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A regional informatics platform for coordinated antibiotic resistant infection tracking, alerting and prevention

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Summary of Key Points (35 words): One in five admissions to a healthcare institution for MRSA or VRE are based on data from a different healthcare system. A regional patient registry and electronic admission notifications can facilitate coordinated infection prevention efforts.

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Abstract

Background. We developed and assessed the impact of a regional antimicrobial resistance (AMR) patient registry and electronic admission notification system on regional AMR infection rates over time. We conducted an observational cohort study of all patients identified as infected or colonized with Methicillin-resistant *Staphyloccus aureus* (MRSA) and/or Vancomycin-resistant enterococci (VRE) on at least one occasion by any of five healthcare systems between 2003 and 2010. The five healthcare systems included a total of 17 hospitals and associated clinics in the Indianapolis, Indiana region.

Methods. We developed and standardized a registry of MRSA and VRE patients and created web forms for infection preventionists (IPs) to maintain the lists. We generated email alerts to IPs whenever a patient previously infected or colonized with MRSA or VRE registered for admission to a study hospital from June 2007 through June 2010.

Results. Over three years, we delivered 12,748 email alerts on 6,270 unique patients to 24 IPs covering 17 hospitals. One in five (22-23%) of all admission alerts were based on data from a healthcare system different than the admitting hospital; a few hospitals accounted for most of this cross-over between facilities and systems.

Conclusions. Regional patient registries identify an important patient cohort with relevant prior antibiotic-resistant infection data from different healthcare institutions. Regional registries can identify trends and inter-institutional movement not otherwise apparent from single institution data. Importantly, electronic alerts can notify of the need to isolate early and to institute other measures to prevent transmission.

Introduction:

Methicillin-resistant *Staphyloccus aureus* (MRSA) and Vancomycin-resistant enterococci (VRE) are two common antibiotic resistant bacteria in healthcare settings.[1, 2] The majority of studies on MRSA and VRE derive from single institutions, however, there is increasing recognition of the role of inter-facility spread of infections, particularly in regions with multiple health care facilities.[3-5]

To better monitor regional rates and track the spread of antibiotic resistant bacterial infections, we built and embedded an AMR registry and tracking system within a regional health information exchange, to register all known MRSA and VRE cases and identify when these patients were admitted to any health care facility within the region.[6] Since May of 2007, we have actively shared information on patient MRSA and VRE colonization or infection status between all major hospitals in Indianapolis and generated e-mail alerts when patients with a history of either are admitted to a hospital.[7] Here we describe initial findings from our citywide network.

Methods:

This study was conducted in Indianapolis, Indiana and included all Indianapolis hospitals participating in the Indiana Network for Patient Care (INPC) at the time the project began.[8] The INPC is an example of an operational Health Information Exchange (and in recent years has expanded beyond the original five hospital systems). This study involved the five major hospital systems (17 total hospitals) in the Indianapolis (Marion County) area. The INPC has stored more than one billion data elements from the Indianapolis region, and more than 85% of the population in Marion County has some data in the system.[9, 10]

We previously described creation of a regional infection control network tying together Infection Preventionists (IPs) between the five hospital systems in Indianapolis.[6] We created a common means for IPs to identify MRSA and VRE cases and to update information on cases as necessary. In mid-May 2007, we instituted email alerts to notify infection control personnel when a patient with a history of MRSA or VRE infection or colonization presented for admission at participating hospital systems. If a patient had both MRSA and VRE in their history, a separate email alert for each was sent at the time of admission. For analysis we included data from June 1, 2007 through June 1, 2010 to include only full months. A simplified flow diagram (Figure 1) outlines the process for generating an email alert. Our system leveraged two key components of the INPC; a robust enterprise master patient index to uniquely link patients across institutions and the transmission of a standardized electronic message (an Admission/Discharge/Transfer or ADT message using the HL7 standard) whenever a patient was admitted to any participating institution.[11] The HL7 messaging standard is used in virtually all health systems, and ADT messages in particular are commonly generated at the time of patient registration within emergency departments.[12]

