Informatics as a tool for antimicrobial stewardship

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The problem : When to start / When to stop

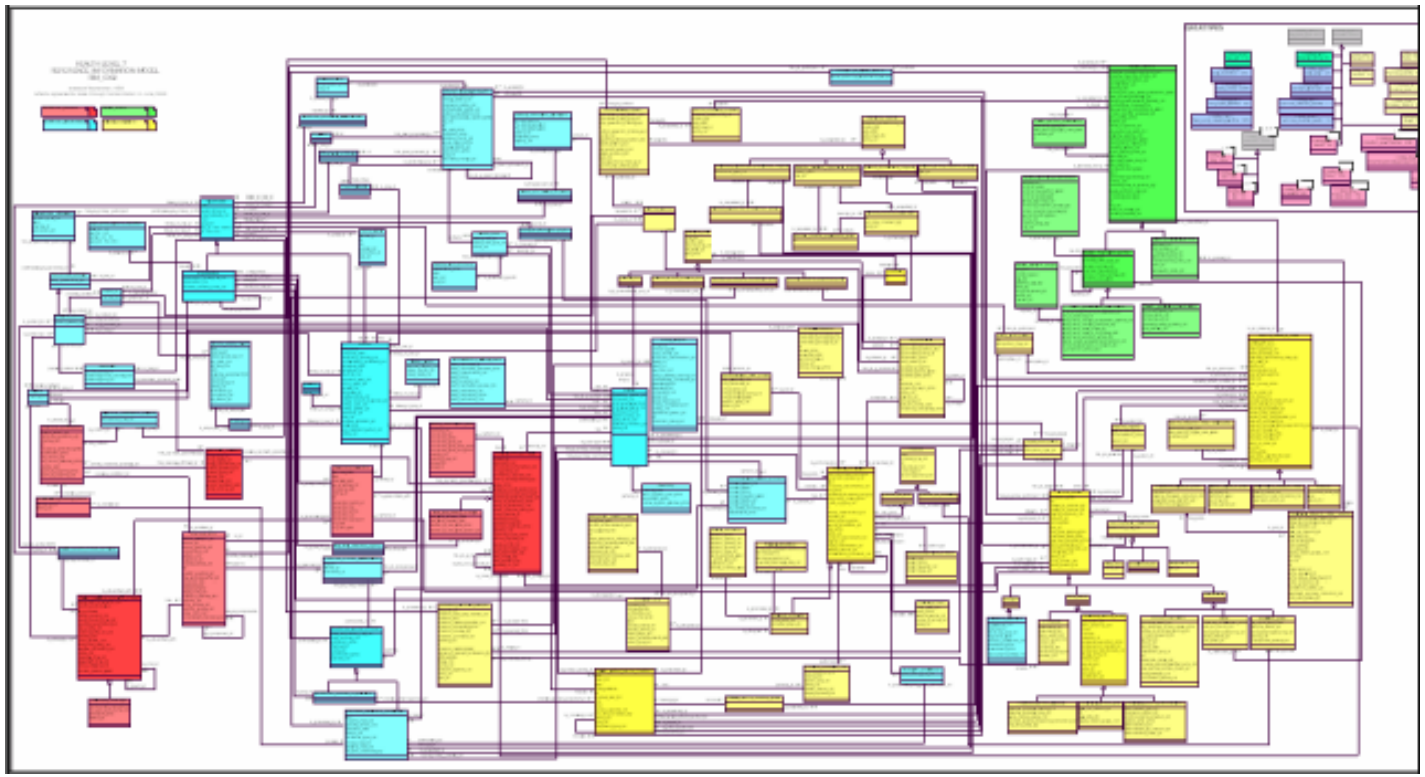
- Diagnosis are difficult & Mistakes are costly !
- Fever : Bacterial vs. viral ? Cancer ? Embolism ? . . .
- The cure of an infection is very difficult to assess :
  - A patient may be cure if no relapse occurs in absence of antibiotics after a certain duration (may be years for bone infections !)
- In other words, we don't know much . . .
- $\Rightarrow$ Need of surrogates for diagnosis of infection and cure :
  - Computerized decision support system are potentially helpful surrogates

What is it

- A program that generates diagnostic and therapeutic recommendations from patient specific information that was input about the suspected diagnosis, such as the presence or absence of specific signs and symptoms
- "Medical artificial intelligence"
- A system that links all the information available in various databases (clinical files, laboratory results, pharmacist...)

