C.1. OVERALL GOAL AND OBJECTIVES

Chronic immunosuppression, diminished functional capacity, and concomitant comorbidities render the impact of vaccine-preventable diseases particularly devastating in individuals with RA. At the same time, estimates of vaccination rates in this population are no better than in the general population, and may even be lower due to the increased complexity of care delivery for these patients. Additional challenges include contraindications to some vaccines among those receiving certain immunomodulators, and the need for appropriate timing of vaccine administration in relation to drug initiation in order to attain protective antibody levels.

Based on a baseline assessment of need at Columbia University Medical Center (CUMC), both vaccine delivery rates and the accuracy in documentation of the vaccinations received by our RA patient population are sub-optimal. Likely contributors to these sub-optimal levels are a general focus on specialty consultant care, higher overall disease severity and acuity among the RA population referred here, and ethnic/socioeconomic disparities. At the same time, RA patients in this setting may be at higher risk of adverse outcomes from infection due to population density, comorbidities, and economic disadvantage. These circumstances are not unique to our facility, but are shared by most large, urban, academic centers. Therefore, the development and testing of an effective intervention to increase vaccination rates within this high risk population is imperative, especially as access to all currently available RA immunomodulators is universal in the New York City metropolitan area for those with both public and private health care reimbursement. Several vaccination optimization initiatives are in place at CUMC, and increasing the rates of recommended vaccinations is a key quality improvement initiative for the coming decade.

Within this context, the overall goal of this quality improvement project is to develop and evaluate the effectiveness of a vaccination optimization program integrated into the out-patient clinical care delivery system for rheumatoid arthritis (RA) patients at a large, urban, tertiary-care medical center. The program to be developed and tested will operate in multiple domains to synergize the effects of provider-based education, a disease-specific electronic medical record (EMR) based information technology (IT) alert system, and support staff tracking and surveillance with the intent to increase vaccination rates within this vulnerable population. Within this context, we propose the following hypothesis-driven aims:

Aim 1: Quantify and compare the change in vaccine uptake rates for common vaccinations among RA patients of providers who are randomized to undergo one of two possible contrasting interventions. For the first intervention (education only) providers will undergo a didactic session aimed at improving their knowledge of appropriate vaccination practices in RA patients. For the second intervention (intensive intervention), providers will receive the same educational intervention in addition to point-of-service prompts and alerts integrated into CUMCs comprehensive EMR developed to identify the vaccines appropriate to the patient at the time of the clinical encounter and efficiently facilitate vaccine ordering, delivery, and documentation. The intensive group will also undergo periodic re-education throughout the study interval and will have nurse-coordinated tracking and surveillance of patients' vaccination status with automated reminders sent to patients who remain unvaccinated. In a sub-aim, changes in uptake rates according to intervention will also be compared between the two

delivery sites for RA care at CUMC differing primarily in patient education level, health literacy, and socioeconomic status.

Hypothesis 1: The more intensive intervention will result in higher vaccine uptake rates compared to the less intensive intervention. Any differences in vaccination rates detected between the two practice sites will be narrowed with adjustment for sociodemographic variables, attitudes toward vaccination, and access to care.

Aim 2: Quantify and compare changes in patient and provider satisfaction, and provider burden between the two interventions.

Hypothesis 2: The change in patient satisfaction will be greater among patients of providers exposed to the more intensive vaccination optimization intervention. We also hypothesize that provider perceived burden will be higher among those randomized to the more intensive intervention, but will be offset by increases in provider satisfaction with the quality of their healthcare delivery.

Aim 3: Quantify and compare the accuracy of EMR documentation of vaccination status between the two interventions.

Hypothesis 3: EMR documentation of vaccination status at the conclusion of the study will more accurately reflect true rates of vaccination (assessed from study-related phone calls of all enrolled patients at the conclusion of each study interval) among the group who received the more intensive intervention.

Upon completion of the project, we expect to have a rigorously determined estimate of the impact of an intensive vaccination optimization program on vaccination rates among our RA population. Along with this, we will have estimates of the patient and clinical practice factors that are associated with both higher and lower rates of vaccination, as well as an evaluation of the magnitude of patient satisfaction and provider burden associated with the intervention. **Perhaps more importantly, the quality-improvement product will benefit from further development based on the findings of the study, has the potential for immediate integration into RA clinical care in a widespread way, and is likely adaptable to the clinical care of patients with other rheumatic diseases and other chronic medical conditions.**

C.2. TECHNICAL APPROACH

It is well established that vaccination rates for vaccine-preventable infections with high potential for morbidity and mortality are suboptimal, particularly among those considered high risk. This is also the case among RA patients[1, 2], a group that presents particular challenges for optimizing vaccination rates due to contraindications to some vaccines among those receiving certain immunomodulators, and the need for appropriate timing of vaccine administration in relation to drug initiation in order to attain protective antibody levels.