We "primed" the system with existing lists of patients with prior history of colonization or infection with MRSA or VRE from all participating institutions, as recorded by their infection control teams. Our system recorded the initial laboratory result as entered by the IP, the source institution, and the culture site which prompted entry of the patient into the merged citywide list of MRSA/VRE cases. We similarly recorded the date/time and location of subsequent admissions of registry patients. Patients could be removed from the citywide list by any infection control provider documenting that the patient had been "cleared." Each site used its institution's criteria to make this determination.

Although the standardized web forms included a "pick list" (or "drop-down menu") of the most common culture sites, IPs could use free text entry to describe the culture site in greater detail, or to overwrite an option on the list. We therefore reclassified all free text entries as one of the common culture sites where possible (e.g. blood, skin and soft tissue, urine, stool, sputum). For patients with more than one positive culture site, we included all cultures sites for analysis. We analyzed patients who had MRSA or VRE or both during the time period of the study.

We created network diagrams to illustrate the connectivity between study hospitals using the open source GraphViz software. [13] Network diagrams can be used to visualize connections (edges) between entities (nodes) with applications in social network analysis or data flow diagrams. In this study, we used Graphviz software to visualize the flow of patients between institutions. We visualized nodes as circles, with area proportional to the number of unique patients identified with MRSA or VRE and admitted only within the same institution. We visualized edges or connections between the institutions with the width of the arrows proportional to the unique patients identified with MRSA or VRE at one institution, but later admitted to a different institution ("crossover" patients).

We compared age, gender, and race for admitted "crossover" patients versus patients who were admitted within the same institution. We used two-sample t-tests to compare mean ages between groups, and chi-square tests to compare gender and race. Missing values were negligible for age and gender. Missing race could not be imputed based on available data and was not included in tests of comparison.

At 18 months after alerts went live, we surveyed IPs at all five participating hospital systems to determine overall burden of alerts, gauge perceived usefulness of the system, estimate time cost or savings in using the alerting system, and elicit suggestions for improvement.

From November, 2006 to February, 2008, one of the investigators (BND) led an AHRQ-funded project aimed at reducing MRSA infection and transmission in hospitals.[14, 15] We formed a regional collaborative to spread effective strategies for Methicillin-resistant *S. aureus* (MRSA) reduction, identify strategies for reducing healthcare associated, community onset (HACO) MRSA, and build a network of people/organizations devoted to MRSA prevention. They conducted a two-phase project, in order to identify and spread successful strategies for reducing MRSA infections in hospitals. The first phase involved four hospitals in Indianapolis over two years. The second phase beginning in mid-2009, was a multisite, multihospital quasi-experimental study of seven hospital systems, including four systems in Indianapolis over four years.

Doebbeling and colleagues also worked closely with hospital leaders and front-line staff in inpatient units to apply organizational changes strategies and evidence-based infection prevention precautions. As part of this project, an intervention bundle was implemented in 4 of the 5 Indianapolis hospital systems. The intervention bundle consisted of active surveillance cultures (including nasal swabs) for all patients admitted to study units, pre-emptive barrier isolation of those identified as either infected or colonized with MRSA, and institution of strict hand-hygiene before and after each patient contact.

Results:

From 2003-2010, the registry included 23,776 unique patients infected or colonized with MRSA, 3,036 unique patients with VRE, and an additional 914 unique patients with both MRSA and VRE (Table 1). Data on race was missing for 19% of the study cohort.

From June 1, 2007 to June 1, 2010, we delivered 12,748 email alerts on 6,270 unique patients (Table 2). As with the larger cohort, race data was missing for a significant proportion (29%). Patients admitted with a history of MRSA colonization or infection were, on average, older than the overall cohort with a history of MRSA colonization or infection (57.0 vs 46.4 years). The same was true among those who had a history of both MRSA and VRE (58.9 for admitted patients vs 51.6 years for all patients).

