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Adoption of Innovation: Impact of Rituximab (Rituxan®) Faster Infusion on Oncology Nurses' Perceptions, Practice, and Resource Utilization

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Abstract

The translation of advances in clinical research into clinical practice in a manner that provides benefits while reducing potential harm is a challenge within the health care delivery system. Data from a phase III multicenter clinical trial led to the 2012 US Food and Drug Administration (FDA) approval of a 90-minute infusion of rituximab (Rituxan®) starting at Cycle 2 for patients with non-Hodgkin's lymphoma who did not experience a Grade 3 or 4 infusion-related adverse event during Cycle 1. The 90-minute rituximab faster infusion will result in a significant change in how nurses in the United States have been administering rituximab since initial FDA approval 15 years ago. This innovative change and its potential impact on patient care demonstrates the need for evidenced-based approaches that integrate the best current knowledge of rituximab administration with nursing clinical expertise to help ensure safe and effective resource utilization when delivering patient care. The aim of this Doctor of Nursing Practice project is to develop an evidenced-based tool kit to assist oncology nurses in adopting rituximab faster infusion while maintaining patient safety, achieving benefits in resource utilization, and promoting both patient and nursing satisfaction. A review of the literature was conducted to identify existing data and a tool kit was created to enable oncology nurses to conduct 30-day pilots to assess the real-world impact of rituximab faster infusion on nursing practice, patient safety, and resource utilization. An interdisciplinary panel of rituximab experts evaluated the clinical accuracy and overall usefulness of the tool kit and confirmed that components were clinically accurate and could inform the adoption of rituximab faster infusion by oncology nurses.

Keywords: rituximab, nursing, innovation, and faster infusion

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Section I: Clinically Relevant Issue

Issue Background and Relevance

Translating scientific innovations into clinical practice in a manner that provides benefits while reducing potential harm is a challenge within the health care delivery system. The nursing profession is on the front line of care delivery, and the task of medication administration is an activity predominately performed by nurses. To incorporate evidenced-based practices into clinical care and achieve a safer health system, leadership and resources are required.

The complexity involved with administering medications creates opportunities for errors and potential harm to patients (Wulff, Cummings, Marck, & Yurtseven, 2011). The Institute of Medicine (IOM) Quality Chasm Report *To Err is Human: Building a Safer Health System* (Kohn, Corrigan, & Donaldson, 2000) called national attention to the fact that up to 100,000 people die in hospitals each year as a result of preventable medical errors, including errors in administering treatment. While the IOM report specifies that achieving safer care must include three agendas (1) identifying what works (efficacy), 2) ensuring appropriate use, and 3) delivering it without errors), few patient safety practices examined in the report that healthcare leaders are working to implement received the "greatest strength of evidence." This disconnect may have been driven by the literature analysis methodology used in the IOM report that prioritized only data from randomized trials (Leape, Berwick, & Bates, 2002). However, the extended time required for new clinical research evidence to be incorporated into clinical practice is an obstacle. For oncology, although there have been many advances in the diagnosis and treatment of cancers, the dissemination and adoption of innovative evidenced-based findings into nursing practice by clinicians remains a challenge for ensuring quality cancer care (Ousley, Swarz, Milliken, & Ellis, 2010).

The US Food and Drug Administration (FDA) is the federal agency responsible for protecting the public health by assuring the safety and effectiveness of human drugs (United States Food and Drug Administration, 2012). In 1979 the FDA established the black-box warning system as the strongest labeling requirement for drugs and drug products that can cause serious adverse events, including death (Halloran & Barash, 2010). The warning provides information enclosed in a black box to highlight essential information regarding the proper prescription and monitoring of severe adverse events. A retrospective study conducted to estimate provider compliance with selected black-box warnings for medications used in the ambulatory care setting found that while 40% of patients received a drug including a black-box warning, provider compliance with following these warnings was variable (Wagner et al., 2006).

Adverse drug events (ADEs) are injuries that result from the use of a drug and account for over 770,000 people being injured or dying each year in hospitals, with resulting costs reaching $5.6 million each year per hospital (Agency for Healthcare Research and Quality, 2001; Hughes & Blegen, 2008). Some ADEs are caused by preventable errors, of which approximately 34% occur at the time of medication administration, an error-prone process stage that primarily involves nurses. A prospective observational study of 107 nurses preparing and administering intravenous medications in hospitals found that nearly 70% of intravenous administrations had at least one error, of which 25.5% were serious (Westbrook, Rob, Woods, & Parry, 2011). For administration errors involving infusion rates, nursing experience played a critical role; serious errors were lowest among nurses with the most clinical experience. These data suggest that targeting experienced nurses first is an optimal strategy for testing interventions to reduce error rates. However, *Patient Safety and Quality: An Evidence-Based Handbook for Nurses* published by the Agency for Healthcare Research and Quality (AHRQ) reviewed the research regarding

medication safety in relation to nursing care and concluded that, while adequate evidence exists regarding the reporting of medication error, there was a lack of evidence about interventions to prevent errors from occurring (Hughes & Blegen, 2008). The challenge is that the safe delivery of patient care requires nursing practices that are consistent with the best available evidence. When evidence is lacking, nursing scholarship must seek to fill the void.

One area where there is a lack of data being collected is in prospective oncology clinical trials, where the impact of medication administration on nursing practice has not been routinely measured (ClinicalTrials.gov, 2012). In such cases, retrospective data collected from nurses may provide useful insights to inform the development and implementation of practices that support safer patient care. These data would augment evidence from other sources, such as pharmaceutical sponsored clinical trials in which medication administration is a component being studied and research sponsored by AHRQ, whose mission is to improve the quality, appropriateness, and effectiveness of health care services (Kohn et al., 2000).

Because of the lack of data that are informative, as new innovations are developed that have an impact on medication administration nurses face a dilemma and must choose to either adopt these innovations without supporting, usable information or continue to use existing practices. The aim of this Doctor of Nursing Practice project is to develop an evidenced-based tool kit to assist oncology nurses in adopting rituximab faster infusion, which is an innovation for NHL patients, while maintaining patient safety, achieving benefits in resource utilization, and promoting both patient and nursing satisfaction.

Non-Hodgkin's Lymphoma (NHL)

The Surveillance, Epidemiology and End Results (SEER) Program of the National Cancer Institute estimates that 70,130 people in 2012 will be diagnosed with, and 18,940 people

will die of, non-Hodgkin's lymphoma (NHL) which are cancers of lymphocytes (white blood cells). Approximately 484,000 men and women in the United States are living with NHL, making this the seventh most common cancer in the United States (National Cancer Institute, 2012a). The World Health Organization (WHO) classification divides NHL into types that are either B-cell origin, T-cell origin, or natural killer (NK)-cell origin (World Health Organization, 2012). Approximately 85 percent of NHL cases are cancerous B-cell origin and include diffuse large B-cell lymphoma (DLBCL), an aggressive (fast-growing) subtype, and follicular lymphoma (FL), an indolent (slow-growing) sub-type (National Cancer Institute, 2012b; The Leukemia & Lymphoma Society, 2012). The incidence of DLBCL and FL are 31% and 22%, respectively, making these the most common NHL subtypes (Rummel, 2010).

Although no standard therapy exists for the initial treatment of indolent FL, data from a large longitudinal, observational study reported that 65% of FL patients in the United States from 2004-2007 received a rituximab based initial treatment strategy (Friedberg et al., 2009). Rituximab (Rituxan\) is a CD20-directed cytolytic antibody that was the first targeted cancer medication approved by the FDA, receiving initial US FDA approval in 1997. Rituximab is an infused medication and indicated for the treatment of patients with B-cell NHL, including DLBCL and FL, as well as other indications (Genentech, 2012). Given that infusion reactions can occur with almost all systemic agents used in cancer treatment (Zetka, 2012), infusion reactions associated with the most widely used initial treatment strategy for FL patients would be of interest to clinicians, and specifically to oncology nurses who administer agents like rituximab.

Rituximab Infusion Related Reactions

The safe administration of medications is an essential element of nursing practice and is a

core competency to ensure patient safety. The American Society of Clinical Oncology (ASCO) and the Oncology Nursing Society (ONS) have created chemotherapy safety administration standards that have been recently revised to add safety measures aimed at reducing timing errors that can result in patients not receiving the intended amount of chemotherapy (Jacobson et al., 2012). This builds upon previous standards for chemotherapy preparation and administration requiring independent verification by a second person of chemotherapy orders, including drug dose, volume, and rate of administration.

An infusion-related reaction (IRR) is defined as a disorder characterized by adverse reaction to the infusion of pharmacological or biological substances (Vogel, 2010). Reactions can range from Grade 1-2 mild transient reactions, when an intervention is either not indicated or intervention responds promptly to symptomatic treatment (e.g., antihistamines, NSAIDS), to Grade 3-4 reactions, requiring hospitalization for prolonged clinical sequelae and which can be life-threatening (United States Department of Health and Human Services, 2010). Monoclonal antibodies like rituximab can induce B-cell lysis predisposing patients to higher cytokine release associated with tumor destruction (Vogel, 2010). Additionally, patients with higher numbers of circulating malignant cells may have an increased risk for infusion reactions due to higher cytokine release.

Infusion related reactions are among the most common adverse reactions associated with rituximab and have an incidence rate ≥25%. Infusion related reactions also are included in rituximab's label as a black box warning. The warning states that:

- Fatal infusion reactions within 24 hours of rituximab infusion may occur
- Approximately 80% of fatal reactions occur with first infusion
- Monitor patients and discontinue rituximab infusion for severe reactions (Genentech,

2012).

Until October 2012, the Rituximab (Rituxan®) United States Package Insert (USPI) recommended 4−6 hour infusion rates for the first infusion and 3−4 hours for each subsequent infusion (Genentech, 2012; Sehn et al., 2007). These administration times make rituximab a time intensive medication to administer, requiring nursing time and chair space resources. Recent data from pilot studies and a large clinical trial (U4391g, aka the RATE study) supported wider implementation of rituximab with a faster infusion rate (Dakhil et al., 2011). In October 2012, the US FDA approved a 90-minute infusion for subsequent infusions administered in Cycle 2 through Cycle 6 or 8 with a glucocorticoid-containing chemotherapy regimen for previously untreated FL and DLBCL patients who did not experience a Grade 3 or 4 infusion related adverse event during Cycle 1, and who tolerated the 90-minute infusion in Cycle 2. Patients who have clinically significant cardiovascular disease or who have a circulating lymphocyte count $\geq 5000/mm^3$ before Cycle 2 should not be administered the 90-minute infusion. Currently there is no literature describing the penetration of faster infusion usage in the United States, although there is evidence that the current adoption rate is approximately 25% and that some institutions are waiting on more data prior to implementation of this innovative method of administration (Montez, 2012; Palkhivala, 2007).

Wider implementation of rituximab faster infusion in a non-research patient population should increase given the recent FDA-approved faster infusion administration guidelines. Studies of the non-initial administration of rituximab at a faster rate have not demonstrated an increased risk for Grade 3 or 4 infusion-related reactions (Chiang et al., 2010; Corey, Go, & Schaper, 2007; Coulter, 2010; Genentech, 2012; Sehn et al., 2007; Swan, Murillo, Cox, Lamoth, & Baker, 2010). Additionally, data from the RATE trial provides the best available evidence to

support this change in how rituximab is administered. The RATE study excluded patients with a circulating lymphocyte count >5,000/μL due to their increased risk of experiencing an IRR. Patients with clinically significant cardiovascular disease, congestive heart failure, ventricular arrhythmia requiring medication, or peripheral vascular disease were also excluded from the RATE study (Dakhil et al., 2011). These exclusions are also included in the October 2012 USPI regarding 90-minute rituximab administration. Clinicians will need to closely assess these excluded patients to ensure that rituximab is safely administered via a faster infusion only to appropriate patients.

Time and labor resources required to administer rituximab according to the current USPI recommended 90-minute infusion rates may decrease. These time and resource savings may also result in increases in both patient and nursing satisfaction. This innovative change in drug administration and the resulting potential positive impacts on patient care demonstrate the need for evidenced-based approaches that integrate the best current knowledge of rituximab administration with nursing clinical expertise to help ensure safe and effective resource utilization when delivering patient care.

Innovation and Nursing Practice

Innovation is *"an idea, practice, or object that is perceived as new by an individual or other unit of adoption."* Two characteristics that determine the rate of adopting an innovation include 1) relative advantage, the degree to which an innovation is perceived as better than the idea it supersedes, and 2) compatibility, the degree to which an innovation is perceived as consistent with the existing values, past experiences, and needs of potential adopters (Rogers, 2003). The American Nurses Association (ANA) Standards of Professional Practice include 1) integrating current evidence findings into practice (i.e., ideas that can be perceived as "new") and

2) utilizing appropriate resources to provide nursing services that are safe, effective, and financially responsible (i.e., consistent with "existing values") (American Nurses Association, 2010).

The development, evaluation, and dissemination of patient-centered, evidence-based interventions that contribute to quality cancer care are central to the practice of oncology nursing and are goals included in the Oncology Nursing Society's 2012–2016 Strategic Plan (Oncology Nursing Society, 2011). A primary focus of the Doctor of Nursing Practice program is on the translation of new science, its application and evaluation, with the goal of nurses delivering the highest quality health care (American Association of Colleges of Nursing, 2006). Oncology nurses face a choice to either adopt the new rituximab administration guidelines or to maintain current practices. In order to adopt this innovation nurses must first assess the impact that this change may have on both nursing practice and patient care. Given the potential growth of rituximab faster infusion with the recent US FDA approval of the 90-minute infusion rate, this is an important topic for nursing to explore using clinical scholarship.

The translation of scientific advances in clinical research that result in new medications and methods of medication administration (such as new rituximab infusion guidelines) into real-world clinical practice is a continuing challenge, resulting in gaps in the adoption of new medical knowledge. Although factors that influence adoption, such as clinicians' information needs, ability to assess information, and make changes to their practices have been studied (Carlson, 2008), no studies investigating the innovativeness of nurses and the adoption of evidence-based practices generated from pharmaceutical company sponsored clinical trials were found in the literature.

Results from a survey administered to over 2,800 health care practitioners, including oncology nurses and physicians, found that although more than 85% of oncology nurses reported having adequate access to the research they need to keep their practice current, only 34% reported having adequate time to study and utilize the research. Moreover, 45% of oncology nurses reported that research findings are often reported in a manner that makes the findings difficult to implement at the bedside or in the office. Designing effective interventions that are tailored to the target practitioner audience is proposed as a strategy to assist with the dissemination and implementation of new research findings (Ousley et al., 2010).

Although the findings from the RATE trial and subsequent US FDA approval support wider implementation of rituximab faster infusion for patients with previously untreated NHL, it is critical to identify the prior conditions that influence nurses' decisions to adopt evidenced-based practices in order to facilitate the implementation of practices by nurses that would both enhance patient safety and reduce resource utilization. As leaders, nurses need to collaborate with other members of the heath care team, including the pharmaceutical industry, when assessing how to best implement innovative practices. Given oncology nurses' key role in medication administration, there is an opportunity for nursing to generate evidence where gaps exist in the literature regarding the adoption of best clinical strategies to deliver medications and to improve the quality of patient care (Institute of Medicine (IOM), 2010).

To address this gap between research and its use, the psychometric properties of a set of four instruments were developed and tested to measure conditions influencing nurses' decisions to adopt evidenced-based pain management practices, including an *Innovativeness Instrument*. The *Innovativeness Instrument* included six items measuring the factors of leadership and reliance on others, with Cronbach alpha's of 0.743 and 0.650, respectively, for these two factors,

and 0.731 for the total instrument. The *Innovativeness Instrument* is suggested as a valid method to identify early adopters of innovation. Early adopters are opinion leaders who evaluate innovations and encourage implementation of the innovation into local nursing practice (Carlson, 2008; Rogers, 2003).

Pharmaceutical research is a key source of new data providing evidence that may promote a change in clinical practice. According to the Pharmaceutical Research and Manufacturers of America (PhRMA), the lobbying organization that represents leading US pharmaceutical research and biotechnology companies, PhRMA member companies have invested an estimated $49.5 billion in 2011 in discovering and developing more than 300 new medicines approved by the US FDA in the last 10 years, making the US biopharmaceutical research sector a global leader in medical innovation (Pharmaceutical Research and Manufacturers of America, 2012). However, for all but one of the active NHL clinical trials recently searched, objectives specific to nursing practice are not included in the clinical trial design. In September 2012, a search of ClinicalTrials.gov, a registry and results database of federally and privately supported clinical trials conducted in the United States and around the world, found 352 open interventional NHL studies recruiting patients in the US. Of these, the trial entitled *"Assessment of Hypersensitivity Reactions and Feasibility of a 60 Minute Rapid Infusion Rituximab Protocol in Patients with B-Cell NHL and Chronic Lymphocytic Leukemia (CLL) at a Comprehensive Cancer Center"* was the only study that included an objective that was specific to nursing practice (ClinicalTrials.gov Identifier: NCT01206777). This study is ongoing and is evaluating both the time savings of a *60*-minute infusion versus standard infusion and the degree of nursing satisfaction as measured with a before and after infusion survey (ClinicalTrials.gov, 2012).

Theoretical Framework

The Iowa Model of Evidence-Based Practice to Promote Quality Care (Titler et al., 2001) was selected as the conceptual model to adopt rituximab faster infusion into nursing practice. Using the Iowa Model, adopting new medication administration practices is a knowledge focused trigger related to new findings from both the RATE trial and a review of literature supporting the administration of rituximab faster infusion for the treatment of appropriate patients with NHL starting at Cycle 2, Day 1. This trigger would be a priority for any practice setting administering rituximab since it has implications for safe medication administration (nursing practice), nursing/patient satisfaction, and resource utilization. Even with US FDA approval of a new 90-minute faster infusion rate, nurses may question if the faster infusion is safe, given a long history of administering rituximab at a standard infusion rate.

If adopting rituximab faster infusion is a priority for a practice setting, a team that includes infusion nurses, clinical trial nurses (if applicable), clinical nurse specialists, and unit managers/educators should be formed, along with clinical pharmacists and prescribing physicians, to critique and synthesize existing research for use within practice settings. The available literature regarding rituximab faster infusion supports piloting the change in practice settings where there is little to no experience with this alternative method of rituximab administration. After completion of a practice-setting, pilot with outcomes supporting safety, resource utilization, and nurse/patient satisfaction benefits, rituximab faster infusion can be implemented within practices as long as outcomes are monitored for continued quality improvement.

Innovation is an idea, practice, or object that is perceived as new by the adopters. Diffusion is the process in which an innovation is communicated through certain channels over

time among members of a social system. Roger's *Diffusion of Innovations* model was selected as the strategy to facilitate the successful adoption of rituximab faster infusion. Attributes of innovations impact their rates of adoption by the social system. Perceived attributes of innovation, including relative advantage and complexity, can determine the rate of an innovation's adoption (Rogers, 2003). For this project, rituximab faster infusion is the innovation perceived as new to oncology nurses.

Definition of Key Terms

The following are key terms used in this project:

- **Adverse Drug Reaction (ADR):** A significant ADR is any unexpected, unintended, undesired, or excessive response to a drug that 1) requires discontinuing the drug (therapeutic or diagnostic), 2) requires changing the drug therapy, 3) requires modifying the dose (except for minor dosage adjustments), 4) necessitates admission to a hospital, 5) prolongs stay in a health care facility, 6) necessitates supportive treatment, 7) significantly complicates diagnosis, 8) negatively affects prognosis, or 9) results in temporary or permanent harm, disability, or death (American Society of Health-System Pharmacists, 1995).
- **Black Box Warning:** US Food and Drug Administration's strongest labeling requirements for high-risk medicines. Rituximab (Rituxan®) includes a Black Box Warning for Infusion Reactions (Wagner et al., 2006).
- **Innovation:** An idea, practice, or object that is perceived as new by an individual or other unit of adoption (Rogers, 2003).

- **Infusion-related reaction (IRR):** A disorder characterized by adverse reaction to the infusion of pharmacological or biological substances (United States Department of Health and Human Services, 2010).
- **Medication Errors:** Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including: prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use (National Coordinating Council for Medication Error, 2012).
- **Rituximab Faster Infusion:** Non-initial rituximab administration that is planned for a 90-minute duration (Genentech, 2012).
- **Rituximab Standard Infusion:** Initial and subsequent rituximab administrations according at an infusion rate > 90 minutes as follows:
    - DO NOT ADMINISTER AS AN INTRAVENOUS PUSH OR BOLUS
    - Pre-medicate before each infusion and administer only as an intravenous (IV) infusion
    - **First Infusion:** Initiate infusion at a rate of 50 mg/hr. In the absence of infusion toxicity, increase infusion rate by 50 mg/hr increments every 30 minutes, to a maximum of 400 mg/hr.
    - **Subsequent Infusions:** Initiate infusion at a rate of 100 mg/hr. In the absence of infusion toxicity, increase rate by 100 mg/hr increments at 30-minute intervals, to a maximum of 400 mg/hr.

    - Interrupt the infusion or slow the infusion rate for infusion reactions.
    - Continue the infusion at one-half the previous rate upon improvement of symptoms.

- **United States Package Insert (USPI):** Prescribing information, also called product information, product labeling, or the package insert ("the PI"). Content is generally drafted by the drug manufacturer and approved by the US FDA. It includes the details and directions healthcare providers need to prescribe the drug properly.

Assumptions and Limitations

Assumptions include that only registered nurses completed the survey and that the sample is representative of oncology nurses who typically administer chemotherapy infusions. However, the survey used a convenience sample of oncology nurses based on available email lists, which may have added bias to survey responses. Therefore, survey results should be interpreted with caution. Limitations of this project include that data were collected retrospectively and those nurses who participated in the RATE trial were surveyed approximately 4 years after the RATE protocol was initially finalized. Patient satisfaction and quality of life assessments were not within the scope of the survey. The survey was completed by convenience sample of 25 survey responders and data were not stratified by RATE study participation versus clinical practice adoption of rituximab faster infusion. Data findings may vary with a larger responding sample.

Project Goals and Expected Outcomes

The PICO evidenced-based decision-making process was used to define the patient population, intervention, comparison group, and expected project outcomes. The PICO evidenced-based decision-making process for rituximab faster infusion is the following:

- **P**: Patient Population: Patients age ≥ 18 years previously untreated NHL who are scheduled to receive treatment with rituximab.
- **I**: Intervention: Starting at Cycle 2, administer rituximab 90-minute infusion to NHL patients who did not experience a Grade 3 or 4 IRR during Cycle 1. Patients with clinically significant cardiovascular disease and high circulating lymphocyte counts ≥ 5000/mcL are not recommended to receive the faster infusion.
- **C**: Comparison: Starting at Cycle 2, administer rituximab infusion at a rate of 100 mg/hr. In the absence of infusion toxicity, increase rate by 100 mg/hr increments at 30-minute intervals, to a maximum of 400 mg/hr.
- **O**: Outcomes: Safety, Resource Utilization, and Nursing Practice Impact.
    - **Safety:** Incidence at clinical site/institution of Grade 3 or 4 IRRs at Cycle 2 and beyond.
    - **Resource Utilization**:
        a) Infusion chair turnover: # chemotherapy infusions, including rituximab infusions, per chair within 30-day period (pre and post pilot).
    - **Nursing Practice Impact**: As measured by positive "Overall Impression" scores ≥ 90%. Nurse survey responses Questions 27-30. Question 27 (impression), Question 28 (recommend to patients), Question 29 (safety), Question 30 (patient preferences).

The goal of this project is to develop an evidenced-based tool kit to support oncology nurses' adoption of rituximab faster infusion. By developing this tool kit, the expected outcomes are that rituximab faster infusion will be adopted so that patient safety is maintained while achieving both resource utilization and patient and nursing satisfaction benefits.

Section II: Review of the Evidence

A review of literature accessing the MEDLINE and CINAHL Plus databases with the keywords rituximab, infusion reactions, nursing, evidence, and rapid/faster infusion was undertaken seeking to answer the following question:

What evidence exists regarding the safety of administrating rituximab faster infusion and the impacts of this innovation on nursing practice and resource utilization?

Data Synthesis

Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 (United States Department of Health and Human Services, 2010) defines infusion-related reactions as "a disorder characterized by adverse reaction to the infusion of pharmacological or biological substances" (see Table 1). The incidence of rituximab infusion-related toxicity is highest with the first infusion (77%) and decreases with subsequent infusions (30% with the fourth infusion, 14% with the eighth infusion). For fatal reactions, approximately 80% occur with the first infusion, with typical onset between 30 and 120 minutes. Rituximab-induced infusion reactions and sequelae include urticaria, hypotension, angioedema, hypoxia, bronchospasm, pulmonary infiltrates, acute respiratory distress syndrome, myocardial infarction, ventricular fibrillation, cardiogenic shock, anaphylactoid events, or death (Genentech, 2012).

Table 1

Common Terminology Criteria for Adverse Events (CTCAE): Infusion Related Reactions

General disorders and administration site conditions					
	Grade				
Adverse Event	**1**	**2**	**3**	**4**	**5**
Infusion related reaction	Mild transient reaction; infusion interruption not indicated; intervention not indicated	Therapy or infusion interruption indicated but responds promptly to symptomatic treatment (e.g., antihistamines, NSAIDS, narcotics, IV fluids); prophylactic medications indicated for <=24 hrs	Prolonged (e.g., not rapidly responsive to symptomatic medication and/or brief interruption of infusion); recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by adverse reaction to the infusion of pharmacological or biological substances (United States Department of Health and Human Services, 2010).					

