Risk Modeling: Applying Evidence-Based Risk Assessment in Oncology Nursing Practice

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Purpose/Objectives: To introduce nurses to the concept of evidence-based risk models and their use in practice.

Data Sources: Poster presentations at meetings and published articles and books.

Data Synthesis: Evidence-based risk models can be used in many clinical situations to identify patients at higher risk for a particular disease or clinical outcome, such as adverse events. These models may be based on molecular, epidemiologic, clinical, or family information obtained from patients. Risk models also may provide information about the cost-effectiveness of prevention, treatment, or support strategies for specific patients.

Conclusions: Determining the risks of disease- or therapy-related adverse events can help healthcare providers and patients. Risk assessment to identify patients who are most likely to benefit from supportive care can lead to the cost-effective use of these supportive care measures and improved clinical outcomes.

Implications for Nursing: Through awareness of relevant evidence-based risk models, nurses can become more effective in actively managing their patients' care. Because of their close and ongoing contact with patients with cancer, oncology nurses are in an ideal position to assess risk factors for adverse events and to use appropriate supportive care for those patients who are at greatest risk.

The concept of risk plays a key role in most decision making. In everyday life, the term "risk" is used in many different contexts to describe probability. Risk generally is perceived to be associated with the negative aspects of a situation and inversely related to benefit (Sokolowska & Pohorille, 2000). In the context of clinical practice, risk commonly is associated with the occurrence of undesirable outcomes, such as a disease- or treatment-related adverse event. An example of a typical disease risk model is the Gail model, developed to predict the five-year risk of invasive breast cancer in women. The model is based on factors such as a family history of breast cancer, personal history of breast biopsies, age at first live birth, current age, age at menarche, and age at menopause (Claus, 2000; Gail et al., 1999).

Assessing risk always has been part of the process through which healthcare providers make decisions about patient care. For many health-related outcomes, key factors have been identified that can help healthcare providers determine patients' levels of risk. Statistical models based on information about these factors can be useful tools in clinical practice. By using models to predict risk, providers can more effectively target patients who are most likely to benefit from risk-reducing strategies. This approach can improve how resources are allocated, which is particularly important with costly procedures or therapies.

Key Points . . .

- ➤ Risk models can be used to predict a patient's likelihood of developing therapy-related adverse events.
- ➤ Nurses who are familiar with evidence-based risk models may be better able to prevent or more effectively ameliorate serious adverse events associated with prevention, treatments, conditions, and diseases.
- ➤ Risk assessment to identify patients who are most likely to benefit from supportive care options can lead to cost-effective use and improved clinical outcomes.

Definitions of Risk in Clinical Practice

Risk generally is categorized as either relative or absolute. A glossary of basic statistical terms is provided in Figure 1. Relative risk (RR) compares the occurrence or likelihood of an outcome among people exposed to a given risk factor (i.e., a characteristic, behavior, or exposure related to the outcome) with the occurrence or likelihood of the outcome among people who lack exposure to the risk factor. The odds ratio (OR) is another measure for comparing risk and, for rare events, is similar to RR. An OR is calculated in logistic regression equations and is a typical measure of risk in meta-analyses. Although RR has value for describing risk at the population level (Claus, 2000), the goal of risk prediction in most clinical situations is to assess the absolute risk (AR) for a patient. This sometimes can be called incidence; it is the predicted probability that a person will experience an outcome in a specified time. Estimates of AR can help healthcare workers make key decisions about the use and effectiveness of interventions (Claus).

Various statistical methods (e.g., multivariate logistic regression, Cox proportional hazards modeling) have been developed to estimate risk. Based on information about the

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Risk Factor
A characteristic, behavior, or exposure that may affect a person's likelihood of having a specified disease or health-related event

Absolute Risk
The probability that a disease-free person with a given set of risk factors (exposed) will develop a specified disease or health-related event in a given period of time in the presence of competing risks; another term for this is incidence

Relative Risk
The probability of a specified disease or health-related event among people with a given risk factor (exposed) compared with the probability of the disease or event among people without the risk factor (unexposed)

Odds Ratio
A measure calculated by comparing (a) the odds of having the disease versus not having the disease observed among those with a given risk factor with (b) the odds of disease versus no disease observed among those without the risk factor.