In twenty-three percent of admissions of patients with a previous history of MRSA, the MRSA had been identified at a hospital system different from the admitting hospital (range 19% to 30% of the admissions each year, over the three years). For VRE, this rate was 22% (range 15% to 35%). Patients in the MRSA group who were admitted to a hospital system different from where the MRSA information had been entered into the registry ("crossover" patients) were younger (54.8 vs 57.7 years, $p<0.001$), and more often female (55% vs 50%, p value = 0.003) than patients who stayed within the same system (Table 3). Patients with a history of VRE admitted to a hospital system different from where VRE had been entered into the registry were similar in age to patients who stayed within the same system, and were more likely to be female (73% vs 59%, p value = 0.004). Patients with a history of both MRSA or VRE admitted to a hospital system different from where MRSA and VRE had been entered into the registry were more likely, compared to those who stayed within the same hospital system, to be black (38% vs 26%, p = 0.01), although race was missing for 17.6% of admitted patients.

Evaluating only the cohort of new patients since the start of email alerts (N= 4016), we observed that email admission alerts occurred an average of 135 days after the patient was first identified as having MRSA or VRE in the registry (SD= 181) with a median of 57 days, and 60% of all alerts occurred within 365 days after the MRSA or VRE data had been first entered into the

registry. The maximum number of alerts across all participating hospitals in any one day was 29, with a maximum of 10 for a single hospital.

Of all patients who generated an alert, 57% had only a single alert over the 3 years, 87% had 3 or fewer, and 99% had 9 or fewer. Sixty-eight patients generated 10 or more alerts, with one patient generating an alert at 47 distinct hospital admissions.

We created network diagrams indicating the flow of patients from initial site of identification of colonization or infection with MRSA or VRE, to sites of subsequent admissions (Figure 2 and 3). Every institution shared patients with every other institution, serving both as a source, and as a receiver, of patients. Different institutions accounted for the highest number of total admissions.

From 2003 to 2006, rates of positive cultures for skin and soft tissue sites (SSTI) increased steadily as a proportion of total MRSA positive cultures (Figure 4). From 2006 until 2010, rates of all MRSA positive culture sites decreased, with sites associated with SSTIs decreasing most rapidly. Over the same years, rates of positive nasal cultures increased rapidly, coincident with regional implementation of the infection control bundle. Over the same time period, rates of SSTI, blood stream, and urinary tract culture sites positive for VRE steadily increased (Figure 5).

Ten IPs representing all of the five institutions completed a subsequent survey at 18 months post go-live. All responded yes to the question, “Do you find the email alerts useful?” IPs estimated an average alert burden of five email alerts per day, of which just over half (55%) were already known to them from data at their own institution. The most common reasons for how IPs used the alerts were to identify patients requiring intervention (e.g. contact isolation), and to identify MRSA cases coming from outside institutions. In considering the time cost of the alerting system (emails and data entry), 6 IPs considered the system to be time neutral overall, 3

responded that use of the system added time, and one responded that the system overall was a time saver. The most common recommended improvements to the system were automated capture of laboratory data into the system to reduce burden of manual entry of new cases.

Discussion:

Since May 2007, Indianapolis infection preventionists have used a common system to collectively track over 20,000 unique patients with a history of infection or colonization with MRSA or VRE. Our network enabled IPs at participating institutions to benefit from the collective infection history of shared patients while continuing to maintain their own historical records. There have been a number of successful regional efforts to coordinate and implement regional infection control, although to our knowledge, ours is the first to implement admission alerts regionally.[16-18]