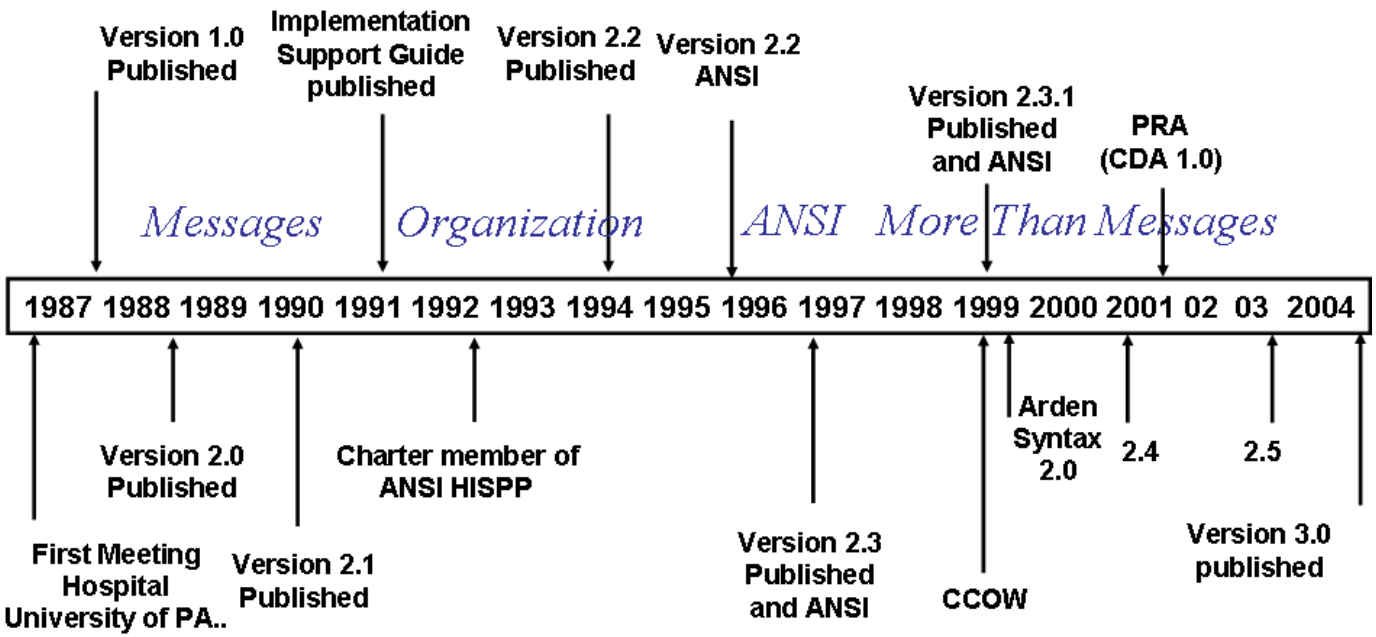
Problem

- Many different systems operating in parallel in hospital
- Not standardized
- Not communicating



Toward a common language for interoperability : HL7

History of HL7



Designed by David Marotta

Sept. 10 and 12, 2006

13

Not that recent

- Electronically identified interventions[1]
- LDS Hospital in Salt Lake City, Utah
- 545 patients in a 12-beds ICU over 1 year
- Outcomes compared to 2 previous years
- $\searrow$ in inappropriate ATB doses, ATB related drug events and total cost of care ...

1. Evans RS. NEJM 1998

Effective even if basic

IHC ANTIBIOTIC ASSISTANT & ORDER PROGRAM

00000000 Doe, John Q. E615 77yr M Dx:PANCREATITIS
Max 24hr WBC=26.3 ↑ (21.1) **Admit:06/21/96.17.50** Max 24hr Temp=38.3 ↑ (37.8)
RENAL FUNCTION: Impaired, CrCl= 28, Max 24hr Cr=2.0 ↓ (2.2) IBW: 77kg
Patient's Diff shows a left shift, Max 24hr Bands = 20 ↑ (8)
ANTIBIOTIC ALLERGIES: Ofloxacin
CURRENT ANTIBIOTICS:
1. 07/14/96.17:23 AMPHOTERICIN B, VIAL 45 Q 24hrs
2. 07/18/96.12:19 VANCOMYCIN (VANCOCIN), VIAL 1000 Q 72hrs
Total amphotericin given = 181mg

IDENTIFIED PATHOGENS	SITE	COLLECTED
Enterococcus	T-Tube	07/17/96.10:57
Staphylococcus aureus	Blood	07/17/96.10:28
Candida albicans	Abdomen	07/14/96.06:23

ABX SUGGESTION	DOSAGE	ROUTE	INTERVAL	
Vancomycin	*1000mg	IV	*q72h	(infuse over 1hr)
Amphotericin B	45mg	IV	q24h	(infuse over 2-4hr)

Suggested Antibiotic Duration: 28 days
*** Adjusted based on patient's renal function**
<1>Micro, <2>OrganismSuscept, <3>Drug Info, <4>ExplainLogic, <5>Empiric Abx
<6>Abx Hx, <7>ID Rnds, <8>Lab/Abx Levels, <9>Xray, <+ or F12>Change Patient
<Esc>EXIT, <F1>Help, <0>User Input, <.>OutpatientModels
ORDERS: <*>Suggested Abx, <Enter>Abx List, </>D/C Abx, <->Modify Abx

- 14 minutes vs. 3.5 seconds [2]
- Decreased cost [3]
- Appropriate antibiotic choice [4]
- Fewer antibiotic doses [5]
- Shorter LOS [6]
- Decreased adverse events [7]
- Decreased mortality [8]

2. Evans RS. NEJM 1998
3. Evans RS. *NEJM* 1998, Barenfanger J *J Clin Microbiol* 2001, Jozefiak ET *Am J Health Syst Pharm* 1995, McGregor JC *J Am Med Inform Assoc* 2006, Paul M *JAC* 2006, Pestotnik SL *Ann Intern Med* 1996, Schentag JJ *Diagn Microbiol Infec Dis* 1993
4. Paul M *JAC* 2006, Samore MH JAMA 2005, Thursky KA Int J Qual Health care 2006
5. Evans RS. NEJM 1998, Pestotnik SL *Ann Intern Med* 1996
6. Evans RS. NEJM 1998, Paul M *JAC* 2006
7. Evans RS. NEJM 1998, Pestotnik SL *Ann Intern Med* 1996
8. Pestotnik SL *Ann Intern Med* 1996

