**1. Overall Goal and Objectives**

The overall goal of this project is to implement and test a system-level intervention designed to achieve very high levels of adherence to pneumococcal vaccination (PVX), annual influenza vaccination INFVX, and zoster vaccination (ZVX) *before* treatment with highly immunosuppressive therapies, including biologics and kinase inhibitors, among patients with rheumatoid arthritis (RA). The intervention will include:

1) electronic quality measurement and individual feedback to physicians,
2) computerized, point-of-care clinical decision support, and
3) population health management facilitated by an electronic data warehouse.

Our specific objectives are to: 1) achieve ≥ 80% rate of initial PVX (or revaccination among those vaccinated only once previously), 2) achieve ≥ 60% rate of INFVX *early* during the 2013-14 season (i.e., prior to December 31, 2013), and 3) achieve ≥ 80% rate of offering ZVX and ≥ 50% rate of actual ZVX. (Note: We have set a lower goal for ZVX because it is often not covered by insurance). We chose these objectives because a) they represent rates substantially above our current rates, and b) we believe these are attainable goals for our practice and other practices around the country that would be interested in implementing this intervention (i.e., these represent rates attainable with best practices and can serve as "achievable benchmarks").

In addition to these primary objectives, our secondary objective is to assess physician and staff engagement in the intervention and to elucidate barriers to achieving optimal vaccination rates. This information will be important for our practice as we strive to improve further and for other practices that want to implement our intervention in their unique practice environment. We will use quantitative and qualitative methods to examine this objective.

**2. Technical Approach**

***a. Current Assessment of Need for the Intervention***

a. i.) Baseline data summary: To determine the need for the intervention, we queried our enterprise data warehouse (EDW) using Structured Query Language. Our EDW stores data from all clinical and administrative sources (e.g., outpatient, inpatient, billing, etc.) in an architecture that facilitates research, quality improvement, and practice management activities. Using a previously developed algorithm by investigators at Northwestern that is more accurate than ICD-9 codes alone,[1] we identified all patients with RA. We then queried the immunization data tables to assess whether patients had received PVX, INFVX, and ZVX.

The immunization rates were as follows:

Pneumococcal (any administration prior to January 2013) - 41%

Influenza (administered at any time during the 2011-12 season) - 19%

Zoster (any administration prior to January 2013) - 2%

a. ii). Primary target audience for the intervention*:* The primary audience will be rheumatologists, internists, and other providers managing RA patients in our healthcare system. We anticipate direct benefit from this project will accrue to RA patients who appropriately receive the three vaccines targeted by this intervention. If the intervention is successful, we hope that other organizations will benefit from this practical, replicable

intervention to improve vaccination rates for population health management of patients with rheumatoid arthritis and other conditions requiring immunosuppression.

a. iii) Innovation of the intervention: A study conducted at Geisinger found that an electronic reminder increased PVX (19 to 41%) and INFVX (47 to 65%) rates among rheumatology patients.[2] Our proposed study goes beyond this in several ways: 1) we are implementing a more comprehensive system that should achieve much higher rates of PVX, 2) we will conduct outreach to achieve high INFVX rates early in the season when it will be most protective, and 3) we will include ZVX as a target and attempt to overcome the common financial barriers faced by patients. This study builds on previous work we have done on the use of computerized algorithms to identify patients with RA,[1] and the effectiveness of complex, multifaceted quality improvement strategies.[3] Our previous intervention targeted a general medical population and did not include pneumococcal vaccination for people < 65 years old, influenza, or zoster as quality improvement targets. Our proposed intervention is innovative because of its use of complex clinical decision support tools and technology-enabled population health management and outreach in a unified system.

***b. Intervention Design and Methods***

b. i. Background and conceptual framework: The intervention will apply the principles and approach used by Dr. Baker in the UPQUAL study. UPQUAL tested a multifaceted system to improve quality of care for chronic diseases and preventive services in our general internal medicine (GIM) clinic.[3-7] The intervention was designed to address the multiple factors that lead to suboptimal quality of care: lack of awareness of a quality deficit, lack of alerts at the point of care and inaccurate or interruptive alert systems, lack of integration of quality measurement and quality improvement tools into routine workflow, and lack of attention to patients who need care but were not coming for visits (and therefore not triggering an alert). An integrated system was designed and implemented that included routine quality measurement, point of care alerts, "asynchronous" alerts to providers about patients who needed outreach to get high-priority services, and routine performance feedback to physicians.

