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Original Article

A National Study of the Impact of Rapid Influenza Testing on Clinical Care in the Emergency Department

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Background. Rapid influenza diagnostic tests (RIDT) may influence physician decision-making. Single-center studies suggest that influenza diagnosed in association with RIDT reduces ancillary testing and antibiotic prescribing. The extent of RIDT use in US emergency departments (EDs) and their impact on patient management are unknown. We examined the use of RIDT and its effect on influenza management, using a national sample of ED visits.

Methods. We performed a retrospective study using data from the National Hospital Ambulatory Medical Care Survey, an annually administered survey capturing a nationally representative sample of visits to US EDs. We identified patient visits in which RIDT was performed and/or influenza was diagnosed across 3 influenza seasons (2007–2009). Ancillary testing and antibiotic and antiviral prescribing were evaluated for 2 groups of patients in whom RIDT was performed (those given or not given a diagnosis of influenza) and a third group in whom influenza was diagnosed but RIDT was not performed.

Results. Rapid influenza diagnostic tests were performed during 4.2 million visits. Forty-two percent of influenza diagnoses were made in association with RIDT. For patients diagnosed with influenza, ancillary test ordering was lower (45% vs 53% of visits) and there were fewer antibiotic prescriptions (11% vs 23%), and antiviral use was higher (56% vs 19%) when the diagnosis was made in association with RIDT.

Conclusions. Influenza diagnoses made in association with RIDT resulted in fewer tests and antibiotic prescriptions and more frequent use of antivirals. This finding suggests that test results influence physician behavior.

Key words. emergency department; influenza; influenza testing; rapid diagnostics; rapid influenza testing.

Influenza-like illness is common among patients who receive care in emergency departments (EDs) during winter. Signs and symptoms of influenza overlap with other respiratory illnesses, including bacterial pneumonia. Uncertainty in the diagnosis of influenza may lead to antibiotic overuse, underprescribing of antiviral medications, and unnecessary ancillary testing [1].

Rapid influenza diagnostic tests (RIDT), based on antigen detection, are widely available. Their sensitivity is variable, ranging from poor to moderate across settings, populations, and tests, but specificity is high [2, 3]. The results of previous studies have shown that the use of RIDT is associated with reduced ancillary testing and antibiotic prescribing and greater use of antiviral drugs for patients with respiratory symptoms who are diagnosed with influenza [2, 4–9]. These studies primarily enrolled children and took place at academic institutions, limiting their generalizability. A Cochrane review found that the

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"current evidence was insufficient, but promising" to support influenza testing to reduce antibiotic prescribing or laboratory intervention [10].

The extent of RIDT use by US ED physicians and the national impact of RIDT on clinical care are unknown. Our objectives were to examine national patterns of RIDT use and the influence of RIDT on clinical care in US ED settings. We hypothesized that a diagnosis of influenza made in association with RIDT would be associated with decreased ancillary testing, reduced antibiotic prescribing, and greater use of antivirals compared with influenza diagnoses made without RIDT.

METHODS

Data Source

This study was a retrospective analysis of data from the National Hospital Ambulatory Medical Care Survey (NHAMCS). The NHAMCS is a yearly sampling of visits to hospital EDs throughout the United States conducted by the National Center for Health Statistics (NCHS) and the Centers for Disease Control and Prevention (CDC) [11]. The EDs included in the study were drawn from all 50 states and the District of Columbia, but all Veterans Administration, military, and other Federal hospitals were excluded. An objective of the survey was to provide an unbiased sampling of visits to EDs in the United States from which to derive nationally representative estimates of clinical care.

The NCHS administers the NHAMCS using a 4-stage probability-based sampling process to identify patient ED visits for inclusion in the dataset. The 4 stages include selection of primary sampling units (which are geographic regions), hospitals within primary sampling units, EDs within selected hospitals, and patient visits within selected EDs. Once an ED is selected to participate, the NCHS assigns a random 4-week reporting period to include patient visits. Representatives from the US Bureau of the Census conduct on site training for hospital staff in the data collection process. The data collection includes patient demographic information, up to 3 assigned clinical diagnoses (using *International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] codes), testing performed, and up to 8 medications prescribed. To derive nationally representative estimates based on the sampled visits included in the database, the NCHS assigns a weight that is associated with each visit that accounts for the 4-stage sampling process and the probability that the individual visit was selected. Patient-level data elements were routinely reviewed for completeness and accuracy and validated by representatives from the NCHS [11].