Classical commercial systems with AMS options

Product Name	Company (also known as)	City, State	Infection Prevention Capabilities
360 Care Insights	Truven	Ann Arbor, MI	Yes
ABX Alert	ICNet	Warrensville, IN	Yes
Antibiotic Assistant	Hospira (Theradoc)	Salt Lake City, UT	Yes
Dynamic Monitoring Suite	Vigilanz	Minneapolis, MN	Yes
Epiquest Live	Epiquest Live	Boca Raton,FL	Yes
Medici	Asolva Inc	Pasadena, CA	Yes
Patient Event Advisor	Care Fusion (Medmined)	Birmingham, AL	Yes
QC Pathfinder	Vecna	Cambridge, MA	Yes
Safety Advisor	Premier	Charlotte, NC	Yes
Sentri 7	Wolters Kluwer (Pharmacy One Source)	Bellevue, WA	Yes

And very sophisticated ones

Common alerts for infectious diseases

- Bug-Drug mismatch
- Positive culture but no antibiotic
- Antibiotic but no positive culture
- IV to PO
- Duration of therapy alerts
- Duplicate antibiotic therapy
- Dose adjustments to renal/liver function
- Target specific antibiotics (carbapenem, costly ATB ...)
- Target organism (MDRO)

Practical examples

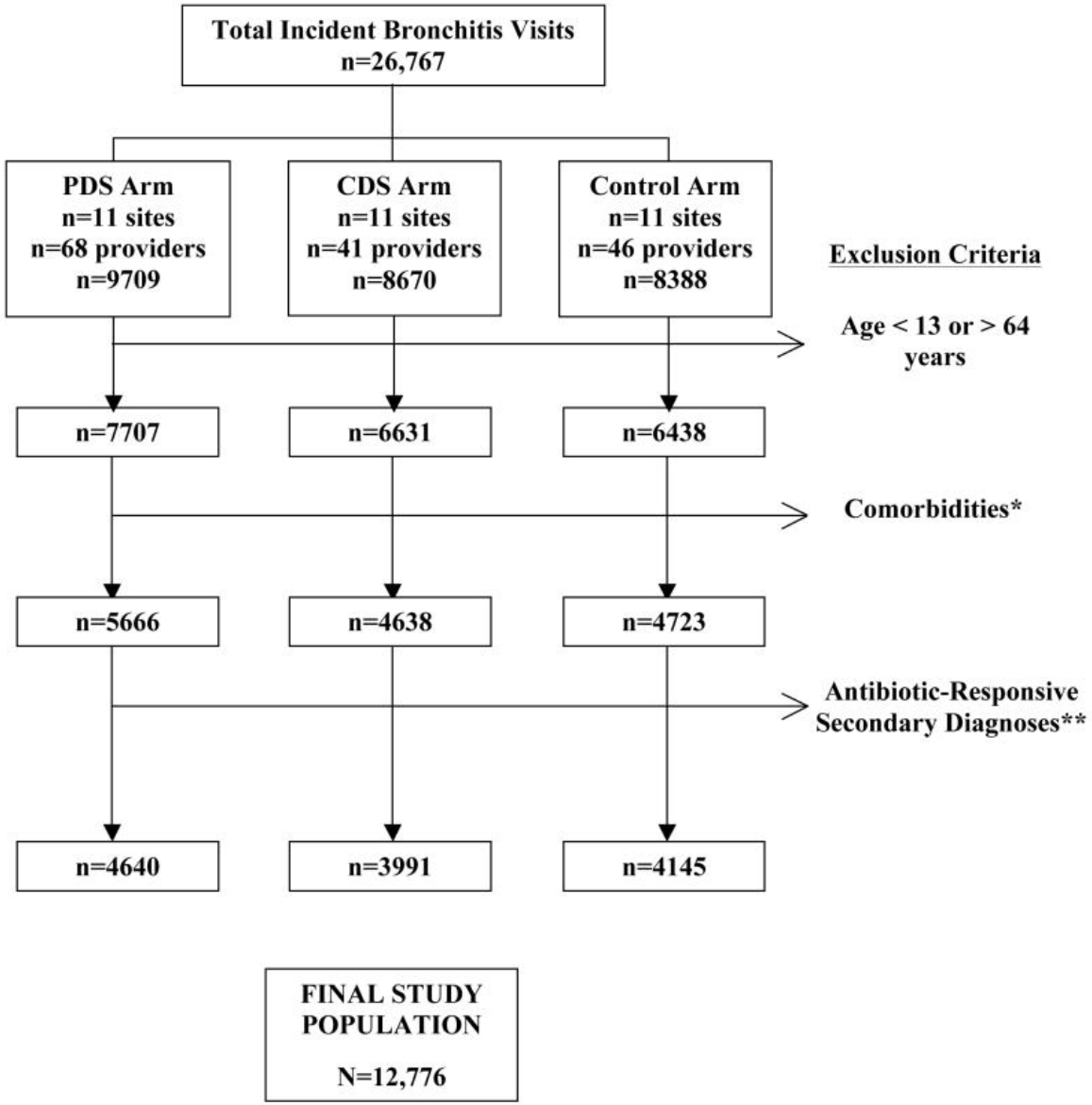
- Patients under Vancomycin >72h without positive culture
- Patients receiving Piperacillin/Tazobactam and Metronidazole
- Patients eligible for conversion from IV to PO linezolid
- Levofloxacin at full dose with renal insufficiency
- Positive blood culture for C. albicans and no antifungal treatment