During the UPQUAL study, quality improved for 14 of 16 targets, and improvement accelerated compared to previous years for nine of 16 measures.[3] Three years after the project ended, the quality measurement, reporting, and improvement tools have remained standard of care. Moreover, the number of active clinical topics addressed by these tools has been expanded from 16 to 22. The basic design principles have been implemented in projects conducted by three other health care systems. If we can achieve similar results for this project, our intervention will serve as a generalizable, sustainable model for improving immunizations among patients with RA and other conditions requiring immunosuppressive medication.

b. ii. Reasons for Failure to Vaccinate and Mitigation Strategies: The underlying assumption with our approach is that failures occur for multiple reasons. Consequently, a multifaceted system is needed to achieve the highest levels of quality. First, providers need valid, trusted data on their individual performance to be motivated to address gaps in their care (e.g., low vaccination rates among their own patients). Second, during a busy visit, providers may forget to assess whether

a patient requires vaccinations. Non-interruptive, highly-visible reminders are needed so that the entire health care team is aware during a visit or other encounter that a patient needs one or more vaccinations; these reminders should be linked to order sets in the electronic health record, making it easy and efficient to do the right thing. Our previous work has shown high rates of physician acceptance and use of these reminders.[3,4] The reminder system also makes it possible to enter medical contraindications, financial barriers, or patient refusals; this information can then be included in performance reports and used to guide outreach. Third, patients who are not seen frequently do not benefit from point of care alerts. Systems are needed to identify patients who need outreach. We have conducted outreach through both asynchronous alerts to clinicians (i.e., sending a monthly list of patients needing medication that should not be delayed until the next visit) and by using care managers to contact patients for important but non-urgent care needs.[5] This is very important for influenza vaccination, since the vaccine should be given early during the influenza season to obtain optimal protection.

b.iii. Setting and Study Population: This project will target patients with RA who are cared for by rheumatologists (10 faculty, 4 fellows) and general internists (37 faculty) in the Northwestern Medical Faculty Foundation (NMFF). NMFF is an academic, multispecialty group practice staffed by the full-time faculty for the Feinberg School of Medicine, Northwestern University. Currently, there are 1771 patients with RA who are regularly cared for by the divisions of Rheumatology and General Internal Medicine. Approximately 50% are treated with a biologic agent. We will not include patients who are cared for by other medical or surgical specialties and receive their rheumatologic and primary care elsewhere. All NMFF physicians use an electronic health record (Epic; Epic Systems Corporation; Verona, Wisconsin) for all clinical encounters (in-person and telephone). All prescriptions for DMARD and biologic therapy are initiated and tracked in Epic.

b. iv. Vaccine Targets: For this project, we will target three vaccines of particular importance to RA patients: PVX, INFVX, and ZVX. We chose these because they are the most commonly indicated vaccinations in this patient population. We limited the intervention to three vaccines so we will not overwhelm clinicians with too many alerts. As vaccination rates increase to high levels, the workload to address gaps is minimized; then, we can expand this to include other vaccines. The specific design elements for this project are described below.

b.v. Intervention Components

*Quality Measurement and Performance Feedback*: Using the same quality of care queries and denominator algorithms used to measure our baseline performance (see 2.a.i. above), we will provide each rheumatologist with a quarterly report of their individual PVX and ZVX rates for RA patients, including the proportion with documented reasons for not giving a vaccination. Group and individual feedback on INFVX will be given *monthly* during influenza season. Group performance and anonymous individual performance will be presented by Dr. Ruderman (the clinical practice director) at standing monthly business meetings. These measures will also be incorporated into the current reporting system used by the GIM clinic (see above).

*Clinical Decision Support and Best Practice Alerts:* Our practice uses the Epic Ambulatory

electronic health record. Epic has a standard tool called “Best Practice Alerts” that allows users to create highly customizable clinical decision support, reminders, and linked order sets. We have extensive experience using these. We will implement point of care alerts and linked order sets for pneumococcal, influenza (seasonally), and zoster vaccinations. The pneumococcal alerts will include an alert for initial vaccination and a second alert for revaccination after five years, as recommended by the Centers for Disease Control and Prevention.[8] The zoster alert will not fire if the patient is receiving a TNF inhibitor or non-TNF biologic agent or tofacitinib, and a warning will be created to prevent ordering the zoster vaccine for patients on biologic agents. If a patient has a medical contraindication or refuses one or more vaccinations, members of the health care team will be able to enter this information into the clinical decision support system so that future point of care alerts will be suppressed; this information will be included as a satisfying condition for performance reports.