Test of Statistical Significance
A test designed to assess whether an observed difference is likely a result of chance alone or, conversely, statistically significant. The appropriate test depends on the type of data being analyzed (e.g., χ^2 test for categorical data, t test for continuous data). In each case, the calculated test statistic is associated with a p value that can be compared with a predefined level of significance (e.g., α is conventionally set at 0.05).

P Value
Based on the calculated test statistic, the probability that the observed difference is the result of chance alone; the smaller the p value, the more likely the observed difference reflects a real difference (statistically significant) (i.e., not caused by chance). If the value is the same as or smaller than a specified significance level α, the difference is considered statistically significant.

Confidence Interval
An interval around the estimate within which the true value has a given probability of occurring. For example, 95% of the intervals from independent samples will include the true population parameter for a 95% confidence interval.

Figure 1. Basic Terms and Concepts

exposure to risk factors and the occurrence of an outcome, statistical models can be constructed to provide risk estimates (Claus, 2000).

Because measures of AR or RR are estimated using statistical methods, patients should be informed not only about their risks for outcomes (such as a particular disease or adverse event), but also about the degree of uncertainty or imprecision associated with those risk estimates. Risk estimates generally are reported in association with standard deviations, confidence intervals, or p values that reflect their precision or significance. In practical terms, confidence intervals around risk estimates indicate a range in which the patient's true risk is likely to fall. However, statistically significant risks may not be clinically significant; conversely, clinically significant effects may not always be corroborated by statistical tests, particularly if the study focuses on a small number of subjects and is underpowered (Fletcher, Fletcher, & Wagner, 1996).

A variety of statistical methods can be used to estimate the risk of a clinical outcome, and developing a reliable risk model is not always straightforward. A good clinical model should minimize bias by clearly stating the hypothesis or purpose in advance, including any subgroup analysis, defining the study population with specific inclusion and exclusion criteria, and limiting missing data, including those on nonassessable subjects (Altman & Lyman, 1998). Models also must be validated independently in a separate set of patients from those used to develop the model. Risk factors included in a model should be associated strongly with the outcome (as shown by the RR) and experienced by a substantial proportion of people in the population (Claus, 2000). Only statistically rigorous analysis of data from representative patient populations can provide systematic and evidence-based risk models for identifying and proactively managing high-risk patients. Most important, clinicians should be able to apply findings from the model in their practice (Claus).

Identifying Patients at High Risk

Sackett, Rosenberg, Gray, Haynes, and Richardson (1996) defined evidence-based medicine as "the conscientious, explicit, and judicious use of the current best evidence in making decisions about the care of individual patients" (p. 71). Ideally, the practice of evidence-based medicine should result in decisions that meet patients' needs and preferences and are based on solid conclusions from randomized trials, meta-analyses, cohort studies, basic science, and clinical expertise (see Figure 2). These research sources are not all given equal weight; levels of evidence should be considered when evaluating information (see Table 1).

For many clinical decisions, research-based evidence is limited or nonexistent. On other topics, a preponderance of information is available. One study estimated that a clinician would have to read 19 new articles each day to keep up with all of the medical advances reported in journals (Sackett et al., 1996). Not all of this information is relevant or ready for clinical application. Thus, clinicians often rely predominantly on their clinical experience to determine which patients are most likely to develop an outcome and how to intervene. Providers must make their decisions about patient care while taking into account many different and often conflicting considerations. These include the expectations of patients and their families, changing reimbursement policies and procedures, and professional issues such as malpractice, peer pressure, the press, and politics (Eddy, 1990). Risk models, systematic reviews,

Evidence-Based Medicine
The conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients

Evidence-Based Practice
Integrating the best available external clinical evidence with individual clinical expertise and patient preference

Clinical Expertise
Judgment, knowledge, and skills gained through clinical experience that can be reflected in the ability to efficiently tailor clinical decisions to each patient's unique circumstances and preferences

Best Evidence
The best available clinically relevant research, especially patient-centered clinical research focusing on assessment, prognosis, and the value of prevention and therapeutic and rehabilitative interventions

Evidence-Based Patient Choice
The use of evidence-based information as a way of enhancing patients' informed choices

Figure 2. Definitions in Evidence-Based Medicine

Note. Based on information from Ropka & Spencer-Cisek, 2001; Sackett et al., 1996.

