PROJECT EXTEND: A COMMUNITY EXTENDED CASE CONFERENCE TO IMPROVE LYMPHOMA CARE

Submitted by the
University of Nebraska Medical Center,
Center for Continuing Education
And
UNMC College of Medicine
Department of Internal Medicine,
Division of Hematology & Oncology

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C. Main Section

C.1 Overall Goal & Objectives:

Overall Goal:

This project has the overall goal of improving the care of patients with lymphoma treated by community oncologists (CO) by implementing an educational program embedded in a community extended multidisciplinary case conferences (MCC) or tumor board meetings (EXTEND Program).

Proposed mechanism of improvement in care: The improvement in care of patients treated by CO will be manifested by an increase in adherence to evidenced-based guidelines or expert panel recommended treatments. The expectation is that the increase in adherence by CO will lead to comparable clinical outcomes of their patients to those treated by university-based oncologists (UO). The proposed educational program will empower CO with knowledge, skills, as well as confidence, to clinically handle patients with lymphoma, to monitor and prevent treatment toxicities, and to enhance their abilities in deciding what treatment options to consider for treatment failure or when patients are best referred for further advanced treatments (example, hematopoietic cell transplantation or clinical trials).

Key Objectives:

This proposal will compare among CO (who are part of the Nebraska Lymphoma Study Group - NLSG) either participating or not participating in the EXTEND program and UO in the following specific aims:

Primary aim: To compare the adherence rates of oncologists to evidence-based guidelines or expert panel recommended lymphoma treatment plans.

Hypothesis: *Adherence to best practice lymphoma treatment will be similar between UO and CO participating in the EXTEND Program and higher compared to CO not participating in the EXTEND Program.*

Secondary aims:

1) To compare patient clinical outcomes after lymphoma treatment including: a) treatment response at restaging, b) 6 month severe medical service utilization (emergency room (ER) visits, and/or hospitalizations), c) 6 month progression-free survival (PFS), and d) 6 month overall survival (OS).

Hypotheses: *Clinical outcomes in the four identified areas will be similar between UO and CO participating in the EXTEND Program and better compared to CO not participating in EXTEND program.*

2) To evaluate the satisfaction of CO participating in the EXTEND program over time (Weeks 1, 12, 24, 36, and 48) in the following areas: a) Conference Satisfaction (adequacy of expertise, quality of information obtained, quality of discussion, level of professionalism, and cordiality of environment); b) Personal Benefits (knowledge acquisition, confidence in treating patients, confidence in treating relapsed disease, confidence in handling complications, confidence in determining when to refer); c) Service Benefits (diagnostic evaluations, consultations); d) Technical satisfaction (format, frequency of meetings, time allotted for meeting, clarity of broadcast); and d) overall satisfaction.

How are the intended key objectives intended to address the established need for this initiative: The EXTEND program is a modification of the well-established MCC or tumor board. Since 2009 the Division of Oncology & Hematology at the University of Nebraska Medical Center (UNMC) had an ongoing weekly lymphoma specialized MCC. This forum will

be extended to CO as a means to educate CO through clinical discussions of the diagnosis, treatment, and follow-up of patients seen in the community. The expectation is that the MCC will provide an environment that provides guidance in the treatment of patients seen in the community which will lead to increased adherence to evidence-based guidelines or expert panel recommended lymphoma treatment plans. The sustained interaction between UO and CO will increase the appreciation of different specialists' perspectives on specific types of lymphoma, diagnostic testing, treatment options and treatment toxicities. These were target areas identified by the national assessments as areas that can be improved by education. [1] It will also assist in the management decisions for specific patients with complex pathology and comorbidities. By extending to our partner CO throughout the state of Nebraska our weekly lymphoma MCC, we are given the unique opportunity to evaluate how extending MCC to the community may improve lymphoma care in the region. When effective, this can serve as a model of cooperation between academic and community oncologists that can be replicated to other cancers where treatments are complex and rapidly changing. Additionally, the proposed initiative allows us to address the identified gaps between actual clinical practice and the low utilization of recommended treatments, as established by the reports on hematologic malignancies accompanying this request for proposal.

C.2 Technical Approach

C.2.A Current assessment of need in target area

C.2.A.1 Quantitative Baseline Data

Figure 1 shows the survival plot of lymphoma patients from the NLSG database according to treatment provider (UO versus CO) and patients' residence (rural versus urban) that we published in 2009. [2] Our study showed that there was no statistically significant difference in the survival probability of lymphoma patients from rural or urban areas that were treated by UO, and urban patients treated by CO (top 3 survival plot). Patients from rural areas treated by CO had a statistically significant worst survival rate (lowest survival plot). In the multivariate analyses, adjusting for type of lymphoma and number of prognostic factors (age = 60, Karnofsky performance score < 80, Ann Arbor stage III or IV, presence of B symptoms, elevated LDH, tumor bulk = 5.0-cm, at least one nodal involvement, at least on extra-nodal involvement), the risk of death among urban and rural patients treated by UO and urban patients treated by CO were not statistically different. However, rural patients treated by CO had a statistically significant higher risk of death when compared with rural patients treated by UO [hazard risk (HR) 1.26 (95% CI 1.06-1.49), p=0.01]. We also observed that urban patients treated by UO were more likely to receive radiation as part of treatment (32%) compared to urban patients treated by CO (27%), rural patients treated by UO (24%), and CO (27%), this difference was no longer noted after stratifying for type of lymphoma. The number of chemotherapy cycles patients received was also not different across groups. However, the use of hematopoietic cell transplantation (HCT), a common treatment for relapsed lymphoma and shown to be curative for diffuse large cell and Hodgkin lymphoma, was significantly higher in patients treated by UO (urban = 19% and rural =16%) compared to patients treated by CO (urban = 11% and rural = 10%, p < 0.01). Additionally, the use of rituximab in diffuse large cell lymphoma from the year 2000 onward was significantly higher in patients treated by UO (urban = 64% and rural = 73%) compared to patients treated by CO (urban = 40% and rural 51%). These findings indicate that some patients treated in the community are less likely to receive optimal treatments

which may explain why their survival outcomes are inferior to those treated by UO. The above findings are compatible with the national assessments and literature accompanying this RFP.

In a separate study by our group of patients with hematologic malignancies (lymphoma, leukemia and multiple myeloma), it was shown that rural patients with lymphoma had a significantly higher risk of death (HR of 1.17, 95% CI of 1.02 – 1.35, p = 0.02) after autologous HCT. No differences in outcomes were noted among patients with leukemia treated with HLA-identical sibling HCT (related allogeneic HCT). [3] It is important to note that autologous HCT patients are transferred back to the care of referring CO soon after HCT, while allogeneic (related or unrelated) HCT patients usually have more rigorous follow-up from both CO and their university-based transplant physicians. In another study we conducted on 6140 patients with leukemia who received unrelated HCT using a US wide sample from the Center for International Blood and Marrow Research, survival rates of patients from rural areas were comparable to patients from urban areas, also likely as a result of the intense follow-up from both CO and their university-based transplant physicians. [4] Both studies on transplant patients suggest that differences in outcomes between rural and urban patients are less pronounced when UO have a role in their treatment or follow-up care. In fact, in a recent prospective study we completed that evaluated the follow-up care of patients with hematological malignancies after treatment from UO, no significant differences in severe medical service utilization between patients seeking follow-up care from UO alone or from both UO and CO were noted.[5]

Our extensive population based studies on hematological malignancies clearly supports the premise that collaborations between UO and CO are essential in reducing, if not eliminating, the disparities in the clinical outcomes between rural and urban patients with hematologic malignancies in Nebraska.

C.2.A.2 Primary audience(s) targeted for intervention / who will benefit.