*Vaccination Care Manager (VCM)*: We will designate a nurse to serve as the VCM for outreach and population management. At the start of the study, the VCM will identify all patients who have not received indicated PVX and ZVX and notify them by mail or through our EHR's secure email system that they should receive these vaccinations. They will be given a list of options for getting vaccinated (e.g., routine visit, special nurse visit for vaccinations, community pharmacy). The mailing will be repeated in three months for those with outstanding vaccinations.

Influenza vaccination should occur in October (2013 for this study); the peak for influenza cases occurs in January or later 80% of the time. Patients may not present for care between October and December, so outreach is crucial. The VCM will use multiple modalities to perform outreach in October, including 1) mailed letters, 2) messages sent through our EHR's secure email system, and 3) automated telephone reminders to notify patients that they should get the INFVX. Patients will be encouraged to obtain the INFVX in the most convenient location; if this is external to NMFF, we will give them our phone and fax numbers to notify the VCM that this was completed so it can be entered into our EHR. The calls and e-mails will be repeated at the start of November and December for those who continue to not have documentation that they were vaccinated. Patients who decline vaccination will have this information entered into the clinical decision support system so that future point of care alerts will be suppressed and reminders will no longer be sent.

The VCM will also work to overcome financial barriers to ZVX use. Many patients will initially not have ZVX covered by their insurance. To address this, we will use data from our EDW to create an active registry of patients who were offered ZVX but could not afford it. The VCM will follow this cohort and notify them when they become eligible (e.g., turn 60 years old, change insurance, or an insurer changes its policy).

b. vi. Implementation of the Intervention

*Creation of Clinical Decision Support Tools in the EHR:* We will develop these using established methods, including a) a yellow “Best Practice” alert visible in all encounters that can show a list of outstanding issues by clicking on the tab (see below, Figure 1); b) “hub and spoke design” that allows clinicians to jump to a location to record previous vaccinations (Figure 2a) or patient reasons for not administering vaccinations (Figure 2b), and c) linked order sets (Figure 3).

Figure 1. Sample Best Practice Alert (BPA) and Advisories visible when the BPA tab is clicked.