Table 1. Priority Symptom Management (PRISM) Levels of Evidence

PRISM Level	Level of Evidence[a]	Evidence Source
I	1	Qualitative systematic review (also called "integrative review") or quantitative systematic review (also called "meta-analysis") of multiple, well-designed, randomized, controlled trials of adequate quality
	2	At least one properly designed, randomized, controlled trial of appropriate size (record if multisite and over 100 subjects, but not required)
	3	Well-designed trial without randomization (e.g., single group pre/post, cohort, time series, meta-analysis of cohort studies)
II	4	Well-conducted, qualitative, systematic review of nonexperimental design studies
	5	Well-conducted case-control study
	6	Poorly controlled study (e.g., randomized controlled trial with major flaws) or uncontrolled studies (e.g., correlational descriptive study, case series)
	7	Conflicting evidence with the weight of evidence supporting the recommendation or meta-analysis showing a trend that did not reach statistical significance
		National Institutes of Health Consensus Reports
		Published practice guidelines, for example, from professional organizations (e.g., Oncology Nursing Society, American Society of Clinical Oncology), healthcare organizations (e.g., American Cancer Society), or federal agencies (e.g., National Cancer Institute, Centers for Disease Control and Prevention)
III	8	Qualitative designs
		Case studies; opinions from expert authorities, agencies, or committees

[a] Levels of evidence range from the strongest evidence at the top to the weakest level of evidence at the bottom.

Note. From "Rating the Quality of Evidence for Clinical Practice Guidelines," by D.C. Hadorn, D. Baker, J.S. Hodges, & N. Hicks, 1996, *Journal of Clinical Epidemiology, 49,* p. 750. Copyright 1996 by Elsevier Inc. Adapted with permission in "PRISM: Priority Symptom Management Project Phase I: Assessment" by M.E. Ropka & P. Spencer-Cisek, 2001, *Oncology Nursing Forum, 28,* p. 1589. Copyright 2001 by the Oncology Nursing Society. Reprinted with permission.

and practice guidelines can assist healthcare providers in the decision-making process.

Information from problem- or disease-specific risk models can be used to identify patients at higher risk for a particular disease or clinical outcome, such as adverse events. This type of information can help providers to (a) focus resources to proactively manage patient care through risk stratification, (b) target high-risk patients more appropriately, and (c) reduce the costs and potential adverse events of prophylactic interventions in low-risk patients. Risk models also can be used to decide among possible treatment interventions for patients with a specific disease or clinical problem.

Risk Models for Prevention

Prophylactic interventions are available to reduce the risk of certain outcomes, but accurate risk assessment is required to identify patients for whom the benefits of such interventions are likely to outweigh disadvantages. As an example, risk-factor charts based on a prognostic algorithm have been developed from findings in the Framingham heart study, which has followed more than 5,000 men and women since 1948 (Anderson, Odell, Wilson, & Kannel, 1991). One such chart makes estimating a person's risk of cardiovascular disease possible on the basis of his or her particular constellation of characteristics and behaviors (Jackson, 2000). According to this chart, a 60-year-old man who does not smoke, has a blood pressure of 180/105 mmHg, has a ratio of total cholesterol to high-density lipoprotein cholesterol of four, and does not have diabetes has a 10%–15% chance or likelihood of suffering a cardiovascular event within the next five years. That likelihood increases to 20%–25% if he also has diabetes and to more than 30% if he is a smoker. These models do not include some known risk factors, such as family history of cardiovascular disease, physical inactivity, obesity, and left ventricular hypertrophy. Using such models gives providers a means of estimating patient risk to guide decisions about appropriate care. Expected benefits should be weighed against cost and potential harm (Jackson).