UNMC has an excellent international reputation in the diagnosis and treatment of lymphoma and is situated in a predominantly rural state. The NLSG was formed in 1982 as a scientific collaboration between UO at UNMC and CO throughout Nebraska and its surrounding states. To date, the NLSG has collected clinical information on over 5400 previously untreated lymphoma patients, 60% of whom are from rural areas. Data from the NLSG was the source for the data discussed in the previous section. There are currently 10 (9 community-based and 1 university-based) participating NLSG sites with 22 practicing medical CO outside of Omaha, the largest city in the state of Nebraska, and 5 UO who are world-renowned experts in lymphoma. The 22 oncologists represent approximately 80% of practicing CO in Nebraska outside Omaha. Community oncology practice can be in the form of solo practice or group practice. The typical CO who participates in the NLSG has a solo or small group practice of 2 to 4. We have surveyed members of the NLSG and identified 10 CO, representing 5 sites who will receive the intervention. There will be 12 CO from 4 sites who will not participate in the EXTEND program and act as control group. Participating sites are also encouraged to have their medical team (mid-levels and nurses) attend the MCC. The participants of the EXTEND Program are expected to benefit from the intervention through acquisition of knowledge and skills which are translated to clinical behaviors (adherence to evidence-based guidelines or expert-panel recommendations) and improvement in clinical outcomes of patients with lymphoma.

C.2.B Intervention Design and Methods

C.2.B.1 The Intervention that will be implemented and tested is the EXTEND Program. It consists of a weekly one hour MCC focused on the discussion of lymphoma patients seen and treated by the CO participating in the EXTEND Program. The MCC will be held at UNMC and be broadcast live via the web. Participants from the community will be able to see and hear the UNMC experts, as well as be seen and heard at UNMC through a HIPAA compliant network. The expertise available during the conferences will include: three recognized lymphoma experts, a hematopathologist with expertise in lymphoma, a radiation oncologist, and a diagnostic radiologist. The EXTEND Program also consists of: 1) providing a Consultation Hotline to lymphoma experts for CO who need to seek advice on cases that need immediate treatment and cannot wait for the weekly MCC; and 2) postings of educational and informational materials, including discussion summaries, follow-up reports and toxicity data discussed during the MCC on the study website that can be accessed privately by the participating CO. Therefore, the intervention consists of: 1) **Clinical Presentation:** clinical features of the patients are presented, followed by pathological examinations and diagnostic tests; 2) **Consensus Formation**: diagnosis is confirmed, then followed by discussions of possible applicable treatment options from evidence-based guidelines or expert recommendations, potential complications and common toxicities of treatment options are provided based on literature and experience of clinical experts; and 3) **Treatment Planning:** choice of treatment plan(s) is reached. The choice of treatment plan(s) is what we will refer to as the equivalent of formation of the 'behavioral intention'. In the theory of planned behavior, intention formation (treatment plan in our study) is the most immediate antecedent to a behavior (adherence in our study) and represent the convergence of the cognitive, motivational, and affective internal processes associated with a given behavior. This behavioral model has supplied the theoretical model for more than 600 empirical studies of behavior prediction and change in the past 20 years, including those geared towards physicians. [6] Table 1 below shows the summary of the intervention.

Table 1: Community Extended Multidisciplinary Case Conference Description (EXTEND Program.

A. Frequency	Weekly 1 hour case conferences hosted by UNMC using videoconferencing equipments of the Nebraska Statewide Telehealth Network to NLSG sites participating in the EXTEND Program. Expected to deliver 42 sessions a year or 80% of the 52 weeks in a year
B. Time frame:	Implementation of the EXTEND Program will last for 15 months of the 24 months study period
C. Experts / Audience:	Experts: 3 lymphoma experts from UNMC, 1 hematopathologist, 1 radiation oncologist and 1 diagnostic radiologist are committed to the EXTEND Program - one of the lymphoma experts will act as facilitator on rotating basis Virtual audience: CO from NLSG sites who have agreed to participate in the EXTEND Program will attend remotely; any mid-levels or nurses are also invited to attend and have access to the MCC broadcast Audience at UNMC: Physicians-in-training as well as nurses, mid-level practitioners and rotating students in Oncology

D. Usual Format:	Cases to be discussed will include patients seen by CO participating in the EXTEND Program. 1. Attending CO will present the salient features of the patients including demographics, brief history, comorbidities, previous treatments, and significant findings on physical examination 2. The Hematopathologist will project low and high-resolution H/E slides. This is broadcast live and is seen by the CO attending. Diagnostic impression is given. 3. The assigned Facilitator will read or show pertinent radiological findings and read out clinical impression. 4. The Facilitator asks for any questions, discussion ensues. 5. Attending CO gives their clinical impressions and treatment plan. 6. Lymphoma experts give their impressions and recommended treatment options. Discussion ensues and agreement on a treatment plan is established. It is anticipated that not all patients will have treatments specified by existing NCCN guidelines. This is where treatment plans developed through collaborative discussion among the physicians involved in the MCC will be of particular value. 7. Facilitator summarizes the agreed upon treatment An average of 5 cases can be discussed during the 1 hour conference, depending on the complexity of the case. Based on weekly reporting of cases to the NLSG, it is very unlikely that there would be more than 5 lymphoma cases per week. However, up to 6 patients has been discussed within an hour in the existing Lymphoma MCC at UNMC.
E. Alternative Consults	In cases where treatment plans are time sensitive (i.e. when patients need to be started on some treatment soon rather than wait for a conference, the 'Consultation Hotline' (see item G below) will be utilized.
F. Other Conference Topics	At least once a month, the following will be incorporated during the conferences: 1. Discussion of common complications of common treatments and remedies. 2. Follow-up on patients previously treated on certain protocols that are unusual, not standard, clinical trials, or modified due to toxicities. 3. Mortality discussions.
G. Augmenters / Boosters	1. Proceedings of every MCC will be summarized and posted on the group's website for retrieval at any time by participants and authorized users. Patients will be de-identified. 2. A printed summary of the cases and the planned treatment approach will be distributed within 2 days after the MCC for reference, and also posted on the secure website 3. A 'Consultation Hotline' to one of the lymphoma experts will be provided on a rotating basis to CO who have agreed to participate in the EXTEND Program in cases where immediate treatment recommendations are sought or when any unexpected complications result from treatment protocols being implemented. CO not participating in the EXTEND Program will not have access to this, but it

	is possible these physicians will contact any of the experts for the usual collegial referrals. The current data abstraction of NLSG captures this referral.
H. Incentives	Free confirmatory diagnosis using immunostains and/or molecular diagnostic tests. Free consultations with experts are provided. CME credits are awarded to attendees. Participating sites will receive an administrative stipend to cover increased cost associated with data collection.

C.2.B.2 Efficacy of multidisciplinary case conference: The increasing complexity of cancer care from the period of diagnosis, to treatment, and survivorship follow-up requires thorough evaluation to implement well-balanced therapeutic options in terms of clinical and personal cost and benefits, and to avoid overtreatment with its consequential adverse effects and toxicities.[7-8] The multidisciplinary team approach is postulated to be one way to attain this well-balanced patient-centered approach and guarantee quality of care. In some European countries, the use of multidisciplinary team approach has become a national health priority for promoting quality cancer care. [9] Multidisciplinary case conferences, a forum meant to systematically incorporate multidisciplinary team approach, are commonly conducted in academic and larger non-academic medical centers to help plan treatment of patients, especially where complex pathology, multiple treatment options and frequent treatment complications exist. In cancer, these conferences are usually broken into disease entities (Breast, Gastrointestinal, Hematological, Lung, etc.) and involve several specialties (Oncologist, Pathologist, Radiologist, Radiation Oncologist, and Surgeons). These conferences are also traditionally used as an educational forum for teaching medical students and trainees. Didactic materials are often presented in the context of specific cases. Medical experts present at the conference provide inputs on cases primarily managed by other physicians. Multidisciplinary discussions of cases have been shown to provide optimal treatment outcomes for patients. [10-12] Some of the compelling studies on multidisciplinary team approach in cancer management have shown that it is able to: 1) change initial physician treatment decisions [13]; 2) improve overall patient survival [14]; 3) enhance communication and coordination between primary care and hospital-based specialists [15]; 4) enhance recruitment of patients to more novel treatments in clinical trials recruitment; [16] and 5) improve staff well-being. [17] On the other hand, a recent study evaluating the role of tumor boards on the quality of cancer care in the US Veterans Affairs health system showed little association. [18] Critics of the study pointed that only 1/3 of the tumors boards were specialized. The intervention in our study is designed to be specialized (lymphoma), intensive (weekly), and comprehensive (diagnosis, treatment and follow-up).

