Diagnostic delays in infectious diseases

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Why are diagnostic delays important?

Diagnostic delays are one of the most important forms of diagnostic error.

Delays in diagnosis may lead to delays in treatment and worse outcomes.

Delays generate excess healthcare costs and unnecessary treatments.
Diagnostic delays are important for ID

Delays in diagnosis can contribute to the inappropriate use of antimicrobials

Delays resulting in inappropriate treatment can influence future treatment options

Some infectious diseases are contagious; delays will generate additional cases
Diagnostic delays for IDs are common

Classic signs and symptoms of an infection are not always present

Fevers (and other symptoms) may also be a symptom of non-infectious diseases

Test results may not be available until days after the test is performed
Temperatures during a febrile episode vary throughout the day

The probability of detecting a fever during a febrile episode varies substantially.
How delays are studied:

Most approaches are resource intensive or limited in scope.

Most prior work has been confined to single academic centers.

Understanding diagnostic delays requires considering sequential visits across a range of healthcare settings.
Our framework for investigating delays

Prior to the correct diagnosis, missed opportunities begin to occur but not all prior visits represent missed opportunities.

Assumptions:

• The likelihood of a visit being a missed opportunity should increase as we get closer to the actual diagnosis date (the index date).

• At these prior visits, patients have symptoms consistent with the disease or symptomatically similar diseases (SSDs).
Computing # of missed opportunities

Number of missed opportunities each day – difference between the observed and expected trends

Total number of missed opportunities – area between the curves (blue region)

Problem: Cannot tell which visits represent a missed opportunity (which fall in red vs blue area)

Our framework for investigating delays

We use a simulation approach that uses iterative resampling to estimate the probability that

• an individual patient experienced a diagnostic delay
• a specific visit represented a missed opportunity
• a patient’s delay lasted a specific duration of time

We can also identify potential risk factors and derive the types of symptoms most or least common among delayed patients

Miller AC, Cavanaugh JE, Arakkal AT, Koeneman SH, Polgreen PM. A comprehensive framework to estimate the frequency, duration, and risk factors for diagnostic delays using bootstrapping-based simulation methods. BMC Med Inform Decis Mak. 2023 Apr 14;23(1):68.
Tuberculosis

SSD visits start to increase around 120 days prior to DX

Average delay: 32 days

Average number of missed opportunities: 4

24% of patients had more than 5 possible missed opportunities

Individual risk factors: asthma, COPD, female sex, age>65 years

Situational risk factors: Emergency department visits, influenza season, weekend visits, rural area

HSV Encephalitis

SSD visits started to increase 28 days prior to DX

Average delay: 5 days

Average number of missed opportunities: 2.23

11.3% of patients had a delay lasting 14 or more days

**Individual risk factors**: age < 65 years, a history of sinusitis or schizophrenia

**Situational risk factors**: Emergency department visits

Miller AC, Koeneman SH, Arakkal AT, Cavanaugh JE, Polgreen PM. Incidence, Duration, and Risk Factors Associated With Missed Opportunities to Diagnose Herpes Simplex Encephalitis: A Population-Based Longitudinal Study. Open Forum Infect Dis. 2021 Jul 26;8(9):ofab400.
Pertussis

SSD visits start to increase 50 days before DX

Average delay: 12 days

Average number of missed opportunities: 2

18% of pertussis patients had a delay of at least 20 days.

**Individual risk factors**: fluoroquinolone prescription, phantom prescribing, teenagers and adults

**Situational risk factors**: emergency department visits

Public health implications of diagnostic delays for pertussis

The odds of secondary household transmission with a diagnostic delay was 5.23 (95%CI: 4.54, 6.02) times the odds of transmission when the index case was not delayed

We found that longer delays were associated with greater risk for secondary transmission (p-value <0.0001)

A one-day increase in duration of delay was associated with ~9% increase in the odds of a secondary transmission

Arakkal AT, Cavanaugh JE, Polgreen PM, Miller AC. The increase in household transmission of pertussis associated with diagnostic delays (under review).
Next Steps…

Continue to investigate different infections

Validate findings using other data sources

Identify themes for risk factors: inappropriate antibiotic use, cognitive bias, visit locations, older populations, vulnerable populations
Develop a **standard approach for reporting delays** (e.g., window period, average delay, average number of misses, % with multiple misses, risk factors)

- identify the diseases, settings, and populations associated with the greatest risk of diagnostic delays

- target diagnostic testing strategies; design interventions to reduce delays; and measure the success of interventions

These metrics should account for the natural history of each disease
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