Although rituximab is generally well tolerated, there are patients who have allergic/anaphylactic reactions and patients who experience infusion reactions believed to be due to cell destruction and the release of cytokines (Breslin, 2007). Either IgE or non-IgE-dependent mechanisms have been suggested as possible etiologies for infusion reactions to monoclonal antibody therapy. Additionally, administration of a monoclonal antibody like rituximab, which can induce B-cell lysis, predisposes patients to have higher cytokine release associated with tumor destruction. Patients with a higher number of circulating malignant cells may have an increased risk for infusion reactions associated with higher cytokine release as well. Patients experiencing allergic/anaphylactic reactions should never be re-challenged. However,

patients who have a cytokine release reaction, rather than a true allergic type 1 hypersensitivity reaction, may be re-challenged with rituximab after accurate assessment and documentation of the infusion reaction (Chung, 2008). Strategies to address potential infusion reactions—such as fractionated dosing of rituximab (i.e., split first dose over two days) and hospitalization—have been used for patients at high risk for cytokine release (Vogel, 2010). In addition, premedication with antihistimines, acetaminophen, and/or corticosteroids are common practices to prevent infusion reactions related to monoclonal antibody therapy (Chung, 2008; Genentech, 2012). Supportive care (i.e., glucocorticoids, epinephrine, bronchodilators, oxygen) is also instituted as needed for infusion reactions. Additional intervention includes slowing the infusion rate, interrupting the infusion, or permanently discontinuing rituximab, depending on the severity of the infusion reaction (Genentech, 2012).

To minimize the potential for infusion-related toxicity, the USPI recommends that, in addition to premedication with an antihistamine and acetaminophen, initiating the first infusion at a rate of 50 mg/hr and, in the absence of infusion toxicity, increasing the infusion rate in 50 mg/hr increments every 30 minutes to a maximum of 400 mg/hr. Subsequent infusions should start at a rate of 100 mg/hr and, in the absence of infusion toxicity, be increased by 100 mg/hr increments every 30 minutes to a maximum of 400 mg/hr. In the event of an infusion reaction, the infusion should be interrupted or slowed and then continued at one half the previous rate upon improvement of symptoms (Genentech, 2012).

For patients with NHL, the majority of infusion-related adverse events typically occurred within 30–120 minutes of beginning the first infusion. As noted previously, slowing or interrupting the rituximab infusion and administering supportive care were effective interventions in resolving the infusion reactions. After symptoms have resolved, the infusion

may be resumed at a minimum 50% reduction in the infusion rate. Patients with pre-existing cardiac or pulmonary conditions, those with prior cardiopulmonary adverse reactions, and those with high numbers of circulating malignant cells ($\geq$25,000/mm^3) should be closely monitored (Genentech, 2012). Even with pre-treatment, patients can have severe infusion related reactions. In a retrospective chart review of 19 community oncology practices, severe infusion reactions for 47 patients treated with rituximab (64% diagnosed with NHL) were identified. Approximately 75% received pre-treatment, with acetaminophen, antihistamine, and corticosteroids being the most common medications given, at 61%, 55%, and 21%, respectively. The majority of severe infusion reactions occurred during the first cycle of therapy. Post-infusion reaction management typically included corticosteroids, oxygen, and intravenous fluids. The incidence of hospitalization after infusion reactions was 5% for Grade 3 infusion reactions and 83% for Grade 4, with a mean of two days in the hospital for Grade 3 and five days for Grade 4 reactions (Schwartzberg, Stepanski, Fortner, & Houts, 2008).

Given rituximab's long infusion duration and data indicating that approximately 80% of fatal infusion reactions occur with the first infusion, several pilot studies have investigated the feasibility and safety of 90-minute rituximab infusion administration times after the first infusion (Chiang et al., 2010; Corey et al., 2007; Coulter, 2010; Sehn et al., 2007; Swan et al., 2010; Zahrani, Ibrahim, & Eid, 2009). The protocols required that 1) patients received their first rituximab infusion according to the USPI, 2) premedication with at least acetaminophen and diphenhydramine prior to the subsequent faster infusion, and 3) the inclusion of a steroid if the chemotherapy regimen required a corticosteroid. For subsequent infusions, rituximab was infused using fixed-volume of 250 mL of normal saline preparation with a maximum

concentration of 4 mg/mL, with a rate titrated to deliver 50 mL (20%) over 30 minutes followed by 200 mL (80%) over 60 minutes (Sehn et al., 2007).

The first report of rituximab faster infusion in the nursing literature was at the 32nd Annual Oncology Nursing Society Congress in 2007 (Corey et al., 2007). The lead author reported treating 46 patients with 135 infusions (mean 3 infusions) with no Grade 3 or 4 infusion-related reactions and, based on these findings, concluded that the 90-minute infusion was safe in the treatment of NHL and well tolerated for patients studied in the community setting. However, the need for additional studies was recognized prior to implementing the 90-minute faster infusion as standard practice at US sites (Palkhivala, 2007).

A prospective study of 79 patients was conducted at an ambulatory cancer center in Singapore with CD20-positive NHL to assess whether the non-initial rituximab dose can safely be administered as a faster 90-minute infusion and to study the impact of a faster 90-minute infusion on resource utilization. Nurses were given detailed administration instructions, patients were pre-medicated with diphenhydramine and paracetamol (acetaminophen), and, if oral corticosteroids were part of the patient's chemotherapy regimen, the day-1 dose of corticosteroids were only administered after the rituximab infusion was complete, in order to avoid masking any potential infusion-related reactions. The study found that rituximab faster infusion was well tolerated with no Grade 3 or 4 infusion-related adverse events (Chiang et al., 2010).

A prospective study of 13 patients at outpatient and inpatient oncology units with CD20-positive B-Cell malignancy, with or without steroid-containing chemotherapy, was conducted to assess if the non-initial rituximab dose can safely be administered at a faster 90-minute infusion rate. All patients received acetaminophen and diphenhydramine premedication; no symptomatic

infusion reactions were observed in 12 patients, while one patient experienced a Grade 3 infusion reaction (nausea, vomiting, syncope) on the second faster-rituximab infusion. A retrospective chart review of 100 patients was also conducted for patients receiving rituximab according to the USPI recommendations. This review found that infusion reactions were experienced by 34% of patients, and that there was an increased risk of infusion reactions for inpatients versus outpatients (23.1% vs. 12.5%; $P < 0.03$) (Swan et al., 2010).

An examination of the safety of rituximab faster infusion for 150 NHL patients with a corticosteroid-containing chemotherapy regimen who received 473 rituximab faster infusions and 56 NHL patients receiving 92 rituximab faster infusions as maintenance therapy found no Grade 3 or 4 infusion-related reactions. In addition, more than 1,200 patients in Canada have received rituximab faster infusion with only one Grade 3 infusion reaction reported. These findings led to the adoption of the 90-minute faster infusion schedule throughout the province of British Columbia (Sehn et al., 2007).

In addition, a systematic review of the literature has been conducted to examine evidence-based data related to the safety of rituximab faster infusion in adult NHL and CLL patients. Data from experimental and non-experimental studies were critically appraised by two independent reviewers for methodological validity (Lang, Hagger, & Pearson, 2011). A meta-analysis of nine studies that included 559 NHL patients who completed 1,799 cycles of a rituximab 90-minute infusion found 2.6% (n=12) acute adverse reactions. Of those reactions, using CTCAE criteria, seven were Grade 1, five were Grade 2, and no Grade 3 or 4 acute adverse reactions were reported. While the Lang et al. systematic review supports a finding of faster rituximab infusion over 90 minutes as a safe practice for NHL patients, it calls for more research and detailed

analysis to develop more specific guidelines, including dosage for antipyretics (i.e., acetaminophen, antihistamine, and corticosteroids).

The RATE trial enrolled approximately 451 patients at 100 centers in the United States. The primary objective of this study was to determine the incidence of Grade 3 or 4 infusion-related reactions resulting from faster infusion of rituximab in patients who have previously received rituximab at the standard infusion rate without experiencing a Grade 3 or 4 infusion-related adverse event (Clinicaltrials.gov, 2011). Patients received the faster infusion (rituximab administered over 90 minutes) in Cycle 2 and, if tolerated, in all subsequent cycles. A total of 363 patients who had not experienced a Grade 3 or 4 IRR while receiving rituximab in combination with chemotherapy during Cycle 1 were evaluated. The incidence of Grade 3 or 4 IRRs was 1.1% at cycle 2 and 2.8% during cycles 2–8, with no fatal IRRs or fatal AEs on days 1–2 at any cycle in this study (Dakhil et al., 2011). Results from this study confirmed that the 90-minute infusion schedule for rituximab is both safe and feasible in NHL patients.

Data from the RATE trial led to the October 19, 2012 US FDA approval of a 90-minute infusion for rituximab starting at Cycle 2 for patients with NHL who did not experience a Grade 3 or 4 infusion-related adverse reaction during Cycle 1. Patients with clinically significant cardiovascular disease and high circulating lymphocyte count greater than or equal to 5000/mcL are not recommended to receive the faster infusion. The RATE trial results are comparable to the results of IRRs during Cycle 2 reported from trials using the standard infusion regimen (Genentech, 2012).

However, FDA approval does not in itself guarantee safe adoption of the new faster infusion rate in real-world clinical practice. Identifying evidenced-based practices to improve patient care and increasing efficiency while managing costs are major issues facing the US health

care system (B. Fortner & Viale, 2009; United States Department of Health and Human Services, 2011). For oncology, this challenge is particularly illustrated by the need to assess new data regarding the feasibility and safety of non-standard methods of immunochemotherapy administration that could impact patient outcomes and resource utilization.

The nursing profession has a critical role in the delivery of quality care for patients. Nurses are seen as partners, educators, advocates, and leaders in cancer prevention, treatment, and symptom management. Developing, evaluating, and disseminating patient-centered, evidence-based interventions that contribute to quality cancer care are central to the practice of oncology nursing and are goals included in the Oncology Nursing Society's 2012–2016 Strategic Plan (Oncology Nursing Society, 2011).

Potential benefits of a faster infusion schedule include the following: reduced infusion times that may in turn provide patients with more scheduling flexibility; improved scheduling efficiency for infusion center chair time; and more nursing time available for other activities (Corey et al., 2007; Swan et al., 2010). A retrospective chart review of 100 patients found that longer infusion time results in longer clinical visits and lengthier utilization of nursing resources. Faster infusion rituximab was 1.7 hours shorter than standard infusion time for the non-initial infusion. Patients were surveyed after their first faster infusion and indicated a preference due to the shortened clinic visits. Although the authors state that nursing staff also preferred the faster-rituximab infusion approach, no survey data were reported in the discussion. The authors caution that adoption of a faster administration protocol "will succeed only if supported by the nursing staff," and that strong nursing leadership and educational in-services highlighting faster rituximab infusion trial safety data contributed to the "support and comfort" required by nursing staff to administer this protocol. The nursing staff was credited with achieving the goal of

decreasing patient time in the infusion clinic through such means as ensuring that premedication was given and that the faster infusion was started in a timely manner (Swan et al., 2010).

Chiang and colleagues (Chiang et al., 2010) reported a "substantial" reduction in resource utilization as measured by reduced facility charges to patients and by savings from faster infusion chair times compared to chair times needed to administer rituximab according to manufacturer recommendations. Implications for nursing include the need to educate patients about relevant rituximab infusion-related reactions so that patients may report these reactions to clinical staff during infusions and possibly prevent a more severe reaction. Given the findings related to patients experiencing post-infusion nausea and vomiting, nursing researchers may want to consider studying the incidence of this adverse event in the context of faster-infusion rituximab and assessing prevention interventions.

As has been noted, evidenced-based recommendations for a 90-minute rituximab faster infusion in the non-initial administration for NHL patients have implications for nursing practice. The briefer administration of a 90-minute infusion, the documented safety profile, and improved resource utilization due to a 50% reduction in nursing workload were reported as advantages of faster infusion. For patients the faster infusion led to less time in clinic and improved patient satisfaction (Sehn et al., 2007). Owing to the shorter duration, the amount of nursing time required for infusion-related monitoring of symptoms and vital signs was reduced (Lang et al., 2011).

With regard to monitoring, few publications report on either the type or frequency of monitoring for adverse events that may occur during infusions. In the community setting, one study found that among 16 patients treated with 51 faster infusions there were no reported Grade 3 or 4 infusion reactions (Coulter, 2010). Patient monitoring included blood pressure, heart, and

respiratory rates before the infusion and at 15, 30, 60, and 90 minutes. Temperature was monitored prior to the infusion, and patients were questioned about adverse reactions throughout the infusion and during each visit. Total infusion time saved (compared to standard rituximab infusions) was 57 minutes per infusion, with both high nursing and patient satisfaction surveys scores reported. One outlier was that nurses had concerns that the intense monitoring schedule used in this study took up the equivalent amount of nursing resources as a standard rituximab infusion. More research is needed focusing on the experiences and perceptions of nurses implementing an evidenced-based monitoring schedule for patients receiving faster infusion rituximab.

The management of infusion-related reactions is a major challenge for nurses when caring for patients receiving monoclonal antibodies. Although monoclonal antibodies used in oncology care are generally well tolerated, a major complication with monoclonal antibodies is the development of mild to life threatening infusion reactions (Carney & Ollom, 2008). In a retrospective study conducted in collaboration with primary care providers, nurses were able to minimize infusion reactions by evaluating quality assurance performance metrics for infusion reactions. The goal of the study was to decrease the number of infusion reactions patients experienced by developing re-challenge programs for patients receiving paclitaxel and carboplatin regimens in the outpatient setting (Huddleston et al., 2005). Tracking quality metrics may be a useful strategy to apply in assessing infusion reaction rates in NHL patients.

Although nurses are recognized as being integral to the management of hypersensitivity reactions, there are limited data regarding the tasks and associated costs that infusion reactions require of patients, caregivers, and providers. A review of the literature examining the specific burden that infusion reactions associated with monoclonal antibodies have on these groups found

that, overall, tasks required to manage infusion reactions fell into categories that align with CTCAE grading criteria (see Table 2). Standing orders or protocols and staff education related to infusion reactions were identified as two strategies to assist nursing staff in managing reactions (B. Fortner & Viale, 2009).

Table 2

IRR Grade, Human Resource Tasks, Time & Costs

Infusion Related Reaction (IRR) Grade	**CTCAE version 4.03 Definition [9]**	**Human Resource Tasks, Time (Minutes) and Increased Costs Required to Manage Patients Experiencing IRRs (B. Fortner & Viale, 2009)**	**Rituximab (N=90) Mean±SD Human Resource Time (Minutes) and Costs Accrued for IRR (Schwartzberg et al., 2009)**
Grade 1 IRR	Mild transient reaction; infusion interruption not indicated; intervention not indicated	Mild IRR not requiring discontinuation Tasks: 13, Time: 72 Costs (USD): $51	N=30 Time: 262.3 ± 64.4 Costs (USD): $79.4 ± 31.0
Grade 2 IRR	Therapy or infusion interruption indicated but responds promptly to symptomatic treatment (e.g., antihistamines, NSAIDS, narcotics, IV fluids); prophylactic medications indicated for =24 hrs		
Grade 3 IRR	Prolonged (e.g., not rapidly responsive to symptomatic medication and/or brief interruption of infusion); recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae	Severe IRR discontinuation of infusion therapy but managed in the outpatient setting Tasks: 20, Time: 139 Costs (USD): $102	N=5 requiring Time: 200.2 ± 152.8 Costs (USD): $117.8 ± 60.9
Grade 4 IRR	Life-threatening consequences; urgent intervention indicated	Severe IRR resulting in hospitalization Tasks: 22, Time: 106 Costs (USD): $134	

Several studies have examined the economic and human resource impact of infusion reactions. In the solid tumor setting, a large United States database that includes patient-level medical and pharmacy claim histories for commercially insured US patients was used to study the clinical and economic impact of infusion reactions on patients with colorectal cancer (CRC) treated with the chimeric antibody cetuximab. A key objective of this study was to quantify the economic burden associated with the management of infusion reactions. The study found that among CRC patients treated with cetuximab 8.4% experienced infusion reactions that required resource-intensive medical interventions, and more than two-thirds of patients with infusion reactions experienced disruptions in their treatment regimen resulting in significant increases in associated costs. This study's methods may have utility in assessing the clinical and economic impacts of infusion reactions associated rituximab faster infusion in patients with NHL (Foley et al., 2010).

Because of a lack of literature pertaining to systematic examination of the drivers of costs associated with administering alternative chemotherapy protocols, de Raad and colleagues (de Raad J. et al., 2010) conducted the first study from a nursing perspective about the time required to perform chemotherapy-related tasks. Focus groups and a survey were used to assess the extent to which evidence-based chemotherapy protocols in Australia accurately capture chemotherapy-related administration tasks and the associated required nursing resources. Patient education, patient assessment (including assessment for infusion reactions), chemotherapy administration, and patient communication were the specific nursing activities assessed. On average, patient education during the first infusion required the most nursing time, followed by patient communication, administration, and patient assessment, with an average of 3.3 hours of staff time required per patient visit. Although details regarding time resources associated with

specific chemotherapy regimens were not described, this information may be used to inform healthcare decision makers—including nursing leaders—about the amount of nursing time required to administer chemotherapy and to make an assessment of the cost-effectiveness of alternative chemotherapy administration protocols.

Time and motion studies have been conducted to examine the human resource implications of infusion reactions (B. V. Fortner, Schwartzberg, Stepanski, & Houts, 2007; Schwartzberg et al., 2009). Severe infusion reactions are intensive events that present significant challenges for patients in the outpatient setting and for oncology practice resource utilization and workflow (Schwartzberg et al., 2008). Schwartzberg and colleagues (Schwartzberg et al., 2009) conducted a prospective multicenter time and motion study of patients receiving their first outpatient infusion of cetuximab or rituximab. Staff time and costs were estimated for the management of infusion reactions. It was found that 41.3 minutes more staff time was required for patients who experienced infusion reactions to rituximab; in mean human resource costs this calculated to a range of $54 to $118. Since awareness can lead to better planning for responding to infusion reactions in the outpatient setting, identifying clinical guidelines for intervention and management was suggested by the authors as a way to reduce time spent on managing infusion reactions effectively.

Only a few studies have explored the impacts of nursing attitudes or interventions and/or patient education on infusion reactions. A qualitative, interviewer-administered, 31-item survey, with a convenience sample of 202 oncology nurses attending the 2005 Oncology Nursing Society's annual congress, assessed the impact of infusion reactions on both nurses and patients. The survey found that 96% of nurses reported that Grade 3 and 4 reactions were "very" or "extremely" disruptive for patients, and 80% felt that these same reactions were also disruptive

for nursing practice. Moreover, 95% agreed with the statement that "infusion reactions can result in lost time and increased patient anxiety," with a statistically significant difference of more outpatient nurses agreeing or strongly agreeing with this statement (98% versus 90%, P≤ .05). Almost all nurses (98%) agreed that infusion reactions take time away from other patients, and two-thirds agreed with the statement "infusion reactions add a tremendous amount of stress and anxiety to the entire staff." Although this survey was limited by nurses having to retrospectively self-report on the severity of infusion reaction grade rather than use actual grading and frequency from chart reviews, it was the first study conducted to examine the impact of infusion reactions on nurses and patients (Colwell et al., 2007).

Oncology nurses' perceptions and experiences regarding the involvement of patients in the prevention of chemotherapy errors have also been explored. A small qualitative descriptive study of 11 oncology nurses in Switzerland found that although patient participation in safety was perceived as a complex learning process, oncology nurses reported positive attitudes and experiences with engaging patients in safety education (Schwappach, Hochreutener, & Wernli, 2010). This finding would need to be studied in US oncology care settings, with a modified design exploring the impact on patient outcomes of nurses' perceptions and strategies associated with educating patients about infusion reactions and about the need for early reporting of symptoms.

In a related survey of 325 ambulatory office nurses, those surveyed perceived that their interventions influenced patient outcomes; with regard to satisfaction and patient education, all respondents reported that they increased patient and family satisfaction either "frequently" or "sometimes," and 94% classified patient education on treatment and related side-effects as a "very important" registered nurse (RN) responsibility. Concerning safety, 97% felt it was "very

important" that a staff RN administer IV medications, and while 88% reported having a policy for hypersensitivity reactions, 84% responded that they actually document patient tolerance to chemotherapy administration. With regard to patient scheduling, an interesting finding was that although only 41% of staff RNs had the primary responsibility for infusion room scheduling, 54% were responsible for fixing scheduling problems and 61% felt that infusion room scheduling was a "very" or "somewhat" important RN responsibility (Ireland, DePalma, Arneson, Stark, & Williamson, 2004). Recommendations based on the survey findings that could impact patient outcomes include developing a standard guide for chemotherapy documentation.

One strategy to avoid delayed responses and improve outcomes is for nurses to educate both patients and family members about infusion reactions and encourage them to report reactions immediately to clinicians (Vogel, 2010). This family-focused intervention may serve both to improve a patient's anxiety and to prevent delayed response times to infusion reactions. However, more data are needed to assess effectiveness.

The goal of this review of the literature was to identify existing data that may support implementation of evidenced-based approaches to improve nursing care and outcomes for patients with NHL receiving rituximab faster infusion in the United States. The findings from the RATE trial support wider implementation of rituximab faster infusion for patients with previously untreated NHL. However, there remains a lack of data regarding the impact of rituximab faster infusion on nursing practice and resource utilization, and in particular on evidenced-based interventions delivered by oncology nurses to minimize adverse events and improve patient outcomes. As leaders, nurses need to collaborate with other members of the care delivery team, which includes the pharmaceutical industry, when making decisions regarding

adopting innovative strategies that impact patient care. Moreover, evidence that both leadership and reliance on others are factors that help determine which nurses may be early adopters of innovations will help inform strategies to support the diffusion of innovation into practice (Carlson, 2008). The review of literature findings calls for additional data to fill data gaps related to how changes in drug administration impacts the approaches to care nurses provide to patients.

Section III: Implementation Plan

In order to identify potential evidenced-based nursing practices to improve the delivery of patient care, in March 2012 a draft survey was created with questions derived from the literature (Carlson, 2008; Colwell et al., 2007; Coulter, 2010; Huddleston et al., 2005; Schwappach et al., 2010; Vogel, 2010) and combined with questions adapted from a global pharmaceutical company's survey of nurses regarding an alternative subcutaneous method to administer rituximab. In April 2012, to obtain instrument face validity for the clinical component of the survey, the draft survey was sent to an expert group of 13 nurses who work in the Medical Science Liaison role within US Medical Affairs for a large global pharmaceutical company. These scientific professionals specialize in oncology and work in collaboration with health care professionals to support of the pharmaceutical company's overall scientific and clinical goals. After the clinical validity was established based on 11 completed responses (85% response rate) as well as discussions with DNP committee chair, broader questions originally designed to assess mental health provider openness to innovation were replaced with questions targeted specifically to nursing practice about conditions that influence nurses' adoption of evidence-based practices. These questions, from Carlson's *Innovativeness Instrument* (Carlson, 2008), were obtained following a search of the CINAHL database using the key words evidenced-based practice, instrument, and nursing.

In September 2012, after receipt of an exemption from University of San Francisco, Institutional Review Board for the Protection of Human Subjects (IRBPHS), a letter that included both appropriate informed consent documentation and a SurveyMonkey ™ link to a 30-item questionnaire was sent via email to selected US nurses. (SurveyMonkey ™ is a web-based survey tool that sends survey responses over a secure, encrypted connection). The objectives of Keith Dawson

the survey were to obtain evidence about oncology nurses attitudes about innovation, their readiness to adopt new evidenced-based ideas/practices, and their perceptions regarding the impact of rituximab faster infusion on nursing practice, safety, patients, and resource utilization

Two groups of US oncology nurses were surveyed. First, on September 6, 2012 an email was sent to 69 active email addresses of Study Coordinators/Study Nurses who participated in the prospective, open-label, multicenter, single-arm clinical trial designed to assess the safety of faster infusion of rituximab in previously untreated NHL patients (RATE study). Second, on September 8, 2012 an email was sent to 72 active email addresses of oncology nurses who participated in the Oncology Nursing Society's (ONS) Chemotherapy (CHE) and Ambulatory/Office Nursing (AON) Special Interest Groups (SIG). (Email addresses were culled from the ONS May 3, 2012 SIG meeting minutes that included email addresses for SIG meeting attendees.) The RATE Study Coordinators/Study Nurses email addresses were selected because of their experience administering rituximab faster infusion in the RATE clinical trial; the ONS SIG email addresses were selected because of an assumption that their self identified clinical interests would increase the likelihood that they would have previously administered rituximab faster infusion. The survey was sent to a total of 141 active email addresses for both groups; a total of 25 surveys were returned between September 6, 2012 and September 21, 2012 generating an 18% response rate.

The survey included 5 sections and 30 items: 1) *Demographics* (4 items); 2) *Innovativeness Instrument* (6 items, 2 factors: Leadership and Reliance on others); 3) *Rituximab Experience* (3 items); 4) *Impact of Rituximab Faster Infusion on Nursing Practice* (13 items); 5) *Overall Impression* (4 items) (see Appendix C). Expected outcomes of the survey were to learn more

about oncology nurses' attitudes about innovation and their perceptions regarding the impact of rituximab faster infusion on patient safety, nursing practice, and resource utilization.

Demographics

The background and demographic characteristics of the 25 nurse respondents are presented in Table D1. Most had a Bachelor's degree (68.0%) as their highest degree received and have been practicing nursing for greater than 15 years (72.0%). These nurses worked in both inpatient (16.0%) and outpatient (32.0%) settings and at both academic (20.0%) and community hospital (20.0%) practices (see Figure 2). Response percent for current role were as follows: Clinical Trial Nurse (40.9%); Infusion Nurse (36.4%); Clinical Nurse Specialist (22.7%) (see Figure 1). A total of 3 skipped this question and 4 specified an "other" response of nurse manager/educator. For the 18 nurses who responded "yes" to having administered rituximab with both the standard infusion and faster infusion schedules, 60% responded that their current role was Clinical Trial Nurse.

