Clinicians can encounter sex and gender disparities in diagnostic and therapeutic responses. These disparities are noted in epidemiology, pathophysiology, clinical manifestations, disease progression, and response to treatment. This Review discusses the fundamental influences of sex and gender as modifiers of the major causes of death and morbidity. We articulate how the genetic, epigenetic, and hormonal influences of biological sex influence physiology and disease, and how the social constructs of gender affect the behavior of the community, clinicians, and patients in the health-care system and interact with pathobiology. We aim to guide clinicians and researchers to consider sex and gender in their approach to diagnosis, prevention, and treatment of diseases as a necessary and fundamental step towards precision medicine, which will benefit men’s and women’s health.

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