Hennepin County Medical Center

Every Life Matters.

Point of Care Testing and the Challenge of Seasonal Influenza;

The Impact of New Evidence

Glen T. Hansen, Ph.D, FCCM, D(ABMM)
Director, Clinical Microbiology & Molecular Diagnostics
Hennepin County Medical Center
Assistant Professor: Pathology & Laboratory Medicine
Assistant Professor: Medicine; division of Infectious Diseases
University of Minnesota School of Medicine
Minneapolis, Mn

Disclosure

Hennepin County Medical Center

Every Life Matters.

A portion of the data shown here was supported by an investigator initiated unrestricted education grant from Roche Molecular

Objectives

- 1. A microbiology lab director's view of POC
  - Why is "microbiology" so special?
- 2. what evidence is there that POC makes any difference?
- WHY influenza? What's the big deal with flu anyway?
- HCMC's Experience with flu testing inside the ED

Final ranking	Biotechnology	Final score
1	Modified molecular technologies for affordable, simple diagnosis of infectious diseases	288
2	Recombinant technologies to develop vaccines against infectious diseases	262
3	Technologies for more efficient drug and vaccine delivery systems	245
4	Technologies for environmental improvement (sanitation, clean water, bioremediation)	193
5	Sequencing pathogen genomes to understand their biology and to identify new antimicrobials	180
6	Female-controlled protection against sexually transmitted diseases, both with and without contraceptive effect	171
7	Bioinformatics to identify drug targets and to examine pathogen-host interactions	168
8	Genetically modified crops with increased nutrients to counter specific deficiencies	159
9	Recombinant technology to make therapeutic products (for example, insulin, interferons) more affordable	155
10	Combinatorial chemistry for drug discovery	129

Daar et al. nature genetics • volume 32 • October 2002

"Top 10 Biotechnologies for improving health in developing countries" 2006. United Nations Educational, Scientific and Cultural Organization

What are our current Gaps in POC and Molecular testing?

- 1. Does new technology actually make a difference?
  - century, innovations and advancements were based on the development and adaptation of new principles and new technologies to meet identified needs
- 2. The role of molecular in infectious disease testing
  - What's changed in the last decade that now presents new challenges?
  - The value of direct specimen testing; a movement away from function of the growth properties
- 3. The right care at the right time
  - Population health……Community based…..
- 4. Stratification for outcomes beyond diagnosis

Is there a standard working Definition for POC testing?

”They [lab tests] are to the physician just as the knife and scalpel are to the surgeon”

Sir William Osler. *JAMA* 1900;35:230\

Is there a standard working Definition for POC testing?

What are we “measuring” to define a successful POC program?

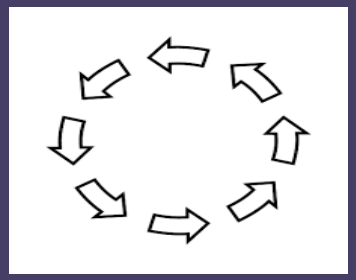
1.) **Length of Stay?**
2.) **Successful Patient “outcome”**
3.) **Waiting Times?**
4.) **Reduced costs**
5.) **Increased efficiency (patient visits; lab utilization)**
6.) **Keeping Dr. X “happy”**
7.) **Time to optimal therapy & Speed to therapeutic response**
8.) **Decreased mortality**
9.) **Reduced Re-admission**
10) **Adherence to CORE measures**
11) **Accessibility to testing---can POC provide “help”**
12) **Increase patient/client satisfaction**

Why point of care for microbiology?

Understanding changes in health care delivery

- 1990s

Why point of care for Microbiology? Circa 2005



POC testing in US pharmacy locations

Source: Alex Adams PharmD, MPH

Why Point of care testing in General?

3 Basic Principles of POC

1.) The value of a POCT lies in the immediacy of the response.

2.) The diagnostic performance of the test has likely already been established in the centralized laboratory but the BENEFITS & OUTCOMES will be capitalized in the POC environment

3.)The result should be actionable

Is POC testing better for patients? Is quicker better?

……Well that Depends

Clinical Chemistry 46:4
543–550 (2000)

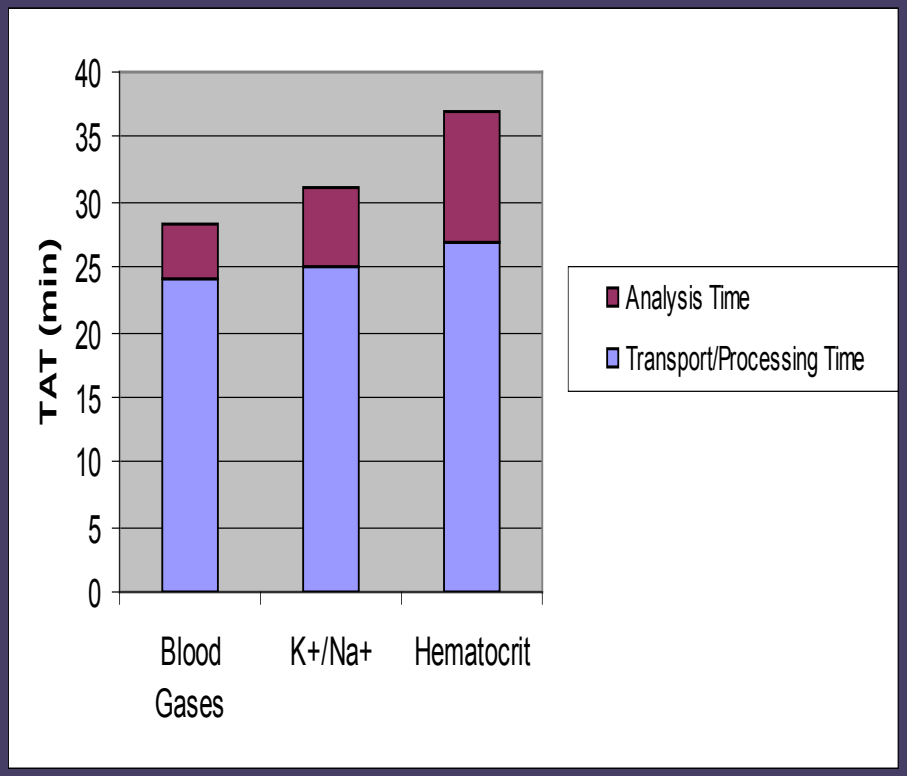
Laboratory Management

Clinical Outcomes of Point-of-Care Testing in the Interventional Radiology and Invasive Cardiology Setting

James H. Nichols,[1*] Thomas S. Kickler,[1] Karen L. Dyer,[1] Sandra K. Humbertson,[1] Peg C. Cooper,[2] William L. Maughan,[3] and Denise G. Oechsle[2]

Conclusions: merely moving testing from a central laboratory to the medical unit does not guarantee improved outcomes. Systematic changes in patient management may be required