Figure 1

Oncology Nurses' Roles

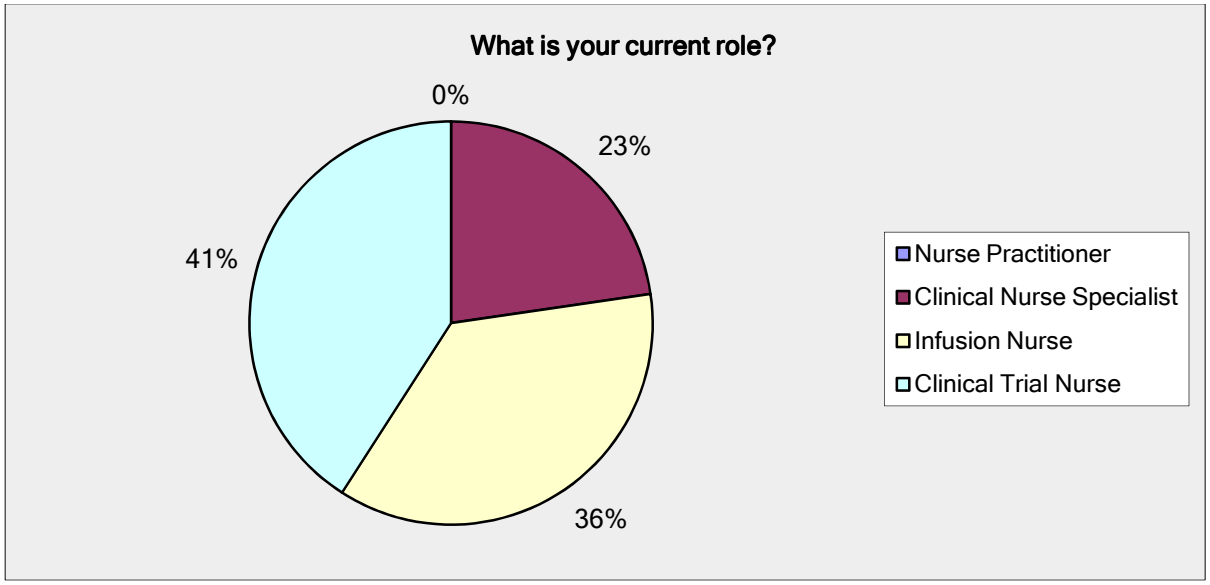
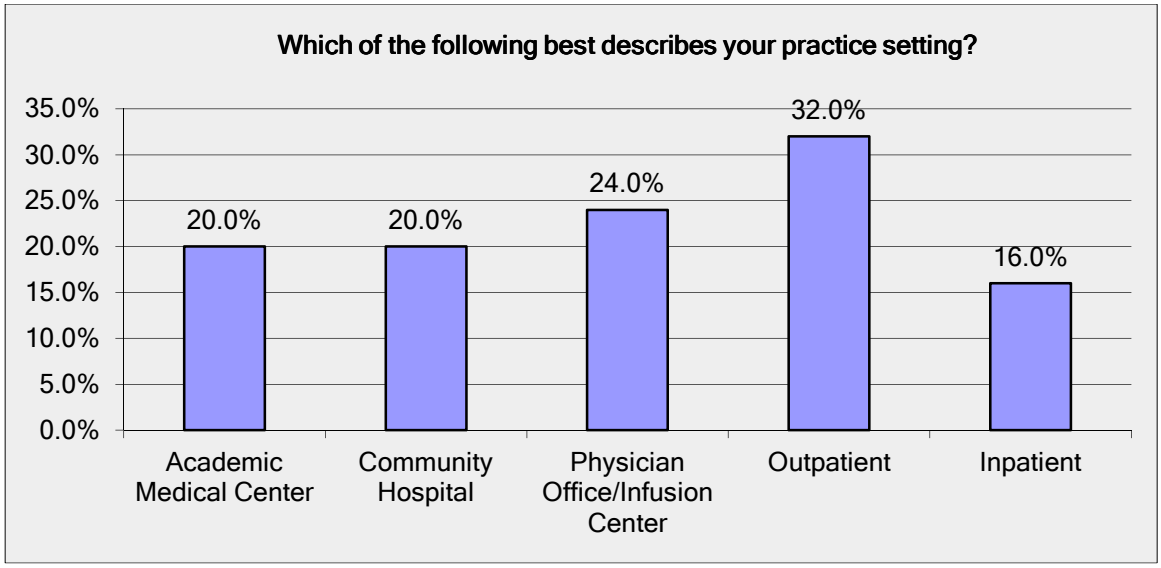


Figure 2

Oncology Nurses' Practice Setting



Innovativeness

Prior conditions that influence the innovativeness of the 25 nurse respondents are presented in Tables D2 and D3 in the Appendix. To identify nurses who may be early adopters of innovations, nurses were asked three questions about leadership and three questions regarding reliance on others (six total questionnaire items). For the innovativeness factor of leadership, greater than 80% of total respondents identified themselves as informal/formal leaders whose co-workers asked them about new ideas/practices either "often" or "almost always" (see Figure 3) and who try new idea/practices when research indicates its value. For the innovativeness factor of reliance on others, 88% are either "seldom" or "sometimes" reluctant to try something new and 72% either "seldom" or "sometimes" needed encouragement from others before doing something new (see Figure 4). Conversely, 72% either "often" or "almost always" network with other nurses outside of their work environment. The innovativeness questions indicate that oncology nurses surveyed are willing to accept new ideas and change practice when research

demonstrates its value and see themselves as opinion leaders who may influence the adoption and dissemination of innovation within their work environments.

Figure 3

Innovativeness: Leadership

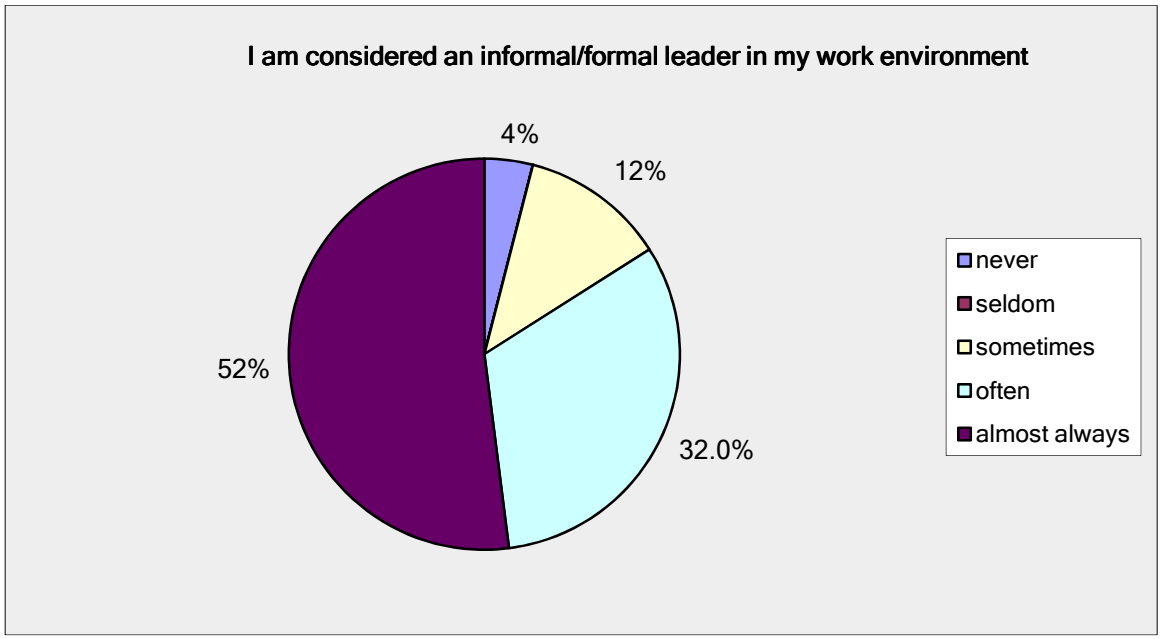
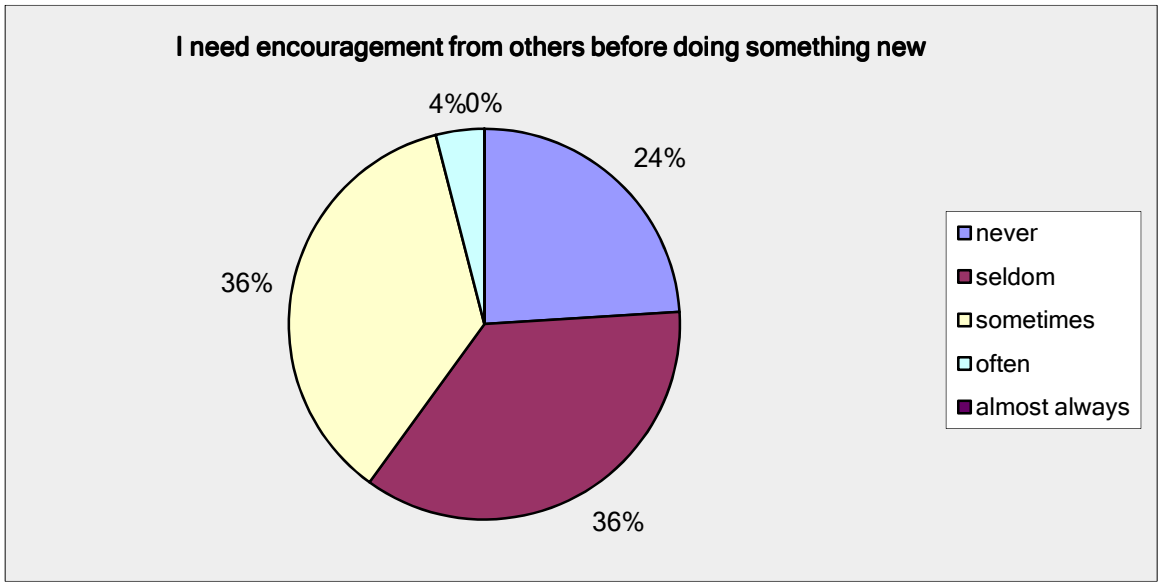


Figure 4

Innovativeness: Reliance on others



The following discussion is limited to the 18 nurses who responded "yes" to having administered rituximab with both the standard infusion and faster infusion schedules. Bar graphs detailing this subset of survey responses are presented in Appendix E: Figures.

Rituximab Faster Infusion: Nursing Experience

Figure E2 shows that one half (50%) of the oncology nurses have treated greater than or equal to 11 patients with rituximab faster infusion, with the majority (88.9%) rating their overall experience with rituximab faster infusion as either "positive" or "very positive."

Rituximab Faster Infusion Impact: Nursing Impact

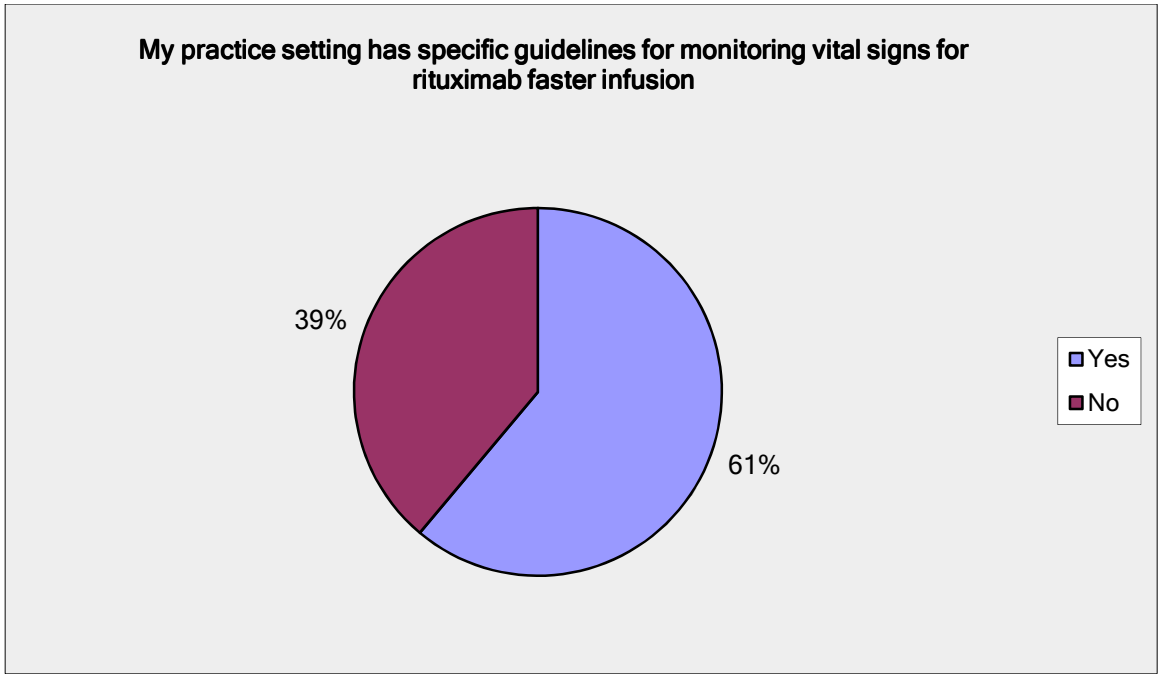
Figure E3 shows that most oncology nurses indicated that they either "agree somewhat" or "strongly agree" that rituximab faster infusion did not impact their abilities to monitor patients for adverse events (94.4%). These same nurses also either "agree somewhat" or "strongly agree" that Grade 3 and 4 infusion reactions are disruptive to nursing practice (83.3%), and that they clearly and accurately document infusion reactions in their practice settings (100%).

Rituximab Faster Infusion Impact: Guidelines, Policies and Procedures

Figure E4 shows that all oncology nurse respondents (100%) either "agree somewhat" or "strongly agree" that their practice settings have specific guidelines in place for the dosage of acetaminophen, antihistamines, and corticosteroids for the administration of rituximab. Although most (83.3%) oncology nurses indicated that they used standing orders or protocols to manage infusion reactions, one-third (33.3%) reported that their practice settings did not track quality metrics to assess infusion reaction rates. In addition, a high percentage (38.9%) (see Figure 5) of oncology nurses responded that they do not have specific guidelines in place for monitoring vital signs for rituximab faster infusion.

Figure 5

Guidelines, Policies and Procedures



Rituximab Faster Infusion Impact: Resource Utilization

Figure E5 shows that all oncology nurse respondents (100%) either "agree somewhat" or "agree strongly" that rituximab faster infusion will improve scheduling efficiency for infusion chair time. For practices that had specific guidelines for monitoring vital signs for rituximab faster infusion, monitoring frequency was split, with 40% monitoring vital signs before the infusion and at 15-minute intervals until infusion completion and 60% with guidelines specifying a 30-minute monitoring interval.

Rituximab Faster Infusion Impact: Patients

Figure E6 shows that all oncology nurses surveyed (100%) either "agree somewhat" or "agree strongly" that nurses in their practice settings educate patients and their families about infusion reactions and encourage reporting of infusion reactions to clinicians. All agreed (100%)

that patients would prefer the administration of rituximab faster infusion, with 83.3% indicating that they "agree strongly."

Rituximab Faster Infusion Impact: Safety

Figure E7 shows that although the majority (82.5%) of oncology nurse respondents either "disagree somewhat" or "disagree strongly" that rituximab faster infusion increases the likelihood of a patient experiencing an infusion-related reaction compared to a standard infusion rate, 17.6% were "not sure." However, all respondents agreed that the administration of rituximab faster infusion was safe, with 66.7% indicating that they "agree strongly."

Rituximab Faster Infusion Impact: Overall Impression

Figure E8 shows that 94.5% of oncology nurses had an overall impression that the process of administering rituximab faster infusion was either "easy" or "very easy," and all agreed that they would recommend rituximab faster infusion to patients, with 72.2% indicating that they "agree strongly" in recommending this to patients.

These new data fill a gap in the existing body of knowledge about nursing perceptions about the safety of rituximab faster infusion and the impact of this innovation on nursing practice and resource utilization. Given that the majority of follicular NHL patients in the United States receive an initial treatment strategy that includes the infusion of rituximab and that the US FDA has approved rituximab faster infusion administration, oncology nurses need to assess how to safely implement this change in drug administration into clinical practice. Both the review of literature and the survey results are crucial to, and inform the content of, an evidenced-based tool kit to support oncology nurses' adoption of rituximab faster infusion.

Section IV: Evaluation Plan

The appraisal of both research and non-research literature found that there is a sufficient research base to support adopting a 90-minute administration of rituximab at the second infusion for patients with NHL. This recommendation is based on literature documenting an incidence of Grade 3 or 4 infusion-related reactions of 1.1% at Cycle 2 and 2.8% during Cycles 2-8, positive impact on resource utilization, and increased nursing and patient satisfaction (see Appendix A: Evidence Table). For a conceptual model to implement rituximab faster infusion into nursing practice, *The Iowa Model of Evidence-Based Practice to Promote Quality Care* (Titler et al., 2001) was selected (see Figure E1). In addition, given that the diffusion of innovation is an identified barrier preventing the adoption and translation of research findings into evidence-based practice, Roger's *Diffusion of Innovations* model was selected as the strategy to facilitate the successful adoption of rituximab faster infusion.

Although the adoption of a 90-minute schedule has been recommended due to both perceived positive impact on resource utilization (reduction in nursing workload and elimination of treatment waiting times for rituximab) and projected increased patient satisfaction, there is still little evidence in the literature that quantifies these positive impacts. Therefore, to support the translation of the rituximab faster infusion innovation into nursing practice, a tool kit was created for oncology nurses to conduct their own 30-day pilot assessments of the real-world impacts of rituximab faster infusion on nursing practice, patient safety, and resource utilization. The target audience for this tool kit is oncology nurse early adopters who are either self identified or identified by nursing leadership within a practice setting.

The tool kit is composed of 3 documents:

- One Page Handout consisting of:

  - Front page: *Process to Minimize Medication Administration Error Risk When Adopting Rituximab Faster Infusion - 5 Rights for Medication Administration* (Table 3)
  - Back page*: Adoption of Rituximab Faster Infusion - Monitor and Analyze Structure, Process and Outcome Data* (Figure E9)
- Innovativeness and Overall Impression Assessment Tool (Figure E10)
- Current version of Rituximab (Rituxan®) Prescribing Information: http://www.gene.com/gene/products/information/pdf/rituxan-prescribing.pdf.

The 5 rights (5 R's) for medication administration include 1) right patient, 2) right drug, 3) right dose, 4) right route, and 5) right time. These 5 R's were developed for nurses as a standardized process to minimize risk of error when administering medications. This process has been critiqued as being inadequate because the process ignores the role of the patient and their families in patient safety (Macdonald, 2010). Given this criticism and data from the survey of oncology nurses supporting the role of patients and their families in reporting infusion reactions, patients were included in the tool kit (see Table 3).

The Innovativeness and Overall Impression Assessment Tool presented in Figure E10 is designed to identify nurses who may be early adopters and to assess nurses' overall impression of rituximab faster infusion (pre and post adoption). These questions may be administered at a practice setting via SurveyMonkey ™, verbally, or on paper.

Table 3

Process to Minimize Medication Administration Error Risk When Adopting Rituximab Faster Infusion - 5 Rights for Medication Administration

BLACK BOX WARNING: FATAL INFUSION REACTIONS, TUMOR LYSIS SYNDROME (TLS), SEVERE MUCOCUTANEOUS REACTIONS, and PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML). Fatal infusion reactions within 24 hours of RITUXAN infusion occur; approximately 80% of fatal reactions occurred with first infusion. Monitor patients and discontinue RITUXAN infusion for severe reactions. See full prescribing information for complete boxed warnings.	
Right Patient	For previously untreated follicular NHL and DLBCL patients. Patients who did not experience a Grade 3 or 4 infusion related adverse event during Cycle 1. Patients who have clinically significant cardiovascular disease or who have a circulating lymphocyte count ≥5000/mm3 before Cycle 2 should not be administered the 90-minute infusion.
Right Drug	Rituximab (Rituxan®) Injection for Intravenous Use • Recommended to pre-medicate before each infusion with acetaminophen and an antihistamine. • In the RATE trial patients with follicular NHL received rituximab 375 mg/m2 plus CVP chemotherapy and patients with DLBCL received rituximab 375 mg/m2 plus CHOP chemotherapy. o All patients received the glucocorticoid component of their chemotherapy prior to Rituximab (Rituxan®) infusion.
Right Dose	The Rituximab (Rituxan®) dose for NHL is 375 mg/m2 Initiate at a rate of: • 20% of the total dose given in the first 30 minutes and the remaining. • 80% of the total dose given over the next 60 minutes. o Total infusion time is 90-minutes. For infusion reactions, interrupt the infusion or slow the infusion rate. Continue the infusion at one-half the previous rate upon improvement of symptoms.
Right Route	Administer only as an Intravenous Infusion. Do not administer as an intravenous push or bolus.
Right Time	If the 90-minute infusion is tolerated in Cycle 2, the same rate can be used when administering the remainder of the treatment regimen (through Cycle 6 or 8). Patients should be monitored after each rituximab infusion according to standard institutional practice.

To obtain expert opinion evidence that the tool kit is clinically accurate and appropriate to assist oncology nurses in adopting rituximab faster infusion, an interdisciplinary panel composed of four members of a US Medical Affairs Medical Team within a large global pharmaceutical company was identified. Panel members included two Master's prepared nurses with the role of Hematology Medical Science Liaison, one PhD prepared Hematology Medical Science Director responsible for the clinical review of materials provided to health care professionals, and one PharmD prepared Project Manager responsible for US Medical Team project management support.

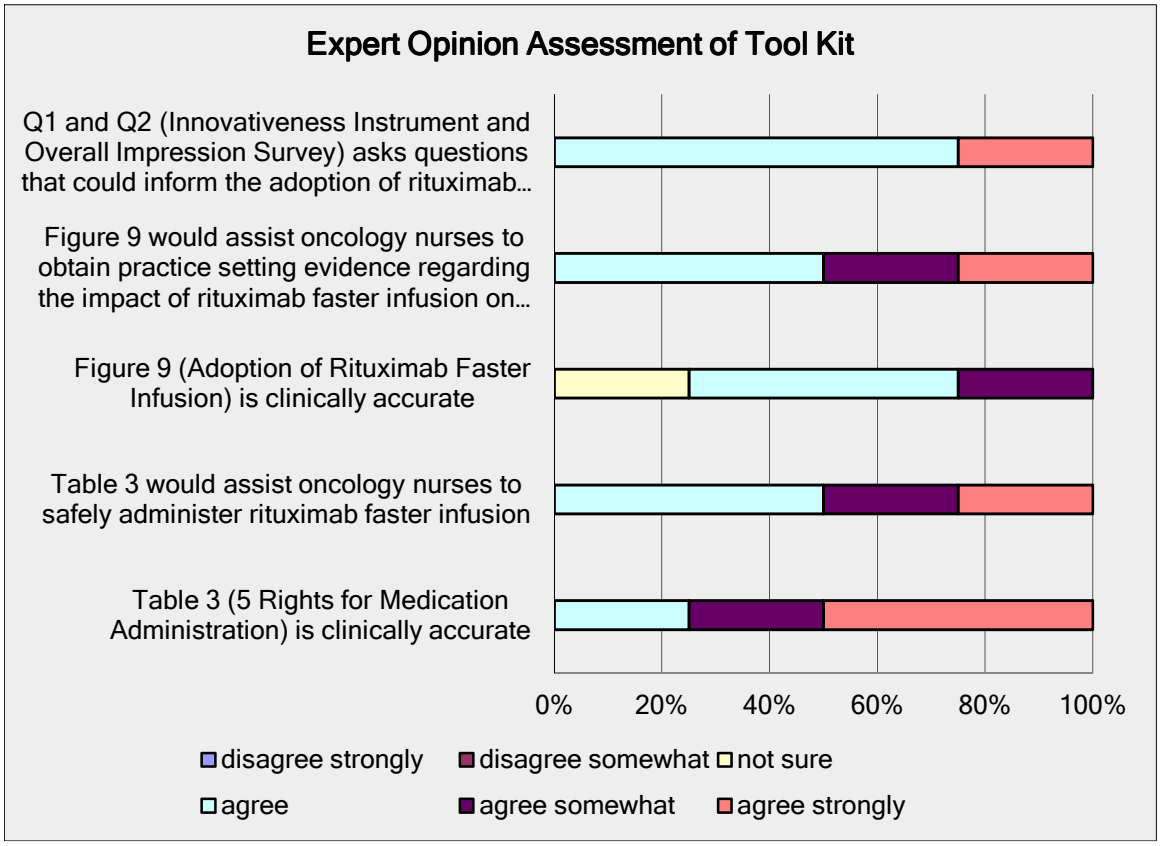
This interdisciplinary panel was sent an email in November 2012 that included a SurveyMonkey ™ link to images of Figures E9, E10, and Table 3 for review/reference and a 5-item questionnaire. The survey included two demographic questions regarding panel member's role within the company and their highest level of education completed. The panel was then asked to evaluate the clinical accuracy and overall usefulness of the tool kit components using a 5-point Likert scale ranging from "agree strongly" to "disagree strongly." Figure 6 shows that at least 75% of panel members either "agree somewhat' or "agree strongly" that the components of the tool kit were clinical accurate, assist with obtaining practice setting evidence, and inform the adoption of rituximab faster infusion by oncology nurses. Table 3 received the strongest agreement (50%) for clinical accuracy, and 100% agreed that the 5 Rights of Medication Administration tool would assist oncology nurses to safely administer rituximab faster infusion.

After receiving expert panel feedback/comments via an open text field, the tool kit was modified to highlight the chemotherapy regimens in the RATE trial and include a reference that the 90-minute infusion was administered in combination with corticosteroid-containing chemotherapy. The entire panel agreed (100%) that Figure E9 would assist oncology nurses to

obtain practice setting evidence regarding the impact of rituximab faster infusion on nursing practice, guidelines, policies and procedures, resource utilization, and patients. The entire panel agreed that the *Innovativeness Instrument* and Overall Impression Survey asks questions that could inform the adoption of rituximab faster infusion by oncology nurses.

Figure 6

Expert Opinion Panel Assessment of Tool Kit



Oncology nurse early adopters who use the tool kit to conduct 30-day pilots to assess the real-world impact of rituximab faster infusion on nursing practice, patient safety, and resource utilization should consider incorporating the proposed Quality Oncology Practice Initiative (QOPI®) measures specific to rituximab faster infusion (see Table 4). QOPI is a quality assessment and improvement program for US-based outpatient hematology-oncology practices

designed to promote excellence in cancer care by providing practices with quality improvement tools and measures to improve cancer care (Neuss, Gilmore, & Kadlubek, 2011). QOPI measures are derived from clinical guidelines or published standards and are adapted from the National Initiative on Cancer Care Quality (NICCQ), American Society of Clinical Oncology (ASCO)/ National Comprehensive Cancer Network (NCCN) Quality Measures, and are consensus-based and clinically relevant. In 2012, there were 97 quality measures, including five specific to NHL, three of which specific to rituximab. Measures 77 and 77a refer to the administration of rituximab when CD□antigen expression is either negative or undocumented and the inverse, when CD□20 antigen expression is positive. Measure 78 refers to obtaining a documented hepatitis B virus infection test, including HBsAg, prior to administration of rituximab for patients with NHL (Quality Oncology Practice Initiative, 2012).