C.2.B.3 Why physician-targeted intervention: Studies have shown that physician targeted interventions meant to increase knowledge of evidence-based recommended screening procedures and treatments result in improve adherence and clinical outcomes.[19-25] Successful implementation of adherence to evidence-based treatments improve quality of care by decreasing variation and expediting the application of effective advances to everyday practice. [26-27] Different approaches used and tested to facilitate or improve adherence among physicians range from low to high intensity interventions.

These approaches include: educational outreach such as the use of academic detailing, tailored reminder letters and phone calls [28]; use of computer generated reminders [29]; and use of computerized decision support systems. [30-32] Giving financial incentives to physicians, as well as patients, have also been shown to improve adherence to evidence-based recommended screening and diagnostic procedures, as well as treatments. [33-34] CO see a wide variety of cancers, thus are not as sub-specialized in one cancer type as those who practice in the academic setting. For example, CO does not see as high a volume of lymphoma patients as lymphoma experts at UNMC. Patient volume, an index of experience, is also shown to be associated with outcomes. [35-38]

C.2.C Evaluation Designs

Overall study design: This is a prospective quasi-experimental study to test if the EXTEND Program administered to a group of CO will improve treatment adherence and outcomes of lymphoma patients. Oncologists will be grouped as follows: group 1 - UO who are recognized lymphoma experts; group 2 - EXTEND Program CO group – group of CO willing to participate in the EXTEND Program and serve as intervention group; and group 3 – non-EXTEND CO group – CO not participating in the EXTEND program and serve as the comparison CO group.

C.2.C.1 Metrics to determine if intervention is effective in addressing gaps identified. The outcome of primary interest will be adherence to best practices in lymphoma treatment (Primary Aim) and will be compared across the 3 groups of oncologists. This outcome will determine if the gaps identified in the national and regional needs assessment was addressed in the intervention group. Secondary outcomes will include: treatment response, severe medical service utilization, progression-free and overall survival (Secondary Aim 1). Analyses will focus on comparing the primary and secondary outcomes according to physician groups adjusting for prognostic clinical factors. Analyses for secondary aim 2 (patient satisfaction) will be descriptive; describing the change in satisfaction among EXTEND participating CO over time.

Primary outcome – Adherence: The choice of adherence as the primary outcome was made because it is the central modifiable behavior that has been shown to account for favorable outcomes. Adherence is defined as percentage of patients receiving treatments in accordance to best practices, i.e. in accordance with National Comprehensive Cancer Network (NCCN) guidelines or expert recommendations (when no guidelines exist). [39-40] Treatments administered to patients will be obtained from medical records as per usual practice by the NLSG. Each case reported to the NLSG and deemed eligible in the study within the 15 month implementation period will be blinded for any patient, physician and institution identifiers, be randomly assigned, and reviewed by 1 of 3 lymphoma experts. Cases will then be labeled if adherent. In instances when no NCCN guidelines applies to a particular case, the blinded case will be reviewed by 2 lymphoma experts to assess whether the treatment provided is something they would recommend the patient (expert recommendation). Concordance between the 2 experts will constitute an adherent treatment. A 3rd expert will be called to review the case when opinions differ between the first 2 lymphoma experts. All lymphoma treatments follow protocols that account for dose modification, treatment delays or discontinuation when toxicities occur. These modifications are considered to be following the protocol. Patients started on adherent protocols who need to be switched to another protocol will still be considered adherent since it is within the realm of 'best practice' to change treatment due to unpredictable

clinical circumstances (i.e. tolerance, toxicities). Establishing inter-rater reliability is presented in the statistical section.

Secondary outcomes. All secondary outcomes will be collected individually for a period of 6 months from the time of treatment initiation using medical records.

Treatment response will be ascertained from radiographic tests performed during re-staging and will be disease appropriate: CT scans, PET scans, MRI. Response to therapy will be classified as complete response (CR), partial response (PR), no response (NR) or stable disease (SD), progressive disease (PD), early death, or not evaluable. Response to therapy will be determined after 2 cycles of therapy according to the standard revised response criteria for malignant lymphoma by Cheson. [41] Responses will be dichotomized into positive (CR or PR) versus negative (all other categories). Individual rates of each response will be computed according to physician group.

Severe medical service utilization is defined as visits to emergency room (ER) or hospitalizations for any medical or surgical conditions related to the patient's lymphoma or treatments received. Each event will be counted and expressed as continuous data according to physician groups.

Progression-free survival will be defined as time to disease progression or death from any cause, while ***overall survival*** will be defined as time to death from any cause. Progression will be ascertained according to the criteria set by Cheson. [42]

Data on treatment response, progression and survival are already routinely collected by the NLSG on a biannual basis. We will add the collection of data on severe medical service utilization for 6 months from the time of treatment. Funds are requested from this application for the additional data submission requirement.

Participant satisfaction: As stated in the Secondary aim 2, we will evaluate the following parameters using a survey questionnaire to be administered electronically quarterly from start of the intervention implementation: a) Conference Satisfaction (adequacy of expertise, quality of information obtained, quality of discussion, level of professionalism, cordiality of atmosphere); b) Personal Benefits (knowledge acquisition, confidence in treating patients, confidence in treating relapsed disease, confidence in handling complications, confidence in determining when to refer); c) Service Benefits (diagnostic evaluations, consultations); d) Technical satisfaction (format, frequency of meetings, time allotted for meeting, clarity of broadcast); and d) overall satisfaction. We will utilize a Likert scale grading in the evaluation of all these parameters. The Center for Continuing Education at UNMC will administer these evaluations.

Statistical Approach: Descriptive statistics will be computed for all variables to ensure data quality and to evaluate the assumptions of the statistical tests. Variable distributions will be described. Patient-, disease-, and treatment-related characteristics will be compared across physician groups. To address the study aims, the following analyses will be performed. All tests will be two-sided.

Statistical analysis for primary aim: Compare the adherence rates across physician groups.

In univariate analyses, the adherence rates will be compared between 1) UO vs. non-EXTEND CO group and 2) EXTEND CO group versus non-EXTEND CO group using t-tests. In this study design, correlation is induced by patients nested within physician. While the assumptions of normality and homogeneity of variance are only partially satisfied in the correlated data setting, simulation studies have demonstrated that the t-test is robust to moderate violations of the assumption of normality and homogeneity of variances. Donner

and Klar (1996) state that the independent samples t-test can be applied to cluster-specific event rates. [43-45] The level of significance for these comparisons is an alpha of 0.025.

In multivariate analyses, the method of Generalized Estimating Equations (GEE) will be used to compare adherence rates among the 3 groups (UO, intervention CO group, standard CO group). [46] The GEE methodology will allow us to account for correlation among patients seen by the same physician. Two indicator variables to denote physician group (UO and CO groups) will be included as categorical variables in the model, with non-EXTEND CO group as the reference group. Patient's place of residence, rural vs. urban, will also be included to examine the association with adherence. An interaction term for physician group and patient's area of residence will also be examined. A p-value < 0.05 will be deemed significant for these analyses. The RUCA designation for rural or urban location will be used to classify patients. A dichotomized classification will allow us better power to detect any statistical difference. Since adherence is a binary outcome, a logit link function will be used. The selection and rule out criteria will be used to specify the working correlation structure. [47] However, if the working correlation is misspecified, the GEE estimators of the variance are generally consistent estimators. [48]

A propensity score, based on the patient's probability of receiving the non-randomized treatment condition (UO, EXTEND and non-EXTEND CO groups) will be included as a covariate in the GEE model. By adjusting for propensity score, treatment allocation is independent of measured covariates and allows us to approximate a randomized controlled trial. [49] Since there are three groups, the multiple propensity score method using a multinomial logistic regression will be used to calculate the propensity score. The covariates to be used in the multinomial logistic regression model to derive the propensity score will include age, sex, level of education, median household income, disease severity based on their IPI or Hasenclever scores, comorbidity score and distance of residence to UNMC. Interaction terms between physician group and place of residence will be forced and tested for statistical significance. Furthermore, an analysis restricted to patients in the intervention CO group will be conducted using a GEE model to examine the association of physician attendance at the case conference with adherence.