A prior study[3], conducted in a rural, community-based rheumatic disease population with a highly integrated health care delivery system, reported relatively modest increases in RA vaccination rates using alerts integrated in the EMR system. While applicable to the population studied, these findings may not be generalizable to RA patients receiving care at non-rural, ethnically-diverse, tertiary-care medical centers. In particular, patients have multiple health

care choices and frequently receive medical care from multiple sources, often with limited communication between them. Also, practice patterns that focus on specialty consultant care, generally higher RA disease severity and more non-RA comorbidities, and ethnic/socioeconomic disparities represent potential barriers to achieving recommended vaccination rates and preventing infection among our population.

Increasing vaccination rates in vulnerable populations is possible, as evidenced through published reports of quality improvement projects occurring at CUMC[4]. In general, strategies that rely on passive methods (such mass-media educational campaigns) result in only modest increases in vaccination rates[5]. While active methods to increase rates, such as clinical prompts, provider and patient reminders, and case management, are associated with an increase in rates[6, 7], they can be difficult and costly to integrate into a busy medical practice even when individually implemented. Indeed, simultaneously incorporating all of these modalities in a consistent way may further optimize outcomes, but may be unsustainable without an efficient and unobtrusive system.

One potential way to more effectively integrate all of these quality improvement modalities into practice is by leveraging the capabilities of an integrated EMR system, such as the one used at CUMC. Providers at CUMC utilize an extensively integrated EMR system with note-writing, computerized provider order entry, ePrescribing, and decision support (see section C.2.b.iv for more detail). The plasticity of the EMR allows it to be programmed in any number of ways to provide efficient, patient and provider-specific decision support at the point-of-service.

The study proposed for this project differs from prior studies of vaccination optimization strategies in RA in that:

1. The populations studied will include both affluent and economically disadvantaged RA patients in the tertiary-care setting, with comparisons made between the two
2. Quantitative comparisons of the effectiveness of implementation of an EMR-based vaccination optimization dashboard (VOD) against a provider-based education program
3. The EMR based VOD developed will uniquely incorporate vaccination decision making and logic anticipating near-term initiation of immunomodulators
4. The impact of nursing-coordinated tracking and reminders as part of the vaccination optimization intervention will be evaluated
5. Provider burden, and patient and provider satisfaction will be measured as outcomes.

C.2.a. Current Assessment of Need

C.2.a.i. Summary of Baseline Data We performed a query of the CUMC EzVac database for vaccine administration of seasonal influenza vaccine, all 23-valent polysacharride and conjugated pneumococcal vaccines, herpes zoster vaccine (Zostavax), HPV (Gardasil), and all Hepatitis B viral vaccines. The query was restricted to patients with a diagnosis code of 714.0 and covered the period of September 1, 2011 to March 31, 2012 (influenza season) for influenza vaccination and January 1, 2011 through December 31, 2011 for the remaining non-seasonal vaccinations. Findings are summarized in the Table (right). We

Table 1. Baseline Vaccine Uptake Rates Among 599 RA Patients: 2011-2012

Vaccine Target	Uptake n (%)
Influenza	20 (3.3%)
Pneumococcus	26 (4.3%)
Zoster	0 (0%)
Human Papillomavirus	4 (0.7%)*
Hepatitis B virus	17 (2.8%)**

* Only n=2 completed full series
** n=14 completed full series

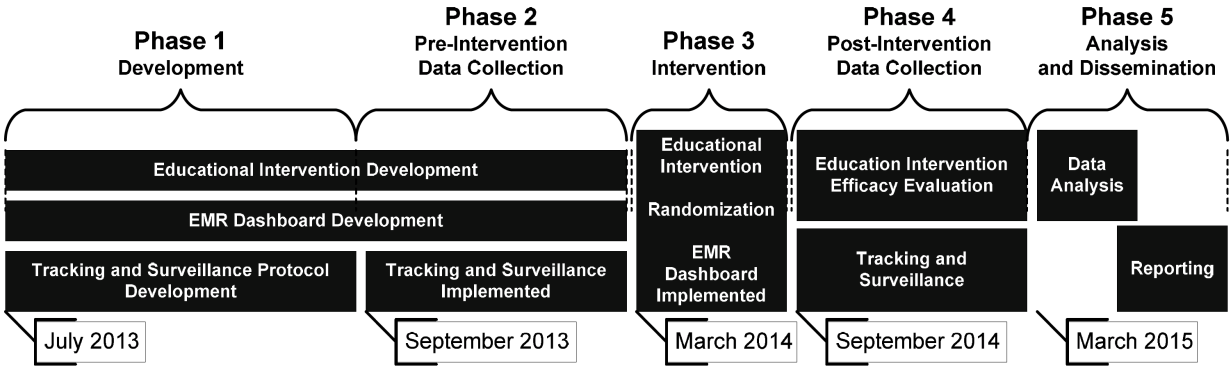
identified 599 unique RA patients with any clinical encounter over this time period. In general, uptake rates for all vaccines were very low. However, there are notable limitations to the data. For one, vaccinations obtained at outside facilities were not included unless specifically entered into the EMR by the provider. This is primarily applicable for influenza vaccination since this vaccine is readily available from multiple sources outside of CUMC during influenza season, but less-so for the other vaccines queried. Another limitation is that the time window of our survey may not fully capture the uptake of vaccines administered at a single time point or infrequently (such as pneumococcal and zoster vaccines). Finally, we did not query corresponding clinical data on the patients to identify vaccine appropriateness in individual patients. This is relevant for the vaccines that are primarily administered to individuals of certain ages (i.e. HPV and zoster vaccines) or potential exposures (HBV vaccine).

