Invasive fungal infections: What to do if there's a fungus among us

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This speaker has no conflicts to disclose

Objectives (Pharmacists)

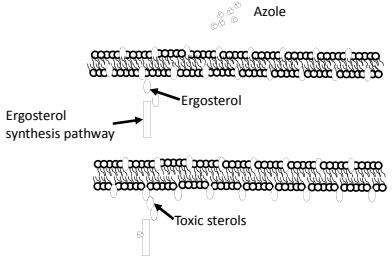
- List three important interactions and monitoring parameters for a given antifungal agent
- Identify two scenarios where empiric antifungal therapy is warranted
- Identify drug(s) of choice for at least one invasive fungal infection

Objectives (Technicians)

- Describe the importance of utilizing an antifungal stewardship program
- State the most commonly used antifungal agents in the hospital setting
- When given a specific pathogen, list the most common antifungal agent(s) used to treat the infection.

Azoles: Mechanism of action

- Inhibit the synthesis of ergosterol, a vital component of the fungal cell membrane



Commercially Available Azoles

- Fluconazole
- Voriconazole
- Itraconazole
- Posaconazole
- Isavuconazole

Fluconazole: Dosing and Administration

- Available as IV or PO tablets
- Dosing ranges from 400-800mg (or 6-12mg/kg) once daily depending on indication and immune status
  - Lower doses are used for candiduria or esophageal candidiasis
- Doses should be reduced by 50% in patients on hemodialysis, CRRT, or with CrCl $\leq$50

Fluconazole package insert. Pfizer; 2014.

Fluconazole: Spectrum

- Fluconazole has reliable activity against most types of *Candida* spp.
  - *C. glabrata* has variable resistance to all azoles, may require aggressive dosing
  - *C. krusei* is intrinsically resistant to fluconazole
- Also has activity against *Cryptococcus* spp.

Clin Infect Dis 2006;43:S28-39.

Fluconazole: Susceptible-Dose Dependent

- *Candida* spp. Isolates with MICs of 16 or 32 are considered susceptible dose-dependent
  - Fluconazole doses of 400-800 mg/day should be used for these isolates
- Fluconazole AUC/MIC ratios of 25 mg·hr/L have been associated with efficacy
- In healthy 70 kg patients doses of 400 mg correlate with an AUC of ~400 mg·hr/L

Clin Microbiol Rev 2006; 19: 435-447

Fluconazole: Interactions and ADEs

Inhibits	CYP 2C9 (strong), 2C19 (strong), 3A4 (moderate)
	• Phenytoin • Warfarin • Dofetilide • Sirolimus • Citalopram
Substrate	N/A Rifampin may decrease serum concentrations
ADEs	• Headache • N/V/D • LFT abnormalities • Additive QTc prolongation (especially in patients receiving ≥400mg/day)

Fluconazole package insert. Pfizer; 2014.

Voriconazole: Spectrum of Activity

- Voriconazole has reliable activity against *Aspergillus* spp., *Candida* spp., as well as *Fusarium* spp.
  - Some studies report variable in vitro susceptibility of *C. glabrata*

Antimicrob Agents Chemother. 1998;42:161-3.
J Antimicrob Chemother. 1999;44:697-700.
J Antimicrob Chemother. 1998;42:253-6
Clin Infect Dis 2006;43:S28-39.

Voriconazole: Dosing and Administration

- Available as IV and PO tablets
- IV dosing is weight based
  - 6mg/kg q12h for 2 doses, then 4mg/kg q12h
- PO dosing is standardized
  - 100mg q12h for patients <40 kg
  - 200mg q12h for patients ≥40 kg
- Dosing should be reduced by 50% in patients with mild to moderate liver dysfunction (Childs-Pugh class A or B)
  - In severe liver dysfunction this should only be used if the benefits outweigh the risk

Voriconazole package insert. Pfizer; 2014.

Voriconazole and Renal Dysfunction

- Voriconazole is not renally cleared
  - No dosage adjustment for renal dysfunction
- Per package insert:
  - Avoid IV administration in patients with a creatinine clearance < 50 mL/min
- Why is this?

Voriconazole package insert. Pfizer; 2014.

Cyclodextrin toxicity

- Cyclodextrin is a solvent agent used in the formulation of IV voriconazole
- Pharmacokinetic data have shown that its clearance is directly correlated with renal function
  - Accumulates even in patients on HD, CRRT and PD
- Data from animal studies suggest accumulation of cyclodextrin can lead to renal and hepatic dysfunction

IV Voriconazole in Renal Impairment

Population (n=128)	Retrospective review of patients receiving fluconazole (n=54), caspofungin (n=55) or voriconazole (n=19) who had CrCl <50 at the time of administration.
Rate of AKI	Rates of AKI were higher in the fluconazole group than for the caspofungin group (p=0.01) however rates of AKI in the voriconazole group was not significantly different
Logistic Regression analysis of causes related to AKI	In a multivariate logistic regression identified only infecting organism as associated with development of AKI
Conclusions	In multivariate analysis of patients with invasive fungal infections and renal dysfunction at baseline, IV voriconazole was not associated with increased risk of AKI

BMC Infect Dis 2013; 13: 14.