Transport/Processing Time vs. Analysis Time



Salem et al. JAMA 1991; 266:382-389

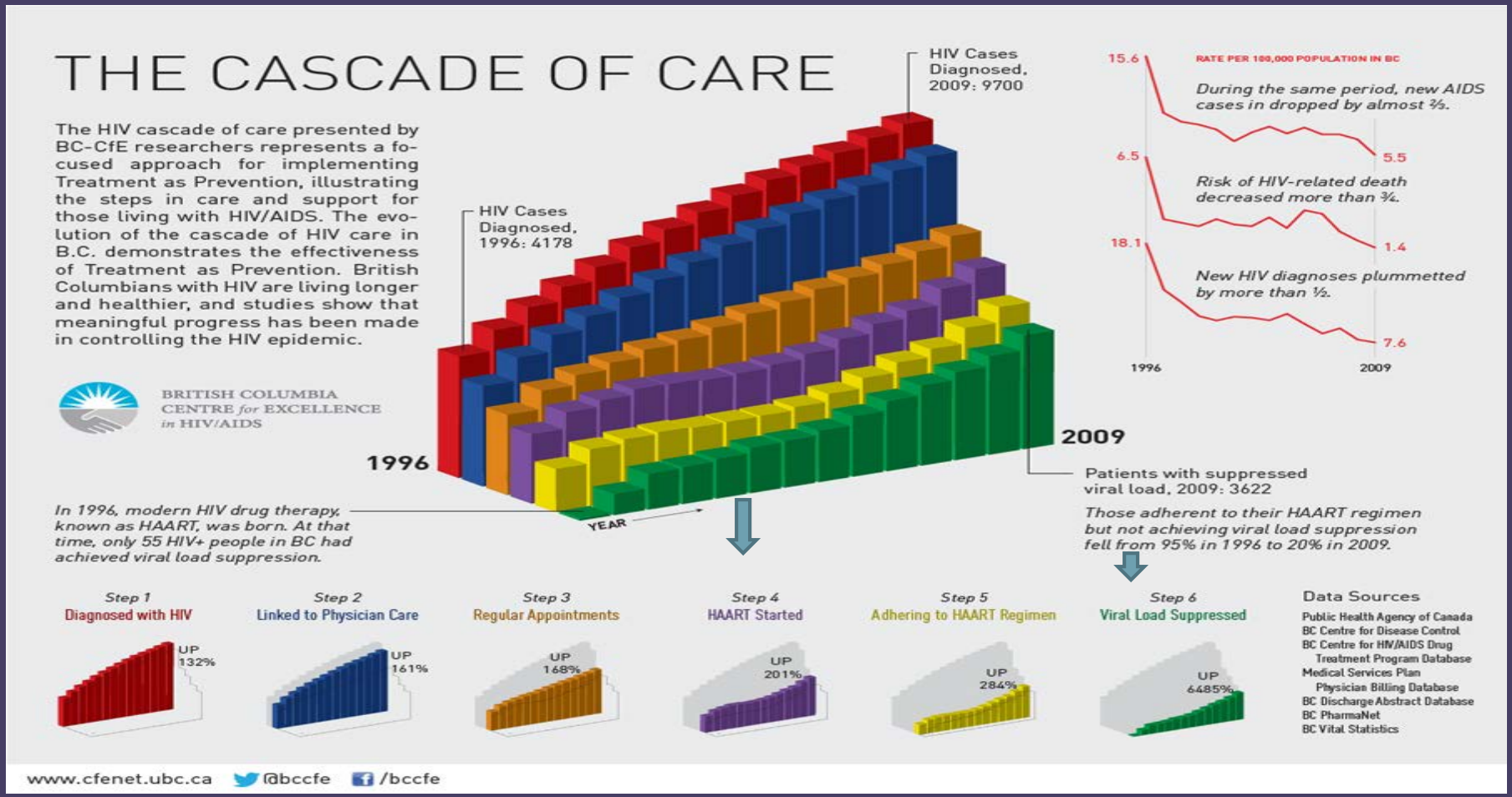
Point of Care Testing in the Post Anesthesia Care Unit

Use of POCT resulted in:

- reduced test TAT from 26 min to 2 min
- decreased length of stay by 18 min
- documented cost savings due to decreased length of stay

Goodwin MLO 1994; 26 (9S):15-18.

Does POCT make a difference?



66% of new infections prevented by 2030
cost avoided 95 Million USD = 368,000/patient

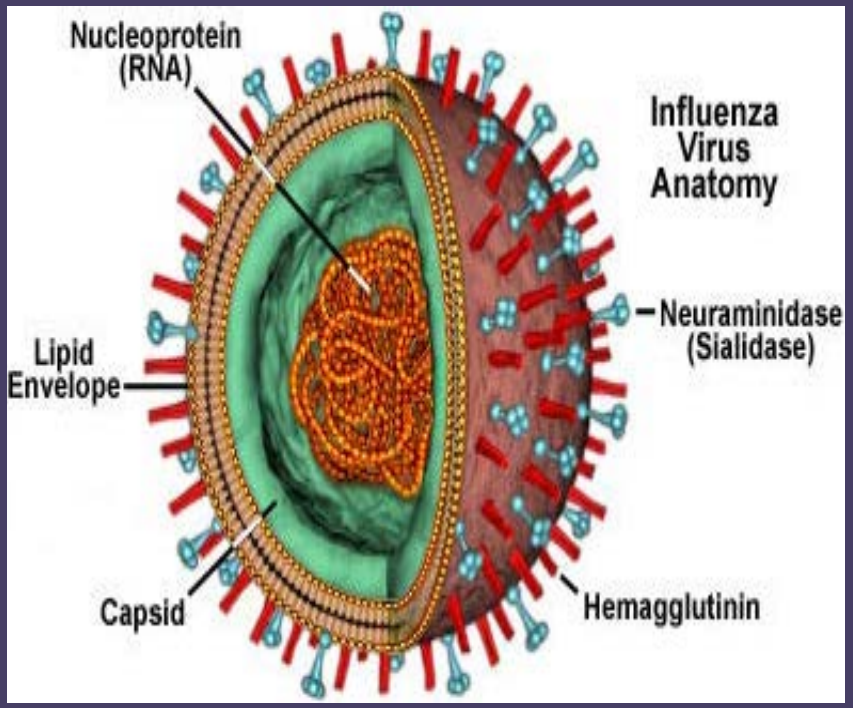
Noysk B et al. Lancet Infec Dis 2014

Lima VD et al. *J Infect Dis* 2008; 198: 59-67.

What are our current Gaps in POC and Microbiology/Molecular

- 1. inferior sensitivity specificity
- 2. versatility
- 3. Costs $
- 4. Contamination QC
- 5. few infectious syndromes are pathognomonic of infection due to a single organism

Influenza Season

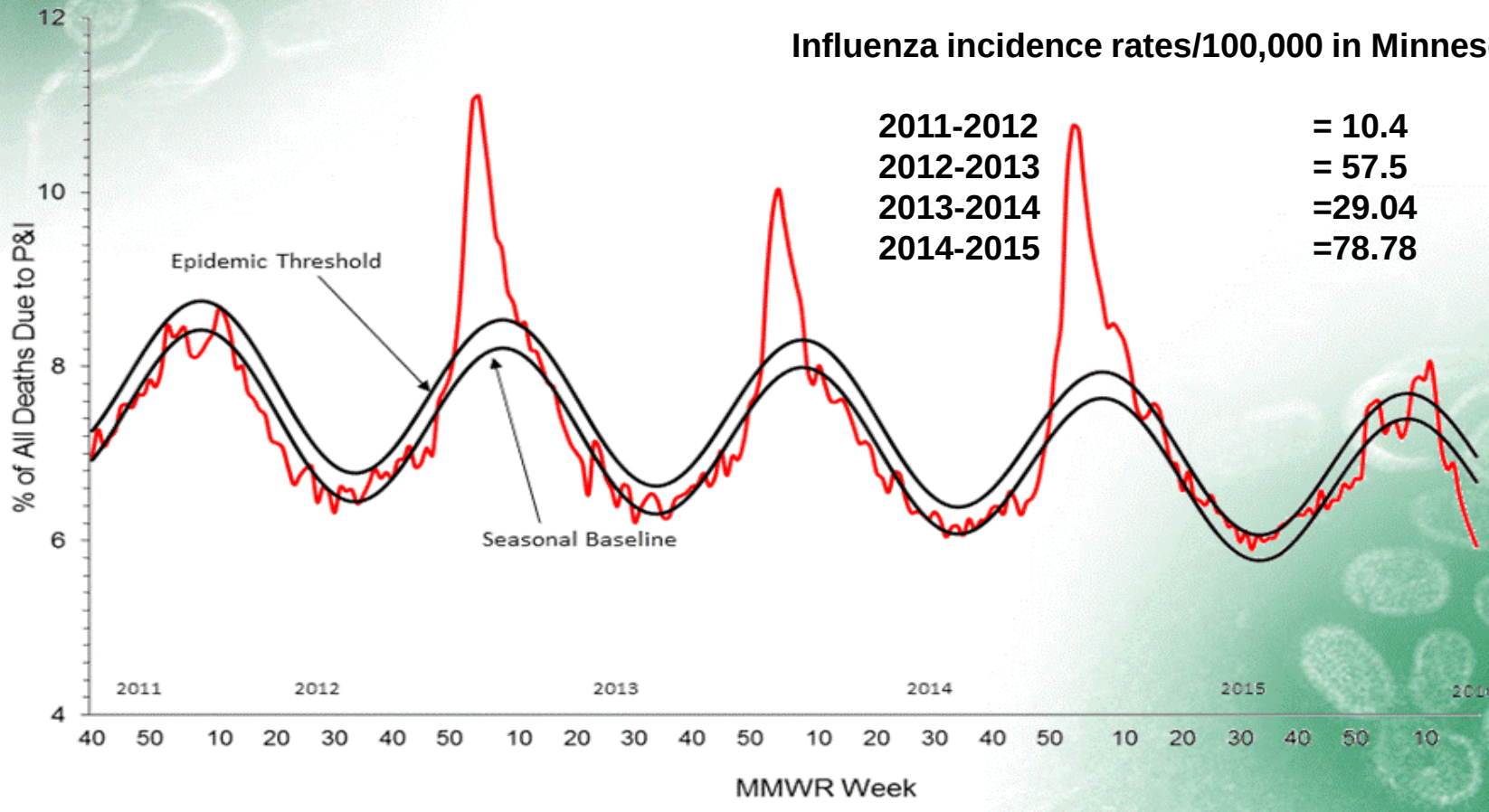


FLUVIEW

A Weekly Influenza Surveillance Report Prepared by the Influenza Division

Pneumonia and Influenza Mortality from the National Center for Health Statistics Mortality Surveillance System