Despite the above limitations, these data readily identify a lack of current documentation of the vaccine experience of RA patients at our center, such that surveillance efforts by providers and staff are incapable of accurately discriminating between patients who are up-to-date with appropriate vaccines and those with multiple deficiencies. Even with a liberal projection that true vaccine uptake rates are 10-fold greater than identified, the background rate of vaccination among our RA cohort remains much less than ideal. ***Thus, these baseline assessments of need demonstrate that a wide margin of improvement is possible status-post the interventions proposed in this project to optimize both vaccine uptake and documentation of administration.***

C.2.a.ii. Target Audience A wide variety of groups can be expected to be benefit from the proposed project. Most proximally are the patients and providers who directly participate in the study, among whom vaccination rates are expected to increase. Upon completion of the project with widespread dissemination of the findings, we anticipate that RA patients and their medical care providers at other sites will broadly benefit from similar interventions integrated into clinical care. More broadly, the technology developed and the strategy for its integration into a clinical care delivery model will be imminently applicable to the care of other rheumatic disease patients and, indeed, any chronic disease population in which vaccine optimization is desired.

C.2.b. Intervention Design and Methods

Figure. Overview of Study Design



C.2.b.i. Study Overview The project is a quality improvement initiative involving the development, implementation, and efficacy assessment of a strategy to optimize the tracking and delivery of recommended vaccines for patients with RA at a single center. The components of the project, according to phase, are outlined in the Figure (above). The project will be conducted in 5 largely sequential phases, with some components overlapping across phases. The study proper is a cluster randomized efficacy trial of an educational intervention combined with an EMR-based VOD + nursing centered tracking and surveillance vs. education alone on uptake rates of recommended vaccines in RA patients. Prior to the intervention, development of the interventions and assessment tools (Phase 1) along with pre-intervention data collection on vaccination rates (Phase 2) will occur. Data collection on vaccination rates (primary outcome) and secondary outcomes will occur in Phase 4, followed by data analysis and data reporting/dissemination in Phase 5. The timing of the phases is structured around the two influenza seasons (September 1 through March 31) of the study period, which will allow several months at the beginning of the project for component development and finalizing regulatory approvals prior to the first influenza season of the project. During the first influenza season, pre-intervention vaccination rates will be assessed using a protocol developed during Phase 1 to capture and record all vaccinations received by RA patients receiving specialist rheumatologic care at CUMC. Just prior to the second influenza season of the project, all providers and support staff will undergo the educational intervention developed in the first part of the study. The providers will then be randomized, with half having an additional "intensive" vaccination optimization intervention (the implementation of a multilayered VOD into the providers' personal EMR along with a systematic nursing-based tracking and reminder system) to be compared to the group that received a single educational session at the beginning of influenza season. Additional details and justification for each component are elaborated in the following sections.

C.2.b.ii. Intervention Rationale and Design There are number of quality improvement strategies with the potential to increase vaccine uptake rates among high-risk populations. These range from passive measures (i.e. mass-media educational campaigns, direct patient- and/or provider-based education[8] to active measures, such as point-of-care alerts and reminders[3]. In general, passive methods have been shown to have modest effects on improving vaccine uptake rates[9]. Among the potential active methods, the propagation of comprehensive integrated health information technology systems over the past decade has introduced a number of potential highly effective strategies for tracking and optimizing the delivery of health services. In particular, the wide-spread use of EMR systems for both documentation of care and the delivery of point-of-care services make this method potentially applicable to vaccine optimization. In a prior study[3], active alerts incorporated into an EMR system were associated with increased influenza and pneumococcal vaccine uptake among RA patients. Interestingly, in the same study, vaccine uptake was higher at sites in which nursing coordination of vaccination was involved, suggesting that the inclusion of nurse management into a vaccine optimization strategy may be superior to a physician-centered strategy alone.

In light of these issues, for the proposed project we will compare vaccine uptake rates in three clinical scenarios: 1) at baseline with no passive or active vaccine optimization intervention involved, 2) after a single physician-oriented education intervention, consisting of

a didactic session with evaluation of learning, and 3) after implementation of a comprehensive initiative involving education, point-of-care EMR based alerts and reminders, and nursing-coordinated tracking, surveillance, and reminders. This design will allow comparison of a "low dose" to a "high dose" intervention. In addition, rather than relying on the background rates collected in a non-systematic way, collecting baseline rates in the same way during the pre- and post-intervention phases will allow for more informative assessment of the efficacy of both the education only and education plus EMR VOD/nursing support interventions.

