Information Technology and Precision Medicine

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Objectives: *To provide oncology nurses with an overview of clinical decision support (CDS) and explore opportunities for genomic CDS interventions. The nation's first personalized cancer decision support tool, My Cancer Genome, is presented as an exemplar of a novel CDS tool.*

Data Sources: *Published nursing and medical literature and the internet for an exemplar.*

Conclusion: *CDS is a sophisticated health information technology that can translate and integrate genomic knowledge with patient information, providing recommendations at the point of care.*

Implications for Nursing Practice: *Nurses, as key stakeholders, must have an understanding of CDS interventions and their application to fully participate in all stages of CDS development and implementation.*

Key Words: *Clinical decision support, web-based application, knowledge base, electronic health record, precision medicine*

Scientific and technologic advances have dramatically increased the understanding of genetics and the molecular basis for the development and proliferation of cancer cells.[1] The translation of genomic discoveries to relevant clinical implications is changing the way cancer is managed. Precision cancer treatment, based on the genomic characteristics of the patient's disease, is quickly becoming a reality. During the past decade numerous gene mutations and pathways have been identified as targets for therapeutic interventions and over 800 experimental drugs are in clinical trial development.[2] As scientific and clinical knowledge of genomics increases, the application of precision medicine will expand beyond treatment to the full spectrum of cancer care. For example, an individual's genomic make-up will be a significant consideration in determining the risk of developing cancer. A genomic-based risk assessment would enable a clinician and patient to establish a highly individualized cancer screening and prevention strategy; leading ultimately to earlier diagnosis and improved outcomes. Subsequently, successful treatment and increased survival rates will warrant personalized survivorship care, with risk-adjusted screening for recurrence and secondary malignancies.[3]

Many health care providers lack the knowledge and formal training to utilize genomic information and the challenge of understanding and interpreting genomic data are compounded by the demands of clinical practice.[4] Even for those who have an

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understanding of genomics, the application of that knowledge and the interpretation of a patient's genomic profile is complex and challenging. For example, approximately 17% of patients with non–small cell lung cancer harbor epidermal growth factor receptor (EGFR) mutations, of which 80% to 90% confer sensitivity to EGFR tyrosine kinase inhibitors (eg, EGFR L858R). However, other EGFR mutations are associated with primary or secondary resistance to the same drugs (eg, EGFR T790M).[5] In addition, mutations that predict responsiveness to therapy in some cancers may be associated with a lack of response in others, as is the case in melanoma and colon cancer. BRAF V600E mutated melanomas are sensitive to BRAF inhibitors such as vemurafenib and dabrafenib, while BRAF V600 mutated colorectal cancers may not be sensitive to these drugs.[6] Consider the busy clinician faced with deciding if erlotinib is the best treatment for a lung cancer patient. The clinical decision is based on a number of patient and disease characteristics including detection of genomic mutations and the clinical implications of all the patient-specific data. Ready access and interpretation of this type of information in the fast-paced clinical environment often proves to be difficult and time-consuming. However, the same busy clinician, utilizing computerized physician order entry and electronic clinical decision support (CDS) receives an electronic alert if the patient's tumor harbors a variant known to confer resistance to erlotinib. The clinician is enabled to quickly make appropriate treatment decisions and avoid patient exposure and expense to a drug that will provide little benefit.

The traditional model of a provider reading current literature to stay abreast of optimal care will be inadequate in light of the increasing scale and complexity of cancer genomics. Realization of precision medicine depends on the ability to collect, disseminate, and process complex genomic information in the context of clinical care.[7] CDS is a sophisticated health information technology (HIT) which can translate and integrate genomic knowledge with patient information, providing intelligently filtered recommendations, and enabling genomic-informed decisions at the point of care.[8] The steady infusion of new HIT solutions, like CDS into the clinical settings, is revolutionizing the way that health care is provided. Nurses, as key stakeholders, must have an understanding of CDS interventions and their application to fully participate in all stages of CDS development and implementation. The purpose of this article is to provide oncology nurses with an overview of CDS and explore opportunities for genomic CDS interventions. The nation's first personalized cancer decision support tool, My Cancer Genome, is presented as an exemplar of a novel CDS tool.