Study Design

Human Subjects Protection. The NHAMCS contains publicly available data and is not considered "human subjects research" as defined by federal regulations [12]. Projects involving NHAMCS data were exempt from institutional review board review.

Study Period. The NHAMCS started recording RIDT use in January 2007; therefore, this date was chosen as the start of our study period. We evaluated 3 influenza seasons: the months of January–April and October–December (inclusive) of 2007 and 2008, respectively, and the months of January–April of 2009 (Figure 1). The months of May–September were excluded each year. Due to poor sensitivity and changing recommendations for RIDT use [13], we ended our study period at the onset of the 2009 H1N1 pandemic.

Study Population. We excluded visits at which RIDT was not performed and influenza was not diagnosed. We only included visits at which influenza was diagnosed by ICD-9-CM code and/or RIDT was performed (Figure 2). An influenza diagnosis was assigned if any of the 3 diagnosis fields contained the ICD-9-CM code for influenza (487.x). Included visits were then classified into 3 groups that reflected what we believed was a range of certainty for the diagnosis of influenza: (1) RIDT performed/influenza diagnosis (RIDT + /INF + ; highest

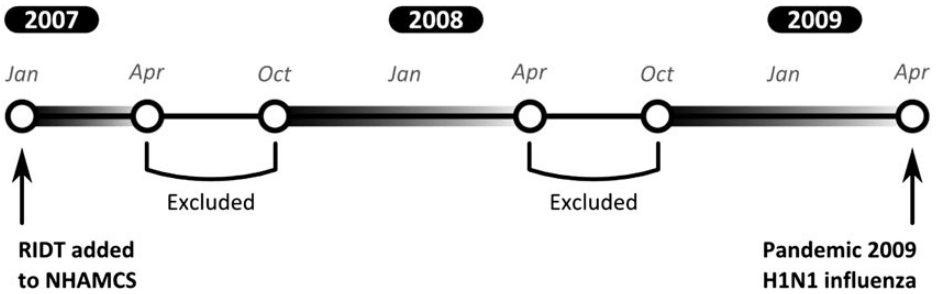

Figure 1. Graphic illustrates the study period. National Hospital Ambulatory Medical Care Survey (NHAMCS) started recording rapid influenza diagnostic tests (RIDT) use in January 2007. Our study period encompassed 3 influenza seasons (shaded in dark gray), including the months of January–April 2007–2009 and October–December 2007 and 2008. The months of May–September were excluded each year. Our study period ended at the onset of the 2009 H1N1 pandemic.