As another example, several risk models are available for assessing the risk of developing breast cancer, each based on a different combination of risk factors. The Gail and Claus models are used most commonly, whereas more recent models such as the BRCAPRO model can estimate individual breast cancer risk based on the probability that a family carries a mutation in one of the BRCAPRO genes (Euhus, 2001). However, none of them integrates family history, surrogate measures of estrogen exposure, and the presence of benign breast disease in a single comprehensive risk assessment tool. The Gail model is the most generally applicable. It estimates breast cancer risk on the basis of the number of first-degree relatives (mother, sisters, offspring) with breast cancer, number of breast biopsies, age at first live birth, current age, age at menarche, and atypical ductal hyperplasia in biopsy. The model does not consider paternal family history of breast cancer, history of breast cancer in second-degree relatives, personal history of lobular neoplasia, family history of ovarian cancer, or the distinction between pre- and postmenopausal breast cancer (Gail et al., 1999).

On the other hand, BRCAPRO and the Claus model consider only paternal and maternal family history, and therefore may

underestimate risk in women with other risk factors (Euhus, 2001). Because each model is associated with strengths and weaknesses, selecting the model best able to account for each patient's circumstances and clinical information is important (Domcheck et al., 2003; Euhus). For example, the Claus model may be the best option for a woman with second-degree relatives with breast cancer, but the Gail model may be more useful for a woman without a family history. Thus, choice of a model depends on the clinical data related to the individual patient as well as the parameters of the model under consideration. Knowledge of the patient's history and other risk factors, as well as understanding how a specific model was generated, is important when choosing which model is most applicable (Domcheck et al.).

For patients identified as high risk, several primary prevention strategies are available to lower their risk of breast cancer. Prophylactic mastectomy or oophorectomy should be considered only in high-risk women because the trade-offs of extensive surgery are significant. Tamoxifen is associated with a 49% reduction in invasive breast cancer in women with a five-year risk of at least 1.7% according to the Gail model (Fisher et al., 1998). However, routine use of tamoxifen in low-risk women is countered by costs and rare side effects such as thromboembolism, endometrial cancer, and cataracts. Women at high risk for breast cancer also may be targeted for enhanced surveillance with mammograms at an earlier age or informed about the increased risk of receiving postmenopausal hormone replacement (Fisher et al.).

Risk Models for Chemotherapy-Induced Neutropenia

Risk models can be used to identify patients at higher risk for developing a particular clinical outcome, such as neutropenia following cancer chemotherapy. Neutropenia has been identified as a leading predisposing factor for infection in patients treated with chemotherapy, and it is the most common dose-limiting adverse effect of cytotoxic treatment. For decades, healthcare providers have known that the severity and duration of neutropenia put patients at risk for life-threatening infection (Bodey, Buckley, Sathe, & Freireich, 1966). Clinical trials have shown that administration of granulocyte–colony-stimulating factor (G-CSF) shortly after chemotherapy reduces the incidence of fever and neutropenia (Crawford et al., 1991; Trillet-Lenoir et al., 1993). The proactive use of growth factors is a better strategy for managing neutropenia than chemotherapy dose reductions and delays because delivering full chemotherapy doses on time and in therapeutic amounts is associated with improved disease-free survival and overall survival in chemosensitive cancers such as early-stage breast cancer and non-Hodgkin lymphoma (Bonadonna, Valagussa, Moliterni, Zambetti, & Brambilla, 1995; Budman et al., 1998; Kwak, Halpern, Olshen, & Horning, 1990).

Significant benefits of G-CSF in the management of neutropenia should be weighed against its potential side effects. The cost of this treatment prevents its routine use in all patients treated with chemotherapy, but cost-effective use of G-CSF can be achieved by targeting proactive G-CSF treatment to patients who are at greatest risk for neutropenia.

Many risk models have been developed to identify independent predictors (stand-alone risk factors) of neutropenia in patients with cancer treated with myelosuppressive chemotherapy. Risk models may be based on unconditional (pretreatment) or conditional (post-treatment) variables. For neutropenia, unconditional variables (pretreatment risk factors) are age, performance status, and extent of the cancer; conditional variables (post-treatment risk factors) are first-cycle absolute neutrophil count (FCANC) or a significant decrease in the neutrophil or platelet count from day one to day eight after chemotherapy (Wilson-Royalty, Lawless, Palmer, & Brown, 2001). Statistically significant predictors of febrile neutropenia and chemotherapy-induced neutropenia- (CIN-) related dose modifications, as identified in a review by Lyman, Lyman, and Agboola (2001), are listed in Table 2.