Voriconazole: Interactions and ADEs

Inhibits	CYP 3A4 (strong), 2C9 (strong), 2C19 (strong)
	• Cyclosporine (Reduce dose by 50%) • Statins (switch to non-CYP metabolized) • Sirolimus (Reduce dose by 90%) • Phenytoin (Reduce dose by 50%, increase voriconazole dose to 400mg PO or 5mg/kg IV) • Tacrolimus (Reduce dose by 66%) • Warfarin (monitor, may require decrease in dose)
Substrate	CYP 3A4, 2C9, 2C19
ADEs	• Visual disturbances • Increased LFTs • Increased SCr • QTc prolongation

Voriconazole package insert. Pfizer; 2014.

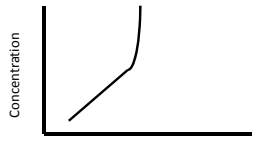
Voriconazole Therapeutic Drug Monitoring

- Voriconazole therapeutic drug monitoring has been associated with improved outcomes and decreased adverse events
- Target troughs: 1-5.5 mg/L
  - Troughs <1 mg/L associated with lack of response in Aspergillosis
  - Troughs > 5.5 mg/L associated with toxicity

Clin Infect Dis 2008; 46: 201-211.
Clin Infect Dis 2012; 55: 1080-1087

Voriconazole Dosing

CAUTION



Non-Linear Pharmacokinetics

Posaconazole: Dosing and Administration

- Now available as oral solution, tablet and IV formulation
- Dosing differs based on indication and formulation used
- **Delayed release tablets and IV solution are currently only FDA approved for fungal prophylaxis**

Formulation	Loading Dose	Maintenance Dose
Oral: Solution	200 mg QID until disease stabilization	400 mg BID
Oral: Delayed Release Tablets	300 mg BID x2 doses	300 mg daily
Intravenous Solution	300 mg BID x2 doses	300 mg daily

Posaconazole: Oral Solution

- Poor absorption and bioavailability
  - Must administer with high fat meal or low pH drink
  - Avoid with administration of antacids
    - Decreases AUC by 32-39%
  - Saturable absorption
    - Max dose 800 mg/day divided 2-4x
  - Absorption decreased in patients with diarrhea and mucositis

Posaconazole package insert. Pfizer; 2014.
Antimicrob Agents Chemother 2009; 53: 24-34.
Antimicrob Agents Chemother 2009; 53: 24-5224-5229.

Posaconazole: Delayed Release Tablet

- Good absorption independent of administration with food
- Less affected by antacids
- 200 mg dose results in average concentrations of 1300 ng/mL
  - Healthy patients
- Substantial accumulation by day 14
  - AUC increased 3x from day 1 to day 14

Posaconazole package insert. Pfizer; 2014.
J Antimicrob Chemother 2012; 67: 2725-2730.

Posaconazole: IV Formulation

- Increased exposure relative to tablets on day 1
- Cyclodextrin used for solubility
  - Per package insert:
    - Should be avoided in patients with CrCl < 50 ml/min unless the benefit outweighs the risk

Posaconazole package insert. Pfizer; 2014.
Antimicrob Agents Chemother 2014; 59: 1246-1251.

Posaconazole: Spectrum of Activity

- Posaconazole is active against all clinically relevant yeasts and molds
  - *In vitro* studies suggest variable resistance with *C. glabrata*

Clin Infect Dis 2006;43:528-39.

Posaconazole: Interactions and ADEs

Inhibits	CYP 3A4 (strong)
	A number of drugs are contraindicated with posaconazole including: • Simvastatin • Sirolimus • 3A4 substrates that may prolong QTc
Substrate	N/A
ADEs	• N/V/D • Fever • Headache • Hypokalemia • Increased LFTs • QTc prolongation • Thrombophebitis (IV only) • Infusion reactions (IV only)

Posaconazole package insert. Pfizer; 2014.

Posaconazole Therapeutic Drug Monitoring

- Posaconazole shows substantial interpatient variability
- Clinical studies have shown correlation between posaconazole levels and efficacy
  - Currently limited to studies of oral solution
- Goal troughs
  - Prophylaxis: > 700 ng/mL
  - Treatment: > 700 ng/mL, can increase to > 1250 ng/mL based on clinical response

Antimicrob Agents Chemother 2009; 53: 24-34.

The new kid on the block: Isavuconazole

- Isavuconazole is a newly approved azole antifungal with broad activity against fungi and molds
- Administered as the prodrug isavuconazonium sodium
  - Rapidly cleaved to active drug via plasma esterases
- FDA approved for the treatment of Aspergillosis and Mucormycosis

Isavuconazole package insert. Astellas; 2015

Isavuconazole: Dosing and Administration

- Available as IV solution and oral capsules
  - Highly bioavailable
- No dose adjustments for renal dysfunction or Childs-Pugh class A or B liver dysfunction

Indication	Loading Dose	Maintenance Dose
Treatment of Aspergillosis or Mucormycosis	372 mg isavuconium sulfate every 8 hours x 6 doses	372 mg isavuconium sulfate daily (12-24h post maintenance doses)

Isavuconazole package insert. Astellas; 2015

Isavuconazole: Spectrum of Activity

- MIC breakpoints for isavuconazole have not yet been established
- Based on in vitro data, isavuconazole appears to have activity against most clinically relevant yeasts and molds
  - Active against Mucorales, variable based on species
  - Limited activity against *Fusarium spp.*

Isavuconazole package insert. Astellas; 2015.
Clin Infect Dis 2015; Online Access.