The tool kit and rituximab faster infusion QOPI proposed measures are resources to assist with the adoption, safe implementation ,and evaluation of this innovation on both patient outcomes and nursing practice. Table 4 lists new QOPI measures proposed for rituximab faster infusion as part of the project's continuous improvement evaluation plan. Since QOPI measures are reassessed every six months by the QOPI Steering Group composed of both community and academic oncologists and nurses, nurse members should propose that results of the RATE study be reviewed for consideration of new QOPI measures.

Table 4

Rituximab Faster Infusion QOPI Proposed Measures

Module	**Quality Indicator**	**Measure**
NHL	Safety	Rituximab 90-minute infusion administered to follicular NHL and DLBCL patients who did not experience a Grade 3 or 4 infusion related adverse event during Cycle 1.
NHL	Safety	Rituximab 90-minute infusion not administered to follicular NHL and DLBCL patients who have clinically significant cardiovascular disease or who have a circulating lymphocyte count $\geq 5000/mm^3$ before Cycle 2.
NHL	Safety	Percentage of Grade 3 and 4 IRRs at Cycle 2 and beyond.

Section V: Implications for Nursing Practice

Rituximab faster infusion will result in a significant change in the administration of this medication in the United States. Data describing oncology nurses' perceptions about alternative immunochemotherapy administration and its impact on safety, resource utilization, and nursing practice are lacking in the literature. Oncology nurses may have concerns about infusion-related reactions related to the new 90-minute administration and will require additional resources to change how they have been administering rituximab over the last 15 years in clinical practice.

The survey of oncology nurses' attitudes about innovation and perceptions regarding the impact of rituximab faster infusion on patient safety, nursing practice, and resource utilization, combined with a systematic review of the literature, provides the best available evidence regarding the impact of this innovation on nursing practice. These data informed the development of an evidenced-based tool kit to assist oncology nurses' adoption of safe and appropriate interventions that may benefit patient care. Based on expert panel review, using a tool that incorporates the 5R's of medication administration may be an effective strategy to minimize medication error risk when adopting rituximab faster infusion and support achievement of positive outcomes for both patients and nursing practice.

Clinical Trial Nurses who had administered rituximab faster infusion represented 60% of survey responders. This finding was influenced by the use of the RATE Study Coordinator/Study Nurse email list. These nurses also had high innovativeness scores for the factors of leadership and reliance on others. This indicates a potential willingness among nurses in this role to accept new ideas and change practice when research demonstrates its value. Clinical Trial Nurses may be a key early stakeholder to support the translation of innovation into

practice, especially for academic and community sites that have clinical research programs as part of their clinical practice.

Additional research exploring oncology nursing interventions related to patient education, adverse event monitoring, patient-reported quality of life, and quantifying the economic impact of new methods of medication administration on nursing resources is needed. These new data will fill gaps in the existing body of knowledge about evidenced-based practices that impact the delivery of patient care.

Dissemination Plan

To support putting into practice the evidence regarding rituximab faster infusion a manuscript detailing findings of the review of the literature and implementation plan for an evidenced-based tool kit may be submitted to nursing journals with high clinical impact (e.g., *Journal of Infusion Nursing, Journal of Oncology Nursing).* In addition, abstracts may be submitted to national clinical oncology conferences such as the Oncology Nursing Society and the American Society of Clinical Oncology annual meetings to disseminate results to oncology nurses.

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Appendix A: Evidence Table

What evidence exists regarding the safety of administrating rituximab faster infusion and the impacts of this innovation on nursing practice and resource utilization?

Study	**Method**	**Sample**	**Intervention**	**Outcomes/ Recommendations**	**Strength of Evidence**	**Quality of Evidence**
					I-V	**A-C**
Lang et al, 2011	Meta-analysis: systematic review based on the Joanna Briggs Institute Model of Evidence-Based Health Care	559 NHL patients	Rituximab 90 min Infusion vs. rate > 120 minutes	12 (2.6%) acute adverse reactions were reported among 559 patients who completed 1799 cycles of rapid rituximab infusion in nine studies. Grade 1: n=7, Grade 2: n=5, Grade 3/4: n=0 Based on best available evidence, a 90 min rapid rituximab infusion is recommended for NHL patient at second infusion and the frequency of nursing monitoring should be readjusted to reduce workforce waste.	II	A
Sehn et al, 2007	Experimental, single arm	150 NHL safety cohort, >1200 treated (Canada)	Rituximab 90 min Infusion in combo with corticosteroid-containing chemo	More than 1,200 patients treated with rapid infusion rituximab in BC with only one Grade III reaction. The authors recommend the adoption of a 90-minute schedule due to a positive impact on resource utilization (reduction in nursing workload and elimination of treatment waiting times for rituximab) and increased patient satisfaction.	!!	A

Study	Method	Sample	Intervention	Outcomes/ Recommendations	Strength of Evidence I-V	Quality of Evidence A-C
Chaing et al, 2010	Experimental, single arm	79 NHL patients (Single center- Singapore)	Rituximab 90 min Infusion (single agent rituximab without corticosteroid therapy)	Patient education regarding infusion-related reactions with rituximab is crucial to aid in the identification of patients who are not suitable for the rapid infusion. Patients who are prone to nausea and vomiting should also be considered for omission from the rapid schedule pending further investigation.	II	A
Corey et al, 2007	Experimental, single arm	33 NHL patients (Single center- US community cancer center)	Rituximab 90 min Infusion in combo with corticosteroid-containing chemo	Rituximab 90-minute was safe and improved resource utilization and patient satisfaction as evidenced by providing patients with more flexibility in treatment scheduling, more time away from the facility and increasing access in the chemotherapy suite.	II	B
Coulter et al, 2010	Experimental, single arm	16 NHL patients (3 US community-based outpatient infusion clinics)	Rituximab 90 min Infusion (pre-medications not standardized)	If medical oncologists adopt rituximab faster infusion as standard practice, an easier monitoring schedule than measuring blood pressure, heart rate and respiratory rate before the infusion and at 15, 30, 60 and 90 minutes to monitor respiratory or cardiac symptoms should be employed to free up nursing time and resources.	II	B

Study	Method	Sample	Intervention	Outcomes/ Recommendations	Strength of Evidence I-V	Quality of Evidence A-C
Swan et al, 2010	Experimental, single arm	13 NHL patients (Single center- US Hospital outpatient and inpatient units)	Rituximab 90 min Infusion (pre-medication with acetaminophen and diphenhydramine, corticosteroids not described)	One Grade 3 reaction of prolonged hypotension, tachycardia, and fever. Adopting a rapid infusion schedule would benefit patients and the institution by reducing clinic chair time for each dose by 1.5–2 hours, compared with standard infusion times. Adoption of a rapid administration protocol will succeed only if supported by the nursing staff. Strong nursing leadership and educational in-services highlighting safety data will help gain support and comfort required for nursing staff to treat patients with rituximab faster infusion and decreasing resource utilization of infusion clinic time by ensuring that premedication is given and that the rituximab faster infusion is started in a timely manner.	II	A
Zahrani et al, 2007	Experimental, single arm	21 NHL patients majority of patients were treated with R-Chemo regimens (Hospital - Saudi Arabia)	Rituximab 90 min Infusion in combo with corticosteroid-containing chemo	No Grade 3/4 infusion-related adverse events observed This shortened infusion schedule has resulted in a substantial reduction in resource utilization. Preliminary data may be used to develop alternative guidelines for administration of rituximab to achieve resource utilization benefits.	II	B

Study	Method	Sample	Intervention	Outcomes/ Recommendations	Strength of Evidence I-V	Quality of Evidence A-C
Schwartzberg et al, 2008	Non-experimental- cross-sectional chart review	76 patients identified with a severe IRR: 47 rituximab cases (19 US community oncology centers)	N/A	21% of rituximab severe IRR cases received corticosteroids before MoAb treatment. Nearly half of the patients who received rituximab and experienced a severe IRR were receiving rituximab alone. 17% of rituximab Grade 3 IRRs resulted in permanent discontinuation. For those not discontinuing, dose delays and infusion rate reductions were common, but actual dose reduction was rare. Well-rehearsed plans and procedures for handling these events can help staff to reassure other patients in general and especially those who may be receiving similar therapies.	III	A
Dakhil et al, 2011	Quasi-experimental- single arm phase III multicenter open label study	451 FL and DLBCL patients	Rituximab 90 min Infusion in combo with corticosteroid-containing chemo	The incidence of Grade 3/4 IRRs at Cycle 2 was low (1.1%) and the rate of IRRs decreased with subsequent administrations Only 10 patients (2.8%) experienced Grade 3/4 IRRs during Cycles 2–8 There were no fatal IRRs or fatal AEs on Days 1–2 at any cycle in this study, and there were no unexpected events or acute fatal events associated with the faster infusion schedule. Results from this study confirm that the 90-minute infusion schedule for rituximab is safe and feasible in	II	A

Study	Method	Sample	Intervention	Outcomes/ Recommendations	Strength of Evidence I-V	Quality of Evidence A-C
				NHL patients who tolerate their first infusion administered at the standard rate and who do not have significant cardiovascular disease or high circulating lymphocytes.		
de Raad et al, 2010	Qualitative-discussion group sessions	36 nurses (6 chemotherapy centers in New South Wales, Australia)	A major limitation of this study is that it is not specific to rituximab faster infusion	Four task types and time averages associated with administering chemotherapy: 1. patient education - 48 minutes during the first visit and 18.5 minutes thereafter 2. patient assessment - 20.3 minutes, 3. administration - 23 minutes, 4. patient communication - 24.2 minutes Each patient received 3.3 hours of staff time (1.7 hours of direct contact time and 1.6 hours of noncontact time). These data will allow healthcare decision makers and evaluators to predict the amount of nursing time required to administer chemotherapy based on the characteristics of a wide range of chemotherapy protocols.	III	A

Study	Method	Sample	Intervention	Outcomes/ Recommendations	Strength of Evidence I-V	Quality of Evidence A-C
Schwartzberg et al, 2009	Qualitative- A prospective multicenter study involving time and motion and activity sampling methods	Of 161 enrolled, 90 patients received rituximab (27 US community oncology sites)	A major limitation of this study is that it is not specific to rituximab faster infusion	IRRs following rituximab administration are common and are associated with measurably increased costs of care Among 161 patients enrolled, 39% of 90 patients on rituximab experienced IRRs. A statistically significant finding was mean human resource costs ranging from $54 to $118 for no IRR to mild/moderate IRR: F (2, 6.448)=5.858, p=.035 (mild/moderate > no IRR). The frequency of IRRs suggests the importance of identifying clinical guidelines for intervention and management. The methods used in this study could be employed for any direct comparison of chemotherapy regimens that purports to examine treatment cost as an outcome.	III	A

Study	Method	Sample	Intervention	Outcomes/ Recommendations	Strength of Evidence I-V	Quality of Evidence A-C
Colwell et al, 2007	Qualitative-Survey	202 nurses (99% women)	A major limitation of this study is that it is not specific to rituximab faster infusion	96% of nurses reported that Grade 3 or 4 infusion reactions were "very" or "extremely" disruptive for patients, and most nurses indicated that Grade 3 or 4 infusion reactions were disruptive to the nurses (80%). 95% of nurses agreed with the statement, "Infusion reactions can result in lost time and increased patient anxiety"), with a greater proportion of outpatient nurses than inpatient nurses agreeing or strongly agreeing with this statement (98% versus 90%, respectively; $P \leq .05$). Infusion reactions associated with parenteral MoAb treatments and chemotherapy are disruptive and emotionally challenging for patients receiving the treatment and the nurses and staff at the institution or practice treating them. The results suggest that further awareness of infusion reaction management and education of patients and clinicians are needed.		
Schwappach et al, 2010	Qualitative-Survey	11 actively practicing US oncology nurses	A major limitation of this study is that it is not specific to rituximab faster infusion	Oncology nurses perceive patient education in safety as a core element of their professional role and are receptive to advancing their expertise in this area. Engaging patients was described as a challenge and nurses acknowledged the diverse needs of patients and deliberately used different strategies to involve patients in safety. Oncology nurses should include patient involvement in error prevention given the reported positive experiences.	III	A

Study	Method	Sample	Intervention	Outcomes/ Recommendations	Strength of Evidence I-V	Quality of Evidence A-C
Breslin, S, 2007	Expert Opinion-Principles related to cytokine-release syndrome in patients receiving MOABs	N/A	N/A	1. Prior to administering any MoAb, nurses should be familiar with its toxicity profile, including the potential for acute and delayed infusion-related side effects. 2. The need for specific pre-medications should be assessed. - For patients with circulating lymphocyte counts of 25,000/mm3 or higher, the addition of corticosteroids and histamine-2 receptor antagonists to the usual pre-medications is recommended. - Hospitalization of such patients for inpatient administration of medication and close monitoring should be strongly considered 3. MoAbs always should be administered piggy-back into the distal port of a main IV line and never should be given as an IV bolus. 4. An infusion pump always should be used for administration. The first infusion should be administered slowly. Subsequent infusions may be given more rapidly as tolerated and per package instructions.	V	A

Study	Method	Sample	Intervention	Outcomes/ Recommendations	Strength of Evidence I-V	Quality of Evidence A-C
Chung, C, 2008	Literature Review-Managing Pre-medications and risk of IRRs with MoAbs	N/A	N/A	Improving risk assessment for infusion reactions has become a compelling medical need. Patients with high circulating malignant cell counts are at risk for severe infusion reactions to rituximab. Pre-medications are considered standard procedure for minimizing the risk for IRRs. Because most infusion reactions with monoclonal antibodies occur after the first or second infusion, the value of premedication on subsequent infusions may decrease.	V	A
Vogel, W, 2010	Expert Opinion-Infusion Reactions, Diagnosis, Assessment & Management	N/A	N/A	Safety assessments from six studies of rituximab used as a single agent in previously treated patients with indolent non-Hodgkin lymphoma gave an incidence of infusion-related reaction in 77% (7% Grades 3–4) of patients during the first infusion, 30% (2% Grades 3–4) during the fourth infusion, and 14% (no Grade 3–4 events) during the eighth infusion. Rituximab is associated with infusion reactions that are caused primarily by cytokine release rather than true allergic reactions. Prompt and accurate documentation of the infusion event including accurate grading of the event will enable the prescribing clinician to decide whether re-challenge is feasible and safe.	V	A

Study	Method	Sample	Intervention	Outcomes/ Recommendations	Strength of Evidence I-V	Quality of Evidence A-C
				Re-challenge may include the re-administration of antihistamines and corticosteroids, followed by administration of the agent at a reduced rate.		
Palkhivala, A, 2007	Expert Opinion-90 minute rituximab infusion	N/A	N/A	*"Patients were pleased with shortened infusion times, more time away from [the] facility, [and] more control and flexibility in [their] treatment scheduling."* Rituximab faster infusion. *"… will make a huge difference to practice to free up those [treatment] chairs."* According to Rogers, before rituximab faster infusion becomes standard practice in the United States more data is needed because of the large impact that faster infusion this will have on nursing practice and resource utilization.	V	B

Study	Method	Sample	Intervention	Outcomes/ Recommendations	Strength of Evidence I-V	Quality of Evidence A-C
Fortner & Viale, 2007	Review of Literature-economic analysis of infusion reactions	N/A	N/A	Time and motion studies are suggested as a model for community oncology centers to assess the tasks involved and the associated costs in treating IRRs caused by therapies such as rituximab and help to evaluate intervention strategies for IRRs that may have a significant impact on centers with limited staff resources. The incidence of an IRR resulted in increased MoAb infusion times and staff time, leading to increased human resource costs. Compared to patients not experiencing IRRs, statistically significant increases in staff time during infusion were observed in patients experiencing IRRs. Prevention, including patient education about IRR risks, and proper management of IRRs may minimize these expenses for patients and families.	V	A

Appendix B: Research and Non-Research Appraisal Forms

Newhouse, R., Dearholt, S., Poe, S., Pugh, L., & White, K. (2007). Johns Hopkins nursing evidence-based practice model and guidelines.

RESEARCH- Appraisal

				Evidence Level: IIA	
Article Title: **Safety of rapid rituximab infusion in adult cancer patients: A systematic review**					
Author(s)	**Lang** DSP, Hagger C, Pearson A.				Date: 2011
Journal:	*International Journal of Nursing Practice*				
Setting:	NHL patients in 90 min regimen			Sample Size: 559 NHL patients	
☐ Experimental	☒ Meta-analysis	☐ Quasi-experimental	☐ Non-experimental	☐ Qualitative	☐ Meta-synthesis
Does this study apply to NHL patients?				☒ Yes	☐ No
If the answer is No, STOP here (unless there are similar characteristics)					
Strength of Study Design					
• Was the sample size adequate and appropriate?				☒ Yes	☐ No
• Were study participants randomized?				☐ Yes	☒ No
• Was there an intervention? *Rituximab infused over 30 min for 20% of the total dose at the beginning and the remaining 80% was infused over 60 min.*				☒ Yes	☐ No
• Was there a control group? *The comparator group was any rituximab infusion rate > 120 min or without a comparison group.*				☒ Yes	☐ No
• If there was more than one group, were groups equally treated, except for the intervention?				☐ Yes N/A	☐ No N/A
• Was there adequate description of the data collection methods?				☒ Yes	☐ No
Study Results					
• Were results clearly presented?				☒ Yes	☐ No
• Was an interpretation/analysis provided?				☒ Yes	☐ No
Study Conclusions					
• Were conclusion based on clearly presented results?				☒ Yes	☐ No
• Were study limitations identified and discussed?				☒ Yes	☐ No

Pertinent Study Findings and Recommendations:

Safety

This systematic review was based on the Joanna Briggs Institute Model of Evidence-Based Health Care to critically appraise, synthesize and present the best available evidence to inform clinical practice. A meta-analysis of NHL patients in 90 min regimen using a random effects model (DerSimonian–Larid) showed a pooled proportion of 0.026 (95% CI, 0.01, 0.048), translated to **2.6% of acute adverse reactions** among nine studies of 559 NHL patients. The studies were homogenous as non-combinability test showed P = 0.0955 and I2 = 40.8% (95% CI, 0%, 71.3%). No publication bias was detected in Harbord bias test, P = 0.30

A total of 12 acute adverse reactions were reported among 559 patients who completed 1799 cycles of rapid rituximab infusion in nine studies, which consisted of NHL patient in 90 min regimen. Grades for acute adverse reactions were reported as follows: Grade 1: n=7, Grade 2: n=5, Grade 3/4: n=0

The most common reported acute adverse reactions were nausea and vomiting followed by rash; chills and rigors; back pain, abdominal pain; sore throat; and hypotension. All these studies used antipyretics, namely acetaminophen/paracetamol, ranging from 375 to 1000 mg either in the form of tablet(s) or by injection.

The most common antihistamine was either oral or parenteral diphenhydramine 25–50 mg. The common choice of corticosteroids was parenteral hydrocortisone 100 mg, prednisolone 100 mg and methylprednisolone

Recommendations
Based on best available evidence, a 90 min rapid rituximab infusion is recommended for NHL patient at second infusion and the frequency of nursing monitoring should be readjusted to reduce workforce waste.

Will the results answer the practice question?	☒ Yes	☐ No

Evidence Rating					
Strength of Evidence	☐ Level I (Strong)	☒ Level II	☐ Level III	☐ Level IV	☐ Level V.
Quality of Evidence (check one)			☒ High (A)	☐ Good (B)	☐ Low/Major flaw (C)

RESEARCH- Appraisal

				Evidence Level: IIA	
Article Title: **Rapid infusion rituximab in combination with corticosteroid-containing chemotherapy or as maintenance therapy is well tolerated and can safely be delivered in the community setting**					
Author(s)	Laurie H. **Sehn,** Jane Donaldson, Allison Filewich, Catherine Fitzgerald, Karamjit K. Gill, Nancy Runzer, Barb Searle, Sheila Souliere, John J. Spinelli, Judy Sutherland, and Joseph M. Connors				Date: 2007
Journal:	*Blood*. 2007;109: 4171-4173				
Setting:	NHL patients planned for treatment with rituximab in combination with corticosteroid-containing chemotherapy at the BC Cancer Agency			Sample Size: 150 patients initial safety cohort, and more than rapid rituximab infusion in > 1200 patients in combination with corticosteroid-containing chemotherapy	
☒ Experimental	☐ Meta-analysis	☐ Quasi-experimental	☐ Non-experimental	☐ Qualitative	☐ Meta-synthesis
Does this study apply to NHL patients?				☒ Yes	☐ No
If the answer is No, STOP here (unless there are similar characteristics)					
Strength of Study Design					
• Was the sample size adequate and appropriate?				☒ Yes	☐ No
• Were study participants randomized?				☐ Yes	☒ No
• Was there an intervention? *Cycle 1 was unaltered and delivered according to the product monograph. All further cycles were administered the same day as chemotherapy over a total infusion time of 90 minutes (20% of the dose in the first 30 minutes and the remaining 80% over 60 minutes; total dose delivered in 250 mL). Patients were encouraged to take their daily corticosteroid dose according to their chemotherapy protocol prior to receiving rituximab.*				☒ Yes	☐ No
• Was there a control group?				☐ Yes	☒No
• If there was more than one group, were groups equally treated, except for the intervention?				☐ Yes N/A	☐ No N/A
• Was there adequate description of the data collection methods?				☒Yes	☐ No
Study Results					
• Were results clearly presented?				☒ Yes	☐ No
• Was an interpretation/analysis provided?				☒ Yes	☐ No
Study Conclusions					
• Were conclusion based on clearly presented results?				☒ Yes	☐ No
• Were study limitations identified and discussed?				☒ Yes	☐ No

Pertinent Study Findings and Recommendations:

Safety

With initial safety cohort, the rapid infusion rituximab schedule was extremely well tolerated with no Grade 3 or 4 infusion reactions observed. The rate of Grade 3 or 4 toxicity was 0% (95% CI, 0%-0.019%), which is not higher than the expected rate with standard administration.

- 10 patients who had experienced an adverse reaction with their first cycle (administered at the standard rate) subsequently tolerated rapid infusion without event.
- 8 patients who did not receive any corticosteroids because of a contraindication also tolerated the rapid infusion without event.
- 0 patients had an elevated circulating lymphocyte count at the time of rapid infusion rituximab; thus, the safety of rapid infusion of rituximab in this setting remains unknown.

More than 1,200 patients treated with rapid infusion rituximab in BC with only one Grade III reaction.

Resource Utilization

- Rituximab administration times have been cut in half or less with a concomitant reduction in nursing workload.

Patient Satisfaction

- Most patients can be conveniently treated with rituximab in a shorter time interval and on the same day as their chemotherapy. As a consequence, patient satisfaction has improved, and treatment waiting times for rituximab have been eliminated.

Recommendations

The authors recommend the adoption of a 90-minute schedule due to a positive impact on resource utilization (reduction in nursing workload and elimination of treatment waiting times for rituximab) and increased patient satisfaction.

Will the results answer the practice question?	☒ Yes	☐ No

Evidence Rating					
Strength of Evidence	☐ Level I (Strong)	☒ Level II	☐ Level III	☐ Level IV	☐ Level V
Quality of Evidence (check one)			☒ High (A)	☐ Good (B)	☐ Low/Major flaw (C)

RESEARCH- Appraisal

				Evidence Level: IIA	
Article Title: **A prospective study to evaluate the feasibility and economic benefits of rapid infusion rituximab at an Asian cancer center**					
Author(s)	Joen **Chiang**, Alexandre Chan, Vivianne Shih, Siew Wan Hee, Miriam Tao, Soon Thye Lim				Date: 2010
Journal:	*Int J Hematol* 91:826–830				
Setting:	This was a prospective, single institution, open label single arm study conducted on non Hodgkin's lymphoma patients who were to receive rituximab at NCCS (Singapore)			Sample Size: 79	
☒ Experimental	☐ Meta-analysis	☐ Quasi-experimental	☐ Non-experimental	☐ Qualitative	☐ Meta-synthesis
Does this study apply to NHL patients?				☒ Yes	☐ No
If the answer is No, STOP here (unless there are similar characteristics)					
Strength of Study Design					
• Was the sample size adequate and appropriate?				☒ Yes	☐ No
• Were study participants randomized?				☐ Yes	☒ No
• Was there an intervention? 90 min infusion given without corticosteroid therapy				☒ Yes	☐ No
• Was there a control group?				☐ Yes	☒ No
• If there was more than one group, were groups equally treated, except for the intervention?				☐ Yes	☒ No
• Was there adequate description of the data collection methods?				☒ Yes	☐ No
Study Results					
• Were results clearly presented?				☒ Yes	☐ No
• Was an interpretation/analysis provided?				☒ Yes	☐ No
Study Conclusions					
• Were conclusion based on clearly presented results?				☒ Yes	☐ No
• Were study limitations identified and discussed?				☒ Yes	☐ No

Pertinent Study Findings and Recommendations:

The rapid infusion of rituximab over 90 min was well tolerated by patients when administered as the second and subsequent infusions in the course of therapy. The shortened infusion schedule helped to reduce resource utilization as well as brought time and cost savings to the patient. Patient education regarding infusion-related reactions with rituximab is crucial to aid in the identification of patients who are not suitable for the rapid infusion. Patients who are prone to nausea and vomiting should also be considered for omission from the rapid schedule pending further investigation.

Safety
A total of 79 patients were recruited with a total of 269 infusions administered. The rapid infusion of

rituximab was well tolerated without any Grade 3/4 infusion-related adverse events observed. In this study, three patients experienced post-infusion nausea and vomiting - not commonly listed as Grade 3 or 4 adverse reactions (1% for NHL patients).

Resource Utilization
Rituximab rapid infusion resulted in both time and costs savings in resource utilization savings as measured by reduced facility charges and total amount of chair time saved for patients and the center.