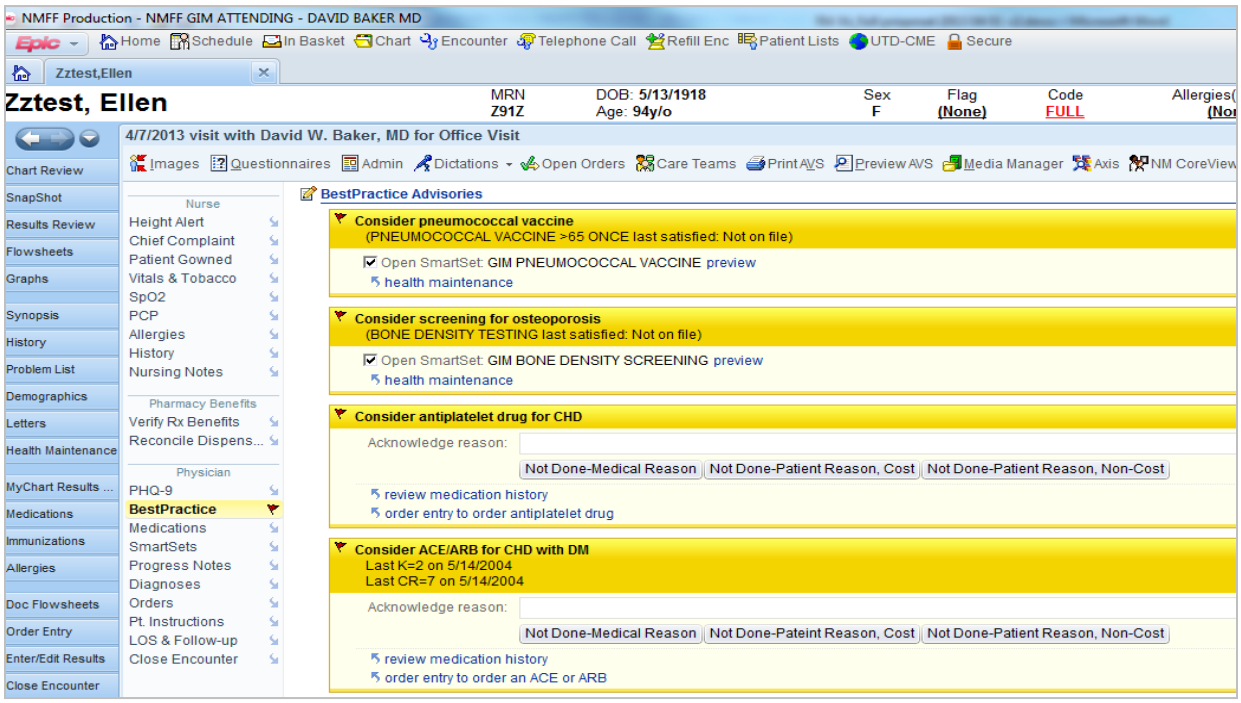



Figure 2a. Example of recording outside vaccinations.

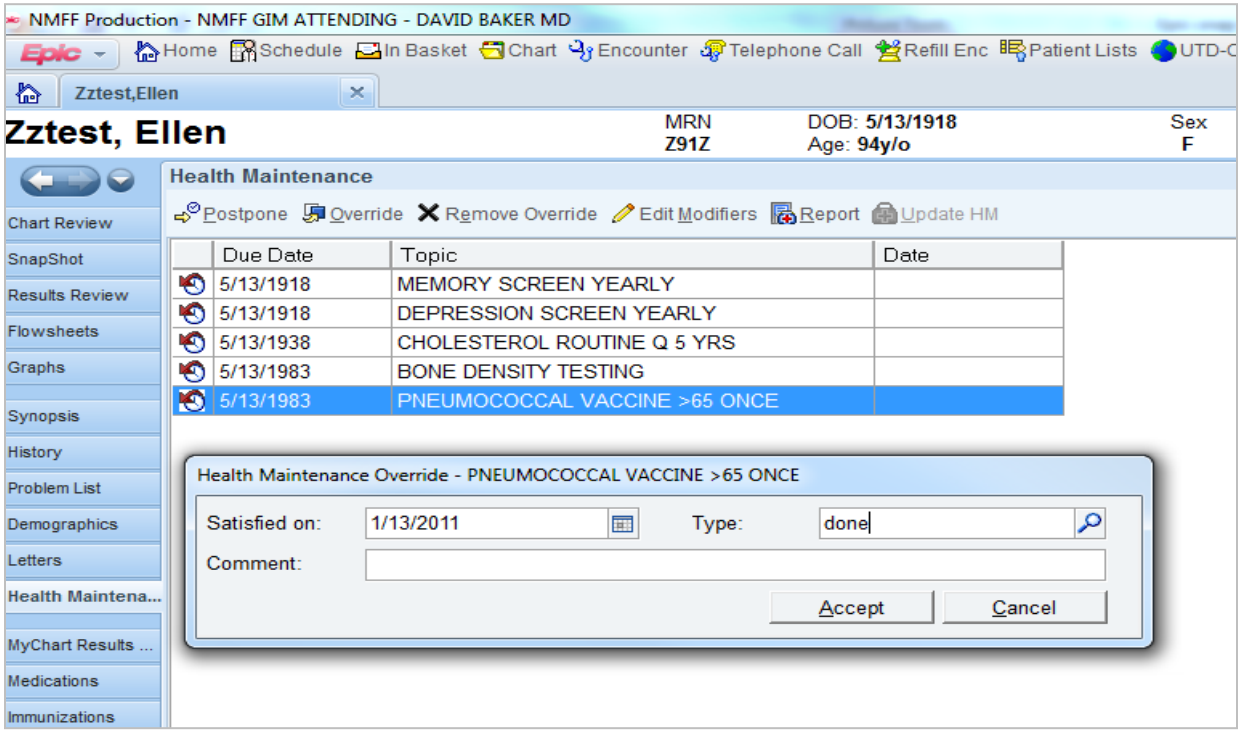


Figure 2b. Example of recording that a patient was not vaccinated due to financial barriers.