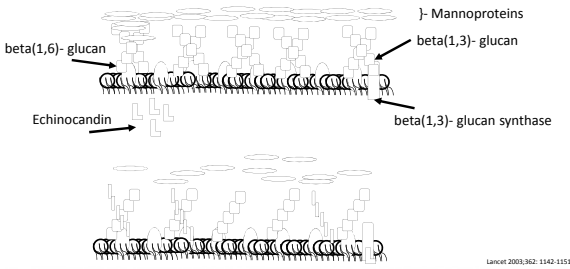
Isavuconazole: Interactions and ADEs

Inhibits	CYP 3A4 (moderate) Induces CYP 2B6
	• Sirolimus • Midazolam • Tacrolimus 2B6 Substrates • Bupropion
Substrate	CYP 3A4 Contraindicated with strong inhibitors or inducers
ADEs	• N/V/D • Headaches • Hypokalemia • Abdominal pain • Increased LFTs

Isavuconazole package insert. Astellas; 2015

Echinocandins: Mechanism of Action

- Inhibit the formation of β-(1,3)-glucan, an important part of the fungal cell wall



Lancet 2003;362: 1142-1151.

Echinocandins: Spectrum of Activity

- All echinocandins have similar spectrums of activity
- Active against *Candida* spp., including *C. glabrata* and *C. krusei*
  - Echinocandins have variable *in vitro* activity against *C. parapsilosis**
- Limited activity against *Aspergillus* spp.
  - Fungistatic
  - May be appropriate in salvage therapy

Lancet 2003;362: 1142-1151.

Echinocandins: Dosing and Administration

- All commercially available echinocandins are IV only

Drug	Loading Dose	Maintenance Dose
Caspofungin	70mg x 1	50mg daily
Micafungin	None	100mg daily
Anidulafungin	200mg x1	100mg daily

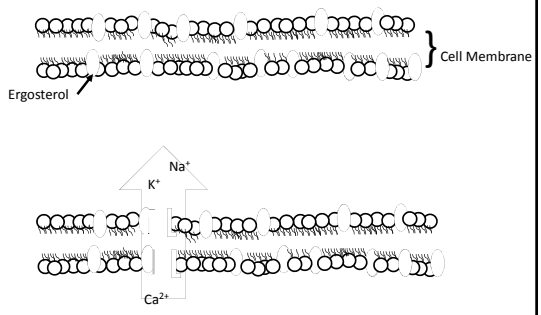
Expert Opin Infect Dis 2003; 12: 1313-1333.

Echinocandins: Interactions and ADEs

Inhibits	Micafungin- CYP 3A4 (minor)
Substrate	Micafungin- CYP 3A4 (minor)
Avoid with concurrent use of	Micafungin may increase levels of sirolimus, usually is not clinically relevant, however monitoring is warranted
ADEs	• LFT elevations • Fever • N/V/D • Hypomagnesemia • Hypokalemia

Lancet 2003;362: 1142-1151.
Expert Opin Infect Dis 2003; 12: 1313-1333.

Amphotericin: Mechanism of Action



Drugs 2009; 69: 361-392.

Amphotericin: Spectrum of Activity

- Amphotericin has activity against most clinically relevant yeasts and molds
  - Variable activity against:
    - *Fusarium* spp.
    - *Zygomycetes*
  - Important gaps in coverage include:
    - *Aspergillus terreus*
    - *Candida lusitaniae*

Clin Infect Dis 2006;43:S28-39.
Drugs 2009; 69: 361-392.

Amphotericin: Dosing and Administration

- Amphotericin B is only commercially available as IV formulation
- Dosing depends on formulations
  - Amphotericin B deoxycholate- 0.6-1.5mg/kg
  - Lipid formulations- generally 3-5 mg/kg
    - Liposomal amphotericin B has been studied in doses up to 12 mg/kg

Drugs 2009; 69: 361-392.
Clin Infect Dis 2007; 44: 1289-1297.

Amphotericin: Interaction and ADEs

Inhibits	N/A
Substrate	N/A
Avoid with concurrent use of	• Other nephrotoxic agents
ADEs	• Renal dysfunction • Infusion reactions • N/V/D • Pulmonary toxicities • Hypokalemia • Hypomagnesemia

- Lipid formulations have been shown to be equally efficacious for most indications
- Lower rates of side effects- especially nephrotoxicity
  - Rates of infusion reactions similar!

Drugs 2009; 69: 361-392.

Antifungal Stewardship

- Unnecessary antifungal therapy can lead to increased costs, ADEs and increased resistance
- Antifungal stewardship has been shown to decrease the number of days of inappropriate and unnecessary antifungals
  - Single center in England showed savings of > $280,000 (~£180,000) in first year

Clin Infect Dis 2015; 69: 361-392.
J Antimicrob Chemother 2014; 69: 1993-1999.