A good example of a well-designed predictive model for CIN complications is the model by Silber, Fridman, DiPaola, et al. (1998). This conditional model was developed from the findings of a study of 95 women treated with standard adjuvant chemotherapy regimens for breast cancer and subsequently was validated in a separate group of 80 women. The incidence of severe neutropenia and chemotherapy dose modifications (dose reductions $\geq$ 15% and treatment delay $\geq$ 7 days) were used as clinical end points. This risk model showed that a FCANC nadir of 500×10^6/L or less is a practical and effective indicator of a high-risk patient who should be given G-CSF preferentially in subsequent cycles. Silber, Fridman, Shpilsky, et al. (1998) went on to show that prophylactic G-CSF was cost-effective in preventing subsequent neutropenic events when its administration was limited to the 50% of patients with early-stage breast cancer who were at greatest risk for CIN as defined by first-cycle blood counts.

The Silber risk model then was used to identify patients at high risk for neutropenic complications for treatment with G-CSF (Rivera et al., 2001). Impact of this targeted use of G-CSF on neutropenic complications and delivery of planned chemotherapy doses on schedule were examined. Rivera et al. showed that patients at high risk for neutropenic complications could be identified effectively on the basis of their FCANC nadir. Furthermore, planned chemotherapy doses could be delivered on time to most patients by targeting prophylactic

Table 2. Independent Risk Factors for Febrile Neutropenia in Patients Treated With Chemotherapy

Tumor Type	Risk Factors
Early-stage breast cancer	Age $\geq$ 65 years (Lyman et al., 2001) Absolute neutrophil count nadir in cycle 1 < 500 x 10^6/L (Silber, Fridman, DiPaola, et al., 1998) Pretreatment white blood cell count < 2,000 x 10^6/L (Lyman et al., 2001)
Non-Hodgkin lymphoma	Age $\geq$ 65 years (Lyman et al., 2003) Poor performance status (Voog et al., 2000) Serum lactate dehydrogenase level > 1 x normal (Intragumtornchai et al., 2000) Bone marrow involvement of lymphoma (Intragumtornchai et al.) Serum albumin level $\leq$ 3.5 g/dl (Intragumtornchai et al.) Chemotherapy dose intensity > 80% of target (Lyman et al., 2003) Renal disease (Lyman et al., 2003) Cardiovascular disease (Lyman et al., 2003) Pretreatment hemoglobin < 12 g/dl (Lyman et al., 2003) No cerebrospinal fluid prophylaxis (Lyman et al., 2003)

G-CSF to the high-risk patients. In 95% of the patients treated prophylactically with G-CSF, healthcare providers could give more than 85% of relative dose intensity. These results show that prophylactic G-CSF support given in accordance with a risk model is feasible and enables the allocation of healthcare resources to patients most likely to benefit.

An important limitation of a conditional model such as this one, based on the results with the initial treatment, is that it does not determine which patients are at risk for neutropenic complications in the first cycle of chemotherapy. This is when the majority of febrile neutropenia episodes and infection-related deaths occur (Gomez et al., 1998; Lyman & Delgado, 2002; Meza, Baselga, Holmes, Liang, & Breddy, 2002). An unconditional model, based on pretreatment characteristics alone, should be developed and validated to ensure that hematopoietic support is provided to patients before the occurrence of any neutropenic complication.

In one study of patients with aggressive non-Hodgkin lymphoma who received chemotherapy, three pretreatment factors were identified as reliable predictors (≥ 50% probability) of life-threatening neutropenia and febrile neutropenia: elevated lactate dehydrogenase level (≥ 460 IU/L), low serum albumin level (≤ 3.5 g/dl), and bone marrow involvement with lymphoma (Intragumtornchai, Sutheesophon, Sutcharitchan, & Swasdikul, 2000). Patients with these risk factors may be candidates for G-CSF started in cycle 1.