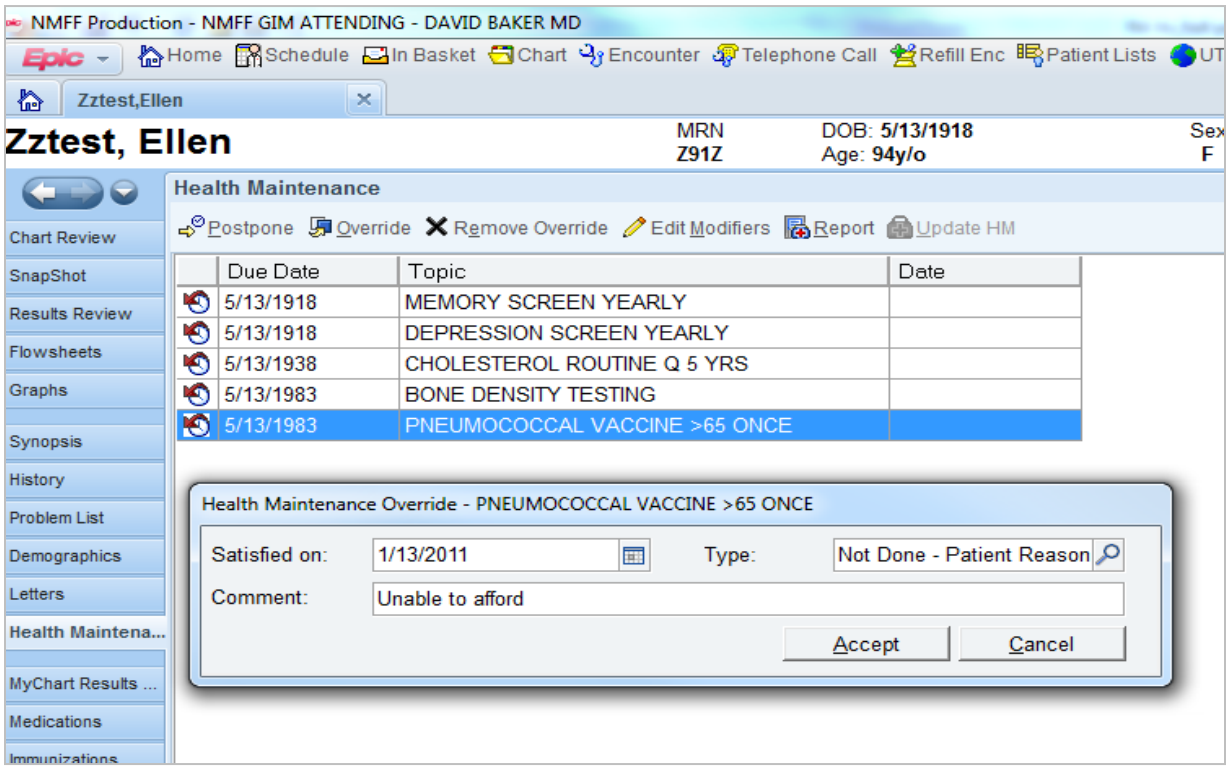
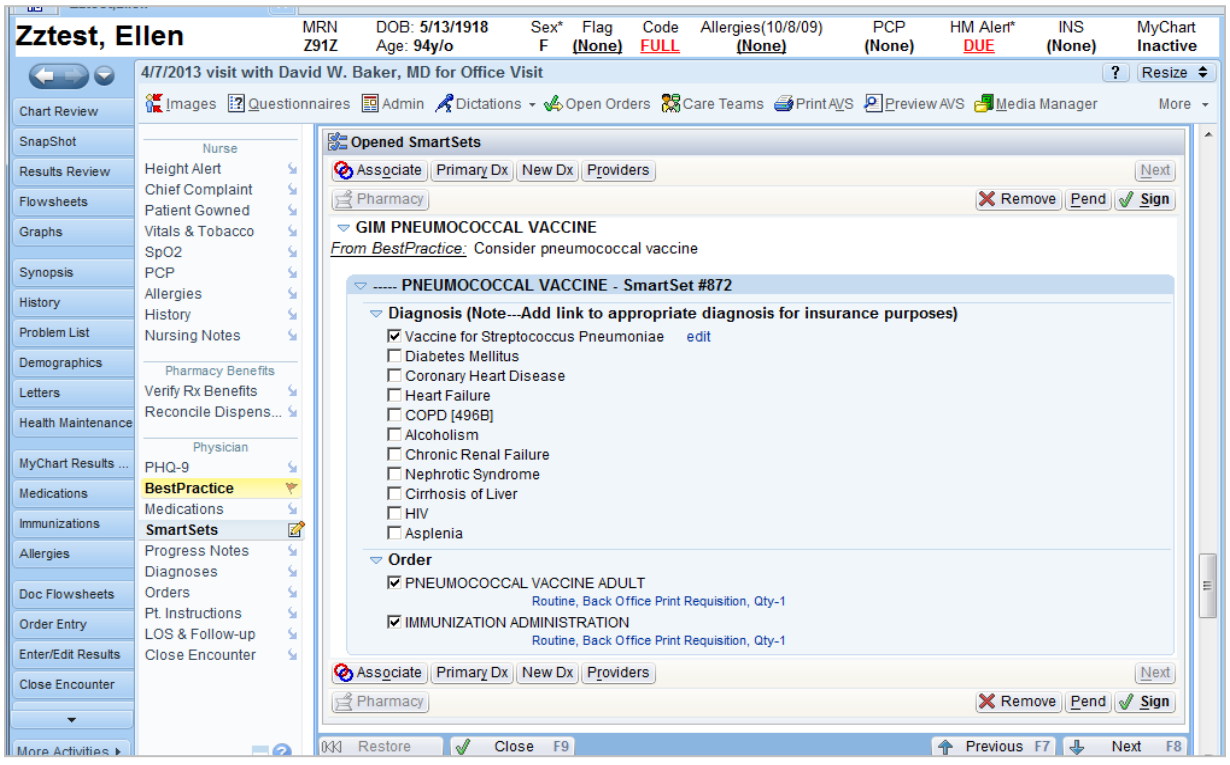