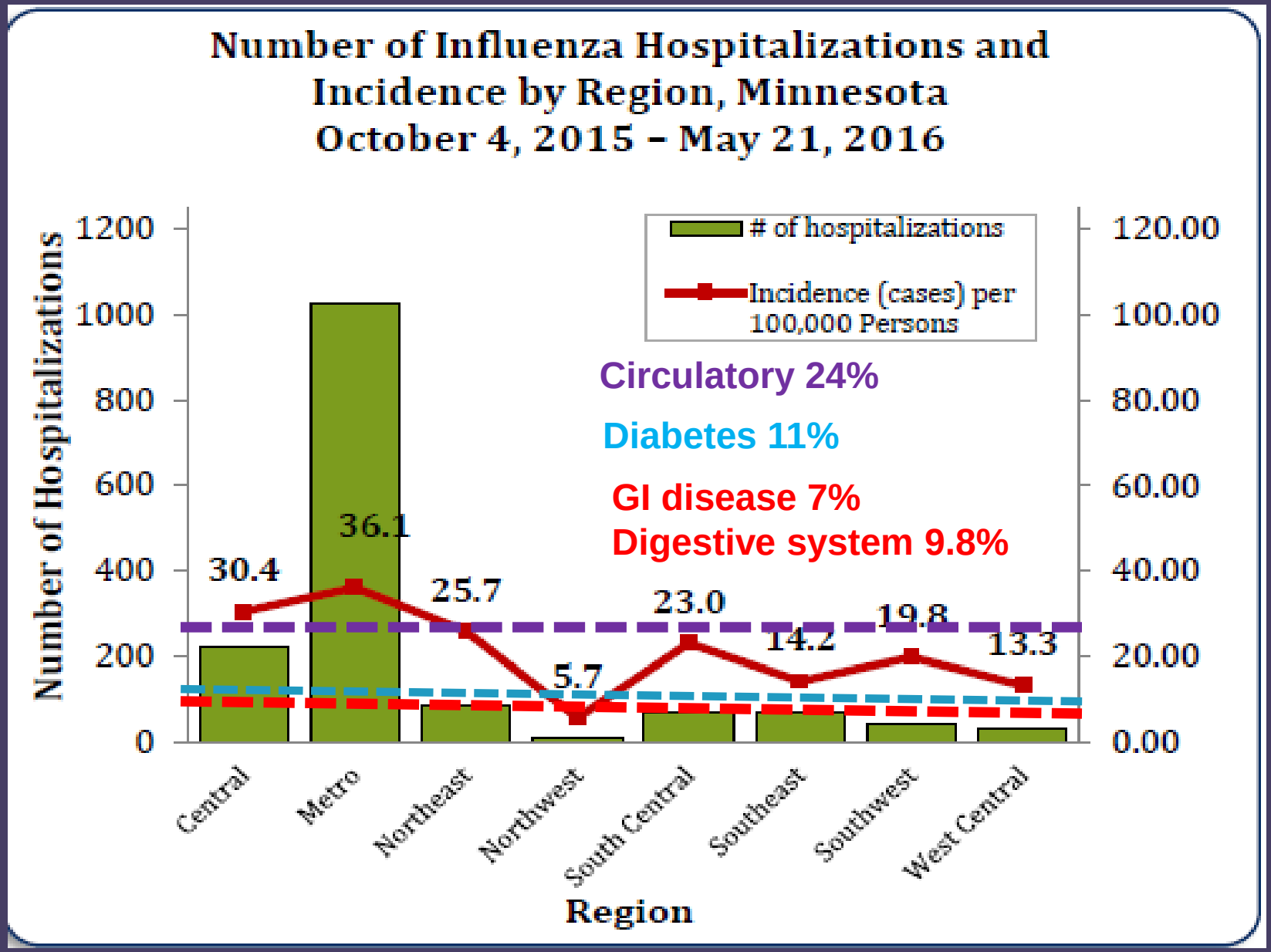
Data through the week ending May 14, 2016, as of June 2, 2016



Influenza incidence rates/100,000 in Minnesota

2011-2012	**= 10.4**
2012-2013	**= 57.5**
2013-2014	**=29.04**
2014-2015	**=78.78**

Source: CDC



Source: Minnesota Dept of Health

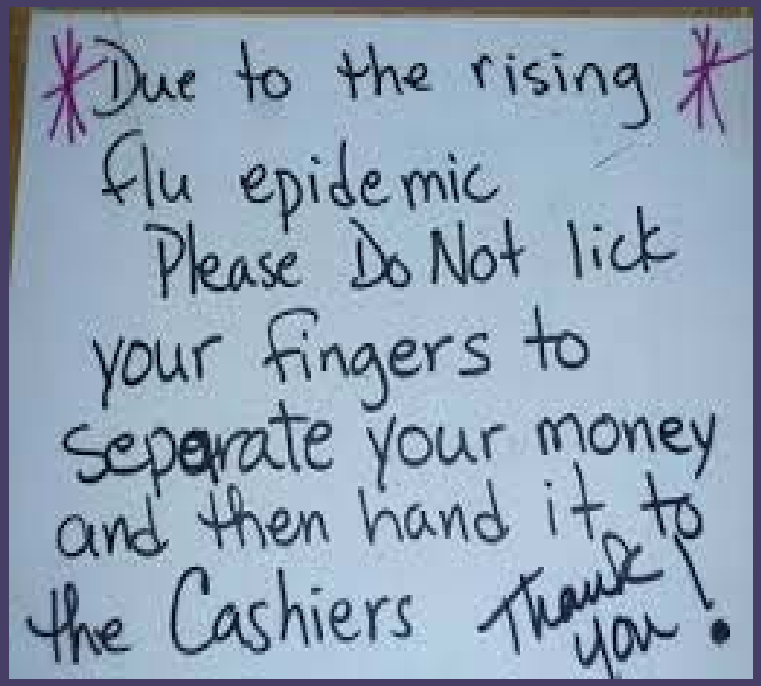
http://www.cdc.gov/diabetes/statistics/hosp/adulttable1.htm

Why test for flu?