Overview of CDS Technology

CDS software is designed to support clinical decision-making by matching the patient characteristics to a computerized clinical knowledge base and patient-specific assessments or recommendations are presented for clinical care decisions.[9] Initially, CDS systems were stand-alone programs designed to provide diagnostic support and medication selection guidance. The early systems had limited availability and required the user to manually enter pertinent patient information. Once the data entry was complete, the user had to interpret the results and determine clinical relevancy.[10] Several limitations associated with initial CDS technology were surmounted by integrating CDS with other clinical systems, such as the electronic health record (EHR) and the computerized physician order entry. One significant advantage of an integrated system is the user does not have to reenter information that is already stored electronically. Secondly, this type of CDS system can be proactive in providing alerts triggered by significant patient data without the user seeking assistance.[7]

CDS technology has been available for several decades; however, adoption has been slow. Implementation has been hindered by inadequate information technology (IT) infrastructure, the exorbitant cost of design, implementation and support of CDS, and a lack of standards and best practice guidelines.[11] Recently, CDS development and implementation has dramatically increased because of the Health Information Technology for Economic and Clinical Health Act (HITECH) of 2009. The HITECH Act establishes incentive payments under the Medicare and Medicaid programs for eligible providers and hospitals that use EHRs to achieve specified improvements in health care delivery. The Federal government, through HITECH, will make available up to 27 billion dollars in incentive payments over 10 years for hospitals and eligible providers who achieve federally defined objectives. The objectives of 'meaningful use' encompass IT functions, like CDS, which enable EHRs to support improved health care.[12]

A wide range of clinical information systems are utilized, including both internally developed 'home grown' systems and commercially available products. The diversity of clinical information systems has resulted in CDS systems that vary in terms of the technology intrastructure, configurations, and interventions.[13] There are three types of CDS, which are characterized by how patient information is submitted and the way patient-specific recommendations are generated. Passive CDS configuration entails the submission of patient information and the generation of recommendations as a manual process. Whereas, active CDS is configured to enable the submission of patient information and the generation of recommendations automatically. With semi-active CDS information, submission is automated and generation of recommendations is manual.[9] Passive configuration requires the clinician to explicitly access available tools or information. Conversely, an active system might modify the clinician's behavior by using alerts and reminders that are automatically triggered by laboratory tests, diagnoses in a problem list, or changes in a patient's clinical condition.[14]

CDS interventions are numerous and designed to provide varying degrees of intervention. Smart documentation forms emphasize data elements pertinent to the patient's condition and health care needs. Order sets, care plans, and protocols that encourage correct and efficient ordering and provide appropriate management recommendations based on the specific patient diagnosis. The most common CDS tools are the 'immediate Alerts' that occur just after a user has entered an order, prescription, or documentation to show a potential hazard, or a recommendation for further information.

There are CDS interventions designed to support information management like single-patient data summaries, which filter and organize patient information to highlight important care management issues. Multi-patient monitors assist providers who are multitasking among patients by displaying activity among all patients on a care unit. Predictive and retrospective analytics are CDS tools that use artificial and statistical intelligence to provide risk predictions, stratify patients, and measure progress on broad initiatives. The interventions mentioned thus far are triggered by the user entering data. However, alerts and reminders can be triggered by events like an abnormal laboratory value or overdue screenings or evaluations. Another CDS intervention provides filtered reference information and knowledge resources in the context of the patient specific data (Table 1).[15] The following section describes My Cancer Genome, a web-based, knowledge resource CDS intervention.

TABLE 1.
Clinical Decision Support Interventions and Examples[15]

Interventions	Examples
Smart documentation forms	Checklist
	Risk assessment
	Conditional work-up sheet
Order sets, care plans and protocols	Order set for management of a chronic condition
	Transfusion care set
	Complex order variation like TPN
Immediate alerts: warnings and critiques	Drug-drug interactions
	Contraindications: allergy warnings
	Drug substitution suggestion
Event-driven alerts and reminders	Abnormal lab result alert
	Annual health screening activities
Parameter guidance	Dosage guidance adjusted for patient condition
	Order guidance: display hematocrit and cross match status when ordering blood products
Relevant data display (single patient)	Health maintenance flow sheets
	Quality-metric status sheet
Multi-patient monitors and dashboards	ED tracking system
	OR status displays
Predictive and retrospective analytics	Retrospective displays of performance
	Benchmarks
Filtered reference information and knowledge resources	Infobutton
	Data or event sensitive reference information
	Patient education programs
Expert workup advisor	Diagnostic systems
	Antibiotic advisors

Abbreviations: TPN, total parenteral nutrition; ED, emergency department; OR, operating room.

