Information for Nurses:

Influenza Diagnosis, Treatment and Surveillance with Xpert Flu

CDC Recommendations

- CDC provides recommendations on antiviral treatment to patients with suspected influenza [1]
  - Guidelines unchanged since 2011
  - Recommendations recognize three groups of patients with suspected influenza
    - Group 1: Patients with severe, complicated or progressive illness
    - Group 2: Patients at high risk of influenza complications
    - Group 3: Otherwise healthy patients with uncomplicated illness

CDC - Severe Illness

- Group 1: Patients with severe, complicated, or progressive illness
  - Antiviral treatment **recommended** as soon as possible in patients with confirmed or suspected influenza
    - Antivirals reduce severity of illness and influenza-related deaths
    - Treatment recommended within 48 hours of symptom onset, but potential benefit up to 5 days in admitted patients
  - Includes patients with hospitalization, lower respiratory tract disease (pneumonia), etc.

"The benefits of antiviral treatment are likely to be greatest if treatment is started as soon as possible after illness onset, and evidence for benefit is strongest in studies in which treatment was started **within 48 hours of illness onset**. **However, treatment of any person with confirmed or suspected influenza who requires hospitalization is recommended, even if the patient presents >48 hours after illness onset."**

Fiore AE, Fry A, Shay D, Gubareva L, Bresee JS, Uyeki T. 2011. Centers for Disease Control and Prevention (CDC). Antiviral agents for the treatment and chemoprophylaxis of influenza --- recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Surveill Summ 60:1-24.

CDC – High Risk

- Group 2 : Patients at high risk of influenza complications
  - Antiviral treatment **recommended** as soon as possible in patients with confirmed or suspected influenza
    - Antivirals reduce severity of illness and influenza-related complications
    - Treatment recommended within 48 hours of symptom onset
  - Includes the following groups:
    - children aged younger than 2 years;*
    - adults aged 65 years and older;
    - persons with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematological (including sickle cell disease), metabolic disorders (including diabetes mellitus), or neurologic and neurodevelopment conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy [seizure disorders], stroke, intellectual disability [mental retardation], moderate to severe developmental delay, muscular dystrophy, or spinal cord injury);
    - persons with immunosuppression, including that caused by medications or by HIV infection;
    - women who are pregnant or postpartum (within 2 weeks after delivery);
    - persons aged younger than 19 years who are receiving long-term aspirin therapy;
    - American Indians/Alaska Natives;
    - persons who are morbidly obese (i.e., body-mass index is equal to or greater than 40); and
    - residents of nursing homes and other chronic-care facilities.

CDC - Healthy

- Group 3: Otherwise healthy patients with uncomplicated illness
  - Antivirals **not recommended** by CDC
    - Antivirals reduce symptoms if given within 48 hours of symptom onset
    - No demonstration of impact on influenza-related complications
  - Treatment according to physician discretion

Study Overview

- Three year cooperative agreement to evaluate influenza testing, surveillance, and antiviral use
- Funded by Health and Human Services/BARDA
  - Biomedical Advanced Research and Development Authority
- Partnership with the Centers for Disease Control and Prevention
- EMERGEncy ID Net – 4 clinical centers
  - Johns Hopkins Hospital – Lead Coordinating Center
  - Olive View Medical Center
  - Maricopa Medical Center
  - Truman Medical Center