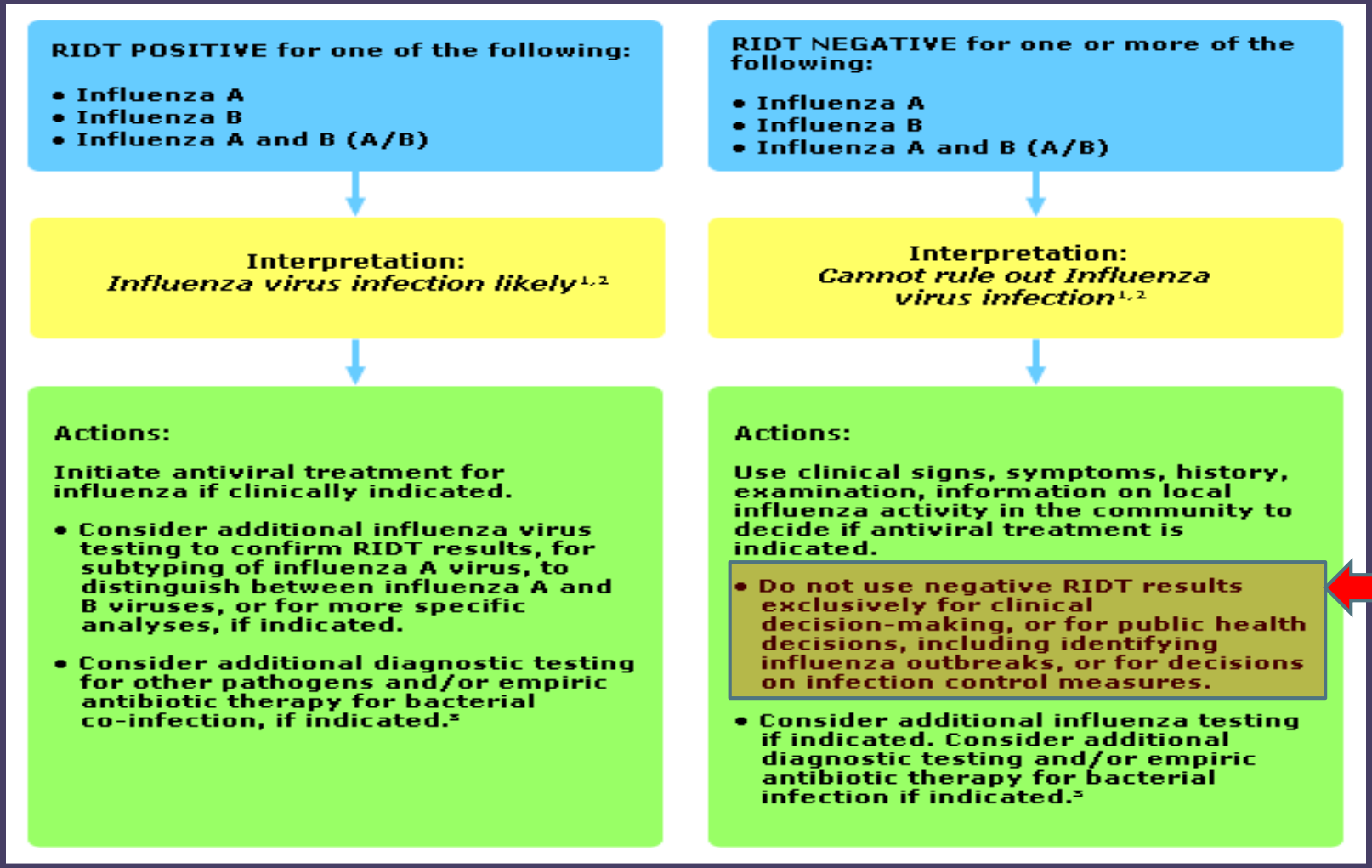
- Help Guide Treatment course
  - CDC recommendations for antiviral treatment
    - Severe or complicated course, those requiring Hospitalization, LTCF, specified chronic medical conditions, immunosuppressive thxp, pregnancy, Native American)
- Further support empiric abx coverag… …itted patients
- Help Guide admission/disch…
- Help guide subseq… …cedures/lab orders?
- Helpful t… …ical staff in predicting course
- Helpful to the patient? Useful to know? Helps to predict course?
- Helpful for patient cohort? Infection prevention at health-care facilities

Does Testing Make Any Difference?

What can we do from a laboratory perspective to help during influenza season?



Guidance for Clinicians on the Use of Rapid Influenza Diagnostic Tests



Can Clinical Symptoms Predict Flu?

DOI:10.1111/irv.12316
www.influenzajournal.com

Original Article

Should clinical case definitions of influenza in hospitalized older adults include fever?

Ann R. Falsey,[a,b] Andrea Baran,[c] Edward E. Walsh[a,b]

[a]Department of Medicine, University of Rochester, Rochester, NY, USA. [b]Rochester General Hospital, Rochester, NY, USA. [c]Biostatistics and Computational Biology, University of Rochester, Rochester, NY, USA.
Correspondence: Ann R. Falsey, Rochester General Hospital, 1425 Portland Avenue, Rochester, NY 14621, USA. E-mail: ann.falsey@rochestergeneral.org

Symptom	Sensitivity	Specificity	PPV	NPV
Temp ≥37.8	57	71	20	93
Temp >37.5	68	61	19	94
Cough	95	13	13	96
Any resp symptom	100	1	12	100
Temp ≥37.8 + cough or sore throat	56	73	21	93
Temp >37.5 + cough	82	47	17	95

DOI:10.1111/irv.12316
www.influenzajournal.com

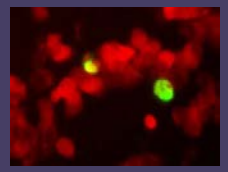
Can Clinical Symptoms Predict Flu in the ED?

	Overall	Symptoms <48	Symptoms >48
Influenza prevalence	16%	15%	16%
Clinical diagnosis			
*sensitivity	**36%**	**39%**	**39%**
*specificity	78%	83%	83%
*+ Like hood ratio	1.63	2.22	2.22
*-- like hood ratio	0.82	0.74	0.74
IIL case definition			
*sensitivity	31%	46%	24%
*specificity	88%	88%	83%
*+ Like hood ratio	2.61	3.85	2.05
*-- like hood ratio	0.78	0.61	0.86

"Clinical diagnosis of ED has a low sensitivity for diagnosing influenza and there is overall low compliance with CDC antiviral treatment recommendations. Improved methods of influenza diagnosis are needed to help guide management in the clinical setting"

Dugas et al. Am. J of Emerg Med. Feb 2015

What's a lab to do? How to test? How do we help our ED?



Rapid Flu tests Lack Sensitivity

Table 1

Sensitivities, specificities, positive predictive values and negative predictive values for the detection of influenza A and influenza B by method.

	%Sensitivity (95% CI)[a]	%Specificity (95% CI)	%PPV[b] (95% CI)	%NPV[c] (95% CI)
Influenza A				
DFA	80.4 (71.2–87.3)	99.2 (97.7–99.7)	96.1 (89.2–98.7)	95.3 (92.8–97.0)
R-Mix	96.9 (91.3–98.9)	100 (99.1–100)	100 (96.1–100)	99.3 (97.9–99.7)
Binax	46.4* (36.8–56.3)	100 (99.1–100)	100 (92.1–100)	88.6 (85.3–91.2)
3MA+B	70.1 (60.4–78.3)	99.8 (98.6–99.96)	98.6 (92.2–99.7)	93.0 (90.5–95.3)
Influenza B				
DFA	74.0 (60.4–84.1)	100 (99.1–100)	100 (90.6–100)	97.0 (94.8–98.2)
R-Mix	98.1 (89.9–99.7)	100 (99.2–100)	100 (93.0–100)	99.8 (98.7–99.96)
Binax	34.6* (23.2–48.2)	100 (99.2–100)	100 (82.4–100)	93.0 (90.3–94.9)
3MA+B	86.5 (74.7–93.3)	98.7 (97.1–99.4)	88.2 (76.6–94.5)	98.4 (96.8–99.2)

Ginocchio CC et al. J. Clin Virol 2009 45(2) 146

Are Panel Based testing options the solution?

Influenza virus	Number of True Positive specimens	% Sensitivity (assay used)		
		FlimArray RP	eSensor RVP	xTag RVPv1.
FluA	30	86.2	100	74.3
Flu A (h1/09)	16	73.3	100	100
Flu A (A3)	14	100	100	92.9
FluB	22	77.3	100	95.5

Time to Results (hr)		FlimArray RP	eSensor RVP	xTag RVPv1.
Instrument time		1.1	5.0	5.5
Time to Result		1.2	7.2	7.8

Popowitch et al. J.Clin.Micro 51(5) 1528; 2013

THE DEBATE OVER THE IDEAL INFLUENZA TEST?