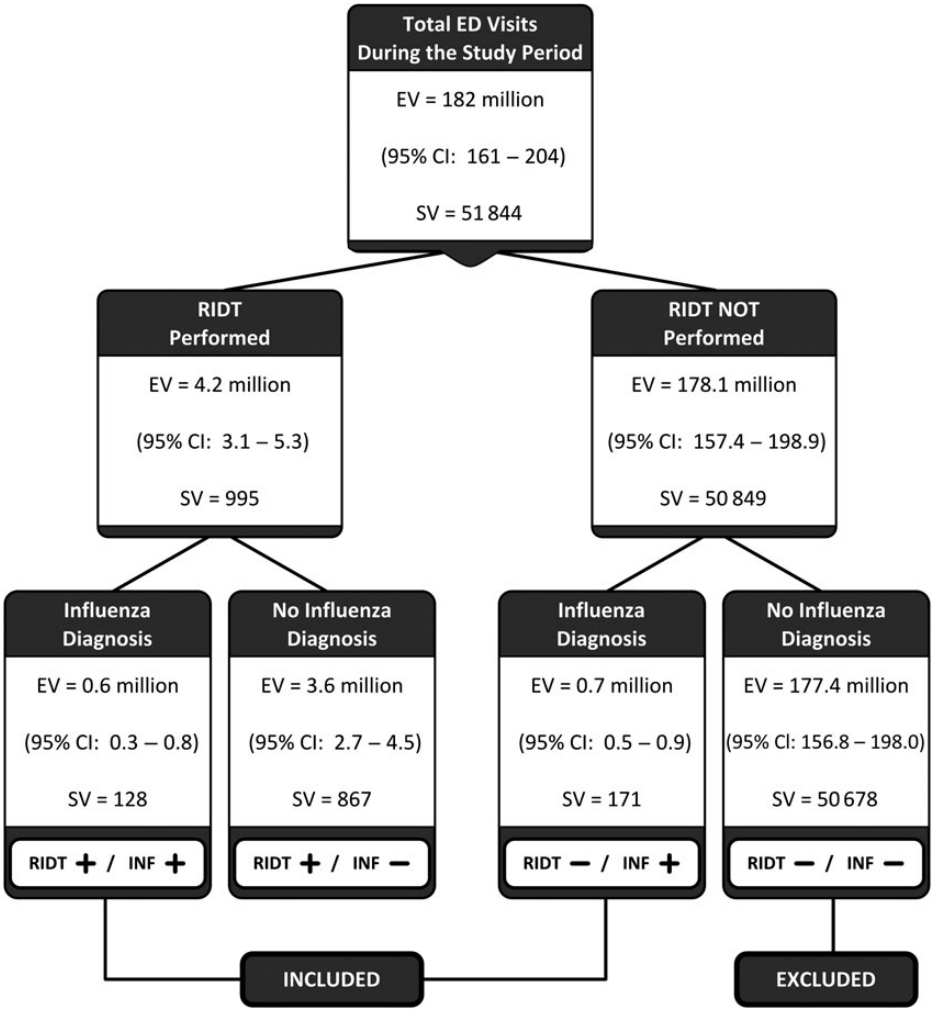

Figure 2. The graphic depicts the study population. From all emergency department visits during the study period, we identified visits with and without rapid influenza diagnostic tests (RIDT) performed. Visits with RIDT performed were divided into those with and without an influenza diagnosis. From visits without RIDT performed, those with an influenza diagnosis were identified and included in the study cohort. Visits with neither RIDT nor an influenza diagnosis were excluded. Abbreviations: CI, confidence interval; EV, estimated visits; SV, sampled visits.

certainty); (2) RIDT not performed/influenza diagnosis (RIDT – /INF+ representing clinical diagnosis without confirmation; intermediate certainty); and (3) RIDT performed/no influenza diagnosis (RIDT + /INF – ; lowest certainty). Both adults and children were included in the primary analysis; subgroup analyses were performed for children <18 and adults ≥18 years.

Study Measures. We analyzed patient- and provider-level characteristics of visits in which RIDT was performed. In addition, we considered the following characteristics: sex; age; whether the patient was admitted to the hospital; temperature (≥100.4°F, <100.4°F); and primary diagnosis (first of the up to 3 diagnoses assigned by the provider). We identified patients with acute upper respiratory tract infection (ARTI) based on previously defined diagnosis codes [14].

For each patient group, we calculated the percentage of visits in which certain clinically relevant measures were performed. These measures included (1) use of ancillary diagnostic tests (chest radiography, blood culture, urinalysis, and complete blood count), (2) prescribing of antibiotics (systemic antibiotics only), and (3) prescribing of antivirals (oseltamivir, zanamivir, amantadine, and rimantadine). Use of diagnostic testing, including RIDT, was documented by providers using check boxes; however, test results are not available in the dataset.

Data Analysis

We calculated the differences in the percentage usage of each of the 3 clinical measures (ancillary testing, antibiotics, and antivirals) between RIDT + /INF+ (highest certainty; used as the reference category) and RIDT – /INF+ (intermediate certainty) and between RIDT + /INF+

(reference) and RIDT + /INF– (lowest certainty). All statistical analyses were performed using Stata11.2 (StataCorp, College Station, TX). Ninety-five percent confidence intervals (CIs) were calculated for each estimate, which accounted for the complex survey design. *P* values for the rate difference CIs were calculated by first calculating the standard error for the differences to derive a z score and then determining the associated *P* value based on a normal distribution [15]. Due to sample size limitations and to maximize the precision of estimates, we combined data for the 3 influenza seasons and data for adult and pediatric patients as recommended by NCHS.