Study Background

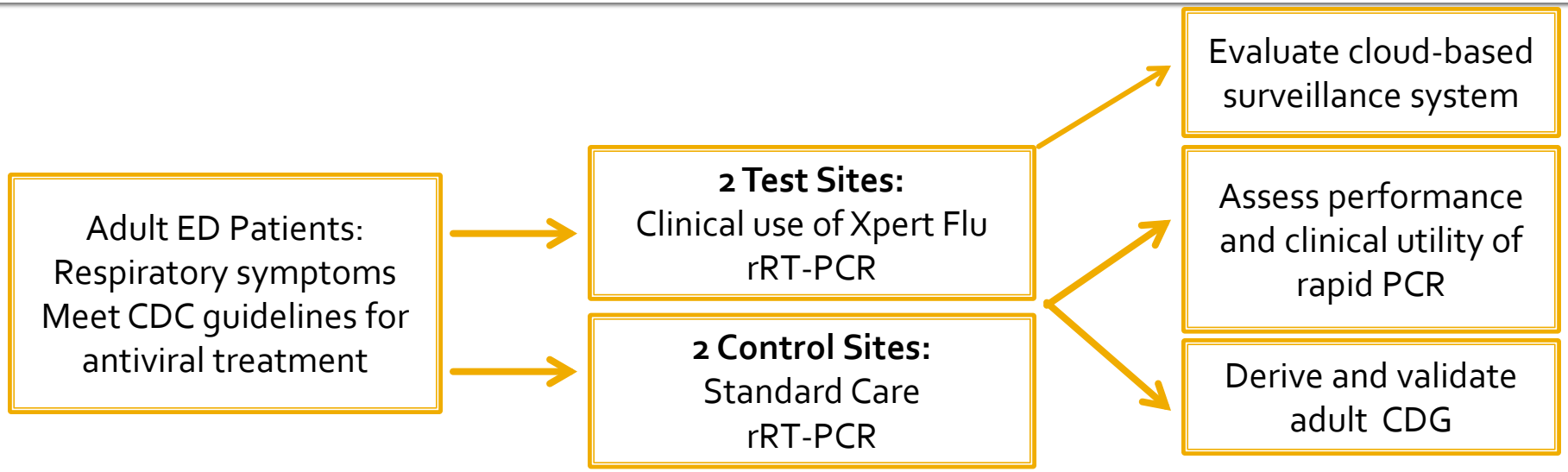
- **CDC recommends antiviral treatment in populations with or at high risk of influenza-related complications**
- **ED providers have poor compliance with CDC guidelines**
  - 36% of patients with influenza recommended to receive antiviral treatment according to CDC guidelines were treated in the ED [2]
- **Diagnosing influenza in the ED is a challenge**
  - Rapid antigen-based tests have poor sensitivity
    - Sensitivity:10-70% [3]
  - Provider decision making has poor sensitivity
    - Sensitivity: 36% in high risk population [2]
  - Clinical decision guidelines based on symptoms such as ILI have poor sensitivity
    - Sensitivity: 31% in high risk population [2]
  - **New PCR-based rapid tests have high sensitivity and rapid turn around time…**

Xpert Flu

- Utilizes GeneXpert platform
  - Rapid rt-PCR multi-use platform
- Assay
  - **FDA Cleared** for clinical use
  - 75 minute turn-around time
  - Single cartridge use (no need to batch tests)
  - Hands on time < 2 minutes
  - Highly sensitive detection of influenza
    - Sensitivity range 90-100% [4]

Figure 1: GeneXpert cartridge (left) and 4-module instrument (right)