Recommendations
Patient education regarding infusion-related reactions with rituximab is crucial to aid in the identification of patients who are not suitable for the rapid infusion. Patients who are prone to nausea and vomiting should also be considered for omission from the rapid schedule pending further investigation**.**

Will the results answer the practice question?	☒ Yes	☐ No

Evidence Rating					
Strength of Evidence	☐ Level I (Strong)	☒ Level II	☐ Level III	☐ Level IV	☐ Level V
Quality of Evidence (check one)			☒ High (A)	☐ Good (B)	☐ Low/Major flaw (C)

RESEARCH- Appraisal

					Evidence Level: IIB	
Article Title: **A NURSE CAN SAFELY DELIVER RITUXIMAB OVER 90 MINUTES**						
Author(s)	Peggy **Corey**, RN, BSN, OCN®, Ronald Go, MD, and Ana Schaper, RN, PhD					Date: 2007
Journal:	*ONCOLOGY NURSING FORUM* – VOL 34, NO 2, 2007					
Setting:	Community-based cancer center			Sample Size: 33		
☒ Experimental	☐ Meta-analysis	☐ Quasi-experimental	☐ Non-experimental	☐ Qualitative		☐ Meta-synthesis
Does this study apply to NHL patients?				☒ Yes		☐ No
If the answer is No, STOP here (unless there are similar characteristics)						
Strength of Study Design						
• Was the sample size adequate and appropriate?				☐ Yes		☒ No
• Were study participants randomized?				☐ Yes		☒ No
• Was there an intervention?				☒ Yes		☐ No
• Was there a control group?				☐ Yes		☒ No
• If there was more than one group, were groups equally treated, except for the intervention?				☐ Yes N/A		☐ No N/A
• Was there adequate description of the data collection methods?				☐ Yes		☒ No
Study Results						
• Were results clearly presented?				☒ Yes		☐ No
• Was an interpretation/analysis provided?				☒ Yes		☐ No
Study Conclusions						
• Were conclusion based on clearly presented results?				☒ Yes		☐ No
• Were study limitations identified and discussed?				☐ Yes		☒ No

Pertinent Study Findings and Recommendations:

Safety

Patients, with NHL, were enrolled in this modified treatment program if they had received rituximab according to product monograph within the last 4 months, no prior Grade 3 or 4 infusion related toxicities, no contra-indication to fluid infusion of 200 ml/hr and an absolute lymphocyte count of <10,000. Patients were pre-medicated with acetaminophen and diphenhydramine.

Thirty-three patients were treated for total of 88 infusions (median 3). No adverse events were observed for the 90-minute rituximab infusions. Rituximab infused over 90-minute was safe in the treatment of NHL and well tolerated in this community cohort.

Patient Satisfaction and Resource Utilization

The reduced infusion time allowed patients more control and flexibility in treatment scheduling, and more time away from the facility. In addition, shorter infusion times improved access in the chemotherapy suite.

Recommendations

The rituximab 90-minute was safe and improved resource utilization and patient satisfaction as evidenced by providing patients with more flexibility in treatment scheduling, more time away from the facility and increasing access in the chemotherapy suite.

Will the results answer the practice question?			☒ Yes	☐ No	
Evidence Rating					
Strength of Evidence	☐ Level I (Strong)	☒ Level II	☐ Level III	☐ Level IV	☐ Level V
Quality of Evidence (check one)			☐ High (A)	☒ Good (B)	☐ Low/Major flaw (C)

RESEARCH- Appraisal

				Evidence Level: IIB	
Article Title: **Rapid Infusion of Rituximab Works in Community Setting**					
Author(s)	Chad **Coulter**, PharmD				Date: 2010
Journal:	*Clinical Oncology News* ISSUE: JANUARY 2010 I VOLUME: 05:01				
Setting:	3 community-based outpatient infusion clinics			Sample Size: 16	
☒ Experimental	☐ Meta-analysis	☐ Quasi-experimental	☐ Non-experimental	☐ Qualitative	☐ Meta-synthesis
Does this study apply to NHL patients?				☒ Yes	☐ No
If the answer is No, STOP here (unless there are similar characteristics)					
Strength of Study Design					
• Was the sample size adequate and appropriate?				☐ Yes	☒ No
• Were study participants randomized?				☐ Yes	☒ No
• Was there an intervention?				☒ Yes	☐ No
• Was there a control group?				☐ Yes	☒ No
• If there was more than one group, were groups equally treated, except for the intervention?				☐ Yes N/A	☐ No N/A
• Was there adequate description of the data collection methods?				☐ Yes	☒ No
Study Results					
• Were results clearly presented?				☒ Yes	☐ No
• Was an interpretation/analysis provided?				☒ Yes	☐ No
Study Conclusions					
• Were conclusion based on clearly presented results?				☒ Yes	☐ No
• Were study limitations identified and discussed?				☐ Yes	☒ No

Pertinent Study Findings and Recommendations:

Safety

Sixteen patients were enrolled and treated with a total of 51 rapid rituximab infusions. The median number of infusions each patient received was three (range, one to seven). Most of the patients were younger than 60 and male. Three patients experienced minor adverse reactions which were expected with rituximab administration.

Premedications were not standardized and could vary per facility protocol. We used a strict safety monitoring algorithm, measuring blood pressure, heart rate and respiratory rate before the infusion and at 15, 30, 60 and 90 minutes to monitor respiratory or cardiac symptoms. We also monitored temperature prior to the infusion
and questioned patients about adverse reactions throughout the infusion and at each visit.

Resource Utilization

The total infusion time saved compared with standard infusion rates was 2,925 minutes (49 hours; 57

minutes per infusion). Nursing staff, however, did feel that the intense monitoring schedule in this trial required equal attention to that of the standard infusion. If medical oncologists at these practice sites adopted this regimen as
standard practice, an easier monitoring schedule should be employed to free up nursing time and resources.

Patient and Nursing Satisfaction
Patient and nursing satisfaction, assessed through surveys, was extremely high in all but one statement

Recommendations
If medical oncologists adopt rituximab faster infusion as standard practice, an easier monitoring schedule than measuring blood pressure, heart rate and respiratory rate before the infusion and at 15, 30, 60 and 90 minutes to monitor respiratory or cardiac symptoms should be employed to free up nursing time and resources.

Will the results answer the practice question?	☒ Yes	☐ No

Evidence Rating					
Strength of Evidence	☐ Level I (Strong)	☒ Level II	☐ Level III	☐ Level IV	☐ Level V
Quality of Evidence (check one)			☐ High (A)	☒ Good (B)	☐ Low/Major flaw (C)

RESEARCH- Appraisal

				Evidence Level: IIA	
Article Title: **Assessment of safety regarding rapid rituximab infusion**					
Author(s)	Joshua T. **Swan**, PharmD, Jose R. Murillo, Jr., PharmD, BCOP, James E. Cox, PharmD, Beverley Lamoth, RN, MSN, OCN, and Kelty R. Baker, MD				Date: 2010
Journal:	*COMMUNITY ONCOLOGY,* Volume 7/Number 10				
Setting:	The Methodist Hospital outpatient and inpatient oncology units.			Sample Size: 13	
☒ Experimental	☐ Meta-analysis	☐ Quasi-experimental	☐ Non-experimental	☐ Qualitative	☐ Meta-synthesis
Does this study apply to NHL patients?				☒ Yes	☐ No
If the answer is No, STOP here (unless there are similar characteristics)					
Strength of Study Design					
• Was the sample size adequate and appropriate?				☐ Yes	☒ No
• Were study participants randomized?				☐ Yes	☒ No
• Was there an intervention?				☒ Yes	☐ No
• Was there a control group?				☐ Yes	☒ No
• If there was more than one group, were groups equally treated, except for the intervention?				☐ Yes N/A	☐ No N/A
• Was there adequate description of the data collection methods?				☒ Yes	☐ No
Study Results					
• Were results clearly presented?				☒ Yes	☐ No
• Was an interpretation/analysis provided?				☒ Yes	☐ No
Study Conclusions					
• Were conclusion based on clearly presented results?				☒ Yes	☐ No
• Were study limitations identified and discussed?				☒ Yes	☐ No

Pertinent Study Findings and Recommendations:

Safety

Thirteen patients were enrolled in this study for a total of 32 rapid rituximab infusions, all of which were administered in an outpatient setting. The rapid rituximab infusions were well tolerated by 12 of the 13 patients in 31 of 32 infusions. There was one Grade 3 reaction of prolonged hypotension, tachycardia, and fever, which resolved within 24 hours. No other symptomatic infusion reactions occurred. These results support previously reported data affirming the safety and tolerability of a rapid, 90-minute infusion for non-initial doses of rituximab in patients with CD20-positive B-cell malignancy.

Resource Utilization

Adopting a rapid infusion schedule would benefit patients and the institution by reducing clinic chair time for each dose by 1.5–2 hours, compared with standard infusion times.

Recommendations Adoption of a rapid administration protocol will succeed only if supported by the nursing staff. Strong nursing leadership and educational in-services highlighting safety data will help gain support and comfort required for nursing staff to treat patients with rituximab faster infusion and decreasing resource utilization of infusion clinic time by ensuring that premedication is given and that the rituximab faster infusion is started in a timely manner					
Will the results answer the practice question?			☒ Yes	☐ No	
Evidence Rating					
Strength of Evidence	☐ Level I	☒ Level II	☐ Level III	☐ Level IV	☐ Level V
Quality of Evidence (check one)			☒ High (A)	☐ Good (B)	☐ Low/Major flaw (C)

RESEARCH- Appraisal

				Evidence Level: IIB	
Article Title: **CASE REPORT: Rapid Infusion Rituximab Changing Practice for Patient Care**					
Author(s)	Ali Al **Zahrani**, MBBS FRCR, Nagwa Ibrahim, Pharm D, Ahmed Al Eid, PhD				Date: 2007
Journal:	*J Oncol Pharm Practice* (2009) 15: 183–186.				
Setting:	Department of Adult Oncology in Riyadh Military Hospital in Saudi Arabia			Sample Size: 21	
☒ Experimental	☐ Meta-analysis	☐ Quasi-experimental	☐ Non-experimental	☐ Qualitative	☐ Meta-synthesis
Does this study apply to NHL patients?				☒ Yes	☐ No
If the answer is No, STOP here (unless there are similar characteristics)					
Strength of Study Design					
• Was the sample size adequate and appropriate?				☐ Yes	☒ No
• Were study participants randomized?				☐ Yes	☒ No
• Was there an intervention?				☒ Yes	☐ No
• Was there a control group?				☐ Yes	☒ No
• If there was more than one group, were groups equally treated, except for the intervention?				☐ Yes N/A	☐ No N/A
• Was there adequate description of the data collection methods?				☒ Yes	☐ No
Study Results					
• Were results clearly presented?				☒ Yes	☐ No
• Was an interpretation/analysis provided?				☒ Yes	☐ No
Study Conclusions					
• Were conclusion based on clearly presented results?				☒ Yes	☐ No
• Were study limitations identified and discussed?				☐ Yes	☒ No

Pertinent Study Findings and Recommendations:

Safety
21 patients with non-Hodgkin's lymphoma were treated with rituximab-based chemotherapy. A total of 126 infusions were administered with average of 6 infusions per patient. The majority of patients were treated with CHOP–Rituximab or CHOP-like regimen. The 90-min Rituximab infusion schedule was well tolerated with no Grade 3/4 infusion related adverse events observed when administered as the second and subsequent infusions in the course of therapy.

Resource Utilization (Discussion- no data provided)
The disadvantages of long infusion times for rituximab include prolonged stays in the Chemotherapy Day Unit for treatment, which is inconvenient for patients, and there is additional workload for nurses. This shortened infusion schedule has resulted in a substantial reduction in resource utilization.

Recommendations

Preliminary data may be used to develop alternative guidelines for administration of rituximab to achieve resource utilization benefits.					
Will the results answer the practice question?			☒ Yes	☐ No	
Evidence Rating					
Strength of Evidence	☐ Level I (Strong)	☒ Level II	☐ Level III	☐ Level IV	☐ Level V
Quality of Evidence (check one)			☐ High (A)	☒ Good (B)	☐ Low/Major flaw (C)

RESEARCH- Appraisal

					Evidence Level: IIIA
Article Title**: Retrospective chart review of severe infusion reactions with rituximab, cetuximab, and bevacizumab in community oncology practices: assessment of clinical consequences**					
Author(s)	Lee S. **Schwartzberg** & Edward J. Stepanski & Barry V. Fortner & Arthur C. Hout				Date: 2008
Journal:	*Support Care Cancer* (2008) 16:393–398				
Setting:	19 community oncology centers affiliated with Accelerated Community Oncology Research Network (ACORN), based in Memphis, TN			Sample Size: 76 patients identified with a severe IR: 47 cases associated with rituximab	
☐ Experimental	☐ Meta-analysis	☐ Quasi-experimental	☒ Nonexperimental	☐ Qualitative	☐ Meta-synthesis
Does this study apply to NHL patients?				☒ Yes	☐ No
If the answer is No, STOP here (unless there are similar characteristics)					
Strength of Study Design					
• Was the sample size adequate and appropriate?				☒ Yes	☐ No
• Were study participants randomized?				☐ Yes	☒ No
• Was there an intervention?				☐ Yes	☒ No
• Was there a control group?				☐ Yes	☒ No
• If there was more than one group, were groups equally treated, except for the intervention?				☐ Yes N/A	☐ No N/A
• Was there adequate description of the data collection methods?				☒ Yes	☐ No
Study Results					
• Were results clearly presented?				☒ Yes	☐ No
• Was an interpretation/analysis provided?				☒ Yes	☐ No
Study Conclusions					
• Were conclusion based on clearly presented results?				☒ Yes	☐ No
• Were study limitations identified and discussed?				☒ Yes	☐ No

Pertinent Study Findings and Recommendations:

Safety

- 47 cases associated with rituximab, All patients treated with rituximab had a hematologic malignancy
- 21% in the rituximab group received corticosteroids before MoAb treatment
- Nearly half of the patients who received rituximab and experienced a severe IR were receiving rituximab alone
- 17% of rituximab Grade 3 IRs resulted in permanent discontinuation. For those not discontinuing, dose delays and infusion rate reductions were common, but actual dose reduction was rare

Resource Utilization (Discussion- no data provided)

Severe IRs have substantial cascading effects in clinical resources and workflow. A severe IR requires chemotherapy nurses, technicians, and doctors to make severe adjustments to maintain care of already scheduled patients. **Recommendations** Having well-rehearsed plans and procedures for handling these events can help staff to reassure other patients in general and especially those who may be receiving similar therapies					
Will the results answer the practice question?			☒ Yes	☐ No	
Evidence Rating					
Strength of Evidence	☐ Level I (Strong)	☐ Level II	☒ Level III	☐ Level IV	☐ Level V
Quality of Evidence (check one)			☒ High (A)	☐ Good (B)	☐ Low/Major flaw (C)

RESEARCH- Appraisal

				Evidence Level: IIA	
Article Title: **Final results of a single arm phase III multicenter, open-label study of rituximab administered by faster infusion in patients with previously untreated diffuse large B-cell (DLBCL) or follicular non-Hodgkin's lymphoma (FL)**					
Author(s)	Shaker **Dakhil**, MD, Robert Hermann, MD, Akiko Chai, MS, Deborah Hurst, MD, Gregg Fine, MD, and Paul Richards, MD				Date: 2011
Journal:	*Poster presented at the 53rd American Society of Hematology Annual Meeting*				
Setting:	82 sites across the US			Sample Size: 451 patients	
☐ Experimental	☐ Meta-analysis	☒ Quasi-experimental	☐ Non-experimental	☐ Qualitative	☐ Meta-synthesis
Does this study apply to NHL patients?				☒ Yes	☐ No
If the answer is No, STOP here (unless there are similar characteristics)					
Strength of Study Design					
• Was the sample size adequate and appropriate?				☒ Yes	☐ No
• Were study participants randomized?				☐ Yes	☒ No
• Was there an intervention?				☒ Yes	☐ No
• Was there a control group?				☐ Yes	☒ No
• If there was more than one group, were groups equally treated, except for the intervention?				☐ Yes N/A	☐ No N/A
• Was there adequate description of the data collection methods?				☒ Yes	☐ No
Study Results					
• Were results clearly presented?				☒ Yes	☐ No
• Was an interpretation/analysis provided?				☒ Yes	☐ No
Study Conclusions					
• Were conclusion based on clearly presented results?				☒ Yes	☐ No
• Were study limitations identified and discussed?				☐ Yes	☒ No

Pertinent Study Findings and Recommendations:

Safety

- Pretreatment: acetaminophen, antihistamine and the oral steroid component of the patient's chemo – no additional steroids were permitted.
- The target duration of 90 minutes for the faster infusions was maintained over Cycles 2–8, reflecting compliance with the protocol and demonstrating the feasibility of the schedule. (Of 1764 infusions administered at the faster rate the median infusion duration was 90 minutes.)
- The incidence of Grade 3/4 IRRs at Cycle 2 was low (1.1%) and the rate of IRRs decreased with subsequent administrations
- **Only 10 patients (2.8%) experienced Grade 3/4 IRRs during Cycles 2–8**
- There were no fatal IRRs or fatal AEs on Days 1–2 at any cycle in this study, and there were no unexpected events or acute fatal events associated with the faster infusion schedule

Recommendations

Results from this study confirm that the 90-minute infusion schedule for rituximab is safe and feasible in NHL patients who tolerate their first infusion administered at the standard rate and who do not have significant cardiovascular disease or high circulating lymphocytes					
Will the results answer the practice question?			☒ Yes	☐ No	
Evidence Rating					
Strength of Evidence	☐ Level I (Strong)	☒ Level II	☐ Level III	☐ Level IV	☐ Level V
Quality of Evidence (check one)			☒ High (A)	☐ Good (B)	☐ Low/Major flaw (C)

RESEARCH- Appraisal

					Evidence Level: IIIA
Article Title: **Nursing Takes Time: Workload Associated With Administering Cancer Protocols**					
Author(s)	Johan **de Raad**, BSc, Kees van Gool, M.Ec, Marion Haas, PhD, Philip Haywood, M.Ec, Margaret Faedo, PhD, Gisselle Gallego, PhD, Sallie Pearson, PhD, and Robyn Ward, PhD				Date: 2010
Journal:	*Clinical Journal of Oncology Nursing* • Volume 14, Number 6				
Setting:	New South Wales, Australia			Sample Size: 36 nurses participated in six discussion group sessions	
☐ Experimental	☐ Meta-analysis	☐ Quasi-experimental	☐ Non-experimental	☒ Qualitative	☐ Meta-synthesis
Does this study apply to NHL patients?				☒ Yes	☐ No
If the answer is No, STOP here (unless there are similar characteristics)					
Strength of Study Design					
• Was the sample size adequate and appropriate?				☒ Yes	☐ No
• Were study participants randomized?				☐ Yes	☒ No
• Was there an intervention?				☐ Yes	☒ No
• Was there a control group?				☐ Yes	☒ No
• If there was more than one group, were groups equally treated, except for the intervention?				☐ Yes N/A	☐ No N/A
• Was there adequate description of the data collection methods?				☒ Yes	☐ No
Study Results					
• Were results clearly presented?				☒ Yes	☐ No
• Was an interpretation/analysis provided?				☒ Yes	☐ No
Study Conclusions					
• Were conclusion based on clearly presented results?				☒ Yes	☐ No
• Were study limitations identified and discussed?				☒ Yes	☐ No

Pertinent Study Findings and Recommendations:

Resource Utilization

Article examines the nursing workload of administering alternative chemotherapy protocols as a driver of costs. Data collection (focus groups with chemotherapy nurses and a survey of nurse unit managers) was conducted to ascertain the time required to undertake chemotherapy-related tasks and the sources of variability in six chemotherapy centers in New South Wales, Australia.

Four task types and time averages associated with administering chemotherapy:

1. patient education - 48 minutes during the first visit and 18.5 minutes thereafter
2. patient assessment - 20.3 minutes,
3. administration - 23 minutes,
4. patient communication - 24.2 minutes

Each patient received 3.3 hours of staff time (1.7 hours of direct contact time and 1.6 hours of

<table>
<tr><td colspan="6">noncontact time).

Recommendations <u>(A major limitation of this study is that it is not specific to rituximab faster infusion)</u>
These data will allow healthcare decision makers and evaluators to predict the amount of nursing time required to administer chemotherapy based on the characteristics of a wide range of chemotherapy protocols.</td></tr>
<tr><td colspan="4">Will the results answer the practice question?</td><td>☒ Yes</td><td>☐ No</td></tr>
<tr><td colspan="6">Evidence Rating</td></tr>
<tr><td>Strength of Evidence</td><td>☐ Level I (Strong)</td><td>☐ Level II</td><td>☒ Level III</td><td>☐ Level IV</td><td>☐ Level V</td></tr>
<tr><td colspan="3">Quality of Evidence (check one)</td><td>☒ High (A)</td><td>☐ Good (B)</td><td>☐ Low/Major flaw (C)</td></tr>
</table>

RESEARCH- Appraisal

				Evidence Level: IIIA	
Article Title: **Implications of IV monoclonal antibody infusion reaction for the patient, caregiver, and practice: results of a multicenter study**					
Author(s)	Lee S. **Schwartzberg**, Edward J. Stepanski, Mark S. Walker, Susan Mathias, Arthur C. Houts & Barry V. Fortner				Date: 2009
Journal:	*Support Care Cancer* (2009) 17:91–98				
Setting:	27 community US oncology sites			Sample Size: 161 were enrolled. Of these, 90 were treated with rituximab	
☐ Experimental	☐ Meta-analysis	☐ Quasi-experimental	☐ Non-experimental	☒ Qualitative	☐ Meta-synthesis
Does this study apply to NHL patients? N=72 (80% rituximab pts)				☒ Yes	☐ No
If the answer is No, STOP here (unless there are similar characteristics)					
Strength of Study Design					
• Was the sample size adequate and appropriate?				☒ Yes	☐ No
• Were study participants randomized?				☐ Yes	☒ No
• Was there an intervention?				☐ Yes	☒ No
• Was there a control group?				☐ Yes	☒ No
• If there was more than one group, were groups equally treated, except for the intervention?				☐ Yes N/A	☐ No N/A
• Was there adequate description of the data collection methods?				☒ Yes	☐ No
Study Results					
• Were results clearly presented?				☒ Yes	☐ No
• Was an interpretation/analysis provided?				☒ Yes	☐ No
Study Conclusions					
• Were conclusion based on clearly presented results?				☒ Yes	☐ No
• Were study limitations identified and discussed?				☒ Yes	☐ No

Pertinent Study Findings and Recommendations:

Resource Utilization

A prospective multicenter study involving time and motion and activity sampling methods was conducted among patients with cancer receiving their first outpatient infusion of cetuximab or rituximab. Patients were observed from initiation of MoAb infusion to the end of the clinic visit. IRRs were classified as absent, mild/moderate, and severe/life threatening. Staff time and costs were estimated for preparation and administration of MoAb, other chemotherapy agents, and for management of IRRs. Resource costs were compared across IR groups within each MoAb. IRRs following rituximab administration are common and are associated with measurably increased costs of care Among 161 patients enrolled, 39% of 90 patients on rituximab experienced IRs.

Treatment of patients who experienced IRs required more staff time (31–80% more time) and resulted in higher human resource costs (increase of 17–65 US dollars) than patients who did not experience

IRs. For rituximab patients, the staff time required for rituximab infusion was 164.6 min for patients who had IRs and 123.3 min for those who did not and a statistically significant finding was mean human resource costs ranging from $54 to $118 for no IR to mild/moderate IR: F (2, 6.448)=5.858, p=.035 (mild/moderate > no IR). **Recommendations** The frequency of IRs suggests the importance of identifying clinical guidelines for intervention and management. The methods used in this study could be employed for any direct comparison of chemotherapy regimens that purports to examine treatment cost as an outcome.					
Will the results answer the practice question?				☒ Yes	☐ No
Evidence Rating					
Strength of Evidence	☐ Level I	☐ Level II	☒ Level III	☐ Level IV	☐ Level V
Quality of Evidence (check one)			☒ High (A)	☐ Good (B)	☐ Low/Major flaw (C)

RESEARCH- Appraisal

					Evidence Level: IIIA
Article Title: **The Impact of Infusion Reactions on Oncology Patients and Clinicians in the Inpatient and Outpatient Practice Settings**					
Author(s)	Hilary H. **Colwell,** MPH, Susan D. Mathias, MPH, Nita H. Ngo, MPH, Matthew Gitlin, PharmD, Z. John Lu, PhD, Teresa Knoop, RN, MSN, AOCN				Date: 2007
Journal:	*Journal of Infusion Nursing, Vol. 30, No. 3, May/June 2007*				
Setting:	Inpatient and Outpatient Practice Settings			Sample Size: 202 nurses (99% women)	
☐ Experimental	☐ Meta-analysis	☐ Quasi-experimental	☐ Non-experimental	☒ Qualitative	☐ Meta-synthesis
Does this study apply to NHL patients?				☒ Yes	☐ No
If the answer is No, STOP here (unless there are similar characteristics)					
Strength of Study Design					
• Was the sample size adequate and appropriate?				☒ Yes	☐ No
• Were study participants randomized?				☐ Yes	☒ No
• Was there an intervention?				☐ Yes	☒ No
• Was there a control group?				☐ Yes	☒ No
• If there was more than one group, were groups equally treated, except for the intervention?				☐ Yes N/A	☐ No N/A
• Was there adequate description of the data collection methods?				☒ Yes	☐ No
Study Results					
• Were results clearly presented?				☒ Yes	☐ No
• Was an interpretation/analysis provided?				☒ Yes	☐ No
Study Conclusions					
• Were conclusion based on clearly presented results?				☒ Yes	☐ No
• Were study limitations identified and discussed?				☒ Yes	☐ No

Pertinent Study Findings and Recommendations:

Nursing Practice

- Most nurses reported that administration with rituximab or paclitaxel resulted in the most frequent infusion reactions (46% and 27%, respectively).
- 96% reported that Grade 3 or 4 infusion reactions were “very” or “extremely” disruptive for patients, and most nurses indicated that Grade 3 or 4 infusion reactions were disruptive to the nurses (80%).
- 95% agreed with the statement, “Infusion reactions can result in lost time and increased patient anxiety”), with a greater proportion of outpatient nurses than inpatient nurses agreeing or strongly agreeing with this statement (98% versus 90%, respectively; $P \leq .05$).
- Infusion reactions associated with parenteral monoclonal antibody treatments and chemotherapy are disruptive and emotionally challenging for patients receiving the treatment

and the nurses and staff at the institution or practice treating them. **Recommendations** • The results suggested that further awareness of infusion reaction management and education of patients and clinicians are needed.					
Will the results answer the practice question?			☒ Yes	☐ No	
Evidence Rating					
Strength of Evidence	☐ Level I	☐ Level II	☒ Level III	☐ Level IV	☐ Level V
Quality of Evidence (check one)			☒ High (A)	☐ Good (B)	☐ Low/Major flaw (C)

RESEARCH- Appraisal

				Evidence Level: IIIA	
Article Title: **Oncology Nurses' Perceptions About Involving Patients in the Prevention of Chemotherapy Administration Errors**					
Author(s)	David L.B. **Schwappach,** MPH, PhD, Marc-Anton Hochreutener, MD, and Martin Wernli, MD				Date: 2010
Journal:	*Oncology Nursing Forum* Vol. 37, No. 2, March 2010				
Setting:	Outpatient oncology units of a community hospital in Switzerland			Sample Size: 11 actively practicing oncology nurses	
☐ Experimental	☐ Meta-analysis	☐ Quasi-experimental	☐ Non-experimental	☒ Qualitative	☐ Meta-synthesis
Does this study apply to NHL patients?				☒ Yes	☐ No
If the answer is No, STOP here (unless there are similar characteristics)					
Strength of Study Design					
• Was the sample size adequate and appropriate? N=11				☐ Yes	☒ No
• Were study participants randomized?				☐ Yes	☒ No
• Was there an intervention?				☐ Yes	☒ No
• Was there a control group?				☐ Yes	☒ No
• If there was more than one group, were groups equally treated, except for the intervention?				☐ Yes N/A	☐ No N/A
• Was there adequate description of the data collection methods?				☒ Yes	☐ No
Study Results					
• Were results clearly presented?				☒ Yes	☐ No
• Was an interpretation/analysis provided?				☒ Yes	☐ No
Study Conclusions					
• Were conclusion based on clearly presented results?				☒ Yes	☐ No
• Were study limitations identified and discussed?				☒ Yes	☐ No

Pertinent Study Findings and Recommendations:

Nursing Practice
Oncology nurses perceive patient education in safety as a core element of their professional role and are receptive to advancing their expertise in this area. Engaging patients was described as a challenge and nurses acknowledged the diverse needs of patients and deliberately used different strategies to involve patients in safety.