Introduction to a new paradigm shift for influenza testing in an ED setting?

cobas® Liat Analyzer

cobas® Liat assay tube

A pencil-sized flexible single-use tube acts as the sample vessel and contains all assay reagents pre-packed in tube segments

Sensitivity of the Cobas Liat® compared to Genmark RVP (n=314 cases)

Cobas Liat Flu A/B per Package Insert:
Flu A
Sensitivity 100%
Specificity 97%
Flu B
Sensitivity 100%
Specificity 94%

N= 293 tests; 293 discrete patients in the ED During Influenza season

	GenMark RVP positive	GenMark RVP negative
Cobas Liat® Influenza positive cases	82 (97%) (100%)	3**
Cobas Liat® Influenza negative cases	3** (98.6%) (100%)	202

**NGS was performed to amplify viral RNA from the original samples and failied to detect viral RNA 5/6 specimens

Key Question

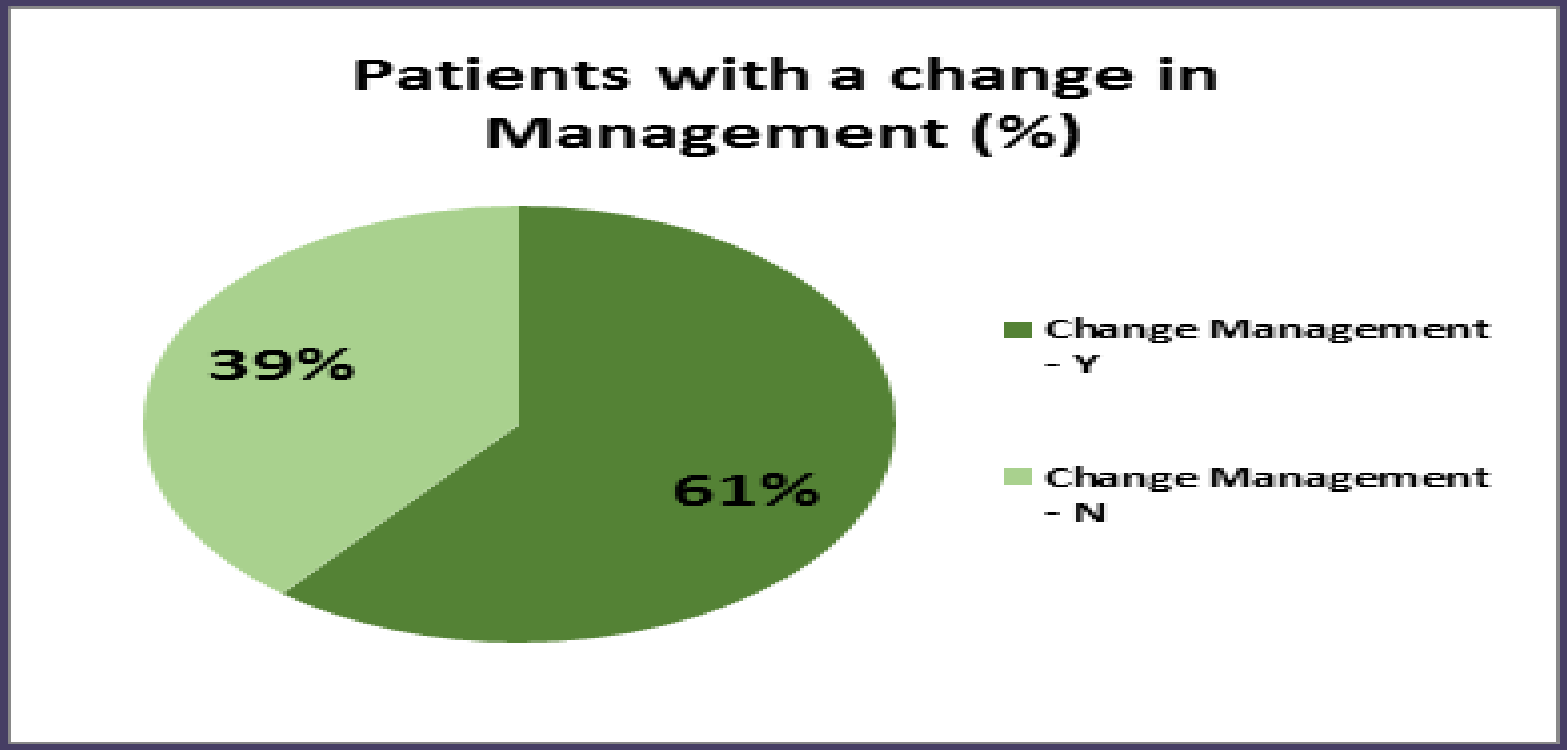
But…. Everything I've shown you to this point IS NOT the key question

Can rapid sensitivity PCR based testing for influenza in an emergency department testing impact patient management?

Impact of the cobas liat® flu assay on clinical decision making in the emergency department setting (CLADE study group)

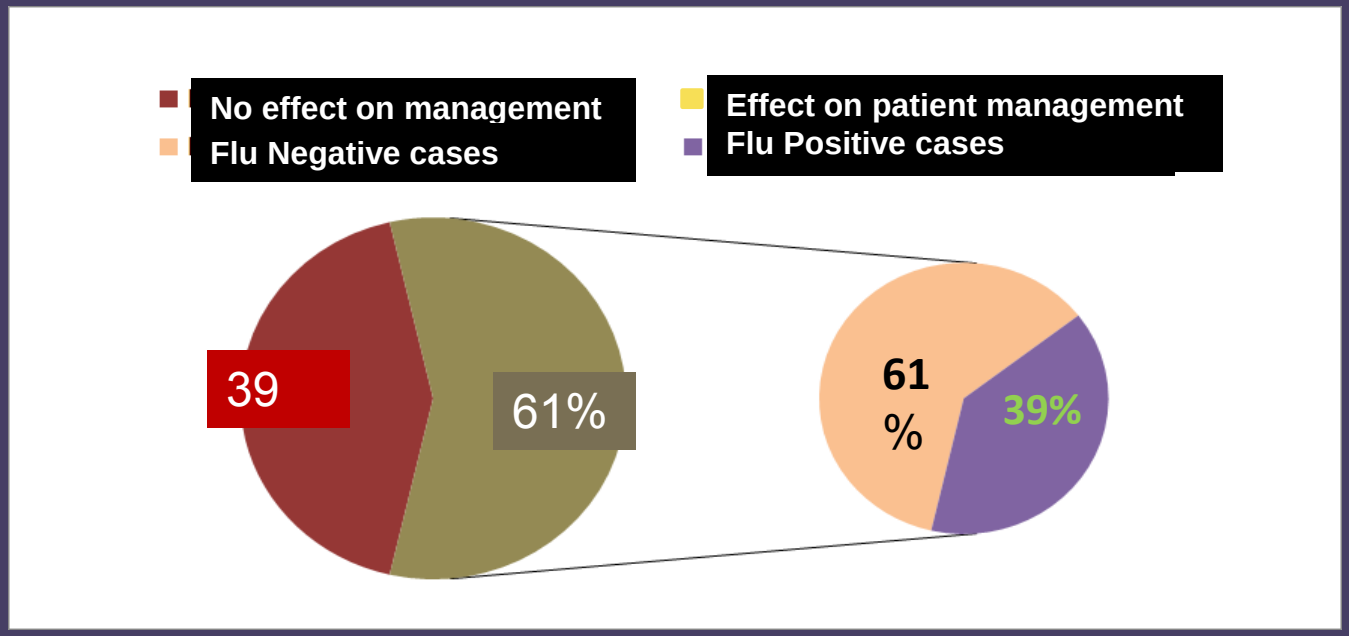
- Prospective observational cohort aimed to determine the impact of a sensitive rapid PCR based assay for influenza on clinical decision making amongst ED physicians
- 314 patients enrolled over three months during the 2015 flu season
- 24-7 study enrollment
- 5 page survey was administered to both ED physician and patient (n=143) (46%)
- Changes in patient management were noted by providers & verified by retrospective chart review
- Test characteristics compared to the Influenza results from the GenMark RVP

Does Rapid Flu results Impact Management of the Patient?