Season 1 Clinical Study Objectives

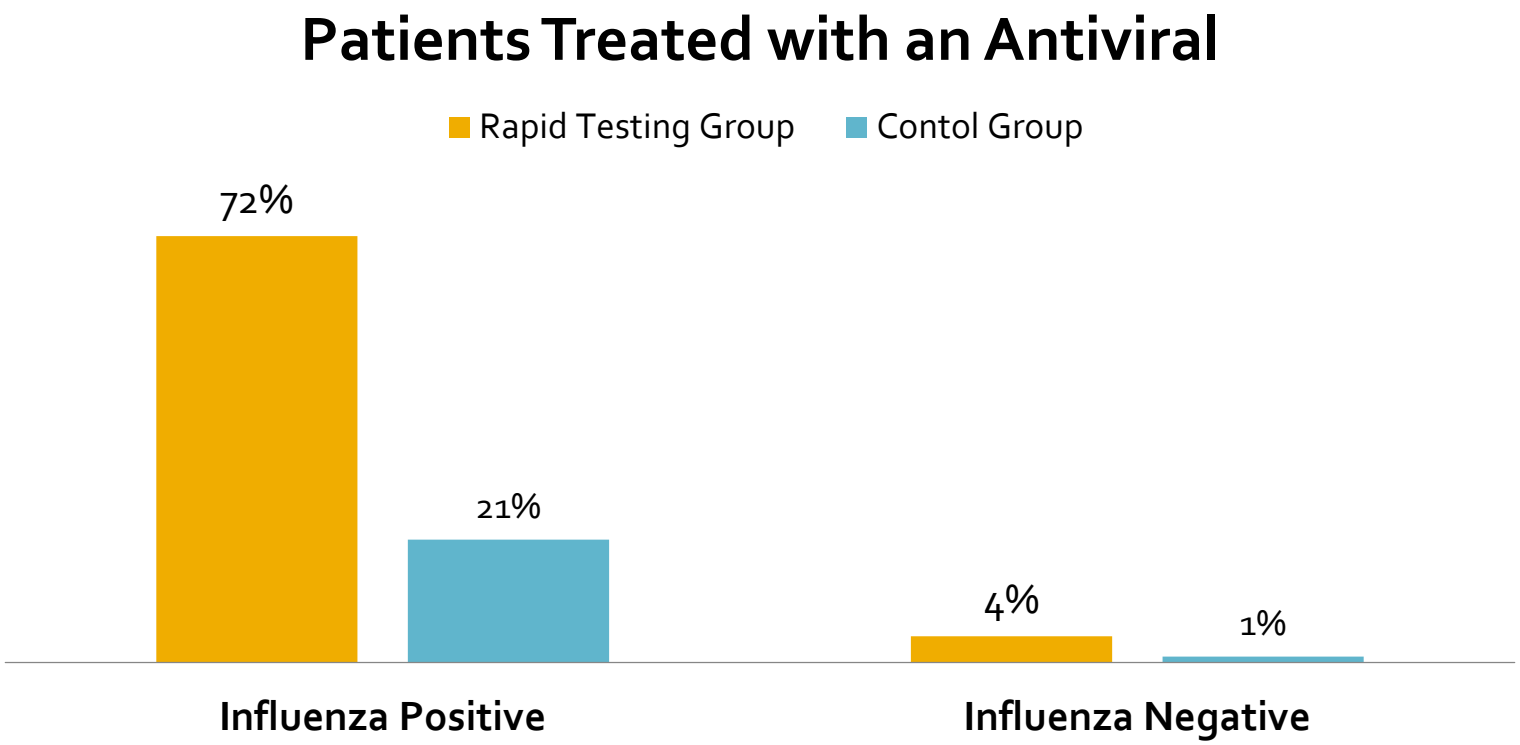


Objectives:

- **Evaluate impact of rapid influenza testing** on antiviral treatment
- **Evaluate the clinical performance** of Xpert Flu
- **Derive and validate** an adult clinical decision guideline (CDG) to guide influenza testing
- **Establish framework and conduct pilot feasibility** of cloud based surveillance *(test sites only)*

Season 1 Outcomes

Clinical Utility of integrating a highly sensitive rapid PCR assay



* Note: All subjects included in study were recommended to receive antiviral treatment according to CDC guidelines

Season 1 Outcomes

Clinical Decision Guideline (CDG) to guide influenza testing

- Anyone with 3 points or greater should be tested for influenza:
  - Cough (2 points)
  - Subjective fever (1 point)
  - Headache (1 point)
  - Triage temperature of 100.4 or greater (1 point)
- Out-of-sample validation:
  - Sensitivity 92% Specificity 28%

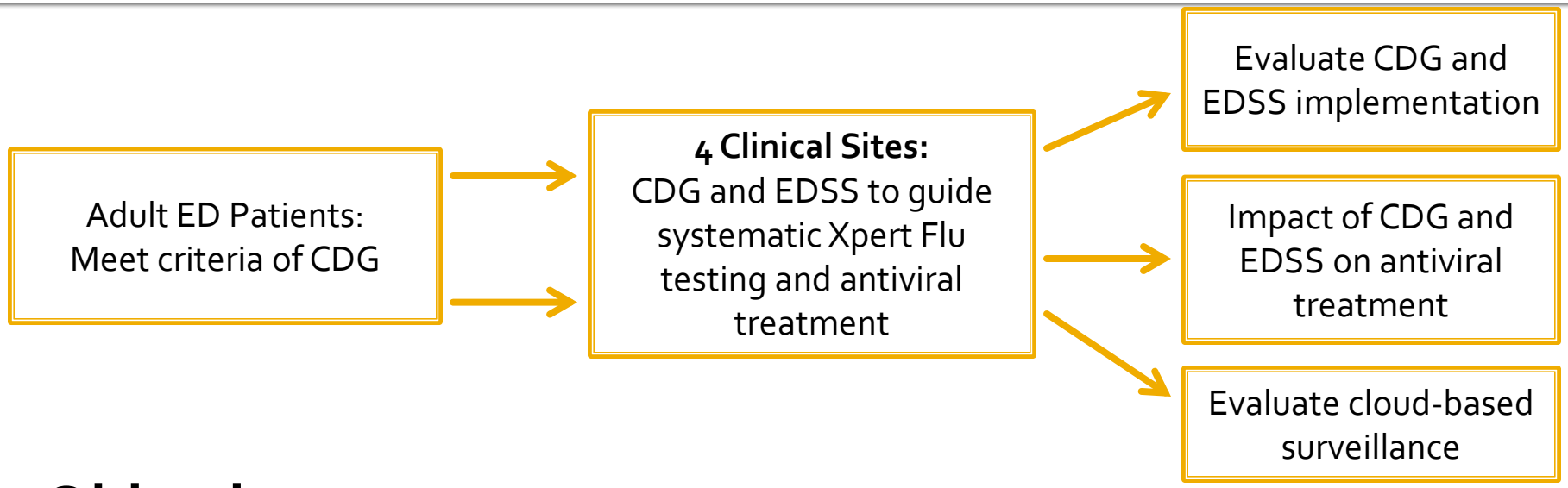
Influenza Like Illness (Fever plus cough or sore throat):
Sensitivity 31% (18-47%) Specificity 88% (83-92%)

