Nearly two decades after the completion of the Human Genome Project, the vision of universal genomic analysis within medicine as a path to disease prevention and greater longevity remains mired in exaggerated risks, misdirected market forces and sparse evidence for clinical utility and cost-effectiveness. The MedSeq and BabySeq Projects are the first randomized clinical trials to rigorously explore the medical, behavioral and economic impact of DNA sequencing in health adults and newborns, respectively. This presentation will summarize results from these and other studies that return unanticipated genomic results, and consider the necessary next steps for harnessing genomic information for population health.