An alternate strategy would forgo randomization, with all providers receiving the education intervention during the first influenza season of the project followed by all providers having the EMR VOD implemented during the second season. While this would provide a basic comparison of rates, it would not allow for a period to collect pre-intervention baseline rates. Furthermore, differences in vaccination practices that may vary between seasons would be problematic to assess and control. Thus, a design that allows comparison of each provider's individual pre vs. post-intervention vaccination rates over same seasons is a more desirable study design.

C.2.b.iii. Education Intervention All of the studied providers will undergo an educational intervention focused on the rationale, efficacy, and recommended uses of vaccination in RA patients. The goals of the education intervention are:

1. Survey providers' attitudes about vaccination in general and their knowledge of recommended vaccine administration in RA patients
2. Increase knowledge of the risks/benefits of vaccination in RA patients, and appropriate delivery according to demographics, exposures, and medication status
3. Evaluate changes in attitudes and knowledge upon immediate completion of the intervention and again at the conclusion of the study interval.

Development of the education intervention questionnaires and the content of didactic session will occur upon project inception and will be implemented in late summer of 2014. We will base the educational session on the most recent ACIP and ACR guidelines[10, 11] as outlined in the request for applications for this project.

C.2.b.iv. EMR Vaccine Optimization Dashboard Intervention The VOD will be developed in conjunction with the IT design staff of the CUMC Department of Bioinformatics and the Informatics Intervention Research Collaboration using logic and decision making programming, beta testing, and phased implementation into the EMR. The EMR system utilizes linked relational frames within a single electronic portal to allow providers to:

1. Document patient encounters using templates personalized to the providers (by document type and specialty)
2. View and update the patient's current and past problem list, social and family history, and allergy list with linkage to billing diagnosis codes
3. View documents for encounters from all of the patient's encounters at CUMC
4. View scanned documents from encounters outside CUMC
5. View current medications uploaded automatically from the patient's pharmacy
6. E-prescribe medications that are linked to the patients problem list and are auto-faxed directly to the patient's pharmacy

7. Order laboratory and imaging studies and review results (laboratory and imaging reports are uploaded automatically into the EMR)
8. View all prior and upcoming patient appointments
9. View the patient's immunization record. Immunization data are automatically entered into the EMR from the CUMC EzVac system when any vaccination is delivered at CUMC, regardless of provider of clinical setting. Immunization data, such as that from immunizations occurring outside CUMC, can also be manually entered by any provider.

These capabilities, in particular the immunization record, will be exploited for this project. In addition, two other functionalities of the CUMC EMR system will be utilized for the project. The first is **automated alerts** that can be programmed using clinical definitions from the other functionalities of the EMR. The alert itself is displayed prominently on the patient's main EMR page as a red triangle with an exclamation point. Clicking on the alert opens a frame that identifies the circumstances of the alert and links to the steps to rectify the issue. In addition, the alert frame also opens when the provider is closing the patient's EMR "chart", at which time rectification of the alert can also be accomplished. Programmable alerts have been used successfully at CUMC for increasing the documentation of Medicare Meaningful Use elements, and a similar system is directly applicable to immunization alerts. Because of the linked systems in the EMR, "smart" alerts can be programmed based on the clinical characteristics of individual patients. For example, the system could identify that the patient has RA based on their problem list, does not have a documented herpes zoster vaccination, is in an appropriate age range for vaccination, does not have a listed allergy to vaccines, is not prescribed contraindicated current immunosuppressants, and that the provider has just generated a first prescription for a biologic DMARD that is awaiting financial authorization. The alert generated would request the provider verify the criteria and would automatically generate a pre-populated order request. The alert could also remind the provider on the recommended time frame between vaccination and initiation of the planned biologic agent. An alert can also be generated to remind the provider to query and record any un-documented vaccines obtained outside of CUMC.

The second functionality that will be exploited for this project is the **programmable task list.** Each provider's task list populates with clinical updates, notifications of results to review, and messages generated by office staff. Clickable menus specific for each task allow the provider to efficiently resolve the task and document the outcome. For this project, the task list will include detailed alerts for patients with recent encounters who are appropriate for vaccination but without documented receipt of vaccination. These will populate into a report for nursing-coordinated reminders (see C.2.b.v. below) and can also populate a daily report for the provider identifying the vaccine-appropriate patients with vaccination deficiencies for all of the RA encounters scheduled for an upcoming day. It would also be possible to pre-populate a personalized vaccination order request for these patients, to facilitate the ordering of appropriate vaccinations after verification that the patients have not received vaccination elsewhere and do not have any additional contraindications not identified by the data in the EMR.