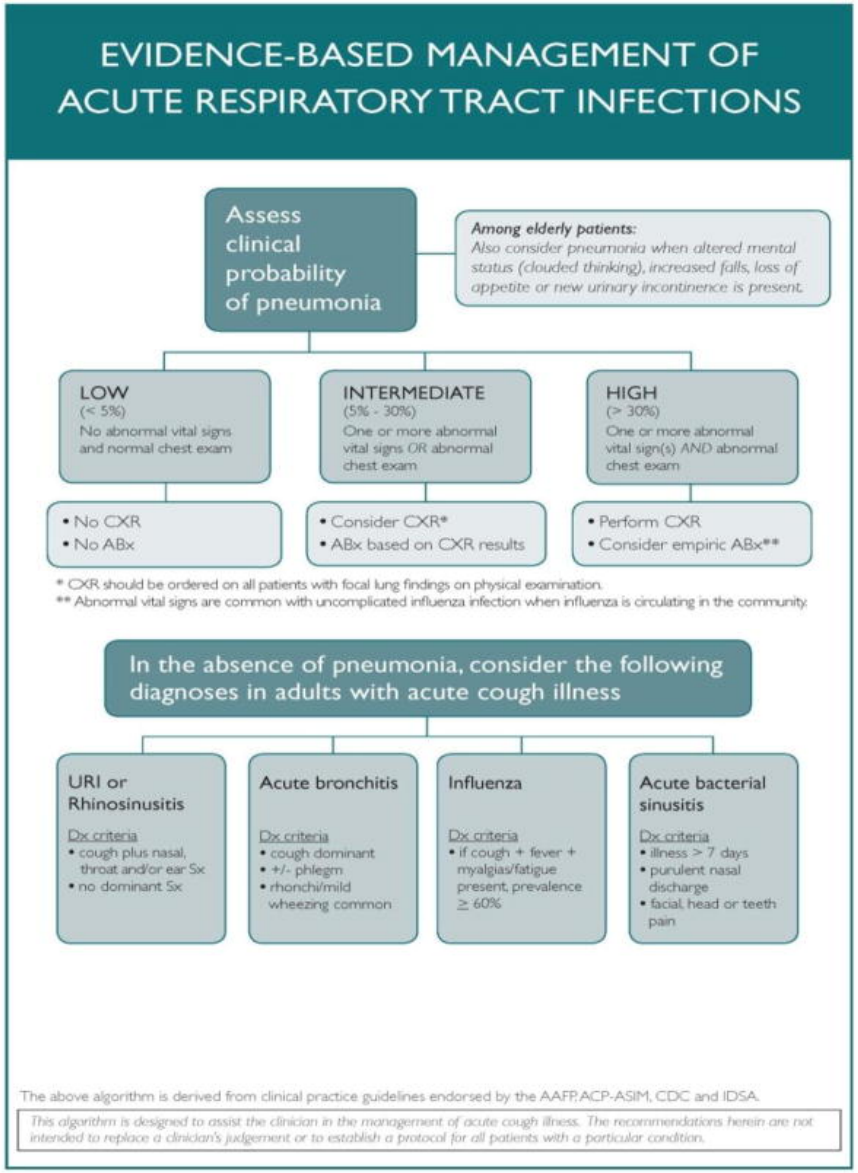
But it is also beneficial for non ID-related problems (anticoagulation...)

Outpatient example

- Three arm cluster randomized trial[9]
- 33 primary care practices in Pennsylvania, USA
- Acute uncomplicated bronchitis
- Control vs. Print Based vs. Decision support

9. Gonzales R JAMA Int Med 2013


Total Incident Bronchitis Visits
n=26,767
PDS Arm
n=11 sites
n=68 providers
n=9709
CDS Arm
n=11 sites
n=41 providers
n=8670
Control Arm
n=11 sites
n=46 providers
n=8388
Exclusion Criteria
Age < 13 or > 64 years
n=7707
n=6631
n=6438
Comorbidities*
n=5666
n=4638
n=4723
Antibiotic-Responsive Secondary Diagnoses**
n=4640
n=3991
n=4145
FINAL STUDY POPULATION
N=12,776



EVIDENCE-BASED MANAGEMENT OF ACUTE RESPIRATORY TRACT INFECTIONS

Assess clinical probability of pneumonia

Among elderly patients: *Also consider pneumonia when altered mental status (clouded thinking), increased falls, loss of appetite or new urinary incontinence is present.*

LOW (< 5%)
No abnormal vital signs and normal chest exam
- No CXR
- No ABx

INTERMEDIATE (5% - 30%)
One or more abnormal vital signs *OR* abnormal chest exam
- Consider CXR*
- ABx based on CXR results

HIGH (> 30%)
One or more abnormal vital sign(s) *AND* abnormal chest exam
- Perform CXR
- Consider empiric ABx**

* CXR should be ordered on all patients with focal lung findings on physical examination.
** Abnormal vital signs are common with uncomplicated influenza infection when influenza is circulating in the community.