Alerts based on regional data identified when a patient with a history of infection or colonization with a drug resistant organism was readmitted to any networked institution and may improve rates of compliance with contact precautions.[19] In this study, we demonstrated that approximately one in five patients with a relatively recent history of MRSA or VRE is readmitted at neighboring institutions, which corroborates and quantifies the estimates of other studies. [3-5, 20] Although we cannot directly relate our regional admission alerts to improved infection control measure compliance, our regional registry captured data likely reflecting compliance with increased surveillance cultures (nasal) as part of a coordinated effort to reduce MRSA infections. Recent models suggest that coordinated infection control efforts in a region can help individual hospitals achieve better control than on their own.[21]

Universal screening has been proposed as an effective means to control MRSA infections.[22] However, controversy remains over the optimal approach given variation in how well infection control measures are implemented and the significant resource investment required.[23-25] In this example, data sharing on prior history of infection or colonization with MRSA or VRE may have reduced the need for repeat culture, and more quickly identified a patient requiring pre-emptive contact precautions. Our data demonstrate that local hospital interactions are asymmetric, with some hospital systems sharing a disproportionate burden of infected or colonized patients. Identification of higher burden hospitals or hospital systems may help guide resources to match relative burden of disease in a community. Institutions also differed in their relative burden of MRSA versus VRE patients. Further study may elucidate institutional factors associated with differing rates of drug-resistance.[26]

Creation of a common registry enabled regional tracking of new cases of MRSA or VRE. During the study period, the incidence of positive cultures involving skin and soft tissue sites increased disproportionately, likely mirroring the increase in CA-MRSA cases noted both locally and nationally.[27, 28] Overall rates of positive MRSA blood cultures decreased gradually over the same time period (a finding similar to that of other studies), although MRSA positive blood culture rates increased slightly at individual institutions.[29] These changes may also have reflected an aggressive program of active surveillance and interventions to reduce hospital-based MRSA instituted during the study period. Notably, however, rates of positive VRE cultures did not change and in fact, trended upwards for urinary tract sites.

Regional surveillance of drug resistant infections provides a broader and potentially more accurate view of infection burden than data from a single institution, and can help coordinate the appropriate use of limited infection prevention resources. Our system reflected national trends in

MRSA incidence and documented evidence of dedicated active surveillance efforts, and potential effects of these efforts on subsequent infection rates.

There are several limitations to our study. We designed our system to capture data entered and verified by IPs, rather than data directly from the laboratory information systems, based on preliminary work that automating case capture could not be considered 100% reliable. As a result, entry dates for new cases sometimes lagged behind the actual time when the infection or colonization was recognized, depending on when the IP was able to manually enter the case information. The requirement for human review and entry into our standardized web forms, likely increased administrative burden on IPs. In fact, the IPs in one of the hospital systems stopped entering data into the system in 2011. However, for the 2007-2010 study period, the system was in continuous use by IPs, which suggests that the benefits of the system may have outweighed (or may have been in approximate balance with) the additional burden of data entry, a fact supported by our mid-study survey. During the time of the study, molecular typing for MRSA strains was not routinely conducted, and neither the hospitals nor the INPC reliably electronically captured enough additional information, in one place, to classify MRSA cases as Healthcare-associated (HA), Community-associated (CA), or Healthcare-associated Community Onset (HACO) classification according to the CDC clinical categories.[1] Instead, our system triggered alerts based on any prior history of MRSA or VRE regardless of classification, or when the original infection or colonization took place. IPs could remove a patient from the regional listing, but may not have done so consistently. The majority of alerts (60%) were triggered based on historical data from within one year of the admission date, and limiting alerts to trigger based on no more than a one-year window may reduce the risk of excess alerts or alert fatigue.[30]

For this study we tracked only cases of MRSA and VRE. We recently expanded our focus to include infection or colonization with gram negative organisms, recognizing that multi-drug resistance in these organisms poses an impending threat.[31-33] To reduce the burden on IPs of manual entry of cases, we are developing the means to extract structured data on new infections directly from electronic messages generated by the laboratory information systems, to limit manual entry only to unusual or uncertain cases.