Figure 3. Example of a linked order set to facilitate ordering needed vaccinations.



*Training Physicians to Use the Best Practice Alerts and Order Sets:* We will use several strategies to encourage physicians and to use the alerts and order sets and to teach them how to use them properly. After the alerts have been developed and are active in Epic, we will demonstrate these to physicians in a one hour session at a monthly business meeting. Physicians will be given their first quarterly quality report at this time to create a "teachable moment." Physicians will also be given a simple pocket reminder card, and they can work through examples using the test patients that are present in our EHR. For the next two months after this, we will send physicians reminder emails about how to use these tools, including a few simple illustrations each time using screen shots from Epic. We anticipate that as some physicians begin to use the tools, their measured performance will improve and those who do not use the codes will look progressively worse compared to their peers. This may create further motivation to learn and use the tools and improve vaccination rates.

*Outreach by the Vaccination Care Manager (VCM)*: The Rheumatology clinic's nurse practitioner, will serve as the VCM. We will train the nurse in the principles of vaccinations and in the use of electronic data sources for population health management.

Our programmer analyst will query our electronic data files to identify all patients with RA who have not received indicated PVX and ZVX. This list will be used by the VCM to notify patients by mail or through our EHR's secure email system that they should receive these vaccinations as soon as possible. The query will be continuously updated so the VCM can see progress. After three months, the VCM will send a second mailing or e-mail to patients who still have not been vaccinated. In October 2013 for this study, the VCM will use a similar approach to notify all patients who our records show have not been vaccinated (some get vaccinated in September) that they should receive the INFVX. The calls and outreach will be repeated monthly for those who continue to not have documentation that they were vaccinated or until they refuse.

Every month, the programmer analyst will query the electronic data to identify patients who did not receive ZVX for financial reasons. These data will be exported to an Access database to create an active registry of patients who were offered ZVX but could not afford it. Every month the VCM will query this database to identify patients who have become eligible for ZVX coverage based on their age and type of insurance. Every quarter, the VCM will contact insurers to assess changes in their coverage policies for ZVX and, if changes occur, query the database to identify those who have become eligible and then contact them.

