Never, throughout human history, have pressures on water resources been greater than they are today. This is important considering that water is a cornerstone natural resource that provides the scaffolding for the natural environment and, thus, drives economic and social development. In response to increasing demands, difficult decisions are being made by managers that often include reallocations of the diminishing quantity and quality of the resource. However, cumulative anthropogenic drivers (e.g., land use, population growth, climate change) confound the uncertainties of decision-making, and many critical information gaps remain. This Special Issue of Water focuses on integrated and multidisciplinary water resources research that advances the understanding and sustainability of water resources. Articles will be considered that address all aspects of integrated and multidisciplinary water resources research, including (but not limited to) water quality, climate, ecohydrology, modeling, water economics, human dimensions of water, water governance, and stakeholder engagement.