Other studies have identified factors that may justify the prophylactic use of G-CSF in the first chemotherapy cycle. Patients older than 65 years are at higher risk for CIN and febrile neutropenia than younger patients. They tend to have longer hospitalizations for febrile neutropenia, resulting in higher costs (Caggiano, Stolshek, Delgado, & Carter, 2001). In older patients, the costs saved by preventing hospitalization are more likely to offset the costs of using G-CSF starting in cycle 1. Indeed, the National Comprehensive Cancer Network recommended routine first-cycle use of prophylactic G-CSF in patients older than 70 years who are treated with cyclophosphamide, hydroxydaunomycin, vincristine, and prednisone (CHOP) or CHOP-equivalent regimens (Balducci & Yates, 2000). In older adults, physiologic age (assessed by performance status) is a better predictor of treatment-related death than chronologic age (Gomez et al., 1998). Therefore, patients younger than 70 years who are physiologically older than their chronologic age also should be considered for prophylactic treatment. Conversely, patients older than 70 years who are physiologically younger may not need prophylactic treatment if no other risk factors are present.

Based on such evidence-based risk models, practice guidelines published by the American Society of Clinical Oncology list factors that may increase the risk of febrile neutropenia or infection. These include bone marrow compromise or comorbidity resulting from disease or prior therapy, a history of febrile episodes with previous chemotherapy, and conditions that potentially impair resistance to serious infection, such as decreased immune function, poor performance status, more advanced cancer, and open wounds or active tissue infection (Ozer et al., 2000).

Risk Models for Treatment

Predictive risk models can be used to aid selection of the most appropriate treatment for adverse events of cancer therapy such as febrile neutropenia. Infections in neutropenic patients can be life threatening (Rolston, 2000). Because the classic inflammatory response to infection in a neutropenic patient may be blunted or absent, patients with cancer and neutropenia who present with fever are presumed to have infection and traditionally were routinely given empiric IV broad-spectrum antibiotics in the hospital (Paesmans, 2000). More recently, healthcare providers have realized that some patients with febrile neutropenia are at a lower risk for infection than others and that intensive, hospital-based antibiotic therapy may not be necessary for every patient. By identifying patients at low risk for infection, healthcare providers could manage febrile episodes in such patients with more appropriate treatments, such as initial empiric oral antibiotics or an early shift from IV to oral antibiotics, and possibly in an outpatient setting. Criteria for identifying patients at low risk for infection are being established in randomized trials because a clear set of guidelines still is lacking (Paesmans).

Two randomized trials in hospitalized neutropenic patients found that in low-risk patients, oral empiric treatment was just as effective and safe as standard regimens of IV antibiotics, with the additional benefits of cost savings and improved quality of life (Freifeld et al., 1999; Kern et al., 1999). The definition of a low-risk patient differed in these two trials, but some eligibility criteria common to both included predicted duration of neutropenia of less than 10 days, absence of catheter-related infection, hemodynamic stability, and normal hepatic and renal function (Paesmans, 2000). Consistent definitions of risk factors (including burden of illness) would make interpreting the results of these and similar clinical trials more reliable.

Several other clinical trials have sought to objectively stratify the risk of complications in patients with chemotherapy-induced febrile neutropenia. Talcott, Finberg, Mayer, and Goldman (1988) and Talcott, Siegel, Finberg, and Goldman (1992) designed a prediction model that divided patients into four risk groups (see Figure 3). The authors observed that neutropenic patients with uncomplicated disease (outpatients when fever developed, absence of comorbidities, and controlled cancer) had the lowest risk of medical complications and death associated with febrile neutropenia. The three higher-risk groups included patients who were hospitalized when fever developed, patients with uncontrolled cancer, and patients with comorbidities. Another model that identified patients at low risk for the development of serious medical complications used data from an observational study conducted by the Multinational Association of Supportive Care in Cancer. This model calculates a risk index score based on points assigned to factors associated with a favorable outcome (see Table 3); scores of 21 or more indicate low risk (Klastersky et al., 2000; Paesmans, 2000). Factors associated with poorer outcomes (and lower scores) included dehydration, previous antifungal therapy, lesions from infection found on chest radiographs, and hypotension.