The following analyses will be performed using descriptive statistics since there are not enough physicians to perform multivariate analyses: 1) Adherence rates over time will be tested by physician group; 2) Individual process variable rates over time within the EXTEND-CO group; 3) Adherence rates by physicians within the EXTEND CO group will be described according to the following process variables. Additionally, physician characteristics (years from graduation from medical school and oncology training, Board certification, distance of practice from patient's residence and UNMC, number of lymphoma patients treated) will be described.

Statistical analysis for secondary Aim 1: Compare the clinical outcomes after lymphoma treatment including: a) treatment response, b) 6-month treatment-specific complications, c) 6-month medical service utilization (non-scheduled consults, emergency room visits, hospitalizations), and d) 6-month progression-free and overall survival.

Treatment response [positive (CR or PR) versus negative (all other categories)], presence or absence of treatment-specific complications and 6-month serious medical service utilization will be analyzed using GEE with physician group, place of residence and propensity score as covariates similar to primary aim. The 6-month serious medical service utilization will be analyzed using a log link function. Here, the hypothesis is that patients treated by non-EXTEND CO group will have more ER visits and hospitalizations. Six-month

progression-free survival and overall survival will be descriptively summarized using the method of Kaplan and Meier. [50] In multivariate analysis, a Cox proportional hazards regression model will be used with physician group, place of residence, type of lymphoma, and propensity score as covariates. In the Cox models, the assumption of proportionality will be tested using a time dependent covariate. [51] In all of the secondary outcomes, an interaction term between physician group and place of residence will be forced and tested for statistical significance. Subset analyses of predominant histology (follicular and diffuse large cell lymphoma) will be performed if numbers are adequate.

Inter-rater reliability: Prior to intervention, the 3 lymphoma experts will convene to review NCCN guidelines. All experts will rate 10 randomly selected cases from sample NLSG records to determine adherence or non-adherence to NCCN guidelines. A 90 % agreement (Cohen's Kappa) will be considered acceptable. [52] If this criterion is not met, discussions on sources of variation will be discussed. Additional records will be reviewed until the desired agreement is achieved.

C.2.C.2 Change expected: The expected result is that groups 1 will have higher adherence rates and clinical outcomes than group 3 (80% vs. 60%), while group 2 will have a 20% higher adherence rate than group 3 (80% vs. 60%). It is also expected that clinical outcomes will be better for group 2 compared to group 3 patients.

The sample size justification is based on comparison of the primary outcome, adherence, between 1) UO vs. non-EXTEND CO group and 2) EXTEND CO group vs. non-EXTEND CO group. Expected accrual based on projected 15 month period with a 5% non-consent rate is 100 patients for group 1 and 75 patients for groups 2 and 3. A Bonferroni adjusted alpha of 0.025 is used to account for multiple comparisons and an intracluster correlation of 0.20 is used to account for the correlation induced by patients clustered within physician. The hypothesis is that adherence rates among non-EXTEND CO group will be 60% compared to 80% for both UO and EXTEND CO group. Given these assumptions, we have 80% to detect 20% difference in adherence rates. A review of adherence to the use of standard CHOP-R in diffuse large cell lymphoma in the NLSG showed that UO have an adherence rate of 87%, while CO have an adherence rate of 60%. Thus the assumptions used in our sample size justifications are reasonable.

C.2.C.3 Covariates and process variables used to determine if target audience was fully engaged in intervention: Table 2 summarizes the variables to be collected according to their use in the analysis. The rural-urban designation based on ZIP codes will be assigned using the Rural Urban Commuting Area Codes (RUCA). [53]

Table 2. Variables to be collected

Variables	Source	Domains
A. Socio-demographic characteristics of patients and treating oncologist	Patient or Patients' records Provider Database [b]	• Age, Sex, ZIP codes, for (rural and urban designation)[a] Race / ethnicity, Level of education, Marital status, Household income • Years from graduation from medical school and oncology training, Board certification, Distance of practice from Patient's residence and UNMC
B. Disease and Treatment	Medical Records, Pathology	• All clinical and laboratory data needed to compute the International Prognostic Index (IPI) or

Covariates	Reports, Ancillary Reports	the Hasenclever Prognostic Index [c] • WHO Classification of Lymphoma; Number of prior treatments given; Charlson Comorbidity Index
C. Process activity variables to be used to determine if target audience was fully engaged in intervention	Case conference proceedings	• Number of conferences held; • Number of cases discussed; • Attendance of participating CO; • Number of incorrect initial diagnoses; • Number of times agreement/disagreement in treatment plan is made without discussions; • Number of times agreement/disagreement in treatment plan is made after discussions; • Number of times 'Consultation Hotline' is used; • Number of times patients are transferred to UO for further treatment or enrolled in clinical trials; • Number of times conference case summaries and recorded conference proceedings are accessed online; Number of technical difficulties (audio and visual)

[a] Rural or urban designation will be based on the Rural Urban Commuting Codes (RUCA); [b] Database source includes UNMC Health Professions Tracking Center, American Board of Internal Medicine, American Board of Family Medicine; [c] The IPI and the Hasenclever Prognostic Index are the two standard indices widely used in non-Hodgkin and Hodgkin lymphoma, respectively. [54-55]

C.2.C.4 Dissemination Plans: Results of the study will be disseminated through publications in leading scientific journals. Prior to this, abstracts will be submitted to annual meetings of the American Society of Clinical Oncology (ASCO) or the American Society of Hematology (ASH). Lay versions of the results will be sent out to local and national news agencies (print, radio, and TV). A written summary report will also be sent out to all CO in the NLSG as well as all NCCN member sites.

C.2.C.5 Sustainability Assessment: The key determinant to sustaining the EXTEND Program is proof of efficacy. Thus, this proposal is designed towards showing this goal. We have also incorporated process variables to evaluate how UO benefits from hosting a community extended case conference (referrals, enrolment in clinical trials). From the perspective of the CO, proof that outcomes are improved, as well as adequate satisfaction should allow for this activity to be sustained. However, an important determinant to sustainability is also the cost associated with running the program. While not part of the study, we will evaluate cost per case discussed and explore options how these services can be reimbursed by insurance companies. Example, incorporating the patient in the discussion can technically be considered as a consult.

C.3 Detailed Work plan and Deliverables Schedule: The first 2 months of the study timeline will involve finalizations of the IRB approval, building of the program website and database, and visiting the 5 NLSG sites participating in the EXTEND Program. All NLSG sites are part of the Nebraska Statewide Telehealth Network and have access to live broadcast of conferences held at UNMC – Omaha campus. All the 10 physicians participating in the EXTEND program will also be given a personal Ipad so they can access the conferences wherever they are. The EXTEND Program will be implemented for a total of 15 months. We are expecting to deliver 52, 1-hour MCC for a period of 15 months. Data abstraction will be

performed from the 1st quarter of year 1 to the end of year 2. Detailed case and data processing procedures are summarized in Table 3 below. We expect that data on primary outcome (adherence) will be available as soon as the EXTEND Program ends in the 1st quarter of year 2. Analysis will follow soon and be the subject of an abstract to be submitted for presentation at ASH or ASCO. The participant satisfaction will be collected every 3 months during the 15 months accrual period. They will be set-up electronically so no further data entry is needed. A 2nd abstract will be focused on the results of the participant satisfaction tool. 6th month follow-up on all secondary outcomes will be collected until the last quarter of year 2. Soon after, the data on secondary outcomes will be analyzed. Results of the analysis of the secondary outcomes will be the subject of a 3rd abstract. While written manuscripts are not part of the timeline, we are committed to publish the results of the study in year 3 after the study has ended. Major activities and deliverables are summarized in Table 4.