CANDIDIASIS

Patient Case #1

- IC is a 44 y/o male, transferred from OSH for abdominal pain and found to have necrotic bowel 2/2 ingestion of cocaine
  - Partial colectomy performed on admit
  - SCr on admit is 11, requiring CRRT
- VS (ICU day 6):
  - HR 115
  - RR 24
  - Tmax 101.5ºF
- Current antimicrobials:
  - Ceftazidime
  - Metronidazole
  - Vancomycin

Patient Case #1

- Patient has had low blood pressures since admit, currently being maintained on norepinepherine drip
- Team would like to start empiric antifungal therapy

Empiric Antifungal Therapy

- Low hanging fruit
  - Febrile neutropenic patients with persistent fever after 72-96 hours of broad spectrum antibiotics
- What about non-neutropenic patients?

Candida Risk Score

Population (n=1,669)	Multicenter prospective observational cohort study of adult patients admitted to the ICU for at least 7 days.
Intervention	Data were collected for all patients that met inclusion criteria Weekly samples were taken to determine colonization of the gastrointestinal, genitourinary or respiratory tracts

Table 4. Calculation of the Candida score: Variables selected in the logistic regression model

Variable	Coefficient (β)	Standard Error	Wald χ^2	*p* Value
Multifocal *Candida* species colonization	1.112	.379	8.625	.003
Surgery on ICU admission	.997	.319	9.761	.002
Severe sepsis	2.038	.314	42.614	.000
Total parenteral nutrition	.908	.389	5.851	.030
Constant	−4.916	.485	102.732	.000

ICU, intensive care unit.

Candida score = .908 × (total parenteral nutrition) + .997 × (surgery) + 1.112 (multifocal *Candida* species colonization) + 2.038 (severe sepsis). Candida score (rounded) = 1 × (total parenteral nutrition) + 1 × (surgery) + 1 (multifocal *Candida* species colonization) + 2 × (severe sepsis). All variables coded as follows: absent, 0; present, 1.

Crit Care Med 2006; 34: 730-737.

Candida Risk Score

B

Cutoff value	Sensitivity	False positive
1.055	.983	.653
1.509	.949	.485
1.963	.898	.426
2.069	.831	.312
2.074	.814	.301
2.526	.814	.259
2.982	.780	.251
3.026	.610	.132
3.093	.593	.130
3.547	.525	.092
4.001	.492	.077

- Determined that a score >2.5 can help to select for patients who may benefit from early antifungal therapy

Crit Care Med 2006; 34: 730-737.

Validation of the Candida Risk Score

Population	Patients admitted to ICU and exhibited signs of hospital-acquired severe sepsis or septic shock (n=94)	Admitted to ICU for sepsis (n=95)
Rate of candidiasis	5.3%	16.8%
Cutoff used	>3	≥3
PPV	23.8%	27.3%
NPV	100%	98.7%

- Very good negative predictor
- Candida risk score can help to identify patients at risk for invasive candidiasis but should be considered in the clinical context of the patient

Critical Care 2011; 15: R249.
Ann Intensive Care 2011;1:50

Patient Case

- What is IC's Candida Score?
  - A. 1
  - B. 2
  - C. 3
  - D. 4

Patient Case #1

- IC is a 44 y/o male, transferred from OSH for abdominal pain and found to have necrotic bowel 2/2 ingestion of cocaine
  - Partial colectomy performed on admit to BIDMC
- SCr on admit is 11, requiring CRRT
- VS (ICU day 6):
  - HR 115
  - RR 24
  - Tmax 101.5°F
- Patient has had low blood pressures since admit, currently being maintained on norepinepherine drip
- Current antimicrobials:
  - Ceftazidime
  - Metronidazole
  - Vancomycin

Patient Case #1

- IC is a 44 y/o male, transferred from OSH for abdominal pain and found to have necrotic bowel 2/2 ingestion of cocaine
  - Partial colectomy performed on admit to BIDMC
- SCr on admit is 11, requiring CRRT **Surgery +1**
- VS (ICU day 6):
  - HR 115
  - RR 24
  - Tmax 101.5°F
- Patient has had low blood pressures since admit, currently being maintained on norepinepherine drip
- Current antimicrobials:
  - Ceftazidime **Septic Shock +2**
  - Metronidazole
  - Vancomycin

(1,3)-β-D-glucan

- Multiple studies have shown widely variable data on the usefulness of this clinical test
- Detects part of fungal cell wall in *Candida* spp. and *Aspergillus* spp.
- Large multicenter trial with 163 patients with proven or probable IFI showed the following:

Table 3. Performance of the (1→3)-β-D-glucan (BG) assay for

BG cutoff value, pg/mL	Sensitivity, %	Specificity, %	Positive predictive value, %	Negative predictive value, %
80	64.4	92.4	80.0	73.0

Clin Infect Dis 2005;41:654-659

(1,3)-β-D-glucan- False positives

- Many factors have been proposed to cause false positive (1,3)-β-D-glucan tests
  - *Pneumocystis jiroveci* pneumonia (PJP)
  - Bacteremia
  - IVIg
  - Certain antibiotics
  - Hemodialysis with cellulose membranes
  - Certain wound care items

Candidemia: Risk Factors

- Central venous catheters
- Prolonged length of stay
- Renal failure
- Hemodialysis
- Parenteral nutrition
- Transplantation
- Immunosuppression
- Surgery
  - Especially abdominal surgery
- Broad spectrum antibiotics

Crit Care Med 2006; 34: 857-863.