My Cancer Genome

Vanderbilt-Ingram Cancer Center (VICC) launched My Cancer Genome (mycancergenome.org), the nation's first personalized CDS, in January 2011. Created by Drs. William Pao and Mia Levy, My Cancer Genome is a web-based tool designed to quickly provide up-to-date information about gene mutations that affect different cancers and mutation-specific treatment options. My Cancer Genome is integrated with Vanderbilt's EHR, thereby providing clinicians with point-of-care decision support for mutation-directed treatment and clinical trial availability. The Web site is freely

available via the internet to any clinician, patient, or researcher who wishes to access the information.[16]

Visitors to My Cancer Genome can easily search for genomic information by disease, gene, or mutation, and the resulting content will be relevant to their selection. For instance, a search of the disease melanoma and the gene *BRAF* results in content describing the oncogene pathway, the significance of the gene *BRAF* in melanoma, the genomic location and prevalence of individual mutations in melanoma, and the implications of each mutation for targeted therapy. The search results also include information about active clinical trials relevant to the gene and disease, and, where available, the results of completed research studies involving targeted therapies for the mutation are summarized with links to the published abstracts.[16]

There are several ways to access gene-associated clinical trial information on My Cancer Genome. As previously mentioned, clinical trial information can be viewed in the content of the Web site when reading about a specific gene or variant. Also, the user can enter a disease and/or gene of interest in the "Find a Clinical Trial" box located on the Web site home page. The user is able to search from a database containing 135 cancer disease types and 490 cancer-related genes. Alternatively, the user can enter the disease and/or gene of interest and the term "clinical trial" in the search box located in the right upper corner of the Web site. Regardless of the search method used, the results will be displayed in the same manner. The user can view a list of clinical trials that match the search criteria and are open for enrollment at VICC, or other national or international locations. Clinical trial information includes the protocol identifier number, title, and phase of the clinical trial. It is important to note that the protocol identifier number is the unique ClinicalTrials.gov identifier and links the user to the detailed trial description on ClinicalTrials.gov. The clinical trial information is downloaded weekly from the National Cancer Institute's Physician Data Query comprehensive database, and the content is annotated to include information on the genes each trial is evaluating.[16]

In addition to information about mutations associated with specific cancers and clinical trials, My Cancer Genome contains a wide variety of content specific to molecular medicine. The Web site visitor can easily access information on targeted therapies and types of molecular testing. An extensive directory of anticancer agents including those with US Food and Drug Administration (FDA) approval and those being studied in clinical trials is available on the Web site. The anticancer drugs are categorized by drug class and drug target. As the anticancer drug list contains both FDA approved and experimental drugs, the drugs are identified by developmental, generic, and trade names. Recently, the My Cancer Genome: Anticancer Agents tool was released as the mobile app, MCG Drug List, which may be freely downloaded to any Apple iOS device from the iTunes store.[16]

To begin to address the needs of patients with rare mutations, Drs. William Pao and Leora Horn developed the DNA-mutation Inventory to Refine and Enhance Cancer Treatment (DIRECT) database. DIRECT is housed on the My Cancer Genome Web site. Clinicians and patients can request information on common and rare EGFR mutations in lung cancer, along with treatments and outcomes experienced by patients with these mutations.[17] There are plans to expand DIRECT to include other cancers and genes.[16]