RESULTS

Nationwide, there were an estimated 182 million (95% CI: 161–204 million; n = 51 844 sampled visits) ED visits during the study period. Rapid influenza diagnostic tests was performed at an estimated 4.2 million (95% CI: 3.1–5.3 million; n = 995 sampled visits), accounting for 2% of these visits (Figure 2). Patient demographics and clinical characteristics from all ED visits during the study period are shown in Table 1. Our final study population of an estimated 4.9 million ED visits (95% CI: 3.7–6.1 million; n = 1166 sampled visits) included the 4.2 million visits in which RIDT was performed as well as 0.7 million visits in which RIDT was not performed but influenza was diagnosed. Fifty-three percent (95% CI: 46%–61%) of patients in the study cohort were children <18 years old. Demographics and clinical characteristics of the study population are shown in Table 2.

Overall, influenza was diagnosed in an estimated 1.3 million ED visits (95% CI: 0.9–1.7 million). Forty-six percent of influenza diagnoses (600 000 estimated visits; 95% CI: 339 000–847 000) were made in association with RIDT. For study visits without an influenza diagnosis, the most common primary diagnoses were as follows: (1) ARTI [14] (43% of visits), (2) unspecified viral infection (9%), and (3) fever (9%). Of all ED visits with a primary diagnosis of ARTI, 11% (95% CI: 8%–13%) of patients received RIDT. Of ED visits by patients <18 years of age with a primary diagnosis of ARTI, 11% (95% CI: 8%–15%) received RIDT (data not shown).

Use of ancillary testing, antibiotics, and antivirals were examined in each of our 3 predefined groups: (1) RIDT performed/influenza diagnosis (RIDT + /INF+), (2) RIDT performed/no influenza diagnosis (RIDT + /INF–), and (3) RIDT not performed/influenza diagnosis (RIDT–/INF+). Comparisons were made using the RIDT + /INF+ group as a reference. Results are shown in Table 3. Findings were comparable when each influenza season was analyzed individually; however, sample sizes were too small for precise estimates.

For patients who had RIDT testing but who did not have an ICD-9-CM code for influenza (RIDT + /INF– group),

Table 1 Demographic and Clinical Characteristics

ED Visits During the Study Period		
Variable	RIDT Performed	RIDT Not Performed
Number of sampled visits	995	50 849
Number of estimated visits	4.2 million	178.1 million
	Weighted Percentage	
Sex		
Male	46%	45%
Age Group		
0–5	34%	12%
6–17	20%	12%
18 +	46%	76%
Hospital Admission?		
Yes	8%	13%
No	92%	87%
Temperature		
≥100.4°F	38%	5%
Primary Diagnosis		
Influenza	12%	<1%
ARTI[a]	45%	11%
Unspecified viral infection	10%	1%
Fever	10%	1%
Other respiratory diagnosis	4%	4%
Other diagnosis	19%	82%

Abbreviations: ARTI, acute respiratory tract infection; ED, emergency department; RIDT, rapid influenza diagnostic tests.
[a]Codes defined in Ref. 14.

Table 2 Demographic and Clinical Characteristics: Study Population

Variable	Study Population
Number of sampled visits	1166
Number of estimated visits	4.9 million
	Weighted Percentage
Sex	
Male	46%
Age Group	
0–5	33%
6–17	20%
18 +	47%
Hospital Admission?	
Yes	7%
No	93%
Temperature	
≥100.4°F	39%
RIDT Performed?	
Yes	14%
Influenza Diagnosed?	
Yes	26%
Primary Diagnosis	
Influenza	20%
ARTI[a]	43%
Unspecified viral infection	9%
Fever	9%
Other respiratory Diagnosis	4%
Other diagnosis	15%

Abbreviations: ARTI, acute respiratory tract infection; RIDT, rapid influenza diagnostic tests.
[a]Codes defined in Ref. 14.