***c. Evaluation Design***

c. i. Study Design: Because this is a system-level intervention targeting the entire population of RA patients, it is not possible to randomize patients or physicians to receive the intervention or not. Therefore, we will use a quasi-experimental design and use time-series modeling (as we have done in previous studies)[3] for the majority of our analyses to assess whether the intervention improved pneumococcal and zoster vaccination rates more than temporal trends. This is a stronger design than a pre-post analysis, which cannot distinguish between the effects of temporal trends and changes resulting from an intervention.

c. ii. Data Sources: We will examine the effectiveness of this intervention using data from the EHR and our Enterprise Data Warehouse.

c. iii. Outcome Assessment and Analyses for Pneumococcal and Zoster Vaccination: Every month, we will extract data from our EHR to identify eligible patients for each measure, as described above. For each measure, we will classify each patient as 1) satisfied measure (yes/no), 2) exception recorded for the measure (yes/no), 3) did not satisfy measure (yes/no). We will then determine the total number of patients in each category ($N_1$, $N_2$ , and $N_3$) and the proportion of patients in each category. Time trends will be graphed in monthly increments.

*Primary Outcome*: The primary outcome for each measure will be the proportion of the entire denominator population that does not satisfy the measure:

$$N_{\text{not satisfied}} / (N_{\text{satisfied}} + N_{\text{exception recorded}} + N_{\text{not satisfied}}) = N_3 / (N_1 + N_2 + N_3)$$

*Statistical Analyses:* We will calculate the primary outcomes for the PVX and ZVX performance measures for each month during the year *prior* to the start of the intervention and for each month during the year *after* the start date. This will yield a 25-point time series for each measure; we expect to see an inflection point at the start of the intervention, indicating a change in the vaccination rates. A linear model will be fitted to each series using time as a continuous predictor, intervention as a dichotomous indicator variable, and a term for the interaction between time and intervention. We will then determine the autoregressive order of the model residuals by minimizing Akaike's information criterion.[9] Finally, we will fit a linear regression model with autoregressive errors (using the appropriate number of autoregressive parameters, if any are necessary) to each series. These fitted models will be used to test statistical significance of changes after the start of the study period.[10] To ensure model validity, we will examine several residual diagnostics, the Jarque-Bera and the Shapiro-Wilk tests for normality of residuals, and normal Q-Q and autocorrelation plots.[11-13]

We will use similar time series modeling to examine changes in the proportion of patients who have been appropriately received a second PVX ((i.e., five years after initial vaccination, according to recommendations from the Centers for Disease Control and Prevention). For this analysis, each month we will identify patients who received PVX five or more years earlier and determine the proportion who have received a second PVX.

In addition to the above analyses of whether the intervention improved vaccination rates beyond what was projected based on temporal trends, we will determine whether we reached our pre-specified goals: 1) ≥ 80% rate of initial PVX, and 2) achieve ≥ 80% rate of *offering* ZVX and ≥ 50% rate of documented *receipt* of ZVX.

c. iv. Outcome Assessment and Analyses for Influenza Vaccination: Assessing changes in INFVX is more challenging because many patients receive it outside of our health care system. Our intervention will increase capture of this information (see Figure 2a). Thus, if we used only data from our EHR to assess changes in INFVX vaccination rates, the increased data capture would bias our results towards an apparent improvement. Therefore, in addition to seeing if we achieve our population goal (≥ 60%) over the 2013-14 influenza season (based on a query of the electronic data as of April 1, 2014), we will conduct interviews with a random sample of eligible patients at the start of the study (e.g., July-August 2013) to assess the rate of self-reported vaccination in the previous season (2012-13) and then repeat this interview after the 2013-14

season (e.g., July-August 2013). We will use the question from the Center for Disease Control and Prevention (CDC) Behavioral Risk Factor Surveillance System to assess self-reported vaccination status. In addition, we will ask questions about knowledge and attitudes towards INFVX from previous surveys. Patients will be called up to six times to try to complete the survey, as per previous protocols.[14]

Differences in the rate of INFVX for the two seasons will be assessed using chi-square tests. Assuming a baseline INFVX rate of 25% for the 2012-13 season, we would need to interview 100 patients in each year to detect a 20% improvement in the rate for the 2013-14 season (alpha 0.05, power 0.80). Assuming a 50% participation rate, we will randomly select 200 patients to interview in each year.

