Abstract. Clinical guideline-based decision-support systems (or computer-interpretable guideline systems CIG systems) used to acquire all of the patient’s data from the clinician who was using the system. The second generation CIG systems were linked to electronic health record (EHR) systems, which enabled them to provide patient-specific recommendations without asking the clinician users to re-enter information that was already available. Futuristic CIG systems will differ in several respects, posing new and exciting challenges. First, they will mine accumulating data on patients’ clinical context, recommendations and actions taken for the patients, and the resulting outcomes to find interesting temporal patterns in the data that could provide new knowledge for clinicians, to assess compliance with the guidelines, and to suggest improvements in clinical care pathways that could improve outcome. Second, they will consider genetic variation between patients (which would be stored in the EHR) that could affect guideline recommendations. And third, they will place the patient at the center, considering personalized information about the patient’s preferences and non-clinical context, which could affect the implementation of recommendations for the patient. Acquiring and representing this personalized information in EHRs or Personal Health Records (PHRs) presents interesting challenges.