C.2.b.v. Nursing-Coordinated Vaccination Tracking, Surveillance, and Reminders Multi-disciplinary care delivery is frequently more successful at optimizing vaccination outcomes[5, 6] and specialized rheumatology nursing has become a feature of many practices. In addition to the point-of-service assessment of vaccine propriety and alerts provided by the physician's EMR VOD, the intensive vaccine improvement intervention will also incorporate an EMR based tracking system for the practice nurse coordinator. The EMR can be programmed to generate audited tasks and reports for patients under specific clinical scenarios using the task list function described in C.2.b.iv. For this project, we will develop and implement a task list that will be generated weekly for patients with prior encounters that do not meet EMR documentation of delivery of those vaccines deemed appropriate at the previous encounter. After nursing review, a reminder will be generated through the system and a recorded auto-call reminder sent. The generated report will also be sent to the provider for review.

C.2.b.vi. Study Sample, Randomization, Recruitment, and Follow-up Study participants will be the clinical providers in the Faculty Practice and AIM clinics of the Division of Rheumatology at CUMC and the RA patients with clinical encounters during the study interval. The unit of randomization will be the provider.

Provider Recruitment Assent of the Divisional Faculty to participate in the project has been obtained in addition to approval by the Division Director (see letter of collaboration from Dr Joan Bathon). After the providers have signed written informed consent to be studied, a study team member will use a random number generator to assign a number to each clinical faculty member. A second study team member will then split the cohort into two equal groups without knowledge of numerical assignment. While both groups will receive the education intervention, those assigned to the education only group will not have the VOD implemented into their personalized EMR, nor will they receive nursing-coordinated surveillance reminders, making unintended cross-over impossible. Although it is also possible that a provider randomized to the intensive vaccine optimization intervention group will not utilize the EMR and nursing based resources maximally, this will not constitute unintended cross-over, since the VOD and nursing surveillance will continue throughout the study interval irrespective of provider participation. Because the design intended for the EMR VOD will be integrated into the current EMR point-of-care workflow and will be purposefully designed to be unobtrusive and efficient, we do not anticipate high rates of lack of participation. In addition, nursing surveillance will not compete with clinical care time required for patient encounters.

Table_2. Inclusion/Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Diagnosis of RA (ICD9 714.0) • Receiving primary outpatient rheumatology specialty care at CUMC (Faculty Practice or AIM clinic) • Age ≥ 18 years	• Contraindication to receiving study vaccines (i.e. allergy, intolerance) • Planning to discontinue care at CUMC • Planning to move out of the area during the study interval

RA Patient Recruitment For the study, two groups of RA patients will be studied. First, we will query the EMR and compile aggregate data on vaccination delivery for all RA patient encounters during each study interval. Second, we will recruit and collect individual-level data for a sub-group of RA patients (n=300) who will be followed in both the pre-and post-intervention periods. For the EMR

query, all patients with RA (ICD.9 assigned diagnosis of 714.0) with an in-office clinical encounter during either study interval will be included. This query will require IRB approval, but will not require individual consent from every RA patient. For the prospective cohort, we will recruit from among consecutive eligible RA out-patient encounters for rheumatology sub-specialty care. In order to construct an unbiased and generalizable sample, inclusion/exclusion criteria are minimal, and are summarized in Table 2. These patients will all provide written informed consent for data collection, tracking of EMR data for all clinical encounters over the study interval, and permission to be contacted at the end of the pre- and post-intervention intervals in order to verify vaccination status.

C.2.b.vii. Study Sites RA patients at CUMC receive outpatient care in two clinic settings. Privately insured patients are followed in the Rheumatology Faculty Practice, made up of nine full-time providers. An additional group of RA patients are followed in the CUMC Associates in Internal Medicine (AIM) clinic, made up primarily of patients with publicly funded medical insurance. AIM clinic patients receive care coordinated by the post-doctoral fellows of the Division of Rheumatology with supervision by faculty who rotate through the clinic. EMR based documentation, work-flow, and clinical orders are solely managed by the fellows. The AIM clinic is functionally and geographically distinct from the Faculty Practice. Accordingly, the AIM patient population is composed of a larger proportion of ethnic minorities and those with lower educational attainment, health literacy, and social/economic deprivation. Comprehensive EMR systems are integrated into both clinic settings, providing an ideal context in which to compare the effectiveness of a quality improvement initiative between patient populations. Enrollment will be stratified to ensure recruitment of equal numbers of study subjects from each site.

C.2.c. Evaluation Design

C.2.c.i.a. Study Assessments Data will be collected from patients and providers. For the patients, individual level data will be collected from the enrolled patients themselves and from the EMR. We will maximize EMR collected data in an effort to reduce patient and provider burden of the study. The data collection schedule is summarized in Table 3. Variables extracted from the EMR will include ***demographics*** (i.e. age, gender, race/ethnicity), number and severity of non-RA ***comorbidities***, patient ***insurance coverage*** (private vs. public), ***RA disease characteristics*** (RA duration, documentation of active synovitis and/or deformity on physical exam, use of biologic and non-biologic DMARDs, prednisone, NSAIDs, and other analgesics), ***frequency of office visits*** to rheumatology and other providers (i.e. level of healthcare exposure) and ***length of time receiving rheumatology care at CUMC***, ***inflammatory markers*** (ESR and CRP) from routine standard-of-care laboratory assessments, ***anthropometrics*** (height, weight, body mass index).