Season 1 Outcomes

Performance of Xpert Flu Assay

- Overall
  - Sensitivity: 91.1% (82.6-96.4)
  - Specificity: 99.6 (98.9-99.9)
- Influenza A
  - Sensitivity: 90.5% (81.5-96.1)
  - Specificity: 99.7 (99.1-99.9)
- Influenza B
  - Sensitivity: 100% (47.8-100)
  - Specificity: 99.9 (99.5-100)

Season 2 Clinical Study



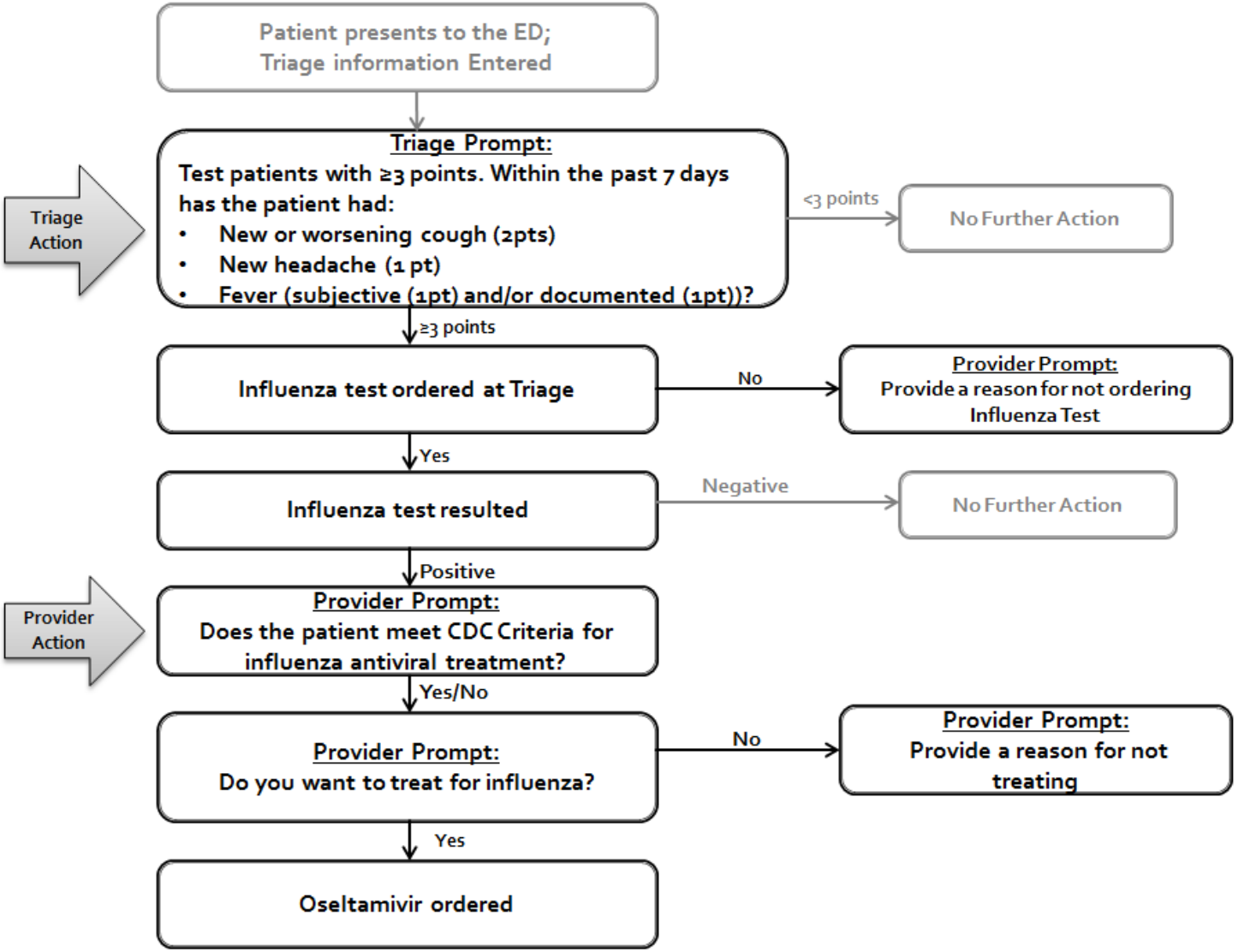
Objectives:

- Integrate derived adult CDG into routine ED practice with an electronic decision support system (EDSS)
- Demonstrate **impact of the CDG with EDSS on antiviral treatment**
- Demonstrate **feasibility and validity** of the cloud-based surveillance system across multiple ED testing sites

Study Implementation - Triage

- Study Period: October 1, 2014 – April 30, 2015
- Triage nurses assess patient symptoms included in the clinical decision guideline on all patients presenting to triage
- If patient has a symptom score of 3 points or greater, a prompt appears to order an influenza test
  - Turn around time 2 hours
- If test is positive, providers receive additional prompts:
  - Determine patient's risk level
  - Antiviral treatment

CDG and Electronic Decision Support System



What to expect - Triage

- CDG Prompts at Triage:
  - Nurse asks: "Within the past 7 days, has this patient experienced.."
    - New or worsening cough (2 points)
    - New headache (1 point)
    - New subjective fever (1 point)
  - Documented triage temperature ≥38° C (1 point)
- The EMR will calculate the patient's symptom score
  - If symptom score ≥3: Prompt appears - Patient is indicated for influenza testing, order test?
    - NO – indicate why not
      - Patient refused
      - Patient diagnosed with influenza within previous 48 hours
      - Other, (provide reason)
    - YES
  - If symptom score <3, no further action