In the absence of pneumonia, consider the following diagnoses in adults with acute cough illness

URI or Rhinosinusitis
Dx criteria
- cough plus nasal, throat and/or ear Sx
- no dominant Sx

Acute bronchitis
Dx criteria
- cough dominant
- +/- phlegm
- rhonchi/mild wheezing common

Influenza
Dx criteria
- if cough + fever + myalgias/fatigue present, prevalence ≥ 60%

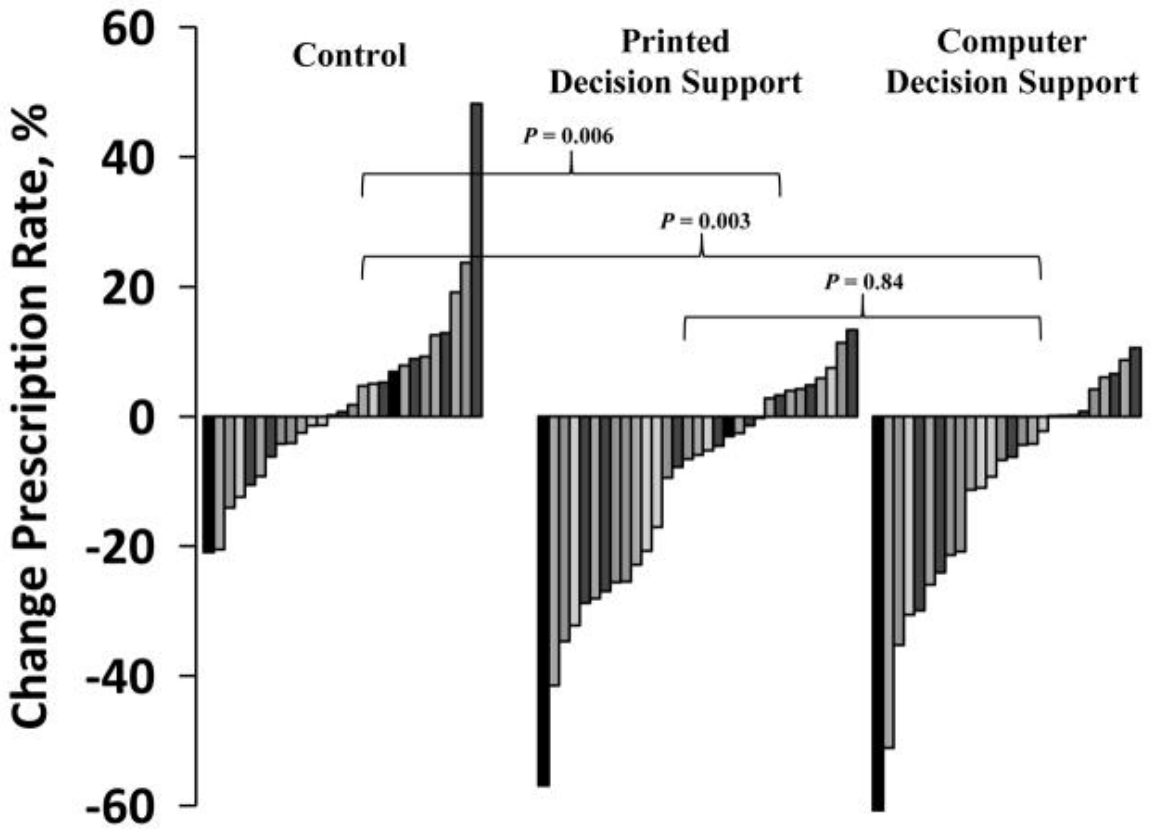
Acute bacterial sinusitis
Dx criteria
- illness > 7 days
- purulent nasal discharge
- facial, head or teeth pain

The above algorithm is derived from clinical practice guidelines endorsed by the AAFP, ACP-ASIM, CDC and IDSA.

This algorithm is designed to assist the clinician in the management of acute cough illness. The recommendations herein are not intended to replace a clinician's judgement or to establish a protocol for all patients with a particular condition.

Results on antibiotic prescribing

- Control arm : $\nearrow$ (72.5%$\rightarrow$74.3%)
- Print-based arm : $\searrow$ (80%$\rightarrow$68.3%)
- Computerized decision support arm : $\searrow\searrow$ (74.0%$\rightarrow$60.7%)


Control
Printed Decision Support
Computer Decision Support
P = 0.006
P = 0.003
P = 0.84
Change Prescription Rate, %
60
40
20
0
-20
-40
-60