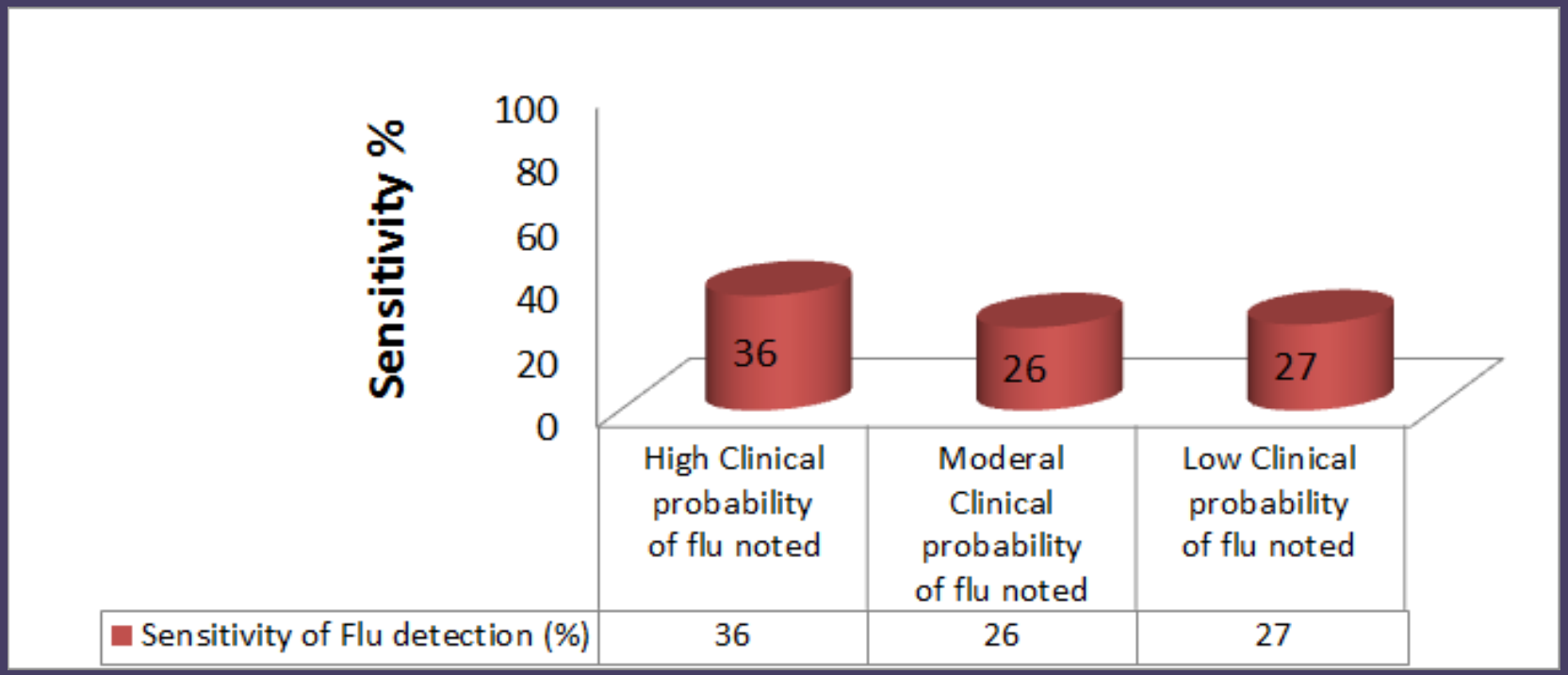
In 61% (n=86/143 patients) of the cases encountered, a documented change in management of patients occurred from base-line upon result of the flu test result

The majority of cases where we see management interventions occur in Flu negative cases?



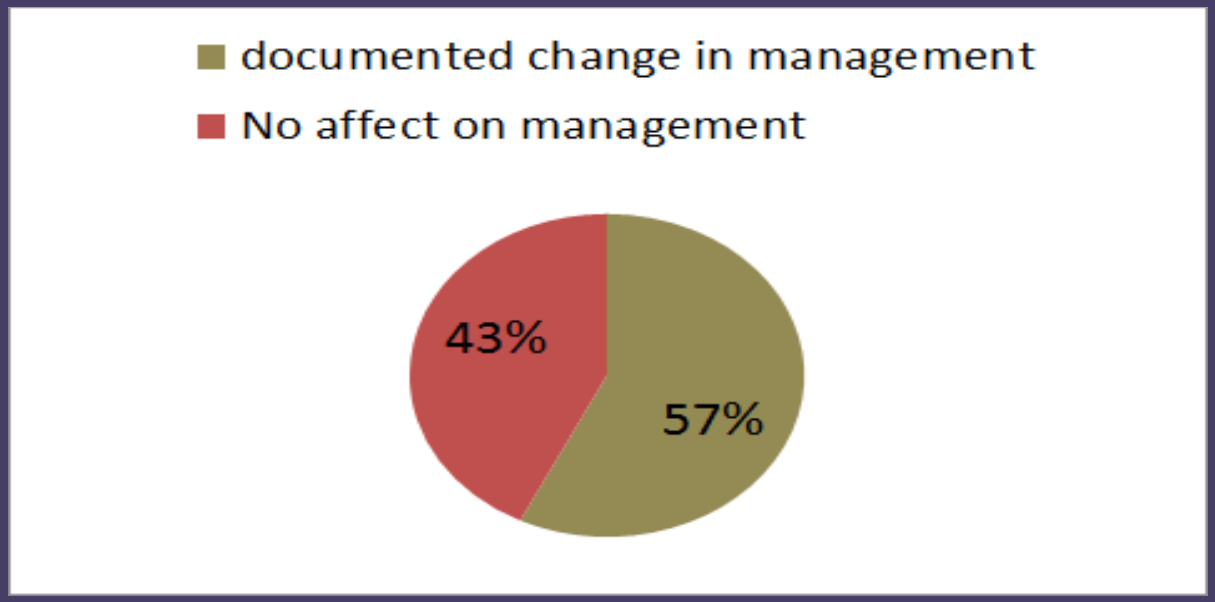
OVER HALF (61%) OF THE CASES WHERE A CHANGE MANAGEMENT OF THE PATIENT OCCURRED WAS REPORTED IN FLU NEGATIVE CASES

A follow up on the sensitivity of predicting flu from clinical symptoms during flu season



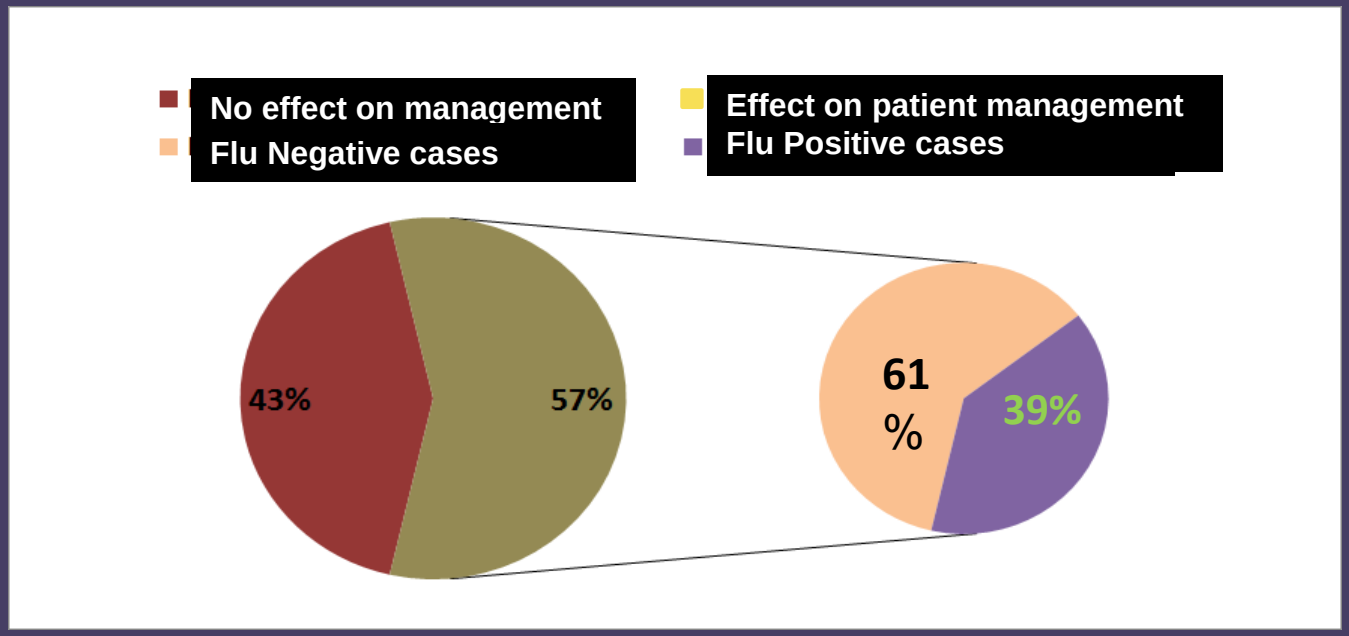
A clinical diagnosis of influenza could be made in on 36% of the cases where flu was denoted as high probability by the physician

Does Rapid Flu results Impact Management of the Patient?