Table 3 Clinical Care Associated With Influenza Diagnosis and Use of RIDT

	Frequency of Ancillary Testing and Medication Use									
Patient Group	Weighted Proportion of Visits in Which Ancillary Testing Was Performed[a]	Rate Difference (95% CI) Compared with Group 1	*P* Value	Weighted Proportion of Visits in Which Antibiotic(s) Were Prescribed[b]	Rate Difference (95% CI) Compared with Group 1	*P* Value	Weighted Proportion of Visits in Which Antivirals Were Prescribed[c]	Rate Difference (95% CI) Compared with Group 1	*P* Value
RIDT performed/ Influenza diagnosis (RIDT + /INF+)	45%	Reference	NA	11%[d]	Reference	NA	56%	Reference	NA
RIDT not performed/ influenza diagnosis (RIDT – /INF+)	53%	8% (–8%, 24%)	.33	23%	12% (0%, 23%)	.05	19%	–37% (–52%, –22%)	.002
RIDT performed/no influenza diagnosis (RIDT + /INF–)	60%	15% (0%, 30%)	.04	47%	36% (25%, 46%)	<.0001	2%[d]	–54% (–68%, –40%)	<.0001

Abbreviations: ARTI, acute respiratory tract infection; CI, confidence interval; NA, not applicable; RIDT, rapid influenza diagnostic tests.

[a] Ancillary testing includes blood culture, complete blood count, urinalysis, and chest x-ray.

[b] Antibiotics include penicillins, cephalosporins, macrolides, quinolones, lyncomycin derivatives, tetracyclines, sulfonamides, aminoglycosides, and carbapenems.

[c] Antivirals included oseltamivir, zanamivir, amantadine, and rimantadine.

[d] Estimates are based on fewer than 30 observations and may not be reliable.

physicians prescribed more antibiotics and ordered more ancillary tests than for either group of patients with an influenza diagnosis. Antiviral prescribing in the absence of an influenza diagnosis was rare. Among patients diagnosed with influenza, antimicrobial prescribing and diagnostic testing were strongly associated with whether or not RIDT was performed. When RIDT was performed (RIDT + /INF+ group), physicians prescribed antibiotics less often (11% vs 23%; absolute difference, 12%; 95% CI: 0–23) and were significantly more likely to prescribe an antiviral agent (56% vs 19%; absolute difference, 37%; 95% CI: 22–52) compared to visits in which influenza was diagnosed without RIDT (RIDT – /INF+ group). In addition, physicians ordered less ancillary testing (–8%) when RIDT was performed. Findings were similar when restricted to pediatric (<18 years) or adult (≥18 years) subpopulations, although sample size limitations precluded calculation of stable estimates.

DISCUSSION

This retrospective study was performed to examine the use of RIDT and the impact of RIDT on influenza management using a nationally representative sample of ED visits. Nearly half of all patients diagnosed with influenza had RIDT performed. Diagnosis of influenza with or without testing decreased the use of antibiotics and ancillary studies. Most importantly, patients diagnosed with influenza when RIDT was performed received the fewest antibiotics and ancillary tests and were the most likely to receive antivirals. Our findings suggest that rapid testing may result in more efficient and appropriate care.

Our findings using a national dataset extend those of several single center studies that have demonstrated decreased antibiotic use and ancillary testing for patients with influenza when RIDT results are known to the physician [4–9]. For example, Bonner et al [4] conducted a randomized trial of RIDT among 418 children in a pediatric ED and showed that when RIDT results were available, children with influenza received significantly fewer antibiotics and diagnostic tests and were more likely to receive antiviral medications. Studies have demonstrated that (1) antibiotics are often prescribed for patients diagnosed with influenza and that (2) antivirals are underused, particularly for patients at high risk for complications [1]. Both results may be a consequence of diagnostic uncertainty that could be mitigated in part by RIDT.

Antigen-based RIDT are limited by their moderate to poor sensitivity. Sensitivity for seasonal influenza strains ranges from 18% to 71% [3, 16]. Current RIDT have relatively poor sensitivity for A/2009 (H1N1)pdm09 [13] and

the swine-origin H3N2v [17]. Despite their limitations, over 4 million RIDT were performed in US EDs during the study period. Widespread use of RIDT may be due to the utility of a positive result; a positive test during influenza season has a high positive predictive value [2, 16].