In this work we successfully implemented a system to track and coordinate infection control efforts within an operational regional health information exchange. Although we benefited from a longstanding history of pioneering informatics work within Indianapolis, recent trends suggest that our work may be generalizable to other communities.[34] Government initiatives to stimulate adoption of EHRs have yielded early success, with steady increase in EHR use nationally.[35, 36] Federal regulations outlining the "Meaningful Use" of EHRs may improve the quality and structure of data captured in EHRs for research or public health purposes.[37, 38] With increased adoption and improved use of EHRs, efforts to connect systems through local and regional health information exchanges are increasingly widespread, although significant barriers still remain.[39] Our work represents a specific use case within a functioning HIE, but one that leverages technology and standards commonly used in health systems and other HIEs (e.g. an enterprise master patient index and HL7 ADT messages generated at admission). With the increasing implementation of EHRs and HIEs, other communities may be well positioned to develop similar electronically coordinated infection control efforts.

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Table 1: Demographics of the patients in the cohort (2003-2010) with MRSA or VRE

		MRSA		VRE		Both	
		N	%	N	%	N	%
Race	White	13212	55.6	2035	67	579	63.3
	Black	4842	20.4	521	17.2	188	20.6
	Other	846	3.6	89	2.9	11	1.2
	Missing	4876	20.5	391	12.9	136	14.9
Gender	Female	11663	49.1	1822	60	505	55.3
	Male	12096	50.9	1214	40	407	44.5
	Unknown	17	0.1	0	0	2	0.2
Age	Under 18	2595	10.9	23	0.8	17	1.9
	18 to 35	4518	19	213	7	95	10.4
	35 to 64	9341	39.3	1408	46.4	446	48.8
	65 and over	6967	29.3	1343	44.2	347	38
	Missing	355	1.5	49	1.6	9	1
Age	mean	46.4		60.8		51.6	
	median	48		62		55.5	
	std	24.5		17		24.5	

Table 2: Demographics of the patients admitted (6/2007 – 6/2010) with a history of MRSA or VRE infection or colonization

		MRSA		VRE		Both	
		N	%	N	%	N	%
Race	White	2414	49.7	435	64.1	424	57.8
	Black	783	16.1	103	15.2	175	23.8
	Other	91	1.9	19	2.8	6	0.8
	Missing	1569	32.3	122	18	129	17.6
Gender	Female	2503	51.5	414	61	406	55.3
	Male	2354	48.5	265	39	328	44.7
Age	Under 18	110	2.3	0	0	1	0.1
	18 to 34	610	12.6	45	6.6	64	8.7
	35 to 64	2287	47.1	340	50.1	390	53.1
	65 and over	1849	38.1	294	43.3	279	38
	(1 age missing in MRSA group)						
Age	mean	57		61.1		58.9	
	median	58		61		60	
	sd	19.6		16.1		15.9	

Table 3. Demographics of "crossover" patients vs. patients staying within same hospital system

	MRSA n=4857			VRE n=679			Both n=734		
	Crossover	Same	P-value	Crossover	Same	P-value	Crossover	Same	P-value
Age in years	54.8	57.7	<.001	62.1	60.1	.48	58.6	59.0	.75
% Female n	55.4	50.3	.003	72.9	58.5	.004	63.0	52.3	.01
% Black	24.0	23.8	.92	19.4	18.4	.87	38.3	26.1	.01

Figure Legends:

Figure 1. Flow diagram outlining process of generating regional email alerts upon hospital admission for patients previously infected or colonized with MRSA or VRE.

Figure 2: Directed graph of admissions for patients with a history of MRSA infection or colonization who stayed within a hospital system (circles or nodes) or who crossed over between hospital systems (arrows or edges).

Figure 3: Directed graph of admissions for patients with a history of VRE infection or colonization who stayed within a hospital system (circles or nodes) or who crossed over between hospital systems (arrows or edges).