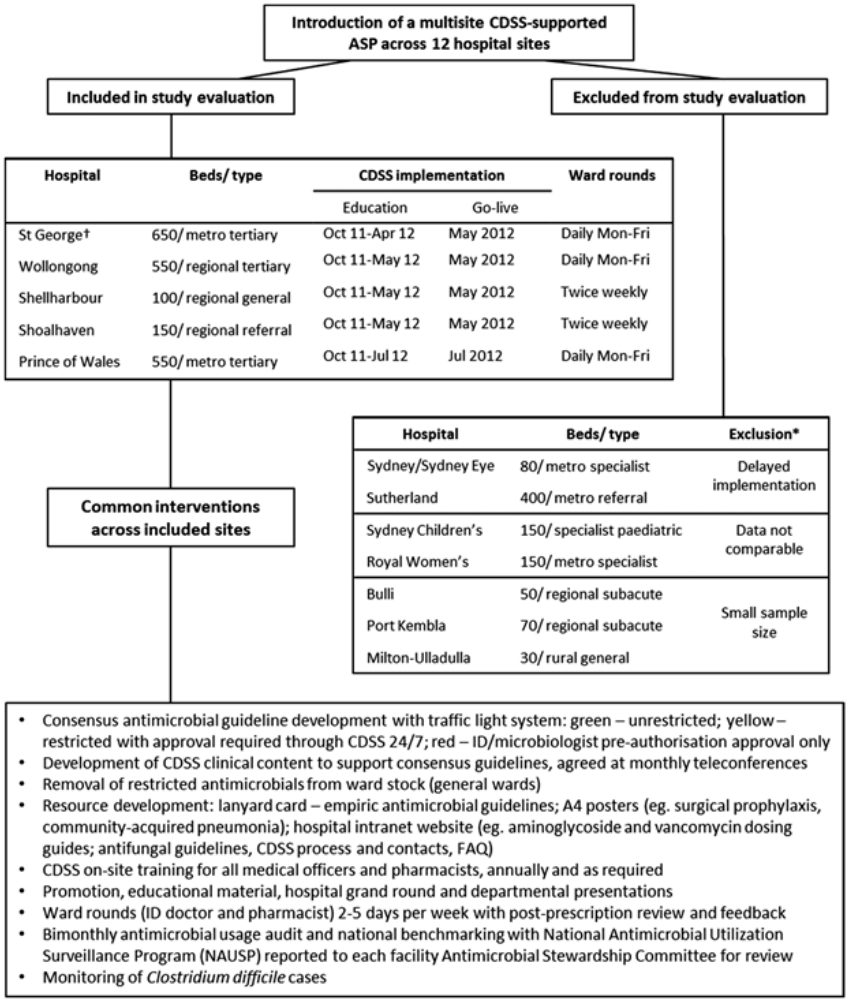
Additional benefits with CDSS

CDSS similarly efficient to printed-based support, but

- Reports can be edited easily
- A general tool that can be easily adapted for many situation, according to new guidelines, new intervention ...
- Adherence can be measured (useful to justify your AMS Team)

Collaboration through CDSS

- Multisite ASP implementation supported by central CDSS
- Five Australian hospitals, 2010-2014
- Bond S. et al, JAC 2017



Hospital	Beds/ type	CDSS implementation		Ward rounds
		Education	Go-live	
St George†	650/ metro tertiary	Oct 11-Apr 12	May 2012	Daily Mon-Fri
Wollongong	550/ regional tertiary	Oct 11-May 12	May 2012	Daily Mon-Fri
Shellharbour	100/ regional general	Oct 11-May 12	May 2012	Twice weekly
Shoalhaven	150/ regional referral	Oct 11-May 12	May 2012	Twice weekly
Prince of Wales	550/ metro tertiary	Oct 11-Jul 12	Jul 2012	Daily Mon-Fri

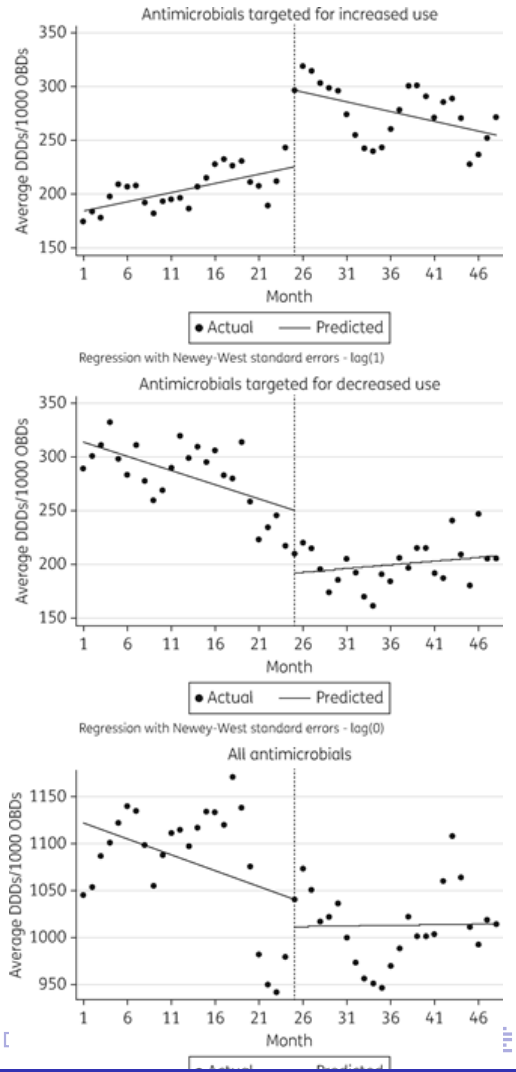
Hospital	Beds/ type	Exclusion*
Sydney/Sydney Eye	80/ metro specialist	Delayed implementation
Sutherland	400/ metro referral	
Sydney Children's	150/ specialist paediatric	Data not comparable
Royal Women's	150/ metro specialist	
Bulli	50/ regional subacute	Small sample size
Port Kembla	70/ regional subacute	
Milton-Ulladulla	30/ rural general	