Patient Case #1

- IC has a Candida Risk Score of 3 and multiple risk factors that have been associated with Candida infection in ICU patients
- Beta-D-Glucan is still pending
- Would you start antifungal therapy?
- What agent would you choose?

Diagnosis

- Yeast is a very uncommon cause of respiratory infection
- Yeast is a common urinary colonizer
  - First line treatment- take out urinary catheter
- No matter the quantity, yeast from blood is not a contaminant

Clin Infect Dis 2009; 48: 503-535.

Candidemia: Treatment

Host/disease factors	Recommended therapy
Immunocompetent **AND** azole naïve within 30 days **AND** hemodynamically stable **AND** no recent history of *C. krusei* or *C. glabrata*	**Fluconazole** 800 mg x 1, then 400 mg IV daily
Immunocompromised **OR** azole experienced within 30 days **OR** hemodynamically unstable **OR** recent history of *C. krusei* or *C. glabrata*	**Micafungin** 100 mg IV Daily OR Liposomal Amphotericin B 3mg/kg daily OR Voriconazole 6mg/kg q12h, then 3mg/kg q12h

Clin Infect Dis 2009; 48: 503-535.

Patient Case

- What agent would be the most appropriate to start in IC?
  - A. No therapy at this time
  - B. Fluconazole 800mg x1 then 400mg daily
  - C. Caspofungin 70mg x1 then 50mg daily
  - D. Liposomal amphotericin B 3mg/kg daily

Fluconazole vs. Anidulafungin for Invasive Candidemia

Population (n=245)	Patients >16 y/o with *Candida* spp recovered from a normally sterile site within 96 hours of enrollment and had signs/symptoms of infection or radiological evidence
Exclusion	• *C. kruseii* infection • Refractory Candida infection • >1 week of azole therapy in past 30 days • >48h of antifungal therapy • Osteomyelitis, endocarditis or meningitis
Intervention	Patients were randomly assigned to receive either fluconazole or anidulafungin therapy and were stratified based on APACHE II score and neutrophil count
Treatment response	Anidulafungin had higher rates of response at the end of IV therapy was found to be non-inferior No difference in 28-day mortality
Conclusions	Echinocandins and fluconazole appear to be equally effective in this population (non-neutropenic patients with APACHE <20)

N Engl J Med 2007; 356: 2472-2482.

Fluconazole vs. echinocandins for *C. glabrata* fungemia

Population (n=224)	Retrospective multicenter study of patients receiving fluconazole or an echinocandin for the treatment of *C. glabrata* candidemia
Exclusion	• Concomitant bacteremia • >48h of antifungal therapy before first positive result
Complete response at day 14	No significant difference in response at day 14 (p=0.383) There was a trend towards decreased response when comparing patients treated with fluconazole with more severe illness
Survival	No difference in mortality at any point (28 day; p=0.944)
Conclusions	Even in the case of *C glabrata*, patients treated with fluconazole who are clinically stable have similar rates of cure and no difference in mortality when compared to echinocandin therapy

J Antimicrob Chemother 2013; 68: 922-926

Patient case #1

- IC was started on fluconazole 400mg daily (with an 800mg load)
- On day 14 yeast from blood culture is speciated to *C. glabrata*
- Still no susceptibilities
- How would this change your current management of this patient?

Patient Case

- IC is clinically improving on fluconazole and is now out of the ICU, however cultures are growing *C. glabrata.*
- What is the best course of action?
  A. Continue fluconazole 400mg daily
  B. Increase fluconazole to 800mg daily
  C. Switch to micafungin 100mg daily
  D. Switch to liposomal amphotericin 3 mg/kg

Candidemia: Other Considerations

- Endocarditis should be a concern in all patients with candidemia
  - TTE or TEE should be obtained in patients with clinical suspicion for endocarditis
- Central lines should be removed, if possible, as *Candida* spp. may form biofilms
- All patients should receive an ophthalmology exam at least once

Clin Infect Dis 2009; 48: 503-535.

Candidal Endocarditis

- Few studies looking at treatment of patients with candidal endocarditis
- Treatment of choice is amphotericin B +/- flucytosine
- However, a small study suggests that echinocandins may have a role
  - All cause mortality of patients treated with caspofungin similar to those treated with amphotericin B in a chart review
- In vitro data suggests that amphotericin B and echinocandins have better penetration into biofilms

Eur J Clin Microbiol Infect Dis 2008; 27: 519-529.

INVASIVE ASPERGILLOSIS

Patient Case

- AG is a 65 year old male admitted for CSF relapse of AML, currently being treated with IT cytarabine
  - Multiple cycles
- On hospital day 30 he develops a fever to 102.3°F
- Currently has WBC count of 1.2, neutrophils are 35%
- Started on cefepime

Patient Case

- On day 3 of treatment with cefepime, patient continues to be febrile
- CT notes nodules in the lungs surrounded by ground glass opacities
- What diagnostic tests could help you determine the best treatment?