A limited number of assessments that are not routinely collected in the EMR in extractable form will need to be collected from the patients at the time of the encounter using questionnaires. These will include ***education level*** (highest education level attained), ***vaccination occurring outside CUMC***, prior ***vaccination history*** (i.e. whether patient has received vaccinations in the past), patient ***attitudes toward vaccination*** (using a previously developed brief 10-question vaccination attitudes questionnaire [9]), ***patient global assessments of RA disease activity, pain, and overall health*** (using 100 mm VAS).

Provider-level data collected will include ***demographics***, ***clinical setting*** (Faculty Practice vs. AIM clinic), ***provider volume*** (average number of new and follow-up patient visits per week), ***provider knowledge*** of RA vaccination recommendations (from the post-evaluation following the education intervention), and ***provider attitudes toward vaccination*** (via questionnaire). Provider attitudes will be assessed pre- and post-intervention implementation.

At the conclusion of the study interval, the study coordinator will contact each participant by phone to confirm which vaccines were administered in the preceding period, the approximate dates of administration, and whether they were administered at CUMC or at an outside facility. These will be used to compare actual vaccination rates compared to those documented in the EMR. In addition, patients will be queried via questionnaire regarding their ***rationale for not receiving specific vaccines*** (if not vaccinated) and ***overall satisfaction with their healthcare delivery*** (Using the Outpatient Short-Form Patient Satisfaction Questionnaire (PSQ-18)[12] which will also be tested at baseline), and ***satisfaction with vaccination*** (if they were vaccinated). Any ***adverse events associated with vaccination*** will be recorded by patient self-report.

Table 3. Schedule of Study Assessments

	Season 1 (pre-intervention)			Season 2 (post-intervention)		
	Visit 1	Follow-up Visit(s)	F/U Call	Visit 1	Follow-up Visit(s)	F/U Call
RA Patient Data						
EMR query of vaccination status	X	X		X	X	
EMR query of demographics, medications, and characteristics	X	X		X	X	
Healthcare utilization	X			X		
Vaccination history	X					
Vaccination verification	X	X	X	X	X	X
Vaccination attitudes questionnaire	X			X		
Patient satisfaction questionnaires	X		X			X
Adverse vaccination events			X			X
Global Assessments of RA, pain, health	X	X		X	X	
Provider Data						
Demographics	X					
Clinical setting and workload	X					
Provider vaccine knowledge/attitudes	X			X		
Provider burden from intervention			X			X
Shaded cells indicate data available for the longitudinally followed RA cohort only						

C.2.c.i.b. Analytical Overview The primary study hypothesis is that efforts to optimize vaccinations in RA patients will result in higher levels of uptake post-intervention compared to pre-intervention. Analytically, we will compare changes in uptake between two interventions; an education only intervention without EMR based prompts or coordinated nursing reinforcement that is expected to have a modest effect on vaccine uptake vs. a comprehensive intervention that includes all of these elements (Aim 1). We hypothesize that the more intensive intervention will result in higher uptake rates compared to the less intensive intervention. We will also compare uptake rates between patients receiving care within the

Faculty Practice (largely private insurance) vs. those receiving care in the AIM clinic (largely public safety-net insurance), with the hypothesis that any differences in vaccination rates detected between the two practices will be narrowed with adjustment for sociodemographic variables, attitudes toward vaccination, and access to care.

In addition to uptake rates, we will compare whether levels of patient health-care satisfaction and provider burden differ according to intensity of intervention (Aim 2). We hypothesize that patient satisfaction will be higher among patients of providers exposed to the more intensive vaccination optimization intervention. We also hypothesize that provider perceived burden will be higher among those randomized to the more intensive intervention.

Finally, we will compare whether EMR documentation of vaccination differs according to intervention (Aim 3), under the hypothesis that EMR documentation of vaccination status at the conclusion of the study will more accurately reflect true rates of vaccination (assessed from study-related phone calls of all enrolled patients at the conclusion of each study interval) among the group who received the more intensive intervention.

Analytical elements of the study are summarized in Table 4.