Recommendations
Oncology nurses should include patient involvement in error prevention given the reported positive experiences.

Will the results answer the practice question?	☒ Yes	☐ No

Evidence Rating					
Strength of	☐ Level I	☐ Level	☒ Level	☐ Level IV	☐ Level V

Evidence	(Strong)	II	III		
Quality of Evidence (check one)			☒ High (A)	☐ Good (B)	☐ Low/Major flaw (C)

NON-RESEACH Appraisal

				Evidence Rating: VA
Article Title: **Cytokine-Release Syndrome: Overview and Nursing Implications**				
Author(s)	**Breslin**, S			Date: 2007
Journal: *Clinical Journal of Oncology Nursing* • Supplement to Volume 11, Number 1 • Cytokine-Release Syndrome				
☐ Systematic Review	☐ Clinical Practice Guidelines	☐ Organizational (QI, QA, PT, financial data)	☒ Expert opinion, case study, literature review	
Does this study apply to the population targeted for my practice question?			☒ Yes	☐ No
If the answer is No, STOP here (unless there are similar characteristics)				

Systemic Review		
• Is the question clear?	☐ Yes	☐ No
• Was a rigorous peer-review process used?	☐ Yes	☐ No
• Are search strategies specified, and reproducible?	☐ Yes	☐ No
• Are search strategies appropriate to include all pertinent studies?	☐ Yes	☐ No
• Are criteria for inclusion and exclusion of studies specified?	☐ Yes	☐ No
• Are details of included studies (design, methods, analysis) presented?	☐ Yes	☐ No
• Are methodological limitations disclosed?	☐ Yes	☐ No
• Are the variables in the studies reviewed similar, so that studies can be combined?	☐ Yes	☐ No
Clinical Practice Guidelines		
• Were appropriate stakeholders involved in the development of this guideline?	☐ Yes	☐ No
• Are groups to which guidelines apply and do apply clearly stated?	☐ Yes	☐ No
• Have potential biases been eliminated?	☐ Yes	☐ No
• Were guidelines valid (reproducible search, expert consensus, independent review, current, and level of supporting evidence identified for each recommendation)?	☐ Yes	☐ No
• Are recommendations clear?	☐ Yes	☐ No
Organizational Experience		
• Was the aim of the project clearly stated?	☐ Yes	☐ No
• Is the setting similar to setting of interest?	☐ Yes	☐ No
• Was the methodology adequately described?	☐ Yes	☐ No
• Were measures identified?	☐ Yes	☐ No
• Were results adequately described?	☐ Yes	☐ No
• Was interpretation clear and appropriate?	☐ Yes	☐ No
Individual expert opinion, case study, literature review		
• Was evidence based in the opinion of an individual?	☒ Yes	☐ No
• Is the individual an expert in the topic?	☒ Yes	☐ No
• Is author's opinion based on scientific evidence?	☒ Yes	☐ No

• Is the author's opinion clearly stated?	☒ Yes	☐ No
• Are potential biases acknowledged?	☒ Yes	☐ No

Pertinent Study Findings and Recommendations:

Safety

Article describes principles related to cytokine-release syndrome in patients receiving MoAbs:

- When a MoAb binds to an antigen on the target cell, chemokines recruit monocytes, macrophages, cytotoxic T cells, natural killer cells, and complement to the area. The immune effector cells bind to the fragment crystallizable or constant portion of the antibody, targeting the cell for destruction by phagocytosis and cytolysis.
- When the cell is destroyed, cytokines are released into the circulation from the targeted cell as well as immune effector cells that have been recruited The constellation of associated symptoms is known as cytokine-release syndrome.
- Massive cytokine-release syndrome is an oncologic emergency; special precautions are necessary for patients at high risk.

Recommendations

1. Prior to administering any MOAB, nurses should be familiar with its toxicity profile, including the potential for acute and delayed infusion-related side effects.
2. The need for specific pre-medications should be assessed.
    a. For patients with circulating lymphocyte counts of 25,000/mm3 or higher, the addition of corticosteroids and histamine-2 receptor antagonists to the usual pre-medications is recommended.
    b. Hospitalization of such patients for inpatient administration of medication and close monitoring should be strongly considered
3. MOABs always should be administered piggy-back into the distal port of a main IV line and never should be given as an IV bolus.
4. An infusion pump always should be used for administration. The first infusion should be administered slowly. Subsequent infusions may be given more rapidly as tolerated and per package instructions.

Will the results answer the practice question?				☒ Yes	☐ No
Evidence Rating					
Strength of Evidence	☐ Level I (Strong)	☐ Level II	☐ Level III	☐ Level IV	☒ Level V
Quality of Evidence (check one)			☒ High (A)	☐ Good (B)	☐ Low/Major flaw (C)

NON-RESEACH Appraisal

				Evidence Rating: VA
Article Title: **Managing Premedications and the Risk for Reactions to Infusional Monoclonal Antibody Therapy**				
Author(s)	**Chung**, C			Date: 2008
Journal: *The Oncologist*;13:725–732 www.TheOncologist.com				
☐ Systematic Review	☐ Clinical Practice Guidelines	☐ Organizational (QI, QA, PT, financial data)	☒ Expert opinion, case study, **literature review**	
Does this study apply to the population targeted for my practice question?			☒ Yes	☐ No
If the answer is No, STOP here (unless there are similar characteristics)				
Systemic Review				
• Is the question clear?			☐ Yes	☐ No
• Was a rigorous peer-review process used?			☐ Yes	☐ No
• Are search strategies specified, and reproducible?			☐ Yes	☐ No
• Are search strategies appropriate to include all pertinent studies?			☐ Yes	☐ No
• Are criteria for inclusion and exclusion of studies specified?			☐ Yes	☐ No
• Are details of included studies (design, methods, analysis) presented?			☐ Yes	☐ No
• Are methodological limitations disclosed?			☐ Yes	☐ No
• Are the variables in the studies reviewed similar, so that studies can be combined?			☐ Yes	☐ No
Clinical Practice Guidelines				
• Were appropriate stakeholders involved in the development of this guideline?			☐ Yes	☐ No
• Are groups to which guidelines apply and do apply clearly stated?			☐ Yes	☐ No
• Have potential biases been eliminated?			☐ Yes	☐ No
• Were guidelines valid (reproducible search, expert consensus, independent review, current, and level of supporting evidence identified for each recommendation)?			☐ Yes	☐ No
• Are recommendations clear?			☐ Yes	☐ No
Organizational Experience				
• Was the aim of the project clearly stated?			☐ Yes	☐ No
• Is the setting similar to setting of interest?			☐ Yes	☐ No
• Was the methodology adequately described?			☐ Yes	☐ No
• Were measures identified?			☐ Yes	☐ No
• Were results adequately described?			☐ Yes	☐ No
• Was interpretation clear and appropriate?			☐ Yes	☐ No
Individual expert opinion, case study, literature review				
• Was evidence based in the opinion of an individual?			☒ Yes	☐ No
• Is the individual an expert in the topic?			☒ Yes	☐ No

• Is author's opinion based on scientific evidence?	☒ Yes	☐ No
• Is the author's opinion clearly stated?	☒ Yes	☐ No
• Are potential biases acknowledged?	☒ Yes	☐ No

Pertinent Study Findings and Recommendations:

Safety
Monoclonal antibodies, like other infused agents, are associated with a risk for infusion reactions, although for most, the incidence of severe events is rare. Improving risk assessment for infusion reactions has become a compelling medical need.

Recommendations

- Patients with high circulating malignant cell counts are at risk for severe infusion reactions to rituximab. Premedications are considered standard procedure for minimizing the risk for infusion reactions.
- Because most infusion reactions with monoclonal antibodies occur after the first or second infusion, the value of premedication on subsequent infusions may decrease.

Will the results answer the practice question?	☒ Yes	☐ No

Evidence Rating

Strength of Evidence	☐ Level I (Strong)	☐ Level II	☐ Level III	☐ Level IV	☒ Level V
Quality of Evidence (check one)			☒ High (A)	☐ Good (B)	☐ Low/Major flaw (C)

NON-RESEACH Appraisal

				Evidence Rating: VA
Article Title: **Infusion Reactions: Diagnosis, Assessment, and Management**				
Author(s)	**Vogel**, W			Date: 2010
Journal: *Clinical Journal of Oncology Nursing*, Volume 14, Number 2 •				
☐ Systematic Review	☐ Clinical Practice Guidelines	☐ Organizational (QI, QA, PT, financial data)	☒ Expert opinion, case study, literature review	
Does this study apply to the population targeted for my practice question?			☒ Yes	☐ No
If the answer is No, STOP here (unless there are similar characteristics)				
Systemic Review				
• Is the question clear?			☐ Yes	☐ No
• Was a rigorous peer-review process used?			☐ Yes	☐ No
• Are search strategies specified, and reproducible?			☐ Yes	☐ No
• Are search strategies appropriate to include all pertinent studies?			☐ Yes	☐ No
• Are criteria for inclusion and exclusion of studies specified?			☐ Yes	☐ No
• Are details of included studies (design, methods, analysis) presented?			☐ Yes	☐ No
• Are methodological limitations disclosed?			☐ Yes	☐ No
• Are the variables in the studies reviewed similar, so that studies can be combined?			☐ Yes	☐ No
Clinical Practice Guidelines				
• Were appropriate stakeholders involved in the development of this guideline?			☐ Yes	☐ No
• Are groups to which guidelines apply and do apply clearly stated?			☐ Yes	☐ No
• Have potential biases been eliminated?			☐ Yes	☐ No
• Were guidelines valid (reproducible search, expert consensus, independent review, current, and level of supporting evidence identified for each recommendation)?			☐ Yes	☐ No
• Are recommendations clear?			☐ Yes	☐ No
Organizational Experience				
• Was the aim of the project clearly stated?			☐ Yes	☐ No
• Is the setting similar to setting of interest?			☐ Yes	☐ No
• Was the methodology adequately described?			☐ Yes	☐ No
• Were measures identified?			☐ Yes	☐ No
• Were results adequately described?			☐ Yes	☐ No
• Was interpretation clear and appropriate?			☐ Yes	☐ No
Individual expert opinion, case study, literature review				
• Was evidence based in the opinion of an individual?			☒ Yes	☐ No
• Is the individual an expert in the topic?			☒ Yes	☐ No
• Is author's opinion based on scientific evidence?			☒ Yes	☐ No
• Is the author's opinion clearly stated?			☒ Yes	☐ No
• Are potential biases acknowledged?			☒ Yes	☐ No

Pertinent Study Findings and Recommendations:

Safety

Safety assessments from six studies of rituximab used as a single agent in previously treated patients with indolent non-Hodgkin lymphoma (Davis et al., 1999, 2000; Maloney et al., 1994; Maloney, Grillo-Lopez, Bodkin, et al., 1997; Maloney, Grillo-Lopez, White, et al., 1997; McLaughlin et al., 1998; Piro et al., 1999) gave an i**ncidence of infusion-related reaction in 77% (7% Grades 3–4) of patients during the first infusion, 30% (2% Grades 3–4) during the fourth infusion, and 14% (no Grade 3–4 events) during the eighth infusion**. The reactions generally occurred within 30 minutes to two hours after initiation of the infusion and resolved with slowing or interruption of the infusion and supportive care.

Rituximab is associated with infusion reactions that are caused primarily by cytokine release rather than true allergic reactions.

Recommendations

- Prompt and accurate documentation of the infusion event including accurate grading of the event will enable the prescribing clinician to decide whether re-challenge is feasible and safe.
- Re-challenge may include the re-administration of antihistamines and corticosteroids, followed by administration of the agent at a reduced rate.

Will the results answer the practice question?				☒ Yes	☐ No
Evidence Rating					
Strength of Evidence	☐ Level I (Strong)	☐ Level II	☐ Level III	☐ Level IV	☒ Level V
Quality of Evidence (check one)			☒ High (A)	☐ Good (B)	☐ Low/Major flaw (C)

NON-RESEACH Appraisal

			Evidence Rating: VB
Article Title: **Ninety-Minute Rituximab Infusions Can Be Performed Safely in Non-Hodgkin's Lymphoma**			
Author(s)	Alison **Palkhivala**		Date: 2007
Journal: *Oncology Nursing Society 32nd Annual Congress*: Abstract 2010. April 24-27, 2007.			
☐ Systematic Review	☐ Clinical Practice Guidelines	☐ Organizational (QI, QA, PT, financial data)	☒ Expert opinion, case study, literature review
Does this study apply to the population targeted for my practice question?		☒ Yes	☐ No
If the answer is No, STOP here (unless there are similar characteristics)			

Systemic Review		
• Is the question clear?	☐ Yes	☐ No
• Was a rigorous peer-review process used?	☐ Yes	☐ No
• Are search strategies specified, and reproducible?	☐ Yes	☐ No
• Are search strategies appropriate to include all pertinent studies?	☐ Yes	☐ No
• Are criteria for inclusion and exclusion of studies specified?	☐ Yes	☐ No
• Are details of included studies (design, methods, analysis) presented?	☐ Yes	☐ No
• Are methodological limitations disclosed?	☐ Yes	☐ No
• Are the variables in the studies reviewed similar, so that studies can be combined?	☐ Yes	☐ No
Clinical Practice Guidelines		
• Were appropriate stakeholders involved in the development of this guideline?	☐ Yes	☐ No
• Are groups to which guidelines apply and do apply clearly stated?	☐ Yes	☐ No
• Have potential biases been eliminated?	☐ Yes	☐ No
• Were guidelines valid (reproducible search, expert consensus, independent review, current, and level of supporting evidence identified for each recommendation)?	☐ Yes	☐ No
• Are recommendations clear?	☐ Yes	☐ No
Organizational Experience		
• Was the aim of the project clearly stated?	☐ Yes	☐ No
• Is the setting similar to setting of interest?	☐ Yes	☐ No
• Was the methodology adequately described?	☐ Yes	☐ No
• Were measures identified?	☐ Yes	☐ No
• Were results adequately described?	☐ Yes	☐ No
• Was interpretation clear and appropriate?	☐ Yes	☐ No
Individual expert opinion, case study, literature review		
• Was evidence based in the opinion of an individual?	☒ Yes	☐ No
• Is the individual an expert in the topic?	☒ Yes	☐ No
• Is author's opinion based on scientific evidence?	☒ Yes	☐ No

• Is the author's opinion clearly stated?	☒ Yes	☐ No
• Are potential biases acknowledged?	☒ Yes	☐ No

Pertinent Study Findings and Recommendations:

Barbara Rogers, CRNP, MN, AOCN, an adult hematology-oncology nurse practitioner at Fox Chase Cancer Center in Philadelphia, Pennsylvania, agreed that rapid infusions of rituximab are highly desirable, if safe, because most major cancer centers have more patients than they have treatment space.

Patient and Nurse Satisfaction
"Patients were pleased with shortened infusion times, more time away from [the] facility, [and] more control and flexibility in [their] treatment scheduling."

Resource Utilization
Rituximab faster infusion*"… will make a huge difference to practice to free up those [treatment] chairs*."

Recommendations
According to Rogers, before rituximab faster infusion becomes standard practice in the United States more data is needed because of the large impact that faster infusion this will have on nursing practice and resource utilization.

Will the results answer the practice question?	☒ Yes	☐ No

Evidence Rating					
Strength of Evidence	☐ Level I (Strong)	☐ Level II	☐ Level III	☐ Level IV	☒ Level V
Quality of Evidence (check one)			☐ High (A)	☒ Good (B)	☐ Low/Major flaw (C)

NON-RESEACH Appraisal

				Evidence Rating: VA
Article Title: **Health Economic Analysis of the Burden of Infusion Reactions on Patients, Caregivers, and Providers**				
Author(s)	Barry **Fortner**, PhD & Pamela Hallquist Viale, RN, MS, CS, ANP, AOCNP			Date: 2009
Journal: *ONCOLOGY*. Vol. 23 No. 2 Supplement				
☐ Systematic Review	☐ Clinical Practice Guidelines	☐ Organizational (QI, QA, PT, financial data)	☒ Expert opinion, case study, literature review	
Does this study apply to the population targeted for my practice question?			☒ Yes	☐ No
If the answer is No, STOP here (unless there are similar characteristics)				
Systemic Review				
• Is the question clear?			☐ Yes	☐ No
• Was a rigorous peer-review process used?			☐ Yes	☐ No
• Are search strategies specified, and reproducible?			☐ Yes	☐ No
• Are search strategies appropriate to include all pertinent studies?			☐ Yes	☐ No
• Are criteria for inclusion and exclusion of studies specified?			☐ Yes	☐ No
• Are details of included studies (design, methods, analysis) presented?			☐ Yes	☐ No
• Are methodological limitations disclosed?			☐ Yes	☐ No
• Are the variables in the studies reviewed similar, so that studies can be combined?			☐ Yes	☐ No
Clinical Practice Guidelines				
• Were appropriate stakeholders involved in the development of this guideline?			☐ Yes	☐ No
• Are groups to which guidelines apply and do apply clearly stated?			☐ Yes	☐ No
• Have potential biases been eliminated?			☐ Yes	☐ No
• Were guidelines valid (reproducible search, expert consensus, independent review, current, and level of supporting evidence identified for each recommendation)?			☐ Yes	☐ No
• Are recommendations clear?			☐ Yes	☐ No
Organizational Experience				
• Was the aim of the project clearly stated?			☐ Yes	☐ No
• Is the setting similar to setting of interest?			☐ Yes	☐ No
• Was the methodology adequately described?			☐ Yes	☐ No
• Were measures identified?			☐ Yes	☐ No
• Were results adequately described?			☐ Yes	☐ No
• Was interpretation clear and appropriate?			☐ Yes	☐ No
Individual expert opinion, case study, literature review				
• Was evidence based in the opinion of an individual?			☒ Yes	☐ No
• Is the individual an expert in the topic?			☒ Yes	☐ No

• Is author's opinion based on scientific evidence?	☒ Yes	☐ No
• Is the author's opinion clearly stated?	☒ Yes	☐ No
• Are potential biases acknowledged?	☒ Yes	☐ No

Pertinent Study Findings and Recommendations:

Review of literature regarding the specific burden, including tasks and associated costs, that IRs have on the patient and caregivers, and application of this information to help manage IRs. The potential burden that MoAb-induced IRs can have on both nurses and patients is reviewed to assist in guiding clinical decisions.

Overall, severe infusion reactions associated with use of monoclonal antibodies (MoAb) resulted in increased estimates of time spent by staff to manage the infusion reactions, which resulted in increased human resource costs.

Of 76 patients who experienced a severe IR (Grades 3–5), 47 were treated with rituximab, 64% were treated for non-Hodgkin's lymphoma and 68% of rituximab patients received MoAb therapy as first-line treatment. 55.3% of rituximab patients were pre-medicated with antihistamines and 61.7% were pre-medicated with acetaminophen. NOTE: premedication is recommended for all patients receiving rituximab.

For the incidence of severe IRs, 87% of rituximab had Grade 3 IRs with 66% of rituximab IRs occurring during the first administration of the agent. For Grade 4 reactions 83% of rituximab IRs required hospitalization, with a mean hospitalization stay of 5 to 6 days.

Time and motion studies are suggested as a model for community oncology centers to assess the tasks involved and the associated costs in treating IRs caused by therapies such as rituximab and help community oncology centers to evaluate their intervention strategies for IRs that may have a significant impact on centers with limited staff resources.

The incidence of an IR resulted in increased MoAb infusion times and staff time, leading to increased human resource costs. Compared to patients not experiencing IRs, statistically significant increases in staff time during infusion were observed in patients experiencing IRs. Prevention, including patient education about IR risks, and proper management of IRs may minimize these expenses for patients and families.

Will the results answer the practice question?	☒ Yes	☐ No

Evidence Rating

Strength of Evidence	☐ Level I (Strong)	☐ Level II	☐ Level III	☐ Level IV	☒ Level V
Quality of Evidence (check one)			☒ High (A)	☐ Good (B)	☐ Low/Major flaw (C)

Appendix C: Rituximab Faster Infusion Survey

#	Question	Answer
I	**This section asks questions about your demographics. Please indicate the best response.**	
1	What is your current role?	**Select one:**
		Nurse Practitioner
		Clinical Nurse Specialist
		Infusion Nurse
		Clinical Trial Nurse
		Other: (please specify)
2	What is the highest degree you have achieved?	Select one:
		Diploma
		Associates
		Bachelor
		Master
		DNP
		DNSc
		PhD
		Other (please specify)
3	Which of the following best describes your practice setting?	(Check all that apply)
		Academic Medical Center
		Community Hospital
		Physician Office/Infusion Center
		Outpatient
		Inpatient
		Other (please specify)
4	How many years have you been practicing nursing?	**Select one:**
		< 1
		1-5
		6-10
		11-15
		> 15

II	**The following questions ask about how innovativeness may influence nurses' decisions to adopt evidence-based practices.**	
#	**Question**	**Answer**
1	I network with other nurses outside of my work environment	Select one: never; seldom; sometimes; often; almost always
2	I am considered an informal/formal leader in my work environment	Select one: never; seldom; sometimes; often; almost always
3	Co-workers ask my opinion about new ideas/practices	Select one: never; seldom; sometimes; often; almost always
4	I try new ideas/practices when research indicates its value	Select one: never; seldom; sometimes; often; almost always
5	Unless I have seen a similar idea/practice work in the past, I am reluctant to try something new	Select one: never; seldom; sometimes; often; almost always
6	I need encouragement from others before doing something new	Select one: never; seldom; sometimes; often; almost always
III	**This section asks questions about your experience with rituximab infusions and infusion reactions. Please indicate the best response.**	
#	**Question**	**Answer**
1	Have you administered rituximab with <u>both</u> the standard infusion according to the Rituxan United States Package insert (USPI) and a rituximab faster infusion schedule?	Select one: Yes; No
2	Approximately how many patients have you treated with rituximab faster infusion?	**Select one:** 0 1-5 6-10 11-15 >15
3	How would you rate your overall experience with rituximab faster infusion?	Select one: very positive; positive; neutral; negative; very negative; N/A

IV	**This next section asks about the impact of rituximab faster infusion on <u>nursing practice</u>. You will be shown a series of statements. Please indicate your level of agreement with each statement. Please do not use the "not sure" option unless you truly do not have an opinion.**	
#	**Question**	**Answer**
1	I find that the administration of rituximab faster infusion did not impact my ability to monitor patients for adverse events	Select one: agree strongly; agree somewhat; not sure; disagree somewhat; disagree strongly; N/A
2	I find that the shorter time associated with the administration of rituximab faster infusion does not impact the quality of patient care compared to the rituximab administered according to the current USPI	Select one: agree strongly; agree somewhat; not sure; disagree somewhat; disagree strongly; N/A
3	My practice setting has specific guidelines in place for the dosage of antipyretics (i.e., acetaminophen, antihistamine, and corticosteroids) for the administration of rituximab	Select one: agree strongly; agree somewhat; not sure; disagree somewhat; disagree strongly; N/A
4	Rituximab faster infusion will improve scheduling efficiency for infusion chair time	Select one: agree strongly; agree somewhat; not sure; disagree somewhat; disagree strongly; N/A
5	My practice setting has specific guidelines for monitoring vital signs for rituximab faster infusion	Select one: Yes; No
6	If YES, please specify vital signs monitored and schedule	**Select one:**
		Vital signs before infusion and at q15 minute intervals until infusion completion.
		Vital signs before infusion and at q30 minute intervals until infusion completion.
		Other schedule: (please specify)