In 57% (n=82/143 patients) of the cases encountered, a documented change in management of patients occurred from base-line upon result of the flu test result

The majority of cases where we see management interventions occur in Flu negative cases?



OVER HALF (61%) OF THE CASES WHERE A CHANGE MANAGEMENT OF THE PATIENT OCCURRED WAS REPORTED IN FLU NEGATIVE CASES

Influenza Testing in the ED-----Four Critical Touch points

17%

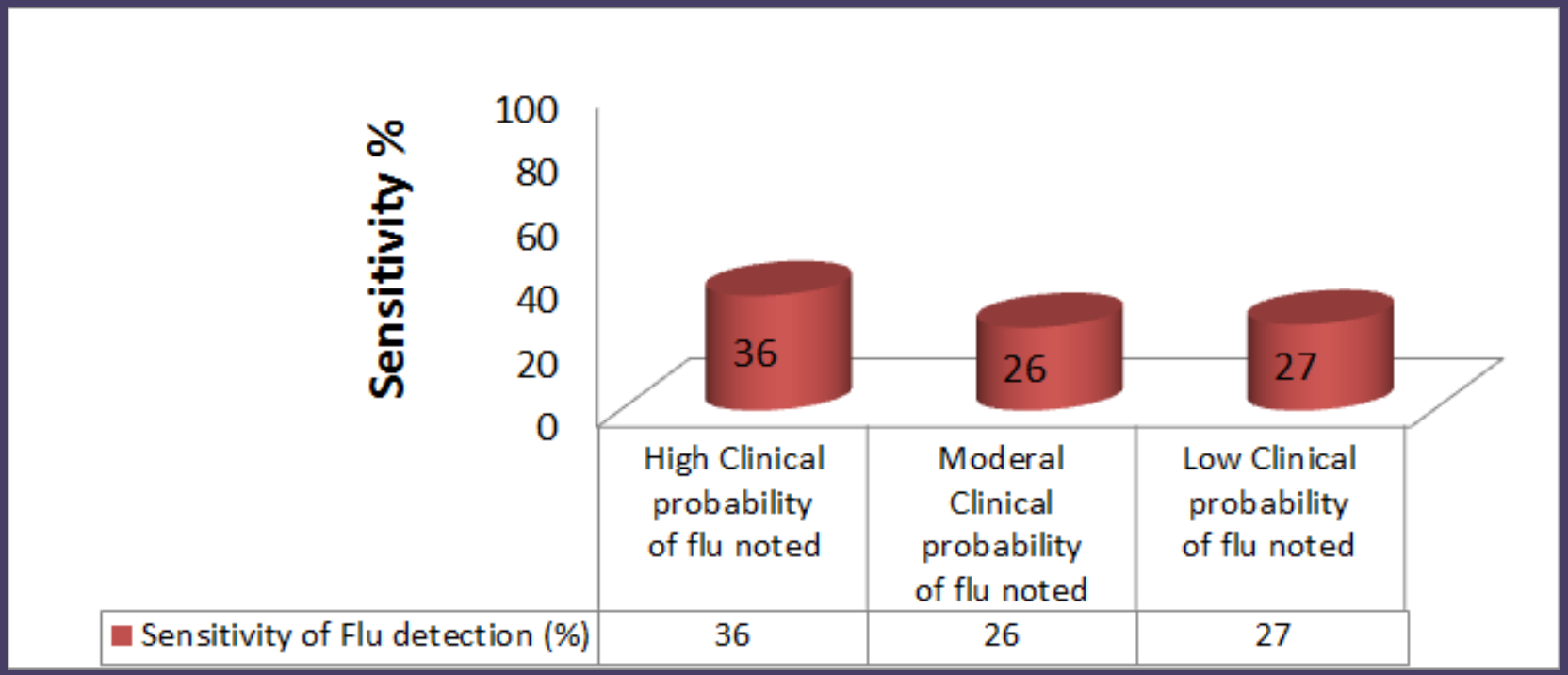
14%

53%

15%

Hansen et al. CVS 2015
Hansen et al AMP 2015

A follow up on the sensitivity of predicting flu from clinical symptoms during flu season



A clinical diagnosis of influenza could be made in on 36% of the cases where flu was denoted as high probability by the physician

RESPIRATORY FAILURE (INCLUDING PNEUMONIA) 6.6% INCREASE IN STAYS PER POPULATION

H-CUP HEALTHCARE COST AND UTILIZATION PROJECT

AHRQ Agency for Healthcare Research and Quality

STATIS

December 2013

Costs for Hospital Stays
States, 2011

Anne Pfuntner, Lauren M. Wier, M.P.H.,
M.P.H.

Introduction

Health care expenditures in the Unite
18 percent of the Gross Domestic Pro
inpatient hospital costs account for ne
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Statistics on costs are included for sta
major diagnostic category, and princip
between estimates noted in the text a
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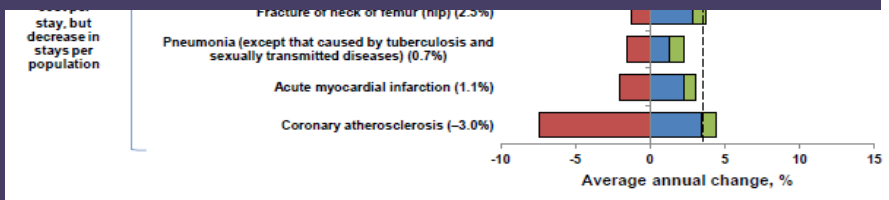
www.hcup-us.ahrq.gov/reports/statbriefs/sb168-Ho…

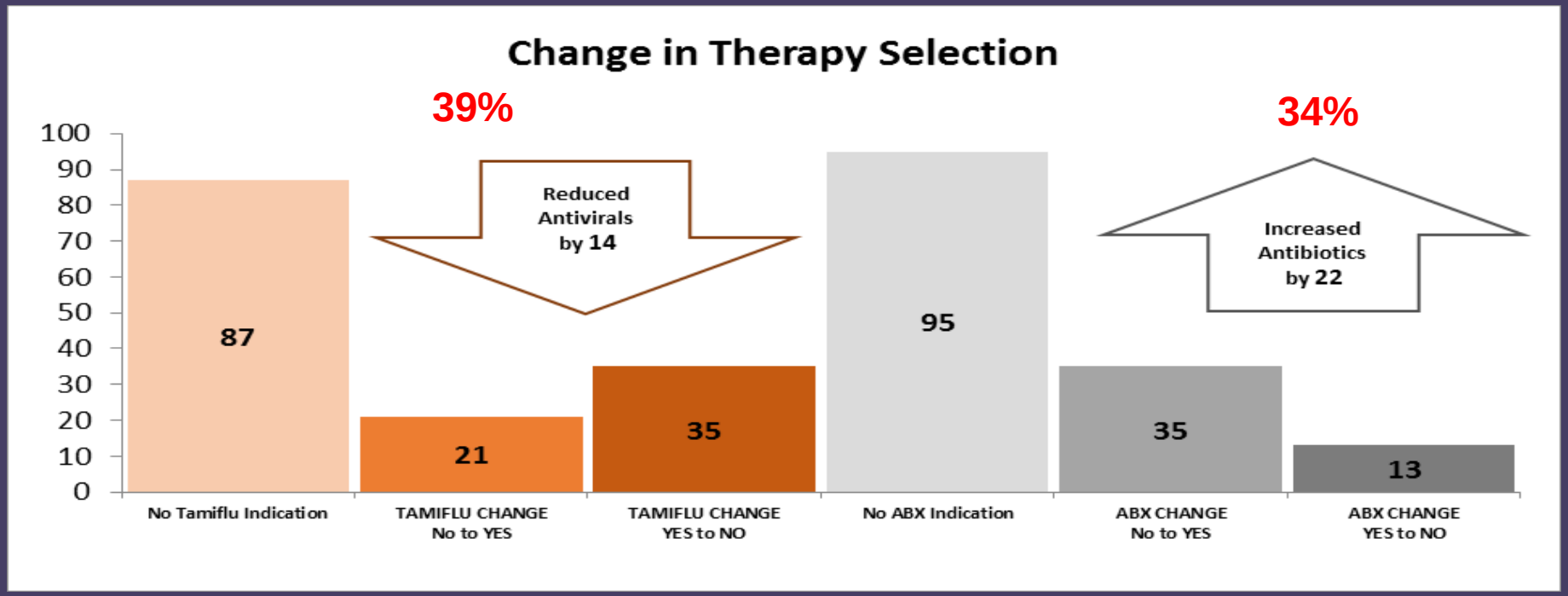
Figure 6. Average annual percentage change* and components of change in inflation-adjusted aggregate hospital costs by principal diagnosis, 1997–2011