Table 3: Case / Data Work Flow

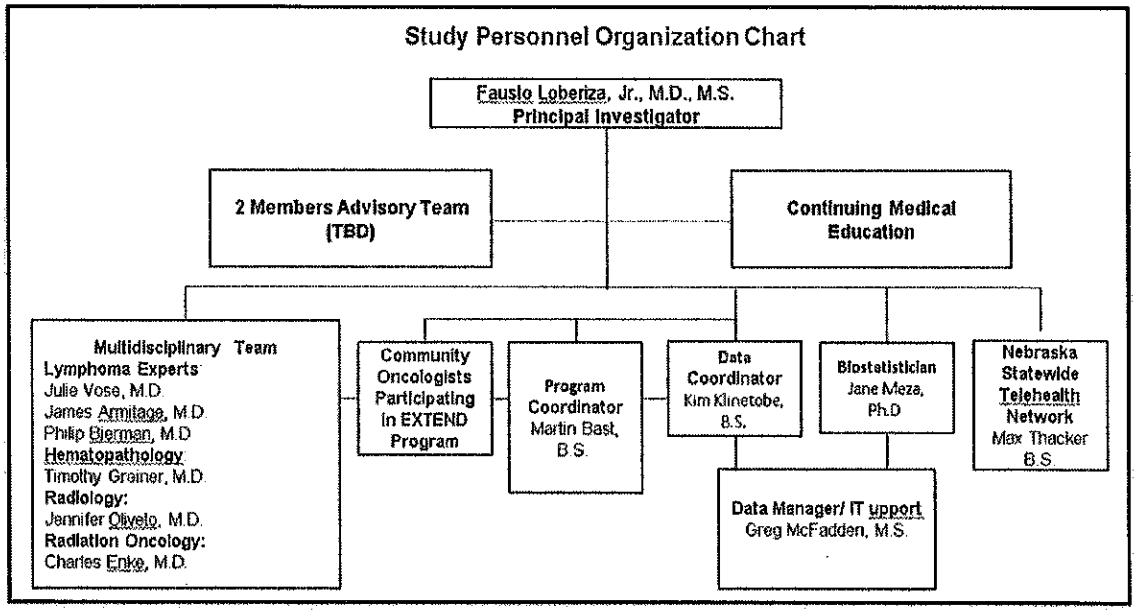
Steps	Description
1. Case Registration	Cases will be registered centrally through a secured website. A unique identifier will be assigned after registration. Informed consent from patient is checked at this time.
2. Clinical Summary	A brief medical history or copy of medical records, ancillary and diagnostic procedure reports are sent to the NLSG Central site at UNMC by fax or mail or by internet. Documents are matched with unique identifier.
3. Tissue / Radiological materials processing	Tissue specimens are sent to the NLSG Central Site using provided tissue sample kits. Actual available radiographs or electronic copies of these radiographs are also sent using overnight express mail. Tissues and radiographs will be matched with clinical information by the Program Coordinator. Tissues will be sent to the UNMC pathology department for 24 hour processing.
4. Case list formation	Study PI examines the list of cases and creates a list for distribution by email to all MCC attendees. Study PI prepares each week's list for distribution every Friday in time for the Monday conference. Weekly cutoff for cases to be discussed will be every Wednesday at 5PM. This allows adequate time for tissue processing.
5. Data Processing	The NLSG has existing policies regarding data transmission. All procedures followed are in accordance with existing federal and state regulations and are covered by existing IRB approvals. Medical records will be requested from NLSG sites every 6 months. Trained data entry personnel will enter all data and the Data Manager will merge the NLSG files with the created study files using SAS for analysis.

Table 4. Study Timeline of Detailed Major Activities and Deliverables

Major Activities	Year 1				Year 2			
Quarter →	1	2	3	4	1	2	3	4
Finalize IRB approval	X							
Train and visit participating CO / Coordinators	X							
Build database for new data / website	X							
Implement EXTEND Program		X	X	X	X	X		
Patient accrual		X	X	X	X	X		
Administer Participant Satisfaction Tool		X	X	X	X	X		
Data abstractions and outcome follow-up			X	X	X	X	X	X
Analysis of Primary Outcome [a]							X	X
Analysis of Participant Satisfaction Tool						X	X	
Analysis of Secondary Outcomes								X
Abstract Submission on Primary outcome								X

[a] Collection of data for primary aim (adherence) will end by the second quarter of year . Data collection for all secondary aims (6^{th} month outcomes) will end by year 2 and be ready for analysis soon after. Data will be constantly cleaned as data are reported throughout the study period.

D. Organizational Detail



Team Members:

Fausto Loberiza MD, MS, Principal Investigator and Team Leader – Dr. Loberiza is Professor in the Section of Oncology/Hematology, Department of Internal Medicine at the UNMC. In this project, Dr. Loberiza will have the following roles:

a) Manage and sustain the organization of the project, b) Hold weekly meetings with study personnel (Program Coordinator, Data and Tissue Coordinator, Data / IT Manager, and IT support person) to discuss, trouble shoot problems related to study implementation, enrolment procedure, data collection, IT related issues, tissue processing and handling of all medical records and radiographic tests.,

b) Monitor the day to day activities related to all aspects of study conduct,

c) Hold monthly meetings with multidisciplinary team and quarterly meetings with Advisory Board to report progress of studies, as well as discuss ways to improve study implementation. Use these meetings to solicit ideas to problem solve or correct study deficiencies,

d) Obtain updated IRB approvals as it relates to additional information required of study,

e) Act as main contact person for all inquiries related to study; maintain in close contact with participating community oncologists and their respective data coordinators. Be responsible for updating the Standard Operating Procedures of the NLSG as it relates to this study,

f) Work with IT support person and Program Coordinator to create study website,

g) Work with data manager regarding formats and coding of new variables to be collected as part of the study, as well as discuss design of study specific database / dataset,

h) Work with Program Coordinator regarding weekly case list for discussion in the case conference,

i) Work with lymphoma experts to make sure formats of case conference are done in a consistent manner,

j) Abstract outcomes data related to severe medical service utilization and treatment-related complications from medical records,
k) Supervise IT support person regarding audio and video requirements during weekly case conferences; making sure recorded videos are posted on time,
l) Create summary reports of weekly case conferences and making sure they are posted on time on the study website,
m) Create Consultation Hotline schedule for lymphoma experts with the help of the Program Coordinator,
n) Work with Biostatistician regarding all aspects of study analysis,
o) Lead team in study presentations, dissemination, and publications,
p) Be responsible for yearly progress reports, as well as final report, and
q) Be responsible for the ethical and responsible conduct of implementing, analyzing, and publishing results of the study.

Dr. Julie Vose will take on project leadership if Dr. Loberiza becomes unable to maintain his responsibilities. She will also be responsible for creating the weekly case list with the help of NLSG clinical research coordinator when Dr. Loberiza is on vacation.

Multidisciplinary Team of Experts:
Lymphoma Experts: Julie M. Vose, MD, James O. Armitage, MD, and Philip J. Bierman, MD.
Hematopathologist: Timothy Greiner, MD
Radiation Oncologist: Charles A. Enke, MD
Radiologist: Jennifer M. Oliveto, MD

This team will act as the university-based multidisciplinary team members who will act as resource people during the MCC. Lymphoma experts will rotate as facilitator of the MCC and provide consultations on a rotating basis. They will also update the group of current clinical trials, and provide insights of treatment toxicities and complications. They will review summary sheets of treatment plans prior to posting to study website. Hematopathologist will examine all tissue samples and provide pathological diagnosis using all immunostains and processes needed. Other expert members of the team will act as consultants during the MCC and will be sought for their expertise in arriving at diagnosis and planning of outcomes.

Biostatistician: Jane L. Meza, Ph.D
Dr. Meza is Director of the Center for Collaboration on Research, Design and Analysis at UNMC. She is also the Co-Director of the Biostatistics Shared resource of the Eppley Cancer Center. She will work closely with Dr. Loberiza to make sure that data collected are coded and collected properly. She will meet with Dr. Loberiza as often as needed and be present during quarterly meetings with the Advisory Team in reviewing procedures and challenges the team may experience in the execution of the study plan.

Advisory Panel: To be determined.
Two members with expertise in technology-based intervention and health outcomes / disparity research will be identified to serve as a scientific advisory board that can be consulted for ideas as we proceed in the proposed project. The panel is also expected to review progress of the study and provide insights in trouble shooting study related problems.

Center for Continuing Education:
Lois Colburn: Under the direction of Ms. Colburn, the Center will be responsible for the monitoring and evaluation of the educational components of the EXTEND Program, as well its accreditation. While it reports under Dr. Loberiza, it will be an independent entity and will supervise the evaluation of the program implementation. Ms. Colburn will also be an active member of the implementation and evaluation team.

