Abstract: The USGS Prompt Assessment of Global Earthquakes for Response (PAGER) system provides rapid and automated alerting of estimated economic and human impacts following earthquakes around the globe. Although PAGER's primary purpose is to quantitatively any earthquake's severity for situational awareness and response decision-making, the underlying tools developed are utilized for many other scientific and mitigation efforts. There are four components of the PAGER system. First, earthquakes trigger rapid source characterization; second, these source parameters inform our estimates of shaking-distribution (e.g., ShakeMap). Third, losses are then modeled by computed populations exposed per shaking intensity level, and country-specific and shaking-dependent loss functions are used to provide estimates of economic impact and potential casualties. Finally, these uncertain loss estimates are communicated in an appropriate form for actionable decision-making among a variety of users. Rapidly and automatically assessing the wide range of seismological, demographic, building inventory, and vulnerability information necessary to make such loss estimates entails a requisite balance of empirical & physics-based modeling strategies. Several aspects of our problem cannot yet be adequately solved with purely empirical, nor solely mechanistic, approaches. The "physics-based" model components of the PAGER system are essential for informing empirical models where they are data-limited, and for providing a framework for better understanding the causative pathways that dominate earthquake losses around the globe. In the course of explaining the end-to-end strategies and science/engineering employed by the PAGER system, I also describe what pragmatic choices were made in balancing the uncertainties in and benefits provided by our empirical, semi-empirical, expert-opinion, and physical models. Recognizing and reconciling the complimentary benefits of data-driven verses theoretical problem-solving is at the core of the PAGER system, as it is for a wide variety of other challenges within the earth sciences.