Table 4. Analytical Elements According to Aim

Aim	Cohort	Outcome	Exposure	Potential Confounders	Stratified Analyses
1a	All RA Encounters (>n=600)	Aggregate Change in Vaccination Rates for Each Vaccine	Intervention group: (Education only vs. Education + EMR VOD + nursing support)	Demographics Socioeconomic variables Education/Health literacy Healthcare exposure Comorbidities RA Characteristics: Disease activity/pain Medications Provider Variables: Volume/Attitudes Knowledge of vaccination	Clinical Setting: (Faculty Practice vs. AIM clinic)
1b	Longitudinal Sub-Cohort (n=300)	Within-Subject Change in Vaccination Rates for Each Vaccine			
2a		Patient Satisfaction			
2c		Provider Burden			
3		Concordance between EMR documented vaccine delivery vs. true vaccine delivery			

EMR=electronic medical record; VOD=vaccine optimization dashboard; AIM=Ambulatory internal Medicine

C.2.c.i.c. Study Metrics and Outcomes The metric that will serve as the primary outcome of the study will be the difference in vaccination uptake pre- and post-intervention for each vaccine studied. In an ideal, yet not logistically possible study, all the RA patients receiving care at our facility would have encounters in both the pre- and post-intervention periods, and all vaccinations would be accurately recorded. However, for this study in which the encounters are arranged according to the patient and provider scheduling of routine clinical follow-up, there will be patients who are observed in either the pre- or post-intervention phase, but not both. In addition, some RA patient encounters will be for one-time visits for second-opinions. Therefore, we will utilize several metrics to assess changes in vaccination rates. For one, we will be able to track aggregate vaccination uptake data as recorded in the EMR for all RA patients with encounters during the pre- and post- intervention intervals. The strength of this metric is that it encompasses all the RA patients with encounters; however, its limits are that 1) the pre- and post- intervention cohorts will not necessarily have the same subjects (i.e. many RA patients will have encounters in both years, but some will also have only one encounter) so unique-subject changes in rates will not be able to be calculated and 2) vaccination rates in the

education only group will likely be underestimated due to under-reporting into the EMR, since this group will not have their EMR personalized with VOD prompts to query and input vaccination occurring outside CUMC.

Therefore, to provide a more robust assessment of changes in vaccination rates, we will also compare changes in pre- and post-intervention vaccination rates for unique RA patients enrolled during the pre-intervention surveillance period and followed through the post-intervention period. These patients will be consented to have study-related contact for verification of vaccination status at the conclusion of each period, so differential misclassification of vaccine uptake according to intervention group will be avoided. Within this cohort, we will be able to categorize the change in vaccination rate in two ways: 1) as the ratio of vaccine actually delivered divided by whether the patient was appropriate for vaccine delivery and 2) the ratio of whether the vaccine was recommended by the provider divided by whether the patient was appropriate for vaccine delivery. This distinction addresses the important question of whether change in vaccine uptake is hampered by lack of the provider recommending the vaccine vs. patient autonomy to refuse vaccines against medical advice. By having complete, individual level data on these patients, we will also be able to explore the associations of patient and provider characteristics on the change in vaccination rates.

C.2.c.i.d. Data Collection, Data Integrity, Confidentiality, and Human Subjects Research Each participant will be identified by a unique confidential study number. Data will be stored on a dedicated, password-protected database server that is backed up daily. Data from scannable forms will be transferred using Teleform software (Cardiff, San Marcus, CA), which features range checking for individual items, within-form consistency and logic checks during entry, between-form checks, and electronic inventory of all forms. All research data will be stored in relational databases, which, among other features, allows for maintaining data integrity for accuracy and consistency across large data sets that are constantly being added to with new results as they are collected.

The risk for subjects assigned to any group in this study is considered minimal. A protocol, manual of operations, and consent form will be prepared for review by the IRB. Informed consent will be obtained by the study coordinator or principal investigator. All procedures will be HIPAA compliant as outlined in CUMC policy procedures.

C.2.c.i.e. Statistical Analysis Plan Analytical parameters of the study are summarized in Table 4. For all analyses, descriptive statistics will be calculated at all time periods. Continuous variables will be examined for normality and, where required, transformation or non-parametric analyses performed. We will compare the crude differences in aggregate vaccination rates pre- and post-intervention for each group using the chi-square goodness-of-fit test. Differences in vaccine rate change according to groups will be statistically compared using Poisson regression. For the entire cohort (i.e. the pooled intervention groups), we will explore factors associated with change in vaccination rate, first in univariate models and then in multivariable (MV) Poisson models incorporating multiple possible covariates. In models exploring the efficacy of the intervention, intervention group will be modeled as the primary independent covariate of interest. We anticipate that randomization will balance confounders across intervention groups, and for these primary analyses of the efficacy of the interventions will not include

adjustment for unbalanced covariates. Sensitivity analyses will explore the impact of these adjustments in the event of unbalanced confounders. Subgroup analyses by site will involve the introduction of intervention by site interaction terms into the models. In general, our modeling strategy for including potential confounders will be those associated with the primary independent variable of interest (at the $p \leq 0.20$ level to allow for residual confounding). Exclusion of non-contributory covariates from the models will be made using the bias-corrected Akaike's Information Criterion for Poisson models. Because of our clustered randomization, we will also model the mean change in vaccination rates using linear mixed-effects models accounting for the clustering of patients within providers. We will use an unstructured covariance structure to allow full flexibility of the likelihood function. Linear mixed-effects models will also be used to model the effect of intervention on mean change in patient and provider satisfaction scores, and provider burden level, accounting for clustering of patients within providers.