The extensive content found at My Cancer Genome is contributed by a collaborative network of 59 clinical and scientific experts from a variety of institutions located in the United States, Europe, Asia, and Australia. The Web site is updated regularly with new content, covering either new genes and/or diseases, and is managed by a multidisciplinary team based at the VICC. My Cancer Genome is supported by private philanthropy, corporate charitable gifts, numerous foundations, and the VICC.[16] Since its launch in 2011, My Cancer Genome has won the National Cancer Institute and the Office of the National Coordinator for Health Information Technology's "Using Public Data for Cancer Prevention and Control: From Innovation to Impact Developer Challenge"[18] and the GE Healthymagination Cancer Challenge.[19] In addition, My Cancer Genome was featured in the New York Times in April 2013[20] and was recently mentioned in the Wall Street Journal.[21]

Genomic CDS: Future Opportunities and Challenges

CDS interventions provide a means to support the consistent, evidence-based application of genomic information in a variety of ways.[11] The following scenarios illustrate the potential use of

genomic CDS interventions in the delivery of personalized, precision patient care.

A breast cancer patient has completed treatment and the oncologist creates a tailored survivorship plan (CDS Type: Smart documentation form), which includes surveillance for long-term side effects associated with treatment and risk-adjusted screening for recurrence or secondary cancer based on type of cancer, genomic data, treatment regimen, and other patient specific data.

A 72-year-old male is admitted to a surgical unit following a right hemi-colectomy for stage 3 colorectal cancer. Procedure-specific admitting orders (CDS Type: Order Sets) have been electronically submitted by the surgeon to the patient's EHR. The patient has a history of adult onset diabetes and hypertension, so the provider orders daily blood chemistries and hourly vital signs with alert parameters set for patient-specific tolerances for abnormal values (CDS Type: Event-driven alerts and reminders). Upon receiving the surgical specimen, the Pathologist electronically orders molecular diagnostic testing (CDS Type: Order Set and Protocol) and submits an appropriate tissue sample to the molecular lab. The order for molecular testing prompts the addition of the patient to both the surgeon and oncologist's provider dashboard (CDS Type: Relevant Data Display), which displays the status of the molecular tests as pending. An email alert (CDS Type: Event-driven alerts and reminders) notifies both providers when the molecular test results are available in the EHR. Viewing the provider dashboard from a secure office computer, the oncologist learns the patient's tumor harbors a BRAF V6000 E mutation and is KRAS wild type. Within the report the oncologist clicks on the VRAF V600E mutation and is taken to a summary of the clinical significance for the specific gene mutation in the patient's specific cancer diagnosis on the My Cancer Genome Web site (CDS Type: Filtered Reference Information and Knowledge Resources). The oncologist has immediate access to the latest findings regarding treatment implication and clinical trials for BRAFV600E mutation in colorectal cancer. At the next tumor board meeting the patient care team reviews metrics (CDS Type: Predictive and Retrospective Analytics) for mutational testing including the average time from test order to availability of results in EHR, frequency detected mutations, and associated treatment regimens.

There are many lessons to be learned from decades of experience with CDS that are applicable to genomic CDS implementation. Settig et al[22] identified and described 10 specific challenges surrounding CDS, which must be addressed if the technology is to reach its potential and improve the quality, safety, and efficiency of patient care. According to the authors, the improvement of the human-computer interface is the most important issue to be addressed if users are to realize the full benefits of the technology. "CDS should unobtrusively, but effectively, remind clinicians of things they have truly overlooked and support corrections, or better yet, put key pieces of data and knowledge seamlessly into the context of the workflow or clinical decision-making process, so the right decisions are made in the first place."[22(p388)] A number of CDS characteristics (Table 2) are identified in the literature as being associated with successful implementation and support the need for improved human- computer interface.[23] There is a clear need for further research on the impact of CDS on care process, resources, and patient outcomes. Those responsible for the future implementation of CDS must be aware that it requires careful integration into the clinical workflow, which requires the effort and involvement of all stakeholders. The science of genomics and CDS design and implementation are each in their infancy. Future progress in biologic science and IT will certainly lead to innovative, individualized approaches to the prevention, detection, and treatment of cancer.

TABLE 2.
Characteristics of Successful Clinical Decision Support Technology[23]

Features are automated as part of the workflow
Interventions are delivered at the time and location of decision making
Provision of recommendation, not just assessment
Integration with charting or order entry system to support workflow
Promotion of action rather than inaction
Requires minimal additional clinician data entry
Stakeholder involvement in development and implementation

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