Figure 4: Counts of positive MRSA culture sites by year.

Figure 5: Counts of positive VRE culture sites by year.

1. Patient A identified as culture positive for MRSA or VRE

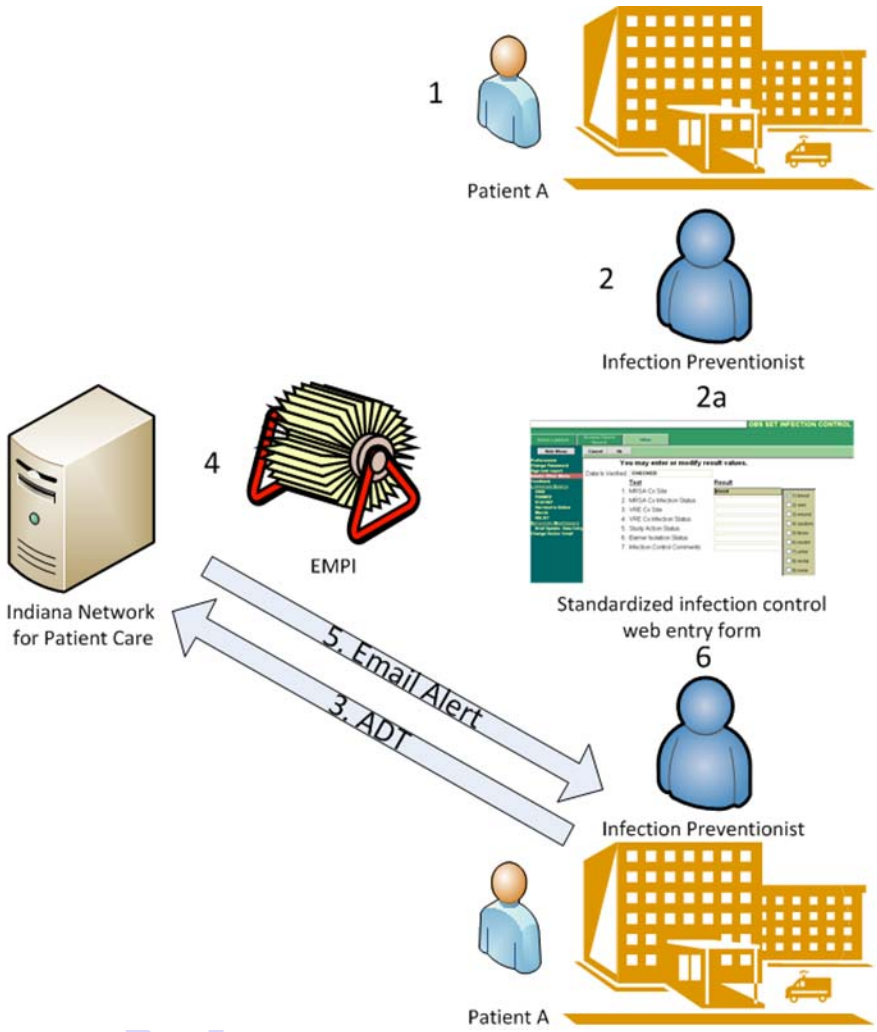
2. Infection Preventionist enters new case using standardized web entry form (2a)