#	Question	Answer
7	My practice setting tracks quality metrics to assess infusion reaction rates	Select one: Yes; No
8	My practice setting uses standing orders or protocols to manage infusion reactions	Select one: Yes; No
9	Nurses at my practice setting educate patients and their families about infusion reactions	Select one: agree strongly; agree somewhat; not sure; disagree somewhat; disagree strongly
10	Nurses at my practice setting encourage patients and their families to report infusion reactions to clinicians	Select one: agree strongly; agree somewhat; not sure; disagree somewhat; disagree strongly
11	Nurses at my practice setting clearly and accurately document infusion reactions	Select one: agree strongly; agree somewhat; not sure; disagree somewhat; disagree strongly
12	Grade 3 & 4 infusion reactions are disruptive for nursing practice	Select one: agree strongly; agree somewhat; not sure; disagree somewhat; disagree strongly
13	Rituximab faster infusion increases the likelihood of a patient experiencing an infusion related reaction as compared to administering rituximab with a standard infusion rate according to the Rituxan United States Package insert (USPI)	Select one: agree strongly; agree somewhat; not sure; disagree somewhat; disagree strongly

V	Overall impression	
#	**Question**	**Answer**
1	What is your overall impression of the process of the administration of rituximab faster infusion as compared to administering rituximab with a standard infusion rate according to the Rituxan United States Package insert (USPI)?	Select one: very demanding; somewhat demanding; not sure; easy; very easy; N/A
2	Based on my present experience with the administration of rituximab faster infusion, I would recommend administration of rituximab faster infusion to patients	Select one: agree strongly; agree somewhat; agree; not sure; disagree somewhat; disagree strongly
3	Would you agree that the administration of rituximab faster infusion is safe?	Select one: agree strongly; agree somewhat; agree; not sure; disagree somewhat; disagree strongly
4	Overall I believe patients would prefer the administration of rituximab faster infusion over rituximab administered according the current USPI	Select one: agree strongly; agree somewhat; agree; not sure; disagree somewhat; disagree strongly
Thank you for completing this questionnaire		

Appendix D: Tables

D1: Background and Demographic Characteristics of Nurses

Questionnaire items	Response Percent*	Response Count (n=25)
What is your current role?		
Nurse Practitioner	0.0%	0
Clinical Nurse Specialist	22.7%	5
Infusion Nurse	36.4%	8
Clinical Trial Nurse	40.9%	9
Other (please specify): 3 Managers & 1 Educator		4
No Response		3
What is the highest level of school you have completed or the highest degree you have received?		
Diploma	4.0%	1
Associates	8.0%	2
Bachelor	68.0%	17
Master	16.0%	4
DNP	0.0%	0
DNSc	0.0%	0
PhD	4.0%	1
Other (please specify)		0
Which of the following best describes your practice setting?		
Academic Medical Center	20.0%	5
Community Hospital	20.0%	5
Physician Office/Infusion Center	24.0%	6
Outpatient	32.0%	8
Inpatient	16.0%	4
Other (please specify): Governmental Agency		1
How many years have you been practicing nursing?		
< 1	0.0%	0
1-5	16.0%	4
6-10	8.0%	2
11-15	4.0%	1
> 15	72.0%	18
* Response percentage reflects responses to answer options only. Other entries are not reflected in percentages		

D2: Innovativeness- Leadership

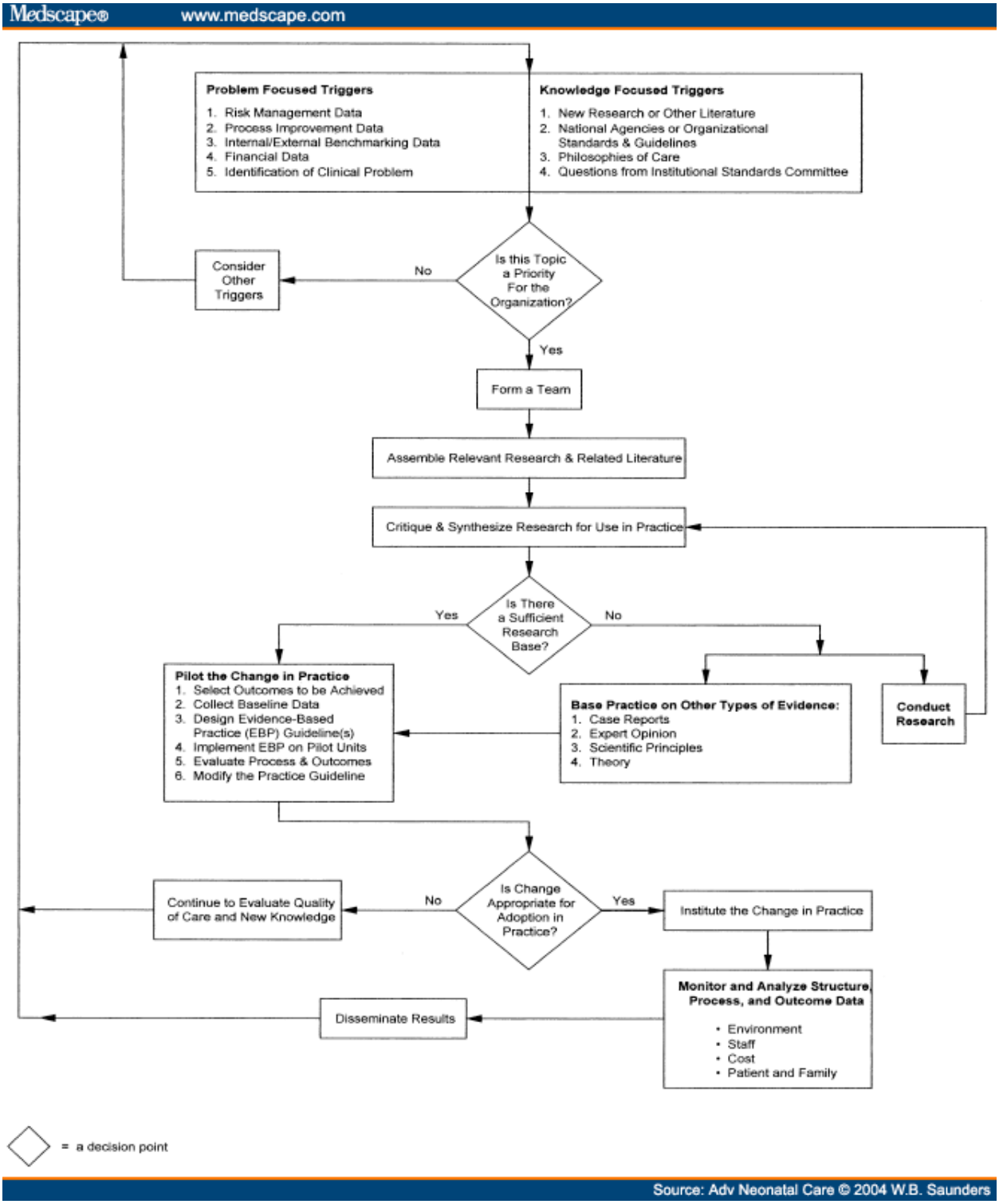
Questionnaire items	Response Percent	Response Count (n=25)
I am considered an informal/formal leader in my work environment		
Never	4.0%	1
Seldom	0.0%	0
Sometimes	12.0%	3
Often	32.0%	8
almost always	52.0%	13
Co-workers ask my opinion about new ideas/practices		
Never	0.0%	0
Seldom	4.0%	1
Sometimes	8.0%	2
Often	56.0%	14
almost always	32.0%	8
I try new ideas/practices when research indicates its value		
Never	0.0%	0
Seldom	0.0%	0
Sometimes	16.0%	4
Often	44.0%	11
almost always	40.0%	10

D3: Innovativeness- Reliance on others

Questionnaire items	Response Percent	Response Count (n=25)
Unless I have seen a similar idea/practice work in the past, I am reluctant to try something new		
Never	12.0%	3
Seldom	48.0%	12
Sometimes	40.0%	10
Often	0.0%	0
almost always	0.0%	0
I need encouragement from others before doing something new		
Never	24.0%	6
Seldom	36.0%	9
Sometimes	36.0%	9
Often	4.0%	1
almost always	0.0%	0
I network with other nurses outside of my work environment		
Never	0.0%	0
Seldom	8.0%	2
Sometimes	20.0%	5
Often	48.0%	12
almost always	24.0%	6

Appendix E: Figures

E1: The Iowa Model of Evidence-Based Practice to Promote Quality Care



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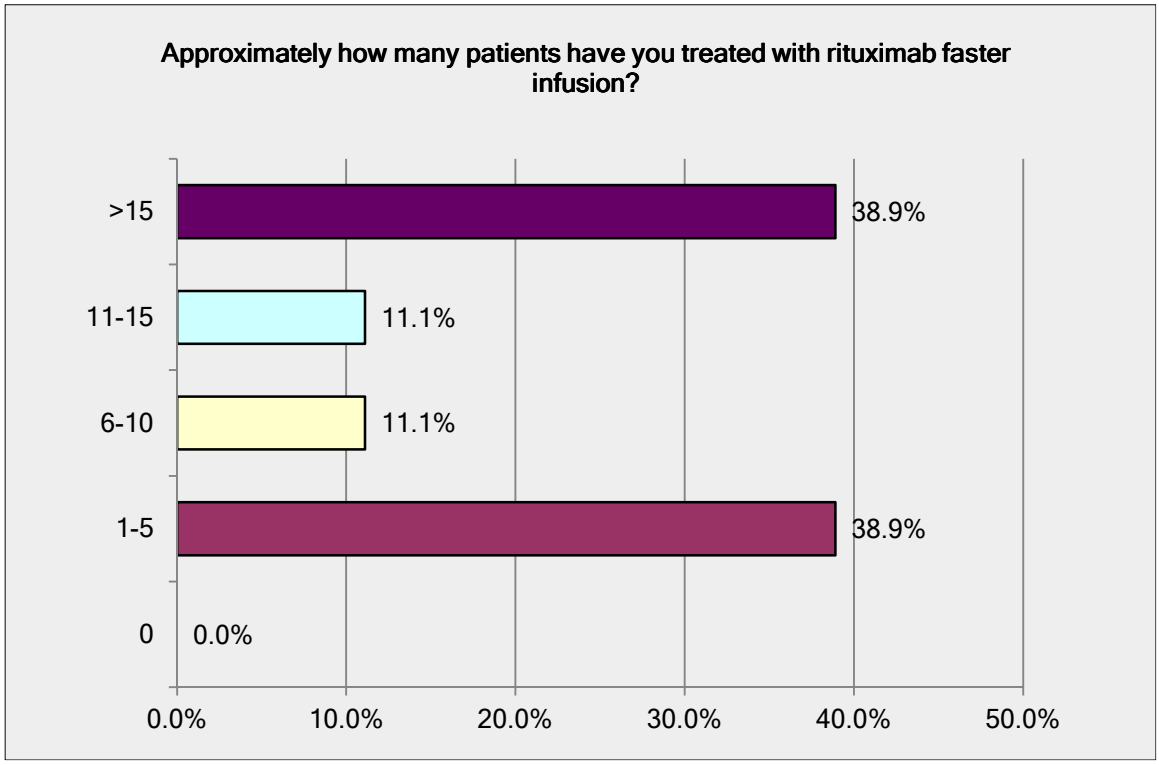
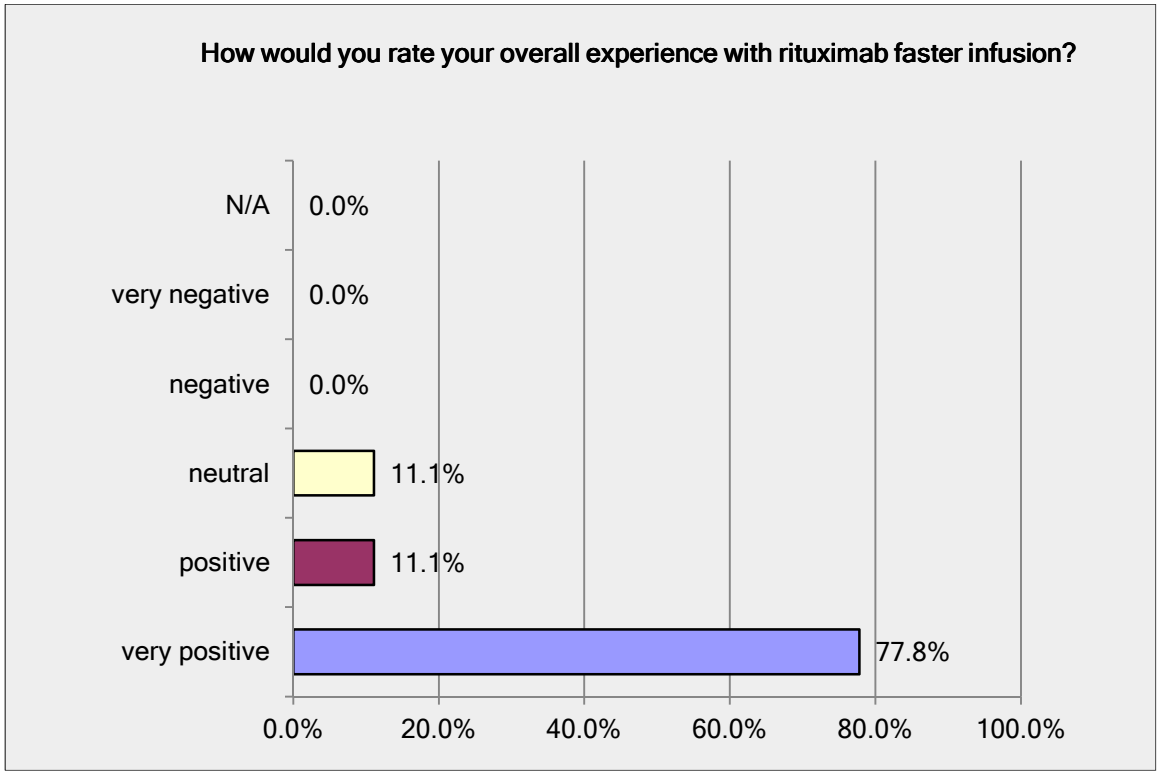
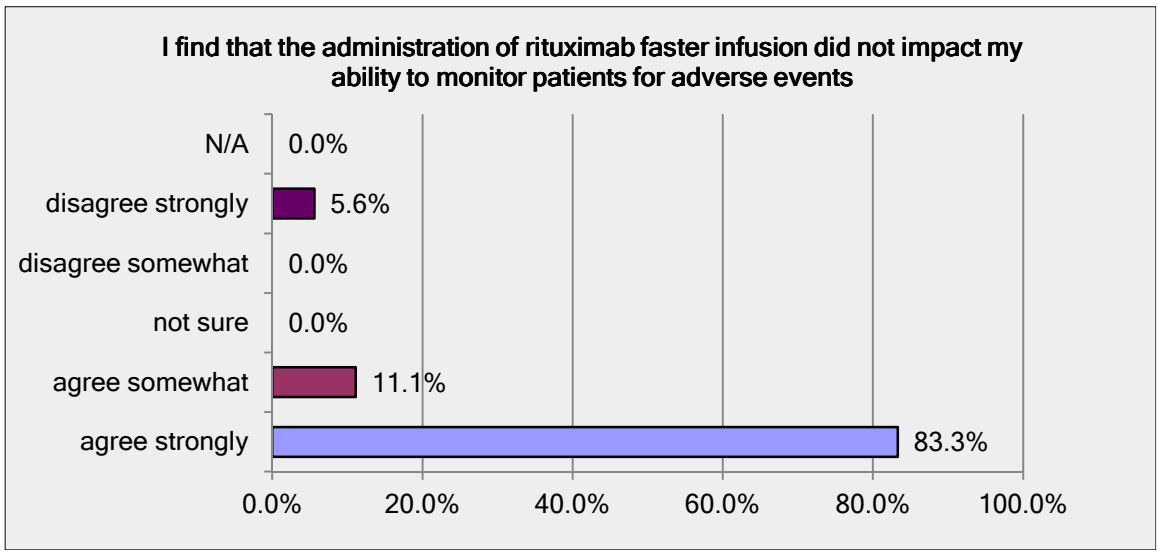
Keith Dawson

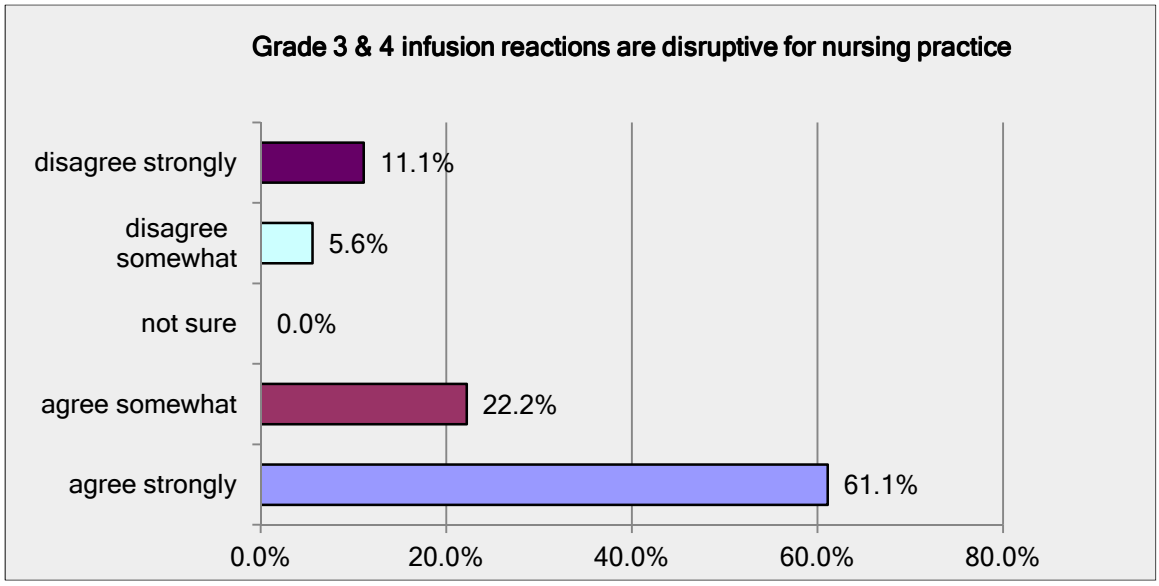
E2: Rituximab Faster Infusion: Nurse Experience

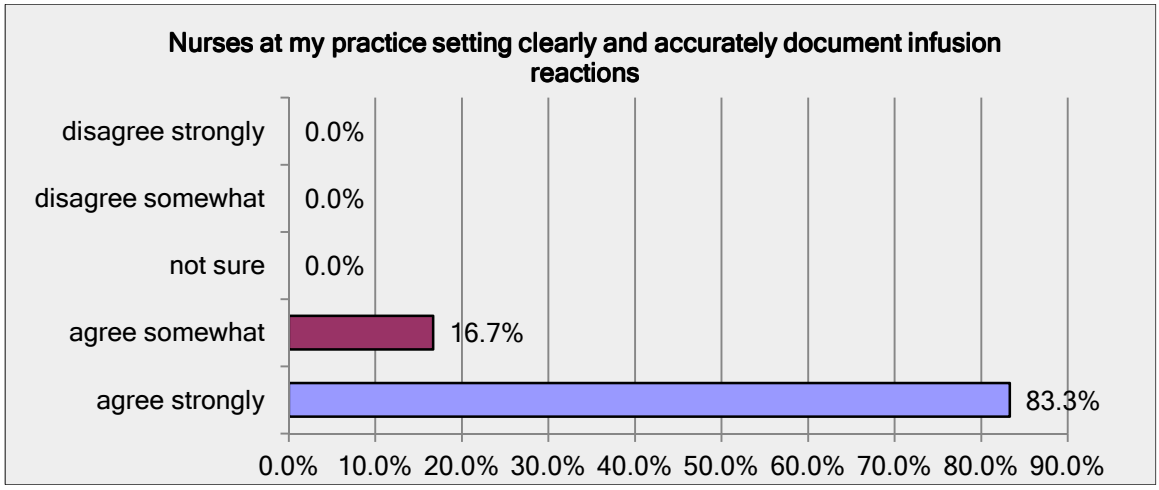




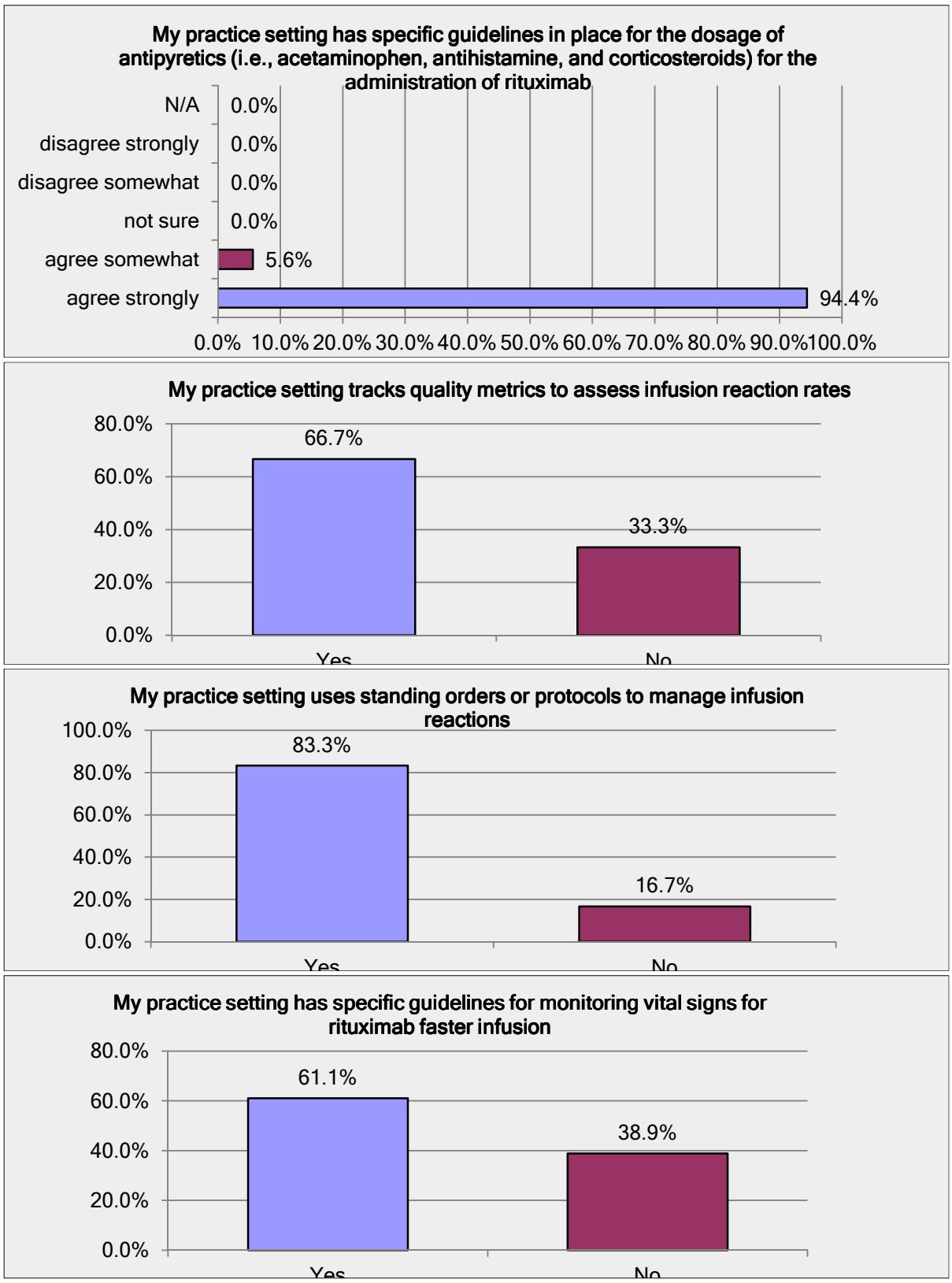
E3: Rituximab Faster Infusion Impact- Nursing Practice