Researchers from the Memorial Sloan-Kettering Cancer Center in New York, NY, have developed a collection of prognostic tools to assist in decision making regarding treatment options for early-stage prostate cancer. These nomograms, charts that represent numerical relationships, predict outcomes based on a combination of disease factors, including stage of cancer, prostate-specific antigen (PSA) level, biopsy pathology, and use of hormone therapy. Actual values of these risk

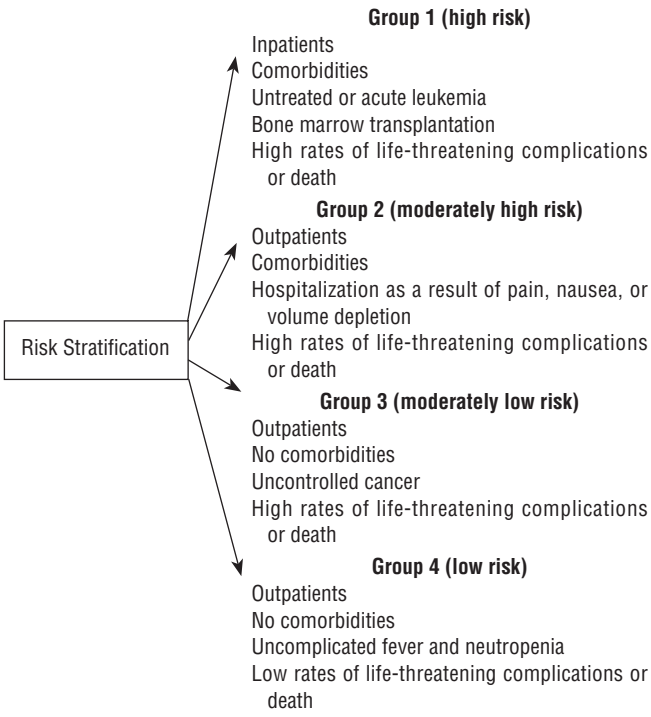

Figure 3. Risk-Stratification Model for Patients With Cancer and Febrile Neutropenia

Note. Based on information from Talcott et al., 1988, 1992.

factors are incorporated into nomograms as continuous values (e.g., exact PSA value) rather than grouped into categories (e.g., PSA 10–20 ng/ml), and similarly, nomograms predict continuous outcomes. This allows accurate, tailored predictions based on the clinical parameters of an individual patient rather than a risk group (Di Blasio, Rhee, Cho, Scardino, & Kattan, 2003).

Among the most important of the prostate cancer treatment nomograms are those that estimate the continuous risk of disease progression following definitive therapy for clinically localized disease with radical prostatectomy (Kattan, Eastham, Stapleton, Wheeler, & Scardino, 1998), external beam radiotherapy (Kattan et al., 2000), or brachytherapy (Kattan et al., 2001). By comparing nomograms, clinicians can find the treatment option with the most favorable probability of preventing disease progression. Another nomogram is available to predict the seven-year probability of disease progression after radical prostatectomy (Kattan, Wheeler, & Scardino, 1999). This information can be used to decide whether adjuvant therapy would be beneficial or to individualize a follow-up regimen. Nomograms should supplement, rather than replace, patient counseling, and many other factors, such the patient's life expectancy and potential side effects associated with available treatments, should be taken into account when deciding on the best treatment option (Di Blasio et al., 2003).

Recommendations for Practice

The use of risk models should help healthcare providers provide the best prevention and treatment options and cost-effective supportive care to patients. For patients who already have been diagnosed with cancer, nurses serve as important resources to educate them regarding risk factors. Nurses can help patients recently diagnosed with prostate cancer to understand the implications of the Memorial Sloan-Kettering Cancer Center prognostic nomograms for prostate cancer or to interpret such results. Similarly, nurses can use risk models to assist family members of a patient with a cancer diagnosis assess their individual risk for developing the same type of cancer (e.g., breast cancer) or an associated tumor (e.g., ovarian cancer). Risk models also can be used by nurses to help families with informed decision making as to whether interventions are desired.

In the area of symptom management and prevention, nurses are well positioned to use evidence-based risk models to help determine supportive patient care because they perform consistent and frequent clinical assessment. By implementing such risk models in their institutions, nurses can provide improved management of treatment-associated side effects and possibly enhance the clinical and quality-of-life outcomes of their patients. By familiarizing themselves with available evidence-based risk models, nurses may be able to decrease the risk and incidence of serious adverse effects, including febrile neutropenia.