Study Implementation and Data Collection Personnel
Martin A. Bast, BS – Project Coordinator – Mr. Bast currently serves as the clinical research coordinator of NLSG and has been in-charge of all its data collection activities since it started in 1985. He has also over the years developed knowledge and skills in dealing with the technical aspects of lymphoma. He coordinates with other coordinators from 9 other sites who are members of the NLSG making sure all data source documents, and biannual follow-ups are sent to the NLSG site in time. He will continue to do this work as part of this study. He will coordinate the list of cases to be discussed in the MCC on a weekly basis. Mr. Bast will help in the creation of the summary of all MCC and be responsible for posting it on the study website. Mr. Bast will report to Dr. Loberiza on a bi-weekly basis activities related to this project.

Kim Klinetobe, BS – Data Coordinator – Ms. Klinetobe has over 8 years of experience as data coordinator and will be responsible for all activities related to obtaining data of patients discussed in the MCC, including data abstraction, follow-up and processing. She will also be responsible for handling all radiological films or disc copies for MCC presentation.

Shelley Lewis, BS – Tissue coordinator – Ms. Lewis will be responsible for all activities related to the handling of tissue specimens of cases discussed in the MCC. She will work closely with Dr. Greiner.

Greg McFadden – Data Manager / IT Support – Mr. McFadden will be responsible for the creation of study specific database, website and data processing for analysis.

Max Thacker, BS – IT Head Nebraska Statewide Telehealth Network. – Mr. Thacker is in charge of the telehealth network and will assist in the setting of all networks to be used in the broadcast of the MCC. He will also be responsible for all technical enhancements of the MCC broadcasts.

References:

1. Educational Needs Assessment to Identify the Decision-making Patterns of Clinicians Managing Patients with Hematologic Malignancies. CE Outcomes, LLC, University of Nebraska Medical Center, Center for Continuing Education. Link to full report: http://www.ceoutcomes.com/wp-content/uploads/2013/07/Hematologic-Malignancies.pdf.
2. Loberiza FR, Jr., Cannon AJ, Weisenburger DD, Vose JM, Moehr JM, Bast MA, Bierman PJ, Bociek RG, Armitage JO. Survival disparities in patients with lymphoma according to place of residence and treatment provider: a population-based study. J Clin Oncol 2009; 27 (32):5376-82.
3. Rao K, Darrington D, Schumacher J, Devetten M, Vose J, Loberiza F. Disparity in Survival Outcome after Hematopoietic Stem Cell Transplantation for Hematologic Malignancies According to Area of Primary Residence. Biology of Blood and Marrow Transplantation 2007; 13:1508-14.
4. Loberiza FR, Jr., Lee SJ, Klein JP, Hassebroek A, Dehn JG, Frangoul HA, Hahn T, Hale G, Lazarus HM, Lemaistre CF, Maziarz RT, Rizzo JD, Majhail NS. Outcomes of Hematologic Malignancies after Unrelated Donor Hematopoietic Cell Transplantation According to Place of Residence. Biol Blood Marrow Transplant; 2010 16 (3):368-75.
5. Cannon AJ, Darrington DL, McIlvain HE, Bauer LK, Vose JM, Armitage JO, Loberiza FR Jr. Association of number of follow-up providers with outcomes in survivors of hematologic malignancies. Leuk Lymphoma. 2010 Oct; 51(10):1862-9.
6. Frances JJ, Eccles MP, Johnston M. Constructing questionnaires based upon the theory of planned behavior. Newcastle Upon Tyne, United Kingdom, ReBECI, 2004.
7. Mohler J, Bahnson RR, Boston B, Busby JE, D'Amico A, Eastham JA, Enke CA, George D, Horwitz EM, Huben RP, Kantoff P, Kawachi M, Kuettel M, Lange PH, Macvicar G, Plimack ER, Pow-Sang JM, Roach M 3rd, Rohren E, Roth BJ, Shrieve DC, Smith MR, Srinivas S, Twardowski P, Walsh PC. NCCN clinical practice guidelines in oncology: prostate cancer. J Natl Compr Canc Netw. 2010 Feb;8(2):162-200.
8. Thompson I, Thrasher JB, Aus G, Burnett AL, Canby-Hagino ED, Cookson MS, D'Amico AV, Dmochowski RR, Eton DT, Forman JD, Goldenberg SL, Hernandez J, Higano CS, Kraus SR, Moul JW, Tangen CM; AUA Prostate Cancer Clinical Guideline Update Panel. Guideline for the management of clinically localized prostate cancer: 2007 update. J Urol. 2007 Jun;177(6):2106-31.
9. Prades J, Borràs JM. Multidisciplinary cancer care in Spain, or when the function creates the organ: qualitative interview study. BMC Public Health. 2011 Feb 28;11:141.
10. Stone EG, Morton SC, Hulscher ME, Maglione MA, Roth EA, Grimshaw JM, Mittman BS, Rubenstein LV, Rubenstein LZ, Shekelle PG. Interventions that increase use of adult immunization and cancer screening services: a meta-analysis. Ann Intern Med 2002; 136 (9):641-51.
11. Stoner TJ, Dowd B, Carr WP, Maldonado G, Church TR, Mandel J. Do vouchers improve breast cancer screening rates? Results from a randomized trial. Health Serv Res 1998; 33 (1):11-28.
12. Nadel MR, Shapiro JA, Klabunde CN, Seeff LC, Uhler R, Smith RA, Ransohoff DF. A national survey of primary care physicians' methods for screening for fecal occult blood. Ann Intern Med 2005; 142 (2):86-94.

13. Foster JA, Abdolrasulnia M, Doroodchi H, McClure J, Casebeer L. Practice patterns and guideline adherence of medical oncologists in managing patients with early breast cancer. J Natl Compr Canc Netw 2009; 7 (7):697-706.
14. Stephens MR, Lewis WG, Brewster AE, Lord I, Blackshaw GR, Hodzovic I, Thomas GV, Roberts SA, Crosby TD, Gent C, Allison MC, Shute K. Multidisciplinary team management is associated with improved outcomes after surgery for esophageal cancer. Dis Esophagus 2006; 19 (3):164-71.
15. Griffith C, Turner J. United Kingdom National Health Service, Cancer Services Collaborative "Improvement Partnership", Redesign of Cancer Services: A National Approach. Eur J Surg Oncol 2004; 30 Suppl 1:1-86.
16. Magee LR, Laroche CM, Gilligan D. Clinical trials in lung cancer: evidence that a programmed investigation unit and a multidisciplinary clinic may improve recruitment. Clin Oncol (R Coll Radiol) 2001; 13 (4):310-1.
17. Haward R, Amir Z, Borrill C, Dawson J, Scully J, West M, Sainsbury R. Breast cancer teams: the impact of constitution, new cancer workload, and methods of operation on their effectiveness. Br J Cancer 2003; 89 (1):15-22.
18. Keating NL, Landrum MB, Lamont EB, Bozeman SR, Shulman LN, McNeil BJ. Tumor boards and the quality of cancer care. J Natl Cancer Inst 2013; 105:113-121.
19. Gandara E, Moniz TT, Dolan ML, Melia C, Dudley J, Smith A, Kachalia A. Improving adherence to treatment guidelines: a blueprint. Crit Pathw Cardiol 2009; 8 (4):139-45.
20. Hardcastle JD, Thomas WM, Chamberlain J, Pye G, Sheffield J, James PD, Balfour TW, Amar SS, Armitage NC, Moss SM. Randomised, controlled trial of faecal occult blood screening for colorectal cancer. Results for first 107,349 subjects. Lancet 1989; 1 (8648):1160-4.
21. Kupets R, Covens A. Strategies for the implementation of cervical and breast cancer screening of women by primary care physicians. Gynecol Oncol 2001; 83 (2):186-97.
22. Mandel JS, Bond JH, Church TR, Snover DC, Bradley GM, Schuman LM, Ederer F. Reducing mortality from colorectal cancer by screening for fecal occult blood. Minnesota Colon Cancer Control Study. N Engl J Med 1993; 328 (19):1365-71.
23. Mandel JS, Church TR, Bond JH, Ederer F, Geisser MS, Mongin SJ, Snover DC, Schuman LM. The effect of fecal occult-blood screening on the incidence of colorectal cancer. N Engl J Med 2000; 343 (22):1603-7.
24. Miaskowski C, Dodd MJ, West C, Paul SM, Tripathy D, Koo P, Schumacher K. Lack of adherence with the analgesic regimen: a significant barrier to effective cancer pain management. J Clin Oncol 2001; 19 (23):4275-9.
25. Myers RE, Turner B, Weinberg D, Hyslop T, Hauck WW, Brigham T, Rothermel T, Grana J, Schlackman N. Impact of a physician-oriented intervention on follow-up in colorectal cancer screening. Prev Med 2004; 38 (4):375-81.
26. Audet AM, Greenfield S, Field M. Medical practice guidelines: current activities and future directions. Ann Intern Med. 1990 Nov 1;113(9):709-14.
27. Chasin MR. Practice guidelines: best hope for quality improvement in the 1990s. J Occup Med. 1990 Dec;32(12):1199-206.
28. Weiner SG, Brown SF, Goetz JD, Webber CA. Weekly E-mail reminders influence emergency physician behavior: a case study using the Joint Commission and Centers for Medicare and Medicaid Services Pneumonia Guidelines. Acad Emerg Med 2009; 16 (7):626-31.