It cost "us" $14,143 for admission to the hospital from the ED with an admission of pneumonia

*HCUP Nationwide Emergency Department Sample (NEDS). Healthcare Cost and Utilization Project (HCUP). 2007, 2008, 2009. Agency for Healthcare Research and Quality, Rockville, MD.www.hcup-us.ahrq.gov/nedsoverview.jsp



documented changes from management plan at H&P



Cost per Antiviral	$92
Cost Incurred	$1,932
Cost Avoided	$3,220
Net Savings	**$1,288**

Cost per ABX	$28
Cost Incurred	$980
Cost Avoided	$364
Net Savings	**-$616**

Clinical Touchpoint	% of overall cases impacted	% reduction in utilization/ change in discharge	% increase i utilization or admission
Total N=143 patients			
Hospital Admission/DC	18.2%	⬇ 10.5%	⬆ 7.7%
Antimicrobial prescribing total	58%	⬇ 10%	⬆ 15%
Antibiotic prescribing	33.5%	⬇ 9%	⬆ 33.6%
Antiviral prescribing	39.2%	⬇ 24.5%	⬆ 14.7%
Medical Procedures/Imaging	15.4%	⬇ 2.1%	⬆ 13.2%
Laboratory studies	14%	⬇ 2.8%	⬆ 11.1%

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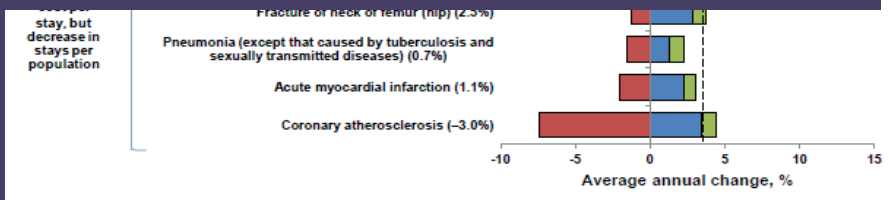
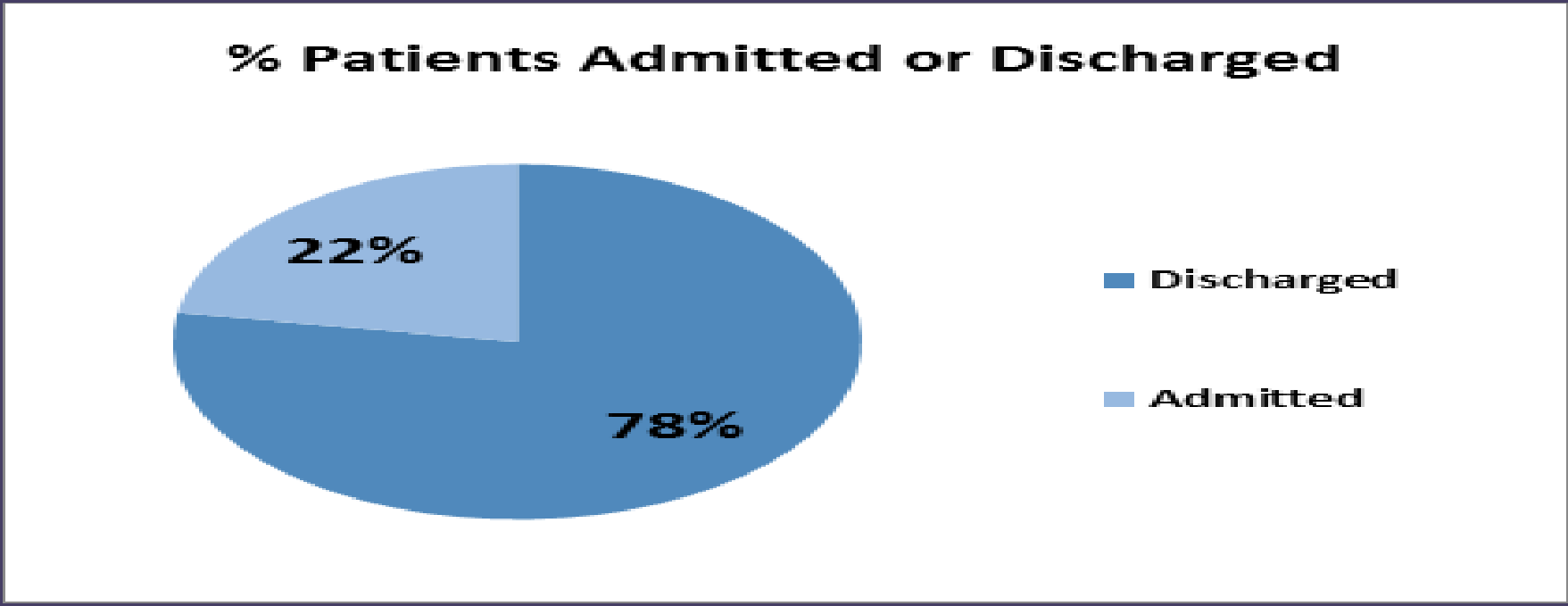


17% of all documented changes from management plan at H&P



Admission/Discharge	377$/patient	
Admission to hospital (incurred)	$155,573	N= 11
Discharge from Hospital (cost avoidance)	$212,145	N= 15
Net Savings	56,572	

. AHRQ, MD.www.hcup-us.ahrq.gov/nedsoverview.jsp

Influenza Testing in the Emergency Department: Four Critical Touch Points

Hospital Admissions / Discharges

17%

Additional Medical Procedures

15%

53%

14%

Antibiotics / Antivirals

Additional Lab Tests

Patients
n = 143

HECON ; Model based on 2000 ED visits for Influenza during season

		Patient involved	Incurred Costs (USD)	Avoided Costs (USD)	Net (USD)
Totals		N=2000			
Tamilfu			27,020	45,034	+18,014
Abx			13,706	5,090	-8,615
Add'tn labs	CBC, micro cult; RVP UA; D-dimer; B. Pertus BMP; C-reactive Legionella; RSV		26,181	6,545	-19,635
Add'tn procedure	Cardiac US; CXR Headt CT; Lumbar p. Renal US; EKG		17,006	2,685	-14,320
Admission change	NO to YES	N= 153	2,163,879		+803,183
Admission Change	YES to NO	N= 209		2,967,062	========== == $778,627

A Final word on the Relative Value of Sensitivity to the patient

In 143 cases documented in our ED.

We saw 35 (24%) cases towards a change away from Tamiflu (Y-N)

We also saw 35 (24%) cases of Abx from N-Y

Assume 20% decrease In sensitivity (100% → 80%) affects 10% of those cases

Over the course of 2000 ED visits that's 49-50 patients who didn't get tamifu who might have upon initial H&P assessment

50 patients who received an antibiotic where the indication might not be there based on a positive flu test

Summary & Conclusions

- 1.) The “Right” information at the “right time” to the “right” people that impacts clinical care
- 2.) When it comes to flu, clinical assessment IS NOT enough
- 3.) Rapid & sensitive access to FLU testing in the ED environment was associated with changes to patient management ($P<0.0001$)
- 4) . The Impact of Sensitive Results Cannot Be Underscored as patient management occurs in negative reporting 1.5x the reporting on positive flu results

A Final question……it access to testing enough impact patient outcome?

It's the integration of testing results

In order for POCT to provide tangible clinical benefit, its results should be actionable and used to make decisions which lead to improved health outcome

Thank you for your time