Several studies have demonstrated that physicians are capable of accurately diagnosing influenza with reasonable accuracy using clinical data or decision rules, without the aid of RIDT [18, 19]. In our study, we did not evaluate the accuracy of influenza diagnosis, but we examined patient management for diagnoses made with or without RIDT. We hypothesized that management would be more appropriate for patients with an influenza diagnosis when RIDT was used in the process. Our research results demonstrated that there was a substantial impact of RIDT use on several aspects of clinical care, suggesting an influence of diagnostic certainty provided by testing on decision making. A German study of community patients diagnosed with influenza with or without the aid of RIDT similarly hypothesized that a threshold "level of confidence" in the diagnosis of influenza was needed to trigger a choice to use antivirals and that confidence was increased by a positive test [20]. This study showed that 60% of patients were prescribed antivirals when RIDT was used, compared to only 25% with a purely clinical diagnosis. In our study, patients diagnosed with influenza were more than twice as likely to receive antivirals if RIDT was performed.

In our cohort, there was an absolute decrease in antibiotic use of 12% for patients diagnosed with influenza when RIDT was used compared to patients diagnosed without RIDT, a relative reduction of over 50%. This result would have translated to 84 000 fewer antibiotic prescriptions in the ED during the influenza seasons of 2007–2009. Certain patients with influenza may have a concomitant bacterial infection and warrant antibiotic therapy [1]. In our study, 11% of patients diagnosed with influenza in the context of RIDT received antibiotics, which may represent a reasonable lower bound.

Our results suggest that even an imperfect test such as RIDT can have a significant impact on clinical decision making. Development of more accurate rapid tests for influenza, including molecular tests, is ongoing. Advancement of improved test methodologies and wider access to them at the point of care should be a public health priority.

Prior studies, limited to single centers, may be subject to local clinical biases and thus have limited generalizability. Using NHAMCS, we confirmed the findings of earlier studies and demonstrated the influence of RIDT on clinical care on a broad, national scale. Although prospective data collection remains the "gold standard," the use of administrative databases offers additional advantages compared with a large multicenter study, including relatively low cost and shorter completion time.

Our study has several limitations. Although the NHAMCS provides information regarding the use of RIDT, it does not provide test results, and we were unable to perform detailed chart reviews for clinical information. We relied on ICD-9-CM coding to identify patients with influenza, a methodology with excellent specificity but moderate sensitivity [21]. Our evaluation made the assumption that a positive RIDT resulted in an influenza diagnosis and negative RIDT was less likely to do so. This assumption was supported by data from our own hospital system. An analysis of >8000 patients seen in our integrated healthcare system facilities (Intermountain Healthcare, Salt Lake City, UT) during the 2007–2009 influenza seasons demonstrated that 93% of patients with a positive RIDT had an influenza diagnosis and 98% of patients who had a negative RIDT test did not have an influenza diagnosis (unpublished data, A. J. B. and A. L. H.).

We found that 46% of influenza diagnoses were made in association with RIDT. Practice variation in the use of RIDT may relate to differences between individual physician practices or between hospitals and the availability of testing options; however, the NHAMCS database does not enable analysis of these potentially important issues. Although we found differences in the use of antibiotics, antivirals, and ancillary tests between patients who did and did not undergo RIDT, we were unable to determine their appropriateness based on illness severity or comorbidities.

CONCLUSIONS

This national study of RIDT in the management of influenza in the ED demonstrated widespread use of these tests and a significant impact of RIDT on physician decision making, patient care, and resource utilization. This practice occurred despite the relatively poor sensitivity of currently available RIDT, which limits their utility. Improvement in the accuracy of rapid influenza testing along with the development of point of care testing for other respiratory pathogens has the potential to improve the appropriateness of antibiotic and antiviral therapy and resource utilization for patients with respiratory illness.

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Potential conflicts of interest. A. J. B., A. T. P., C. L. B., K. K. A., and A. L. H. collaborated with BioFire Diagnostics, Inc (formerly, Idaho Technology, Inc) on several National Institutes of Health– and Centers for Disease Control and Prevention–funded projects. A. J. B. and C. L. B. have intellectual property in BioFire Diagnostics, Inc.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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