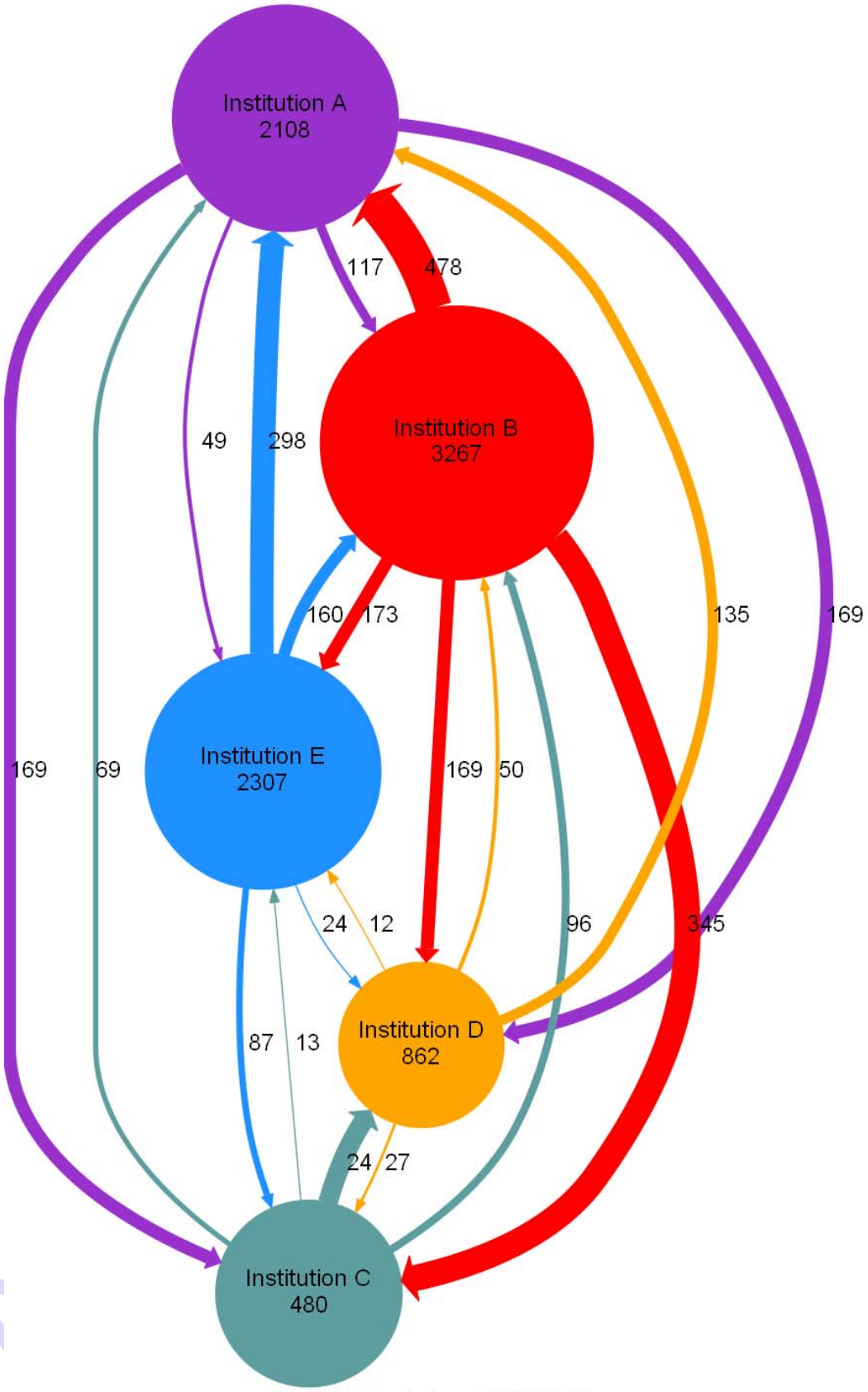
3. During a subsequent visit to an institution within the INPC, Patient A is registered for admission, generating an outbound HL7 Admission, Discharge or Transfer (ADT) message to the Indiana Network for Patient Care

4. Patient A uniquely identified through Enterprise Master Patient Index (EMPI), prompting retrieval of any record of IP entered MRSA or VRE infections or colonizations