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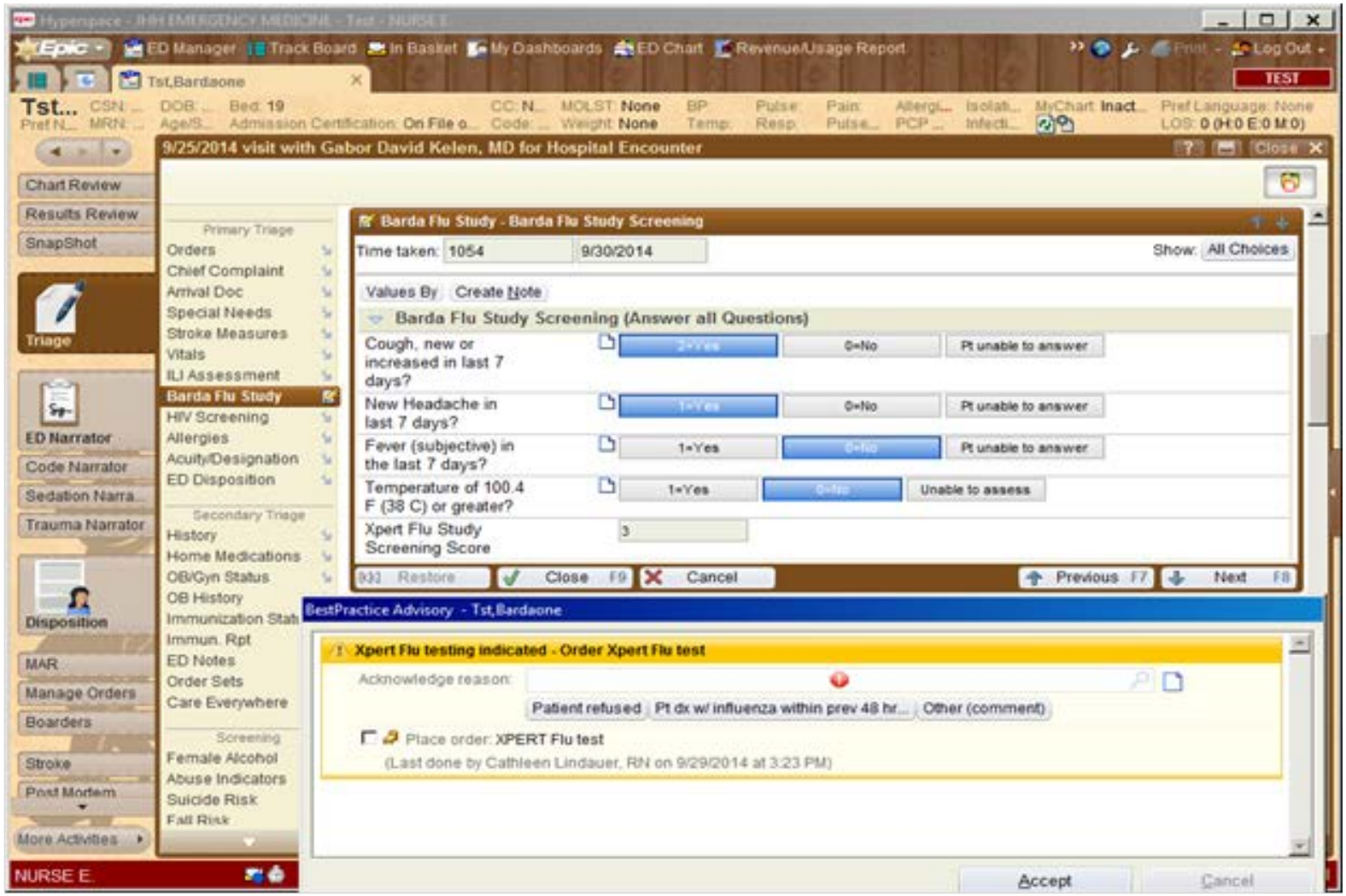
Epic
ED Manager
Track Board
In Basket
My Dashboards
ED Chart
Revenue/Usage Report
Log Out
TEST
Tst,Bardaone
9/25/2014 visit with Gabor David Kelen, MD for Hospital Encounter
Close
Chart Review
Results Review
SnapShot
Triage
ED Narrator
Code Narrator
Sedation Narra...
Trauma Narrator
Disposition
MAR
Manage Orders
Boarders
Stroke
Post Mortem
More Activities
NURSE E
Primary Triage
Orders
Chief Complaint
Arrival Doc
Special Needs
Stroke Measures
Vitals
ILI Assessment
Barda Flu Study
HIV Screening
Allergies
Acuity/Designation
ED Disposition
Secondary Triage
History
Home Medications
OB/Gyn Status
OB History
Immunization Stat
Immun. Rpt
ED Notes
Order Sets
Care Everywhere
Screening
Female Alcohol
Abuse Indicators
Suicide Risk
Fall Risk
Barda Flu Study - Barda Flu Study Screening
Time taken: 1054
9/30/2014
Show: All Choices
Values By
Create Note
Barda Flu Study Screening (Answer all Questions)
Cough, new or increased in last 7 days?
New Headache in last 7 days?
Fever (subjective) in the last 7 days?
Temperature of 100.4 F (38 C) or greater?
Xpert Flu Study Screening Score
1=Yes
0=No
Pt unable to answer
Unable to assess
Restore
Close F9
Cancel
Previous F7
Next F8
BestPractice Advisory - Tst,Bardaone
Xpert Flu testing indicated - Order Xpert Flu test
Acknowledge reason:
Patient refused
Pt dx w/ influenza within prev 48 hr...
Other (comment)
Place order: XPERT Flu test
(Last done by Cathleen Lindauer, RN on 9/29/2014 at 3:23 PM)
Accept
Cancel