In addition to the American Society of Clinical Oncology guidelines mentioned previously, many healthcare institutions have established guidelines to identify patients with cancer who are at risk for neutropenia (Maxwell, Winkler, & Lottenberg, 2002; Michelson et al., 2002; White & Keehne-Miron, 2002). Initial assessment of these patients often includes a thorough physical examination, a complete blood cell count, consideration of the type and intensity of the proposed therapy, and examination of trends and nadirs in the blood cell counts in previous chemotherapy courses if the patient has had prior treatment. Serum albumin and lactate dehydrogenase levels also may be monitored. Either primary or secondary prophylaxis with G-CSF is initiated in those patients who are identified as being at risk for neutropenic complications. The implementation of such guidelines shows promising results, with fewer chemotherapy dose

Table 3. Numeric Risk Score From the Multinational Association of Supportive Care in Cancer

Patient Features	Score
Burden of illness indicating	
Absent or mild symptoms	5
Moderate symptoms	3
Absence of hypotension	5
Absence of chronic obstructive pulmonary disease	4
Solid or hematologic tumor with no previous fungal infection	4
Outpatient status	3
Absence of dehydration	3
Age less than 60 years	2

Note. A score of 12 or higher indicates that the patient is at low risk of complications associated with chemotherapy-induced febrile neutropenia.

Note. From "The Multinational Association for Supportive Care in Cancer Risk Index: A Multinational Scoring System for Identifying Low-Risk Febrile Neutropenic Cancer Patients," by J. Klastersky, M. Paesmans, E.B. Rubenstein, M. Boyer, L. Elting, R. Feld, et al., 2000, *Journal of Clinical Oncology, 18,* p. 3046. Copyright 2000 by the American Society of Clinical Oncology (ASCO). Reprinted with permission from ASCO.

modifications and hospitalizations resulting from febrile neutropenia (Maxwell et al.).

The key to the success of guidelines in managing patients who are at risk for neutropenia is the nursing staff's responsibility and autonomy. Nurses should be able to interpret and explain these findings and their implications to patients. Determining a patient's prognosis and risk of complications before healthcare interventions are initiated can be useful for making treatment decisions. Nurses also are responsible for the education of patients and caregivers to familiarize them with the risk of infection and instruct them on monitoring for infection as well as the importance of prompt reporting. Such education also can help healthcare providers to prepare for postintervention care and assist the patient and family in making informed choices about prevention, treatment, and management options.

Recommendations for Future Research

Risk modeling changes over time as more information is gained about specific risk factors or more studies are published that reveal novel factors that must be added to current models. Differences in methodology, sample size, and characteristics of the study population all influence the effectiveness and applicability to specific clinical situations of any model (Domchek et al., 2003). Data derived from randomized, controlled clinical trials with adequate sample size are optimal for risk model development. They are, however, lacking in important cases, such as risk of first-cycle neutropenia (Gomez et al., 1998) or low risk of infection associated with febrile neutropenia (Paesmans, 2000). New models of other cancers, particularly those that currently are diagnosed most often at later stages (e.g., ovarian and pancreatic cancers), will require extensive research for their development. Nurses are in key positions to observe and report outcomes associated with specific clinical factors that are essential elements for the generation of accurate, effective risk models.

Summary

Ideally, evidence-based medicine integrates the best information available from research with the healthcare provider's clinical expertise and with the patient's preferences. The provider's clinical expertise often is most instrumental in determining the extent to which the evidence applies to the individual patient (e.g., for therapy-related adverse events such as neutropenia) and how this evidence should be integrated into clinical decisions. Risk assessment to identify patients who are most likely to benefit from specific interventions, such as prophylactic G-CSF, can lead to the cost-effective use of supportive care measures and improve clinical outcomes. Ultimately, healthcare providers rely on their professional judgment and experience to make clinical decisions. Because they interact with patients on a daily basis, nurses, in particular, are in an ideal position to support those decisions. By assessing risk factors and applying relevant risk models, they can better identify patients who would benefit from particular treatment choices or additional supportive care.

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