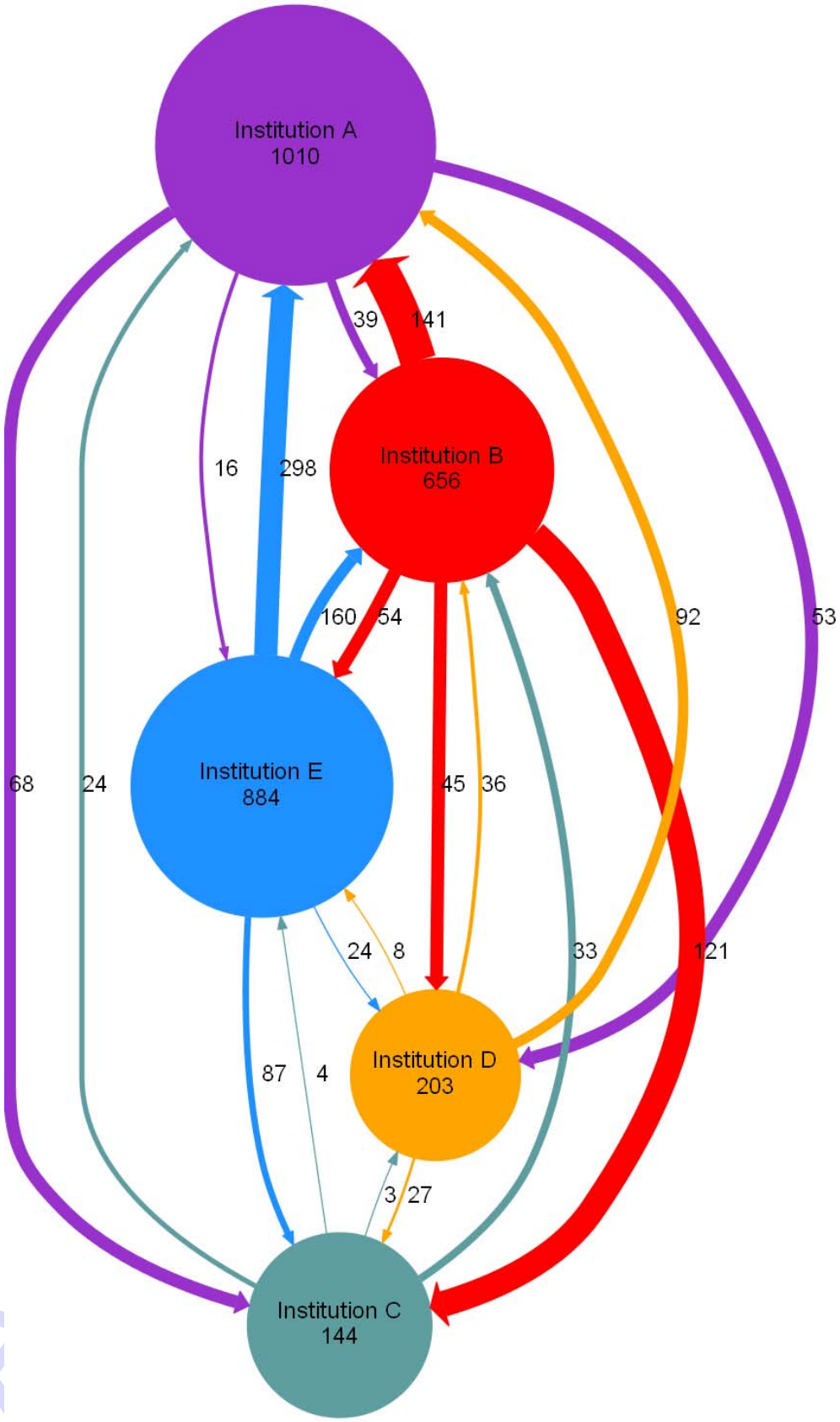
5. Secure email alert generated to IPs at admitting institution, and also to bed control/admitting office

6. IP can update/edit/comment through web entry form to note changes in Patient A status for future admissions





MRSA Admissions 2007-2010



VRE Admissions 2007-2010