyses is that the effect between a certain risk factor and disease remains the same over time. By ignoring the possibility of heterogeneity, that is that the effect of the risk factor changes over time, it is likely that valuable information is being overlooked. However, accounting for heterogeneity requires more complicated statistical analyses, especially when the risk factor is a variable that is measured repeatedly over time, such as height or diet. Statisticians on the Diabetes

Autoimmunity Study in the Young (DAISY) are working to better understand how to analyze these types of data, and how to appropriately interpret results of those analyses.



Heterogeneity of Height

As a result of this work, the association between height and development of islet autoimmunity (IA), the pre-clinical phase in T1D, has been modeled as a function that can change over time. The results from this analysis indicate that this association does, in fact, change with age, and that for young children, being taller is protective against development of IA, but this protective effect lessens with age. In the future, DAISY researchers will investigate heterogeneity within dietary factors, as they hypothesize that a dietary factor that is protective against T1D development in the early years may increase disease risk later in childhood (or vice versa), due to the changing demands of a growing and developing body. By acknowledging the possibility of heterogeneity, valuable information may be learned that can help us better understand these complex diseases.