Patient Case

- At this point, based on consensus definitions what level of certainty do we have that AG has Aspergillosis?
  A. Possible
  B. Probable
  C. Proven

Aspergillus spp.

- Aspergillus spp. are molds that are ubiquitous worldwide
- Important cause of morbidity and mortality in immunocompromised patients
- Invasive infections most commonly occur in the lungs
- Most common species is *Aspergillus fumigatus*
  - May change based on location

Clin Infect Dis 2008; 46: 327-360.

Pulmonary Aspergillosis: Risk Factors

- Prolonged neutropenia
- Advanced HIV
- Inherited immunodeficiency syndrome
- Hematopoietic stem cell transplantation
- Lung transplantation

Clin Infect Dis 2008; 46: 327-360.

Pulmonary Aspergillosis: Signs and symptoms

- Nodules with halo sign on CT
- Positive fungal markers
  - Galactomannan
  - β-D-Glucan
- Cultures obtained via BAL, needle aspiration or thorascopic biopsy

Clin Infect Dis 2008; 46: 327-360.

Pulmonary Aspergillosis: Diagnosis

Consensus Definition for Invasive Fungal Disease	
Proven	Recovery of Aspergillus spp. from a normally sterile site with evidence of tissue damage or clinical correlation with infectious process at that site --Excludes BAL and sinus cavity specimen
Probable	Combination of host factors, clinical criteria and mycological evidence 1) Host is immunosuppressed 2) Pulmonary infection: CT with dense lesions, air crescent signs or cavitary lesions 3) Positive galactomannan or recovery of *Aspergillus* spp. from respiratory cultures
Possible	Combination of host factors and clinical criteria WITHOUT mycological evidence

Clin Infect Dis 2008; 46: 1813-1821.

Galactomannan Assay

- Galactomannan is a cell wall component of *Aspergillus* spp.
  - Released during invasive infection
- Large meta-analysis showed sensitivity of 71% and specificity of 89%
  - Better negative predictor than positive predictor
- False positives have been reported in patients receiving concurrent piperacillin-tazobactam therapy

Blood 2001; 97: 1604-1610.
Clin Infect Dise 2006; 42: 1417-1422.

Patient Case

- What test would move our certainty of *Aspergillus* spp. infection from possible to probable?
  A. β-(1,3)-D-glucan assay
  B. Galactomannan assay
  C. Sputum culture with yeast
  D. Repeat CT to confirm halo

Pulmonary Aspergillosis: Treatment

- Voriconazole is the treatment of choice
  - 6mg/kg q12 for 2 doses, then 4mg/kg
- Amphotericin B may also be effective
  - Amphotericin B deoxycholate dosed 1mg/kg daily
  - Lipid formulations better tolerated
    - Liposomal amphotericin B dosed 3-5 mg/kg/day
  - *A. terreus* is intrinsically resistant to amphotericin

Clin Infect Dis 2008; 46: 327-360.

Voriconazole vs. D-AMB for invasive aspergillosis

Population (n=277)	Randomized open label study of patients with probable or definite invasive aspergillosis and were immunocompromised. Mostly with lung involvement only and hematologic cancers.
Exclusion	Received 96 hours of therapy with amphotericin B or itraconazole, received interacting medications had LFTs >5x ULN, or were on mechanical ventilation.
Intervention	Randomized to receive amphotericin B deoxycholate 1-1.5mg/kg daily **OR** Voriconazole 6mg/kg q12h for two doses then 4mg/kg q12h
Response at week 12	Complete or partial response was 52.8% in voriconazole group and 31.6% in the amphotericin group (CI: 10.4-32.9)
Survival at week 12	Survival in voriconazole group was 70.8% and 57.9% in the amphotericin B group (CI: 0.4-0.88)
Conclusion	Voriconazole was found to have superior outcomes with respect to amphotericin B deoxycholate. Additionally voriconazole was better tolerated but had higher rates of visual disturbances.

N Engl J Med 2002; 347: 408-415

Combination Therapy

Population (n=454)	Randomized double blind placebo controlled trial of combination therapy in proven or probable invasive aspergillosis. Patients had to be >16 years of age
Exclusion	Progressive hematologic malignancies not likely to response to treatment, life expectancy <30 days, **mechanical ventilation**, >96 hours of antifungals before enrollment, pregnant or lactating, severe liver dysfunction
Intervention	Randomized to receive voriconazole 6 mg/kg q12 x2 doses then 4mg/kg BID for a total of 6 weeks of treatment (could switch to PO after 7 days) **OR** Voriconazole 6mg/kg q12h for two doses then 4mg/kg q12h PLUS anidulafungin 200mg x1 then 100mg daily for 2-4 weeks
Mortality at week 6 (mITT)	Mortality in combination therapy was 19.5% vs 27.8% in the monotherapy group (Difference -8.3% CI: -19 to 1.5, p=0.086)
Conclusion	Combination of voriconazole with anidulafungin resulted in a decrease in mortality in the mITT group, however this was not statistically significant. Multivariate analyses identified initial galactomannan level as being predictive of mortality.