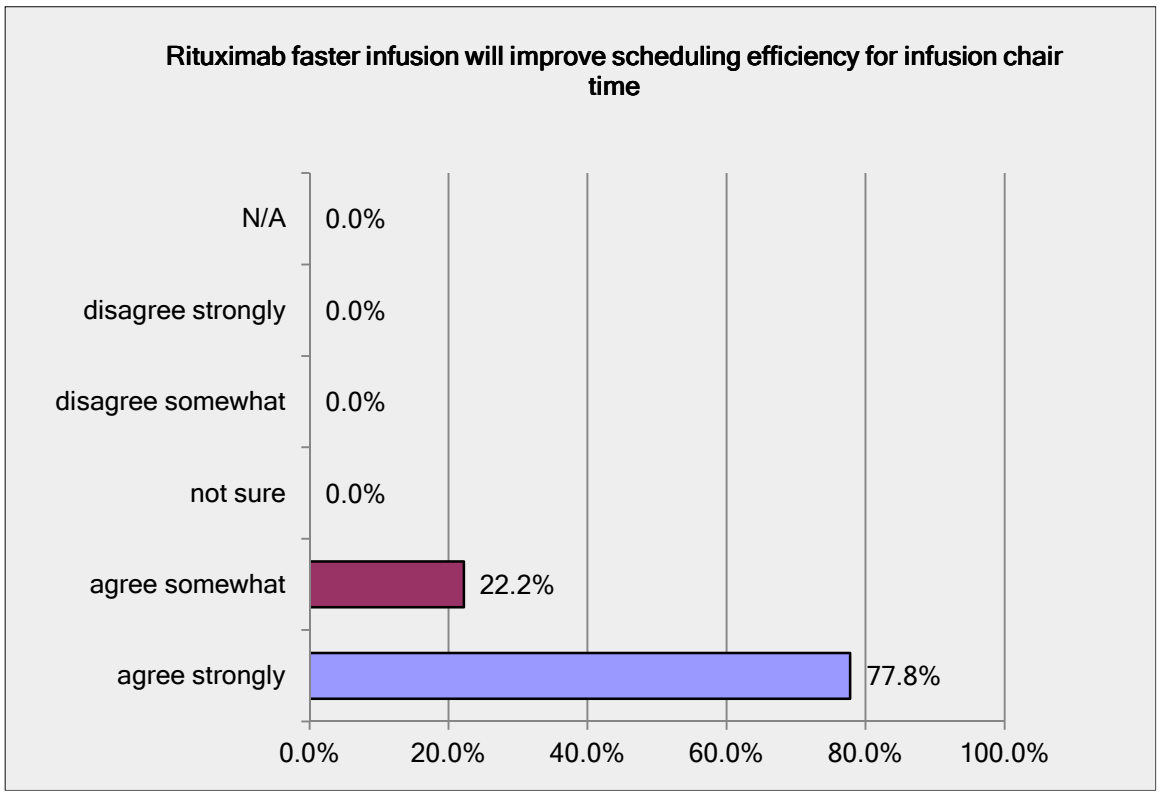


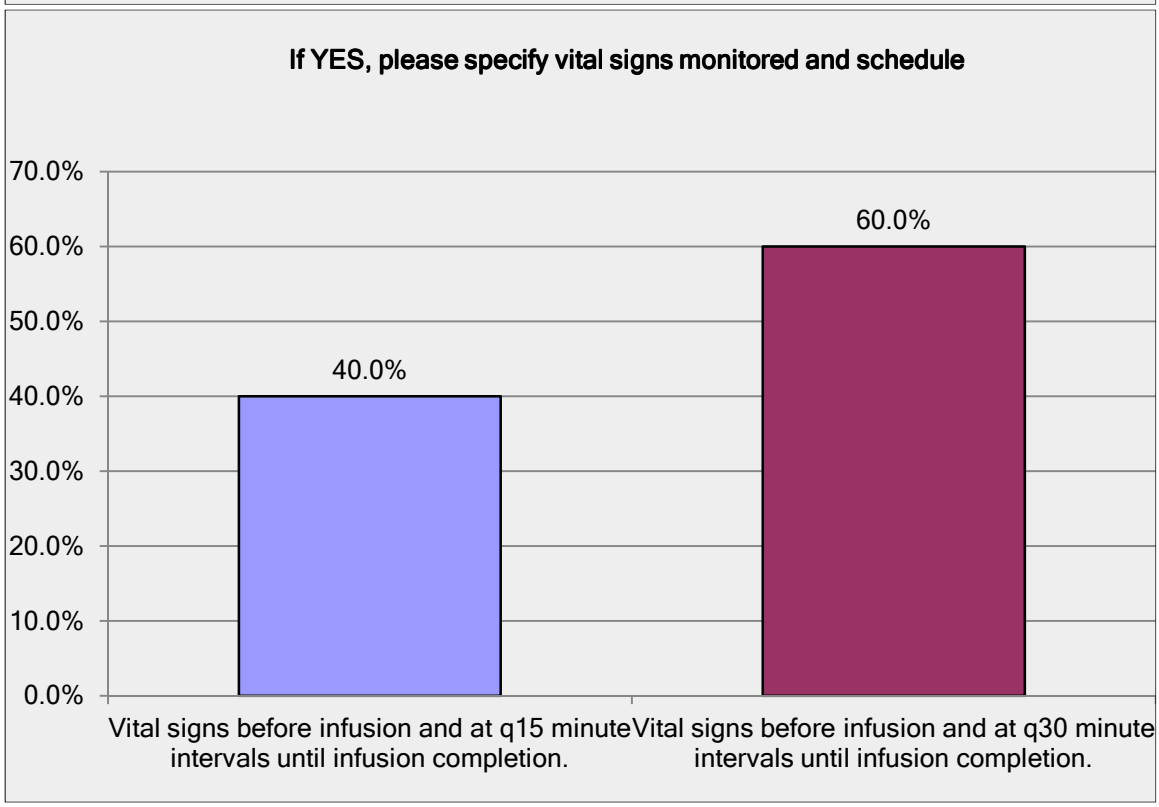


E4: Rituximab Faster Infusion Impact: Guidelines, Policies and Procedures

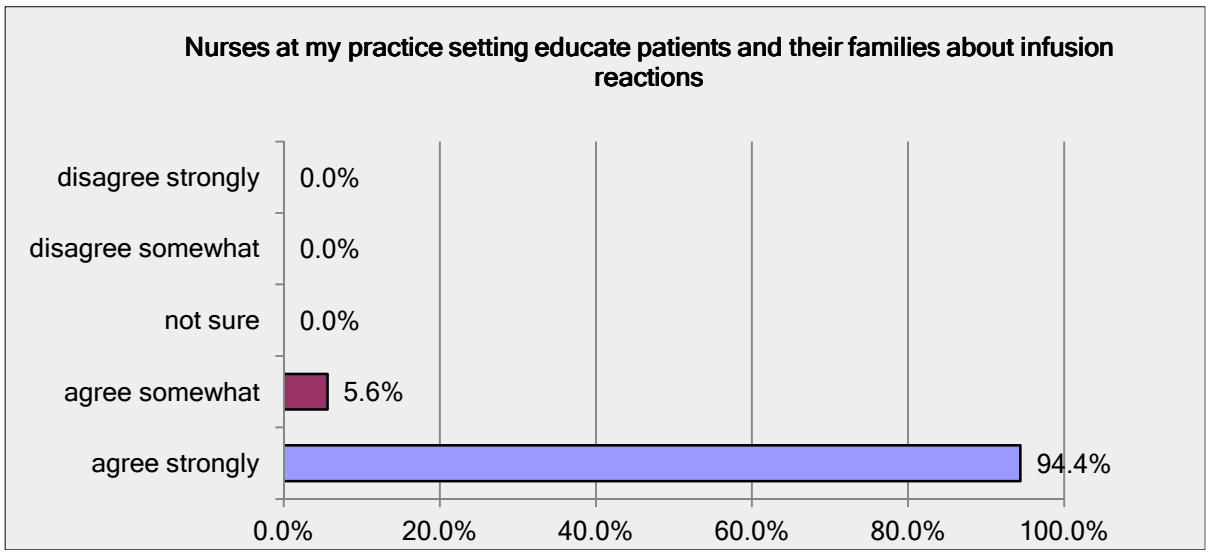


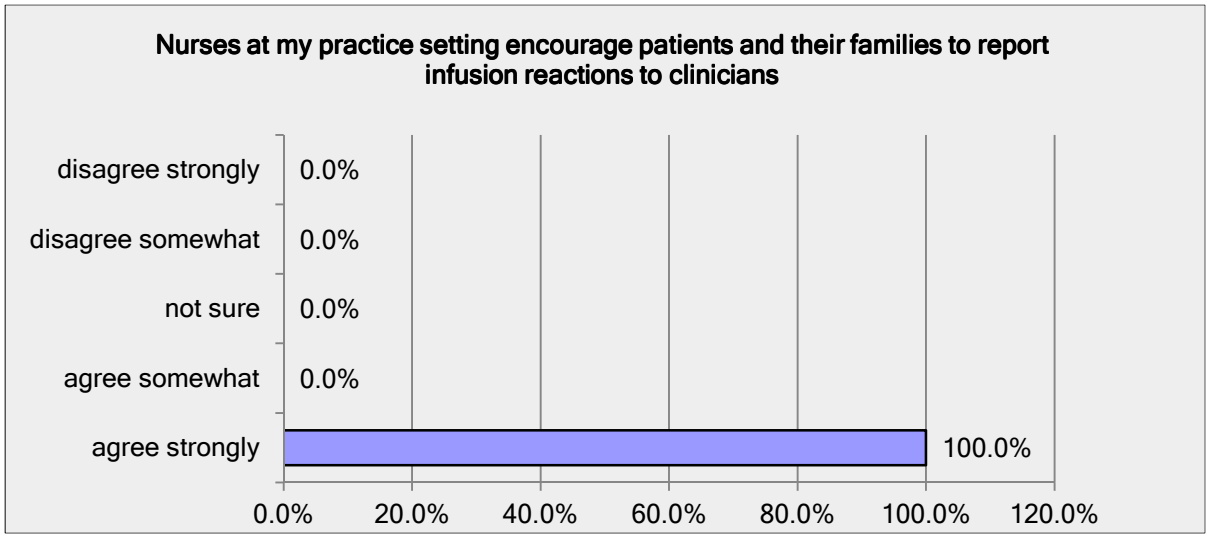
E5: Rituximab Faster Infusion Impact- Resource Utilization

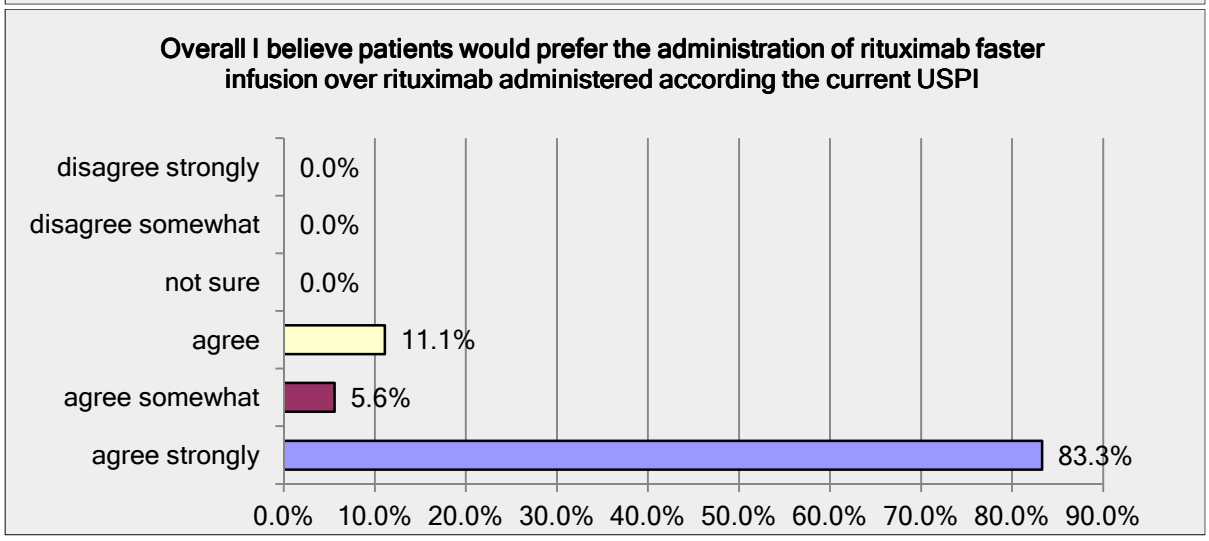




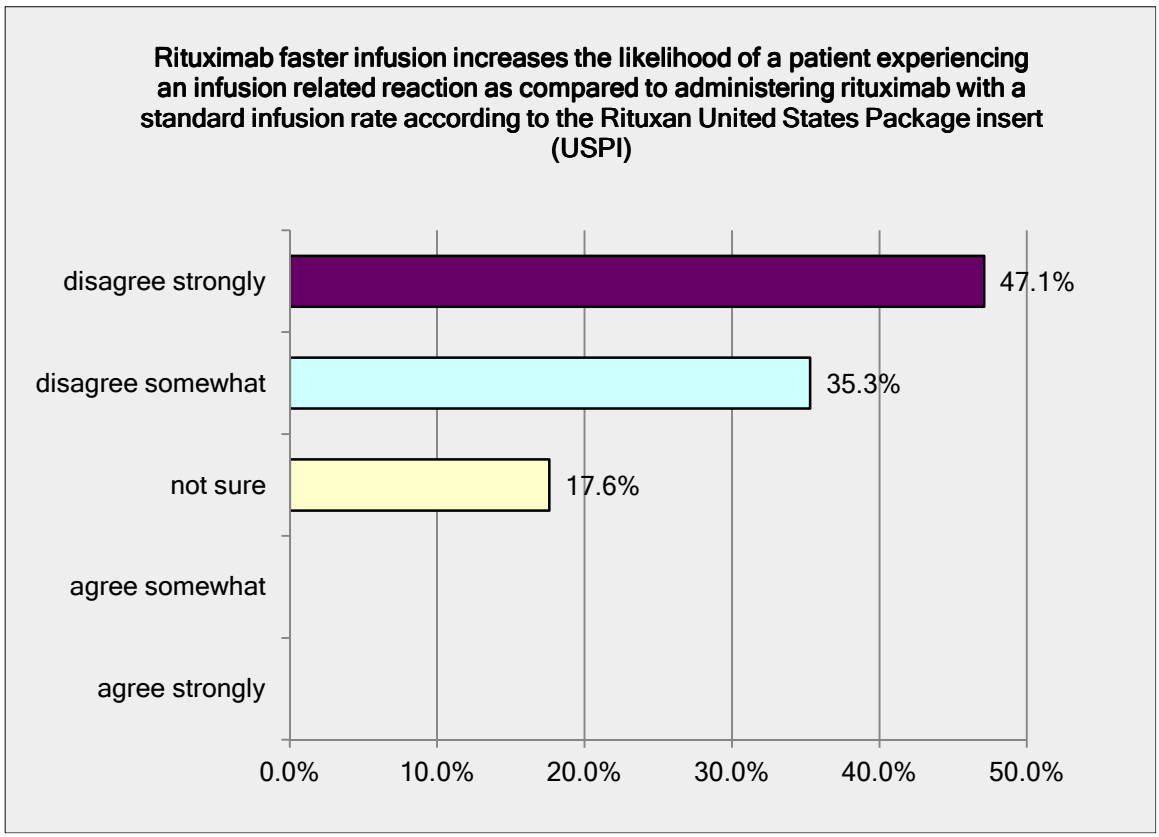
E6: Rituximab Faster Infusion Impact- Patients

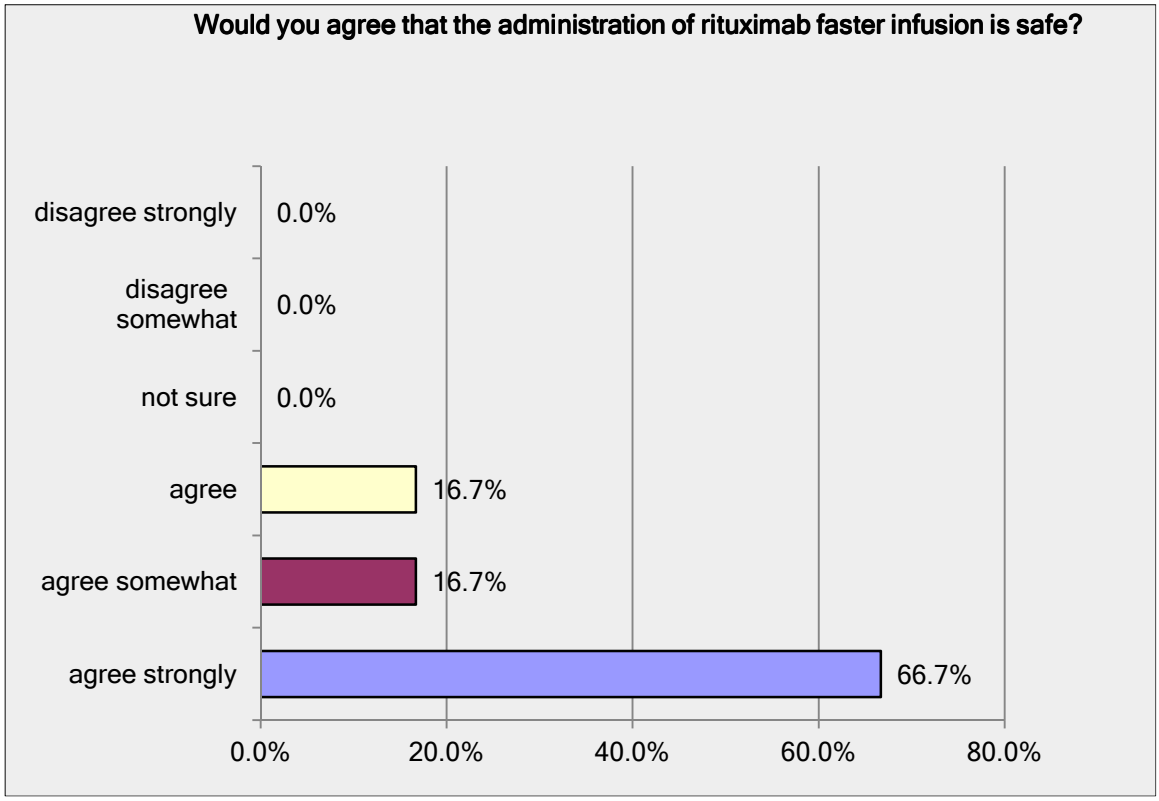




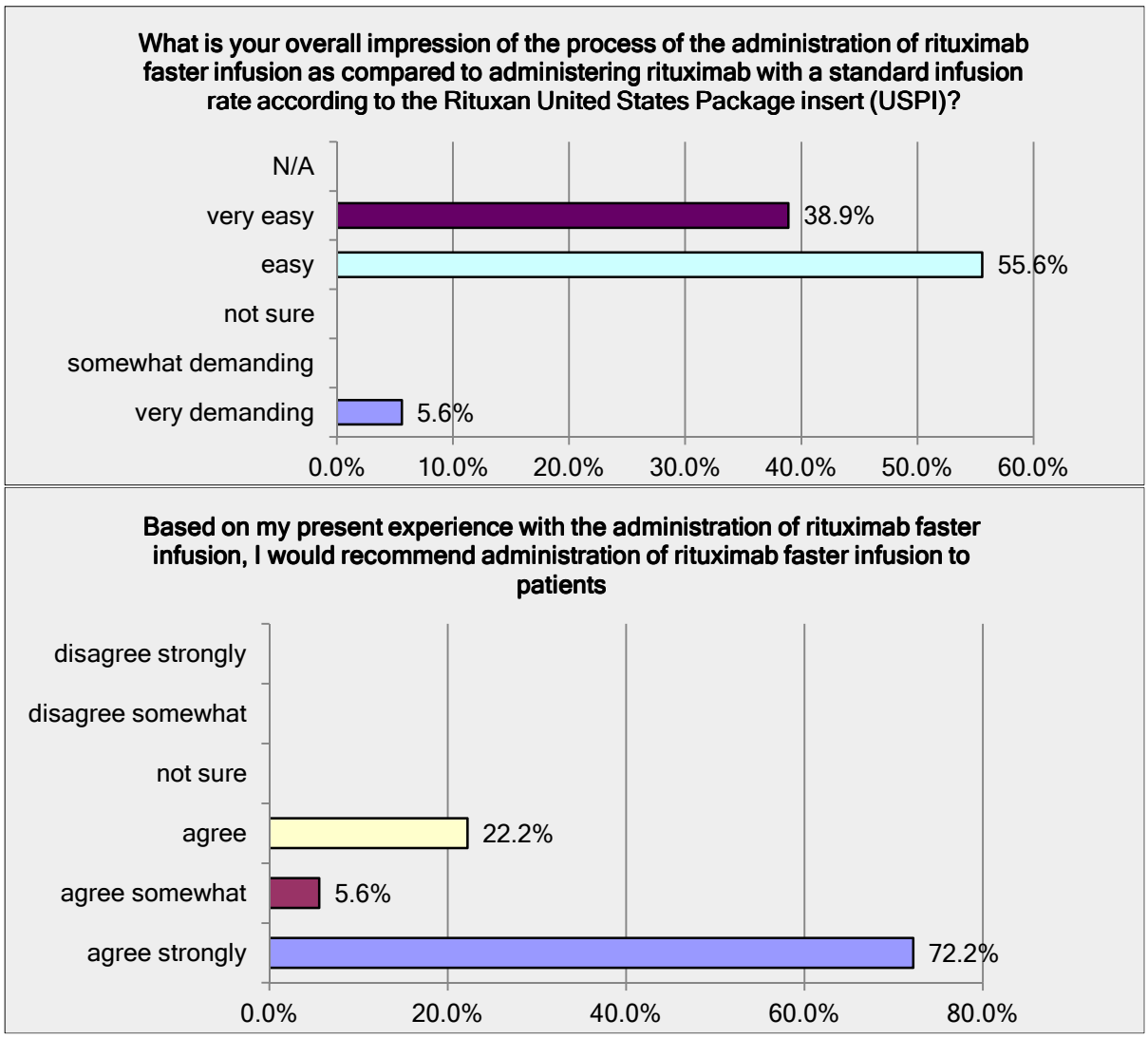


E7: Rituximab Faster Infusion Impact- Safety





E8: Overall Impression



E9: Monitor and Analyze Structure, Process and Outcome Data

E10: Innovativeness and Overall Impression Assessment Tool (Part 1)

Rituximab Faster Infusion Tool Kit for Expert Review

Innovative Instrument (Adapted from C. Carlson, PhD, RN, Innovativeness Instrument, 2008)
Please Read- no need to take survey

3. Figure 10 (Part 1): Innovativeness Instrument

	never	seldom	sometimes	often	almost always
I network with other nurses outside of my work environment	◯	◯	◯	◯	◯
I am considered an informal/formal leader in my work environment	◯	◯	◯	◯	◯
Co-workers ask my opinion about new ideas/practices	◯	◯	◯	◯	◯
I try new ideas/practices when research indicates its value	◯	◯	◯	◯	◯
Unless I have seen a similar idea/practice work in the past, I am reluctant to try something new	◯	◯	◯	◯	◯
I need encouragement from others before doing something new	◯	◯	◯	◯	◯

Overall Impression items adapted from Roche Global survey of nursing regarding subcutaneous rituximab
Please Review- no need to take survey

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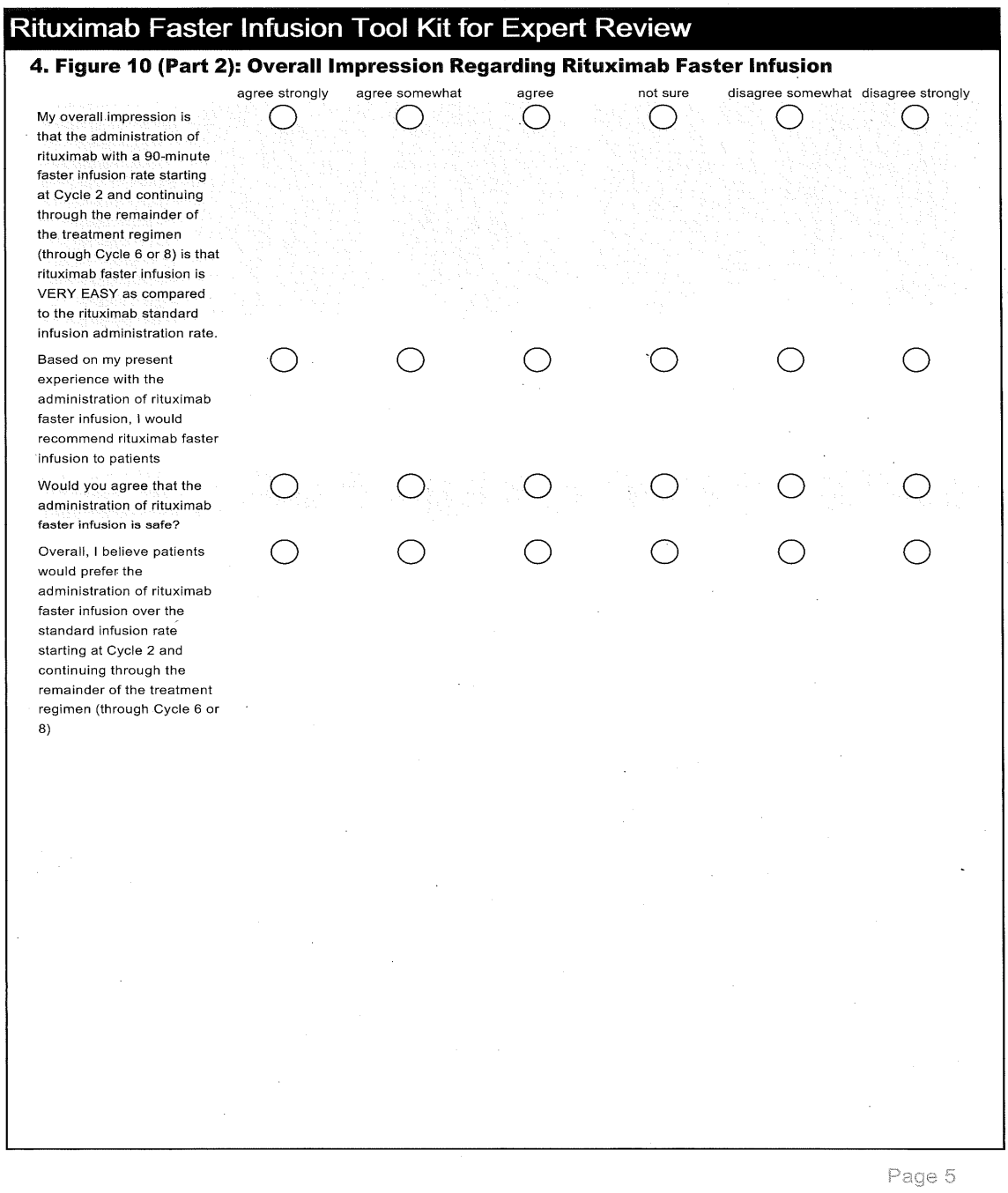
E10: Innovativeness and Overall Impression Assessment Tool (Part 2)



Rituximab Faster Infusion Tool Kit for Expert Review

4. Figure 10 (Part 2): Overall Impression Regarding Rituximab Faster Infusion

	agree strongly	agree somewhat	agree	not sure	disagree somewhat	disagree strongly
My overall impression is that the administration of rituximab with a 90-minute faster infusion rate starting at Cycle 2 and continuing through the remainder of the treatment regimen (through Cycle 6 or 8) is that rituximab faster infusion is VERY EASY as compared to the rituximab standard infusion administration rate.	◯	◯	◯	◯	◯	◯
Based on my present experience with the administration of rituximab faster infusion, I would recommend rituximab faster infusion to patients	◯	◯	◯	◯	◯	◯
Would you agree that the administration of rituximab faster infusion is safe?	◯	◯	◯	◯	◯	◯
Overall, I believe patients would prefer the administration of rituximab faster infusion over the standard infusion rate starting at Cycle 2 and continuing through the remainder of the treatment regimen (through Cycle 6 or 8)	◯	◯	◯	◯	◯	◯

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Carlson, C. (2008). Development and testing of four instruments to assess prior conditions that influence nurses' adoption of evidence-based pain management practices. [Evaluation Studies, Review]. *J Adv Nurs*, 64(6), 632-643. doi: 10.1111/j.1365-2648.2008.04833.x