In addition to the above analyses of difference in INFVX vaccination between the 2012-13 and the 2013-14 years, we will determine whether we reached our pre-specified goal ≥ 60% rate of INFVX *early* during the 2013-14 season (i.e., prior to December 31, 2013).

c. v. Assessment of Whether the Target Audience Was Fully Engaged:

Our secondary objective for this study is to assess physician and staff engagement in the intervention and to elucidate barriers to achieving optimal vaccination rates. We will use quantitative and qualitative methods to examine this objective.

*Physician Survey*: One year after implementing the intervention, we will conduct a survey of all board-certified physicians in the NMFF rheumatology clinic to determine their attitudes towards the intervention. We will use an adaptation of the physician survey used by Dr. Baker for the UPQUAL study (see section b.i.). Rheumatology fellows who see patients in the rheumatology clinic during the course of the study will also be surveyed. Residents will not be included because most will transition into or out of the clinic (i.e., start or finish residency) during the course of the study. Paper versions of the survey will be mailed to physicians, and they will be sent an email with a link that will allow them to complete the survey on line. Written informed consent will be obtained as part of the survey. We have done several surveys with this methodology over the last few years, with good response rates.[15, 16] All surveys will be confidential, but a tracking number will allow the project coordinator to determine who has not responded. Two weeks after the initial mailing/email, non-responders will be sent a postcard and email reminder. To ensure the validity of the study as well as to protect physicians from feeling coerced into participating, Dr. Baker and Dr. Ruderman will not have access to data on who responded to the survey. The project coordinator will create a completely anonymous dataset for analysis.

*Analysis of Physician and Provider Factors Affecting Success*: Variations in vaccination rates by provider will be analyzed using previously published methods.[7] To determine patient and provider-level predictors of vaccination, we will use multivariable, hierarchical logistic regression. Separate models will be analyzed for PVX, ZVX, and INFVX. The dependent variable will be the primary outcome (not vaccinated); we will also analyze a composite variable for whether patients were up to date on all three vaccinations (yes/no). Patient variables included in the model will be age, gender, race/ethnicity, and a continuous variable measuring the number of chronic medical conditions.[17] Provider characteristics will include age, gender, and

years on staff (a proxy for experience with the EHR). All analyses will be conducted using Stata SE 12. A physician identifier variable will entered as a fixed effect, and we will use the cluster function in Stata to adjust variances for the nesting of patients within physician practices.

*Qualitative Analysis*: At the end of the study, we will hold a focus group with physicians, the Vaccination Care Manager, and other staff involved in the intervention to assess a) factors that facilitated success and b) system, provider, and patient-level barriers to success. Written informed consent will be obtained from participants prior to the meeting. The meeting will be audiotaped, and key themes will be identified by team members.

c.vi. Dissemination of Findings from the Project:

Project findings will be disseminated through publications and national meetings. In addition, since Epic is the most frequently used EHR at academic health centers, we will present at the Epic Users Group annual meeting and work with Epic to develop methods and manuals to facilitate implementation. The Rheumatology Division at Northwestern communicates regularly with divisions at other academic medical centers, many of which are also using Epic. We will be able to guide them on working with their information technology support to implement similar protocols at their own institutions.

**3. Detailed Workplan and Deliverables Schedule**

The timeline for the project is shown in Table 1 below; the timeline assumes a start date of July 1, 2013 and an 18-month total study duration.

**Table 1. Project Timeline**

| TASK | 2013 | | 2014 | | | |
|---|---|---|---|---|---|---|
| | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 |
| PREPARATION AND IMPLEMENTATION | | | | | | |
| Create clinical decision support and performance reports | X | | | | | |
| Develop registry, outreach database, patient communication materials; train the Vaccination Care Manager, train physicians in the use of the clinical decision support tools | X | | | | | |
| Activate clinical decision supports; provide quarterly performance feedback; outreach by care manager | | X | X | X | X | X |
| EVALUATION AND DISSEMINATION | | | | | | |
| Conduct patient survey of influenza vaccination (pre, post) | X | | | | X | |
| Conduct provider survey and focus groups | | | | | | X |
| Data analysis ($X_i$ = INFVX survey; others are for PVX and ZVX) | | $X_i$ | X | X | X | $X_i$ X |
| Write abstracts, manuscripts, present at meetings | | | | | X | X |
| Develop implementation and dissemination materials | | | | | X | X |

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