Ann Intern Med 2015; 162: 81-89.

Isavuconazole in Aspergillosis

- Studies have not yet been published
- Randomized double blind study of patients with possible, probable or proven infection (n=231)
- No differences noted in 6 week all cause mortality or overall response at end of treatment
- Less ADEs in patients on isavuconazole,
  - No difference in serious ADEs or ADEs leading to d/c

Abstract 1211, Idweek 2014, IDSA
Ann Intern Med 2015; 162: 81-89.

Salvage Therapy

- Other agents have been studied in salvage therapy
  - Posaconazole 200mg QID
  - Caspofungin 70mg once then 50mg daily
  - Micafungin 100mg daily

Clin Infect Dis 2008; 46: 327-360.

Patient Case

- The team would like to know which medication to start for the treatment of AG's suspected Aspergilosis. What is the best option?
  A. Caspofungin
  B. Liposomal amphotericin B
  C. Voriconazole
  D. Posaconazole

Patient Case

- AG is started on voriconazole per your recommendations. What is the most clinically relevant interaction with AG's medications?
  A. Cefepime
  B. Prochlorperazine
  C. Citalopram
  D. Diphenoxylate/atropine

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Thinking Like an Engineer: Utilizing Human Factor Methodologies to Improve IV Medication Safety in the Peri-operative Setting

Chris Fortier, PharmD, FASHP
Chief Pharmacy Officer
Massachusetts General Hospital
Boston, MA

DISCLOSURE

- The speaker has no conflicts of interest to disclose in relation to this presentation

Learning Objectives for Pharmacists and Pharmacy Technicians

1. Describe the medication use process during the administration of anesthesia.
2. Identify the differences between the system vulnerabilities for preparing medications from a manufacturers drug vial vs. a pharmacy prepared prefilled syringe.
3. Discuss the severity of the system vulnerabilities for preparing medications from a manufacturers drug vial vs. a pharmacy prepared prefilled syringe.
4. Explain strategies to improve medication safety during the course of administering an anesthetic for surgery.
5. State the basic elements involved when considering prefilled syringe adoption in the O.R.

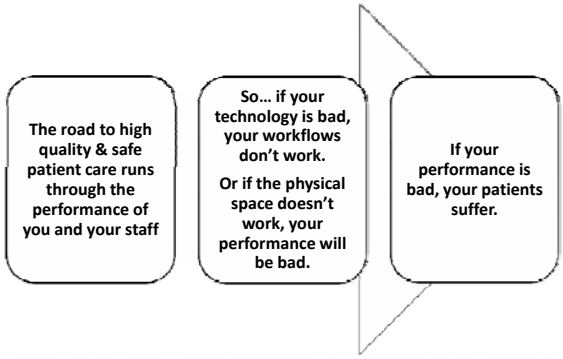
A Call from the Institute of Medicine

- IOM report *To Err is Human: Building a Safer Health System* released in 2000
- Led to many human factors engineering efforts designed to reduce:
  - Error rates in hospitals
  - Consequences of errors
- Much of the focus has been on nursing work, ICUs, surgery

Take Away Messages...

This is what we know:	
• Quality and safety emerge from the interaction between people and the system in which they work. • **Human factors engineering** helps us to understand that interaction so that we can better design systems to improve quality and safety.	**Learn about it!**
• We have tools, standards, guidelines, and principles for improving human performance, safety, and productivity.	**Use & apply them!**
• Human factors engineering improves performance and safety…	**…when used and implemented appropriately**

Main Take-Away Message



Common Healthcare Thinking

- Errors are personal failings
  - When something bad happens, someone must be at fault
- Policies create safety
- And recently…
  - ***Technology will save us!***

What Is Human Factors Engineering?

Science

- Discovers and applies information about human behavior, abilities, limitations, and other characteristics to…
- … the design of tools, machines, systems, tasks, jobs, and environments…
- … for productive, safe, comfortable, and effective human use

Practice

- Designing the fit between people and:
  - Products
  - Equipment
  - Facilities
  - Procedures
  - Environments

HFE Topics of Study

- Usability
- Organizational changes
- Workflow
- Handoffs
- Mental workload
- Situation awareness
- Human-automation interaction
- Training
- Teamwork and team training
- Information processing
- Naturalistic decision making
- Interruptions/distractions
- Violations
- Human error
- Safety
- Resilience
- Alerts
- Lifting

Who *Requires* Human Factors Engineering In Their Designs?

- US Federal Aviation Administration
- Department of Defense
- Department of Transportation
- Nuclear Regulatory Commission
- Department of Energy
- National Aviation and Space Administration
- FDA – Medical Device Testing

What Are the Objectives?

- **Reduce** errors, fatigue, stress and injuries at work, while at the same time…
- **Improve** productivity, ease of use, safety, comfort, acceptance, job satisfaction, and quality of life

Or simply –
improve safety, quality, efficiency, and productivity
all at the same time

Too good to be true?

Raise your hand when you know
HOW MANY results are out of range!!!

Ready…?