For the comparisons of outcomes between randomized intervention groups, we will perform intention-to-treat (ITT) analyses regardless of participation or adherence to the intervention by the providers. For the patient level data, we will only be able to calculate the rate of change in vaccination rates for patients with complete data on the outcome. Recognizing that drop-out may be associated with vaccination status, we will make it an imperative of study execution to obtain post-intervention vaccination status on all patients enrolled in the longitudinal cohort component for which pre-intervention vaccine status was verified. For other non-outcome data, we anticipate a low rate of missing data since most will be collected at enrollment. However, there will undoubtedly be participants for whom complete data will not be available. For these, we will use a number of strategies, including informative approaches using multiple imputation. Intercooled STATA 12 will be used for analysis, and a two-tailed alpha of 0.05 adopted for all comparisons.

C.2.c.ii. Anticipated Effect Size and Sample Size Estimates Prior investigations have identified an increase in influenza and pneumococcal vaccination rates in RA patients of between 40 and 100% after implementation of EMR based alerts[3], albeit with low baseline rates (i.e. 47 and 19%, respectively). For this investigation, we anticipate a pre- vs. post-intervention change in vaccination rate for any specific vaccine of 20% to be a minimally clinically meaningful change. Assuming the same baseline rates, we will need at least n=240 RA patient vaccination-appropriate encounters to observe a minimum of 20% increase in influenza vaccination rate pre vs.post VOD implementation, assuming 80% power and a two-tailed alpha of 0.05. Assuming the same number of RA encounters and similar statistical parameters for the education only group, then we will have 80% power to detect a 10 percentage point difference in the increase in vaccination rate after intensive intervention vs. education only (i.e. the finding that vaccination rates in the intensive intervention group increase 20% vs. 10% in the education group would reach statistical significance). Larger projected differences would require fewer vaccination-appropriate encounters; however, given the size of the CUMC RA population, a sample size of 240 per group will be the primary projection. Inflation for cluster randomization (rho assumption=0.02 with 13 clusters) increases the required sample size to n=300 to achieve the same power.

C.2.c.iii. Target Audience Participation A direct assessment of patient and provider participation with the project will be readily assessable from the satisfaction surveys that will be assessed in both patients and providers involved in the study.

C.2.c.iv. Results Reporting and Dissemination We anticipate a wide audience for reporting the findings of the study upon completion. A primary audience will be RA providers, practice managers, and health care administrators. RA patients and the advocacy groups that represent them (i.e. the Arthritis Foundation and American College of Rheumatology) are also targets for results reporting. Additionally, extending beyond the scope of RA, the quality improvement measures developed for the project are directly transferable to quality improvement measures in other rheumatic diseases and, indeed, non-rheumatic chronic diseases, as well.

In order to disseminate the study findings to these target groups, we will plan to report the study results in multiple formats. First, a scientific abstract will be written and submitted to the 2015 American College of Rheumatology meeting, with a manuscript elaborating the findings in more detail soon to follow. Target journals will include both rheumatic disease focused and general internal medicine journals (i.e. NEJM, JAMA, Annals of Internal Medicine). As there are multiple components to the project, multiple manuscripts are likely. We will also utilize the resources of the CUMC Communications and Public Affairs Department to facilitate the dissemination of press releases to media outlets and other relevant groups. Finally, partnering with the administration of the Columbia Faculty Practice Office, we will facilitate the dissemination of study findings the New York Presbyterian Hospital administration and governance in an effort to more widely implement and evaluate the product.

C.3. DETAILED WORKPLAN AND DELIVERABLES SCHEDULE

The workplan will follow closely the temporal schedule outlined in the Figure (described in section C.2.b.). The first 3 months after study inception in July 2013 will involve regulatory approvals (i.e. IRB), finalizing the manual of operations, initiating the development of the education intervention, and meeting with the IT programming staff on operationallizing the EMR VOD.

By September 1, 2013 IRB approval, study protocols and manuals will be complete. This is also the date marking the beginning of influenza season, after which RA patient enrollment will begin for the pre-intervention assessments.

By March 31, 2014 (the end-of the 2013/2014 influenza season), the entire RA cohort will have been enrolled and all pre-intervention data collected. In addition, the educational intervention will be complete and final beta testing of the EMR VOD in anticipation of implementation post-randomization.

In late summer 2014, providers will undergo the education intervention and providers will be randomized to either education alone or the more intensive intervention group.

On September 1, 2014, post-intervention data collection will begin with all data collected and finalized ***by March 31, 2014***. Data analysis and abstract/manuscript preparation will begin ***by March 31, 2014***. This will allow time for submission of an American College of Rheumatology (ACR) abstract ***for late May, 2015*** that will be presented at the 2015 ACR meeting.

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