29. Du Pen SL, Du Pen AR, Polissar N, Hansberry J, Kraybill BM, Stillman M, Panke J, Everly R, Syrjala K. Implementing guidelines for cancer pain management: results of a randomized controlled clinical trial. J Clin Oncol 1999; 17 (1):361-70.
30. Eccher C, Seyfang A, Ferro A, Miksch S. Embedding oncologic protocols into the provision of care: the Oncocure project. Stud Health Technol Inform 2009; 150:663-7.
31. Lobach DF, Hammond WE. Computerized decision support based on a clinical practice guideline improves compliance with care standards. Am J Med 1997; 102 (1):89-98.
32. Stone EG, Morton SC, Hulscher ME, Maglione MA, Roth EA, Grimshaw JM, Mittman BS, Rubenstein LV, Rubenstein LZ, Shekelle PG. Interventions that increase use of adult immunization and cancer screening services: a meta-analysis. Ann Intern Med 2002; 136 (9):641-51.
33. Stoner TJ, Dowd B, Carr WP, Maldonado G, Church TR, Mandel J. Do vouchers improve breast cancer screening rates? Results from a randomized trial. Health Serv Res 1998; 33 (1):11-28.
34. Hillner BE, Smith TJ, Desch CE. Hospital and physician volume or specialization and outcomes in cancer treatment: importance in quality of cancer care. J Clin Oncol 2000; 18 (11):2327-40.
35. Loberiza FR, Jr., Zhang MJ, Lee SJ, Klein JP, LeMaistre CF, Serna DS, Eapen M, Bredeson CN, Horowitz MM, Rizzo JD. Association of transplant center and physician factors on mortality after hematopoietic stem cell transplantation in the United States. Blood 2005; 105 (7):2979-87.
36. Luft HS, Bunker JP, Enthoven AC. Should operations be regionalized? The empirical relation between surgical volume and mortality. N Engl J Med 1979; 301 (25):1364-9.
37. Nathens AB, Jurkovich GJ, Maier RV, Grossman DC, MacKenzie EJ, Moore M, Rivara FP. Relationship between trauma center volume and outcomes. Jama 2001; 285 (9):1164-71.
38. Tu JV, Austin PC, Chan BT. Relationship between annual volume of patients treated by admitting physician and mortality after acute myocardial infarction. Jama 2001; 285 (24):3116-22.
39. Romanus D, Weiser MR, Skibber JM, Ter Veer A, Niland JC, Wilson JL, Rajput A, Wong YN, Benson AB 3rd, Shibata S, Schrag D. Concordance with NCCN Colorectal Cancer Guidelines and ASCO/NCCN Quality Measures: an NCCN institutional analysis. J Natl Compr Canc Netw 2009; 7 (8):895-904.
40. Punglia RS, Hughes ME, Edge SB, Theriault RL, Bookman MA, Wilson JL, Ottesen RA, Niland JC, Weeks JC. Factors associated with guideline-concordant use of radiotherapy after mastectomy in the national comprehensive cancer network. Int J Radiat Oncol Biol Phys 2008; 72 (5):1434-40.
41. Cheson BD, Pfistner B, Juweid M, Gascoyne RD, Specht L, Horning SJ, Coiffier B, Fisher RI, Hagenbeek A, Zucca E, Rosen ST, Stroobants S, Lister TA, Hoppe RT, Dreyling M, Tobinai K, Vose JM, Connors JM, Federico M, Diehl V. Revised Response Criteria for Malignant Lymphoma. JCO 2007: 579-586.
42. Cheson BD, Horning SJ, Coiffier B, Shipp MA, Fisher RI, Connors JM, Lister TA, Vose J, Grillo-López A, Hagenbeek A, Cabanillas F, Klippensten D, Hiddemann W, Castellino R, Harris NL, Armitage JO, Carter W, Hoppe R, Canellos GP. Report of an international workshop to standardize response criteria for non-Hodgkin's lymphomas. NCI Sponsored International Working Group. J Clin Oncol. 1999 Apr;17(4):1244.

43. Donner A, Klar N. Statistical considerations in the design and analysis of community intervention trials. J Clin Epidemiol 1996; 49 (4):435-9.
44. Harwell MR, Rubinstein EN, Hayes WS, Olds CC. Summarizing Monte Carlo results in methodological research: The one- and two- factor fixed effects ANOVA cases. J Educ Stat 1992 17(4): 315-339.
45. Heeren T, D'Agostino R. Robustness of the two-independent samples t-test when applied to ordinal scaled data. Stat Med 1987; 6(1): 79-90.
46. Liang Ky and Zeger SL. Longitudinal data analysis using generalized linear models. Biometrika 1986;73:13-22.
47. Shults J, Sun W, Tu X, Kim H, Amsterdam J, Hilbe JM, Ten-Have T. 2009 A comparison of several approaches for choosing between working correlation structures in generalized estimating equation analysis of longitudinal binary data. Stat Med. 28(18):2338-55.
48. Lee JH, Herzog TA, Meade CD, Webb MS, Brandon TH. 2007 The use of GEE for analyzing longitudinal binomial data: A primer using data from a tobacco intervention. Addictive Behaviors 32 (2007) 187–193.
49. Austin PC. The performance of different propensity score methods for estimating marginal odds ratios. Statist. Med. 2007; 26:3078–3094.
50. Kaplan EL, Meier P (1958). Nonparametric estimation from incomplete observations. J Am Stat Assoc 53: 457-481.
51. Cox D. Regression models and life tables. Journal of the Royal Statistical Society 1972; 34:187-220.
52. Fleiss JL and J Cohen. The equivalence of weighted Kappa and the intraclass correlation coefficient as measures of reliability. Educ Psychol Meas. 1973; 33: 613-619.
53. Hart LG, Larson EH, Lishner DM. Rural definitions for health policy and research. Am J Public Health 2005; 95 (7):1149-55.
54. The International Non-Hodgkin's Lymphoma Prognostic Factors Project: A predictive model for aggressive non-Hodgkin's lymphoma. N Engl J of Med 1993; 329:987-94.
55. Hasenclever D and V Diehl. A prognostic score for advanced Hodgkin's disease. International prognostic factors project on advanced Hodgkin's disease. N Engl J Med. 1998 Nov 19;339(21):1506-14.

February 22, 2014

Dr. Fausto Loberiza
Division of Hematology/Oncology
Department of Internal Medicine
University of Nebraska Medical Center
987680 Nebraska Medical Center
Omaha, NE 68198-7680

Re: "Community Extended Case Conference to Improve Lymphoma Care"

Dear Fausto,

I enthusiastically support your application and invitation to serve as co-investigator. I will participate in all of your planned multidisciplinary case conferences and serve as a lymphoma expert. Based on my review of your application, I think you have planned for an innovative study that will be appreciated by community oncologists and more importantly, can improve the care and outcomes of lymphoma patients in general. I will also take over your leadership responsibilities as study PI when called to do so. I will participate in reviewing cases for relevant clinical outcomes and attend all discussions regarding study implementation and data interpretation. As the Chief of the Division of Hematology/Oncology at the University of Nebraska Medical Center (UNMC) and the Medical Director for Oncology Services at the Nebraska Medical Center, I will assure that adequate support through the division resources be made available to you as needed to support this project.