Interrupted Time Series

- Antibiotics targeted to decrease ↘ (+32%, p<0.01)
- Antibiotics targeted to increase ↗ (-23%, p<0.01)
- No increase in length of stay or mortality
- But influence decreased over time

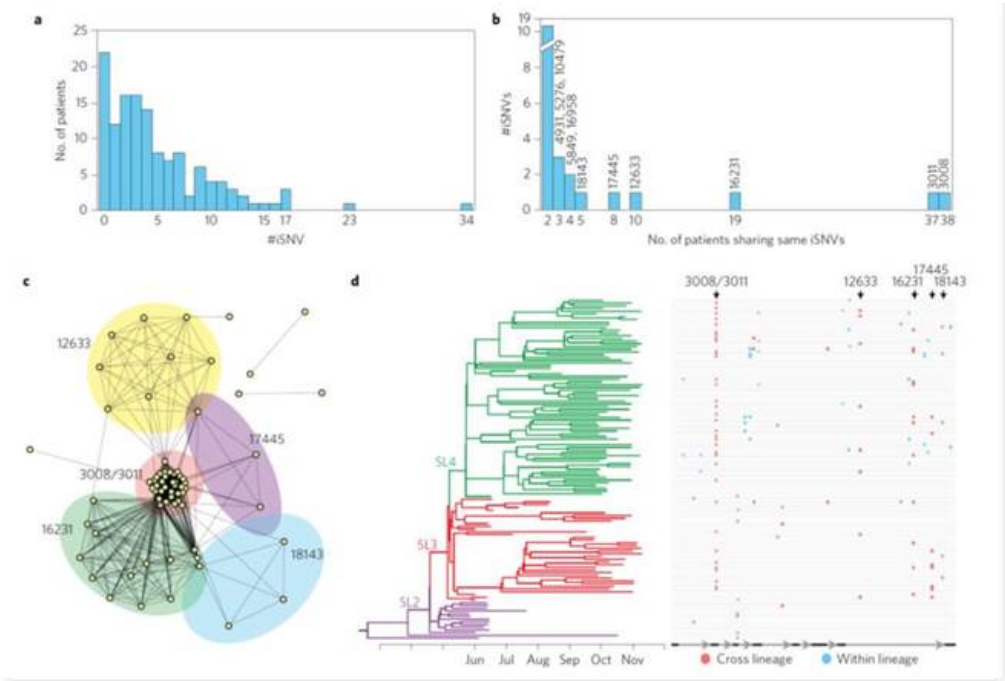
...

1. ⇒ An efficient tool
2. But just a tool
3. which won't replace the AMS team



A source for Big Data

- Data mining on the gathered information
- New patterns to be discovered
- Which will results in new algorithms to feed the AI