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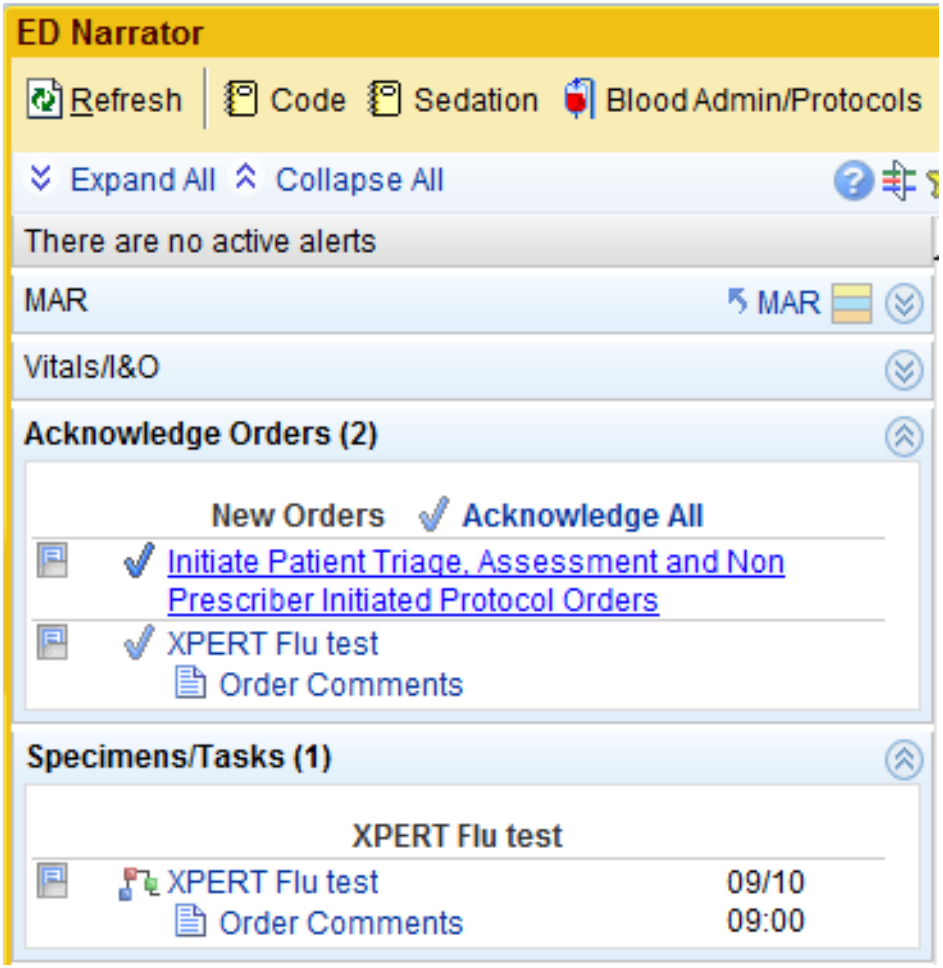
ED Narrator
Refresh
Code
Sedation
Blood Admin/Protocols
Expand All
Collapse All
There are no active alerts
MAR
MAR
Vitals/I&O
Acknowledge Orders (2)
New Orders
Acknowledge All
Initiate Patient Triage, Assessment and Non Prescriber Initiated Protocol Orders
XPERT Flu test
Order Comments
Specimens/Tasks (1)
XPERT Flu test
XPERT Flu test
09/10 09:00
Order Comments

Analysis

Retrospective chart review to determine clinical impact of rapid testing with the CDG and EDSS

- Antiviral and antibiotic treatment in:
  - Those recommended to receive antiviral treatment
    - **High Risk** patients who test **Influenza Positive**
  - Those NOT recommended to receive antiviral treatment
    - High Risk patients who test Influenza Negative
    - Low Risk patients who test Influenza Positive
    - Low Risk patients who test Influenza Negative

Questions?

Thank you!

Citations

1. **Fiore AE, Fry A, Shay D, Gubareva L, Bresee JS, Uyeki T.** 2011. Centers for Disease Control and Prevention (CDC). Antiviral agents for the treatment and chemoprophylaxis of influenza --- recommendations of the Advisory Committee on Immunization ractices (ACIP). MMWR Surveill Summ **60:**1-24.

2. **Dugas AF, Valsamakis A, Gaydos CA, Rothman RE.** 2014. Diagnosis and Management of Influenza in the Emergency Department. Society for Academic Emergency Medicine Annual Meeting, Dallas, Tx.

3. **Centers for Disease Control and Prevention (CDC).** 2009. Evaluation of rapid influenza diagnostic tests for detection of novel influenza A (H1N1) Virus - United States, 2009. MMWR Morb Mortal Wkly Rep **58:**826-829.

4. **Sambol AR, Iwena PC, Pieretti M, Basuc S, Levic MH, Gilonsked KD, Mosesd KD, Marolae JL, Ramamoorthye P.** 2010. Validation of the Cepheid Xpert Flu A Real Time RT-PCR detection panel for Emergency Use Authorization. Journal of Clinical Virology **48:**234-238.