I feel your background in health services and population-based research is ideal to support the EXTEND Program. Since we practice in a state that is predominantly rural, your planned study should benefit a wide range of patients with lymphoma. I also view it as a way to guarantee patients the highest standard of care.

I wish you success in moving forward with the project.

Sincerely,

Julie Vose

Julie M. Vose, M.D.
Neumann M. and Mildred E. Harris Professor
Chief, Division of Hematology/Oncology
Professor of Medicine

February 24, 2014

Dr. Fausto Loberiza
Division of Hematology/Oncology
Department of Internal Medicine
University of Nebraska Medical Center
987680 Nebraska Medical Center
Omaha NE 68198-7680
Phone: 402-559-5166
Fax: 402-559-6520

Dear Fausto,

It is with great enthusiasm that I support your grant application entitled: "Community Extended Case Conference to Improve Lymphoma Care". Your proposal to set-up a multidisciplinary case conference dedicated to planning of treatment for patients with lymphoma that are seen by community oncologists in the state of Nebraska, outstandingly complements our efforts at The Nebraska Lymphoma Study Group. As you may know, this is the kind of project I envisioned the NLSG would get involved in when I helped founded it over 25 years ago. The EXTEND program you have envisioned can potentially change how we best interact with our colleagues in the community. I am particularly excited by it's potential to improve lymphoma outcomes.

You have assembled a pool of investigators who have an outstanding track record in the clinical care of cancer patients and health services research. I have no doubt that the program will flourish under your leadership and the support that will be made available to you at UNMC. As member of the lymphoma expert team in your application, I will participate in the case conferences and assist in abstracting critical adherence data and clinical outcomes from patients records. I will also participate in discussions related to study implementation and data analyses.

I am excited to work with you on this project and wish you the best in all your endeavors.

Sincerely,

James O. Armitage, M.D.
Professor of Medicine

February 24, 2014

Dr. Fausto Loberiza
Division of Hematology/Oncology
Department of Internal Medicine
University of Nebraska Medical Center
987680 Nebraska Medical Center
Omaha NE 68198-7680
Phone: 402-559-5166
Fax: 402-559-6520

Dear Fausto,

I am pleased to participate as co-investigator in your grant application entitled: "Community Extended Case Conference to Improve Lymphoma Care". As a member of the lymphoma expert team you have organized, I will participate in the discussion of cases during the conferences and help extract information from patients records related to your proposed study outcomes. I will also attend meetings tackling issues related to the implementation of your study design and give advice as I see fit. I also look forward to giving my inputs when data are ready for interpretation.

I believe the use of our current multidisciplinary case conferences have helped improve the care of lymphoma patients we see at the university, and I am delighted to see how this translates in to the community. In my opinion, the project you proposed is significant and has the potential to be applied in all types of malignancies. It can represent a new way on how us in the university can help the most in assuring equal outcomes for cancer patients regardless of where they live.

I am sure your enthusiasm and leadership would bring success to this project and I look forward to more interactions with you and the team you have assembled.

Sincerely,

Philip Bierman, MD
Professor of Medicine

Timothy C. Greiner, M.D.
Department of Pathology and Microbiology
983135 Nebraska Medical Center
Omaha, NE 68198-3135
Telephone: 402/559-8707 Fax: 402/559-6018
Email: tgreiner@unmc.edu
PATHOLOGY AND MICROBIOLOGY

February 24, 2014

Dr. Fausto Loberiza
Section of Hematology/Oncology
Department of Internal Medicine
University of Nebraska Medical Center
987680 Nebraska Medical Center
Omaha NE 68198-7680
Phone: 402-559-5166
Fax: 402-559-6520

Dear Fausto,

I am delighted to be a co-investigator in your study entitled: **"Community Extended Case Conference to Improve Lymphoma Care".** Specifically, I am happy to be hematopathologist in-charge of performing confirmatory tests on cases submitted to us as part of the study. As Chief of Hematopathology at UNMC, I assure you that tissues submitted to us will be handled as priority and with due care so they can be presented during our scheduled multidisciplinary case conference on time. I will be happy to attend the scheduled conferences and give my clinical impression of the case based on best evidence available. As you know, the role of the pathologist in the multidisciplinary case conference is essential as proper treatment starts from correct diagnosis. I will perform my role with due diligence. I also look forward to extensive discussion with other members of the excellent team you have assembled.

Thank you for the opportunity to be a part of a project that I know will contribute to the improvement of outcomes of patients with lymphoma.

Sincerely,

Timothy C. Greiner, M.D.
Director of Hematopathology
Professor of Pathology and Microbiology

COLLEGE OF PUBLIC HEALTH
Department of Biostatistics

February 24, 2014

Dr. Fausto Loberiza
Division of Hematology/Oncology
Department of Internal Medicine
University of Nebraska Medical Center
987680 Nebraska Medical Center
Omaha NE 68198-7680
Phone: 402-559-5166
Fax: 402-559-6520

Dear Fausto,

I am writing this letter in support of your application entitled: "Community Extended Case Conference to Improve Lymphoma Care". I am delighted to be part of your investigative team and act as project Biostatistician. Based on discussions and planning of your proposal, I believe we have put forward a sound scientific study that in my opinion can have a significant impact on the health. As Director of the Center for Collaboration of Research Design and Analysis, you have my utmost commitment that the facilities and resources we have shall be made available to you in all aspects of your study implementation, data acquisition and data analysis. I also look forward to attending any team meetings you will schedule as we discuss approaches to different study issues that may ensue as we implement the study design, especially those that pertain to data analysis.

Thank you inviting me to be a part of your team and I know that this will be a productive partnership.

Sincerely,

Jane L Meza

Jane Meza, Ph.D
Professor
Director of Center for Collaboration of Research and Design and Analysis
Interim Chair, Department of Biostatistics

COLLEGE OF MEDICINE
Department of Radiation Oncology

February 23, 2014

Dr. Fausto Loberiza
Section of Hematology/Oncology
Department of Internal Medicine
University of Nebraska Medical Center
987680 Nebraska Medical Center
Omaha NE 68198-7680
Phone: 402-559-5166
Fax: 402-559-6520

Re: "Community Extended Case Conference to Improve Lymphoma Care"

Dear Fausto,

I am delighted to be a co-investigator in your NIH proposed study. Specifically, I am happy to participate in the multidisciplinary case conferences and act as the team radiation oncologist. As you know, I have participated in a similar role during the weekly Lymphoma Multidisciplinary Team Conference here at UNMC and I believe that the discussions related to the diagnosis and treatment plan of these cases significantly impact the patient's outcomes. I am truly excited to be part of the team and look forward to supporting and enhancing this conference in expanded venues. As Chairman of the Department of Radiation Oncology, I would also endorse your project to other faculty and trainees which would allow them to learn from this process. I commend your efforts in organizing the team and reinforcing the role of the team approach in securing better outcomes for our patients.

Thank you for letting me be part of the team and I look forward to our further discussions.

Sincerely,

Charles Enke MD

Charles A. Enke, M.D.
Professor & Chairman
Department of Radiation Oncology
UNMC

DEPARTMENT OF RADIOLOGY

February 22, 2014

Dr. Fausto Loberiza
Division of Hematology/Oncology
Department of Internal Medicine
University of Nebraska Medical Center
987680 Nebraska Medical Center
Omaha, NE 68198-7680

Re: "Community Extended Case Conference to Improve Lymphoma Care"

Dear Fausto,

I am delighted to be a co-investigator in your proposal referenced above. Specifically, I will be part of your multidisciplinary team of experts in your planned case conferences and act as the team's expert radiologist. In this role, I will review all clinical and radiographs submitted to us from patients seen in the community and give my independent clinical impression of the case presented so it may help in the planning of appropriate treatment of the patient. I believe my clinical training and extensive experience with reading CT, MRI and other radiological modalities will help in this project. I also have the expertise of many colleagues in the Department of Radiology at UNMC available and who we can seek opinions when needed.

I look forward to interacting with you and the team as we move forward.

Sincerely,

Jennifer M. Oliveto, M.D.
Assistant Professor of Radiology

981045 Nebraska Medical Center / Omaha, NE 68198-1045
Phone: 492-559-1010 / Fax: 402-559-1011