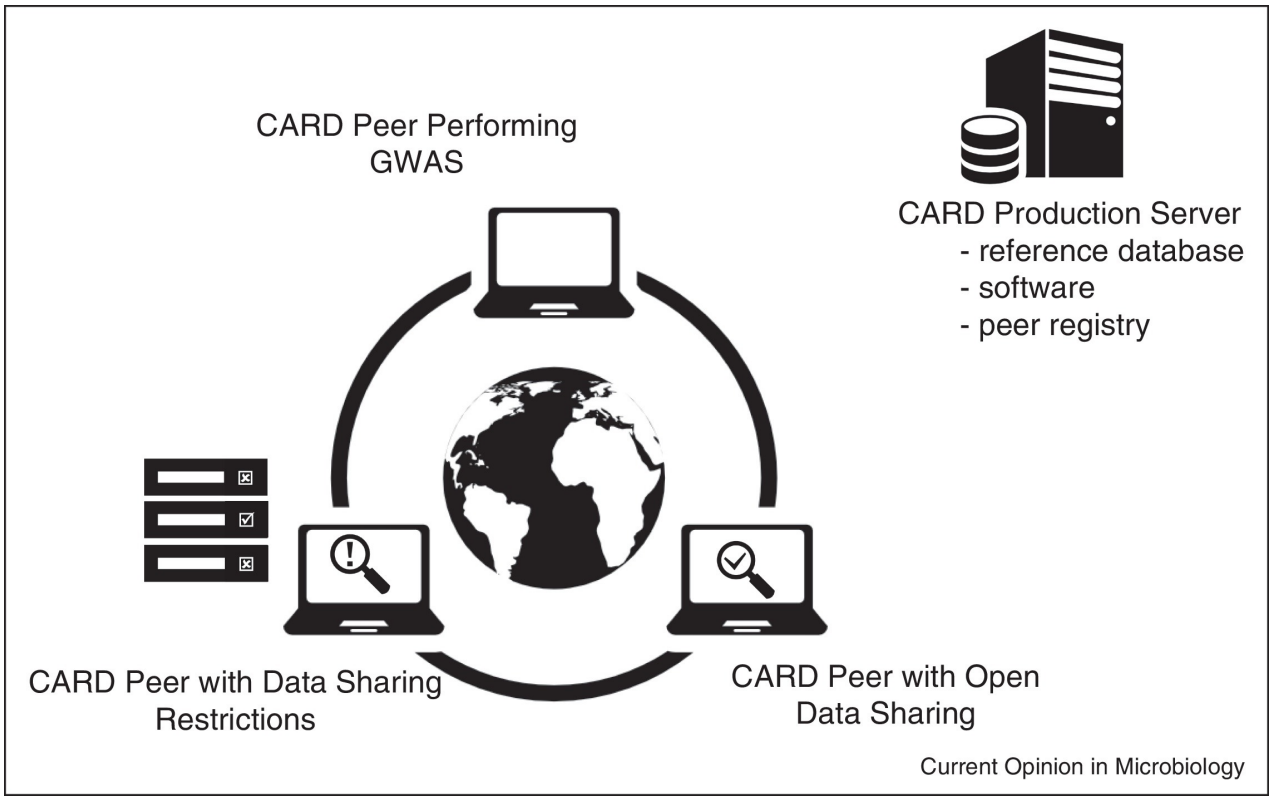


If you want to implement a CDSS

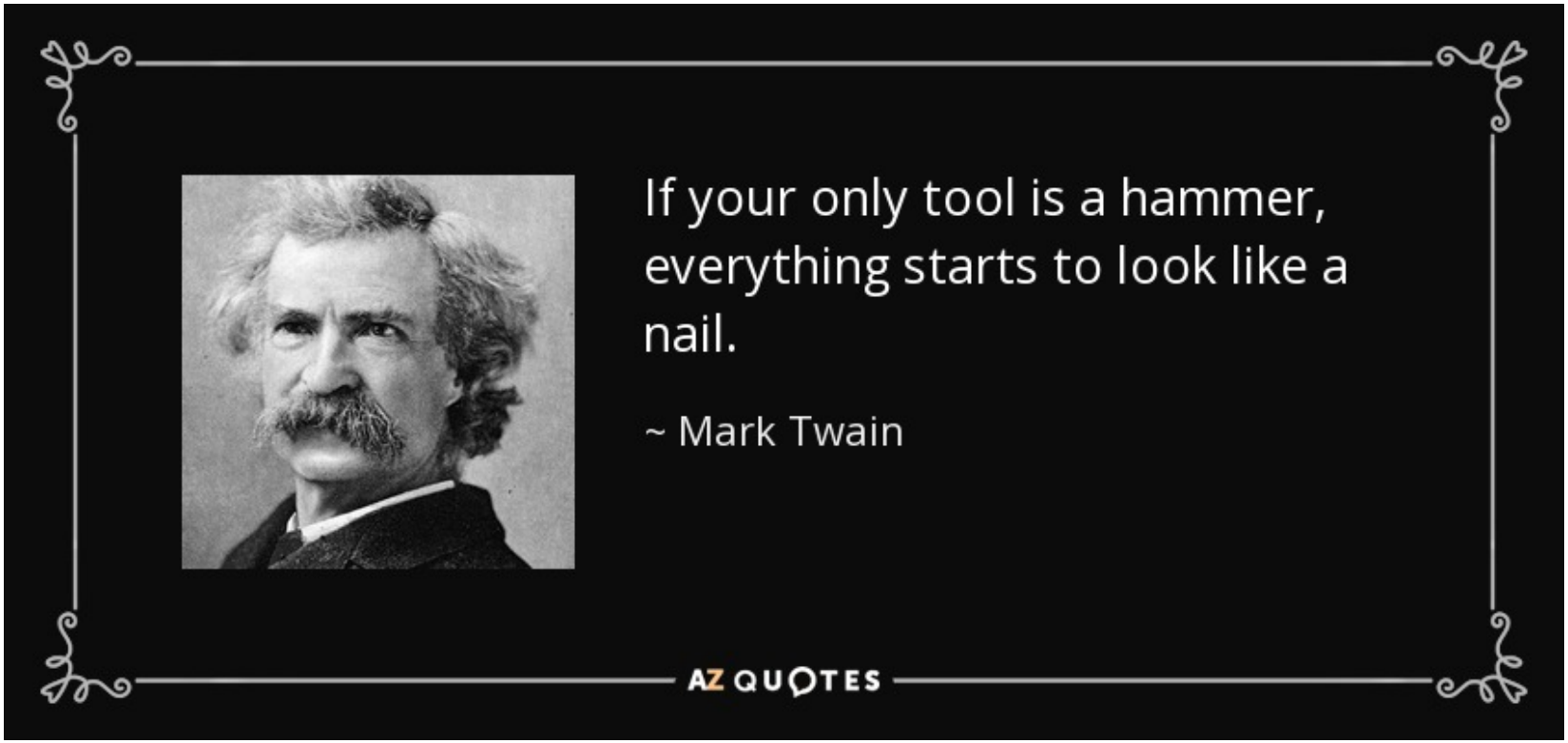
1. Determine your objectives (and take your time)
   - information needs
   - gap within your current digital tools
   - workflow interruptions requiring manual intervention
   - ...
2. Choose a modular system (the tool should be adapted to your needs, you shouldn't need to adapt)
3. Implement a system with option for Big Data tools (e.g. CARD)

Bioinformatics for AMS

- *Comprehensive Antibiotic Resistance Database* (CARD ; arpcard.mcmaster.ca)
- From phenotype of resistance to genotype → data collection
- From genotype to prediicting phenotype → an AMS tool



Tools


If your only tool is a hammer, everything starts to look like a nail.
~ Mark Twain
AZ QUOTES

Thank you for your attention

Whatever you do, your kids will be geek