Species : Adult Canine
Patient : SYDNEY
Client : SUE B

Test		Results	Reference Range
ALKP	=	85 U/L	23 - 212
ALT	=	23 U/L	10 - 100
BUN	=	16.6 mg/dl	7.0 - 27.0
CREA	=	0.77 mg/dl	0.50 - 1.80
GLU	=	130.6 mg/dl	77.0 - 125.0
TP	=	6.21 g/dl	5.20 - 8.20
Na	=	148.9 mmol/l	144.0 - 160.0
K	=	4.44 mmol/l	3.50 - 5.80
Cl	=	116.9 mmol/l	109.0 - 122.0

Okay, try again.

Raise your hand when you know
HOW MANY results are out of range!!!

Ready…?

Test	Results	Reference Range	Indicator (LOW / NORMAL / HIGH)
ALKP	= 85 U/L	23 - 212	
ALT	= 23 U/L	10 - 100	
BUN	= 16.6 mg/dl	7.0 - 27.0	
CREA	= 0.77 mg/dl	0.50 - 1.80	
GLU	= 130.6 mg/dl	77.0 - 125.0	
TP	= 6.21 g/dl	5.20 - 8.20	
Na	= 149.9 mmol/l	144.0 - 160.0	
K	= 4.44 mmol/l	3.50 - 5.80	
Cl	= 116.9 mmol/l	109.0 - 122.0	

What Was the Difference?

The first data presentation:	The second data presentation:	Both presentations:
• Was cognitively challenging because you needed to mentally find the lab value, and then interpret whether or not the value was in range • Each comparison was an opportunity for error	• Provided what we call a **direct perception** display to answer the cognitive challenge I posed to you	• Are typical of types of displays you might encounter every day • Affected accuracy (quality/safety) and response time (productivity) • Only one was good

Can HFE Really Do All That?

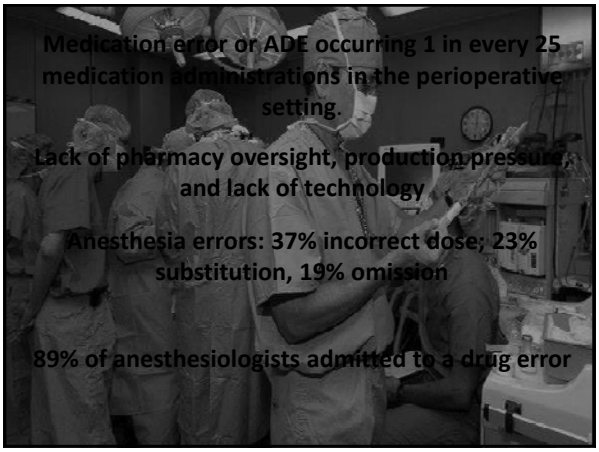
- Yes, because we focus on designing systems to support human performance
- It's about human performance **in context** or **in the system**

What Does HFE Focus on to Meet the Objectives?

- **Identification** of performance: what are people actually doing?
- **Analysis** of the interaction between human performance and work systems
- **Design** of work systems to support/extend performance & eliminate/reduce performance obstacles

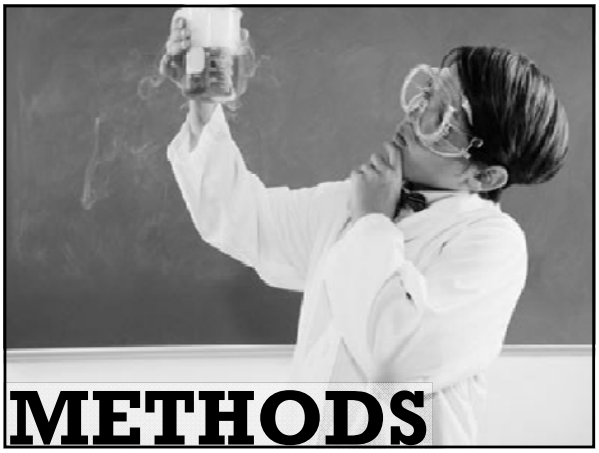
Use "HFE Thinking"

- Systems (e.g., machines or hospitals) need to be designed for people, and to work with people
- Systems must be designed to accommodate the range of users
- How systems are designed will influence human behavior and therefore system performance
- Design needs to be evidence-based, not "common sense" or designer driven
- All design must take into account the system of use



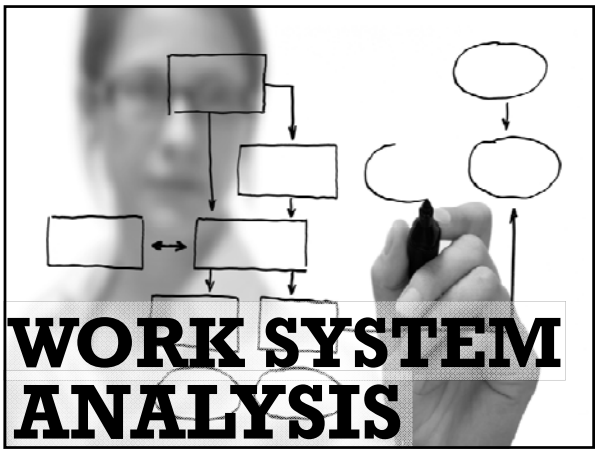
Medical Univ. of South Carolina

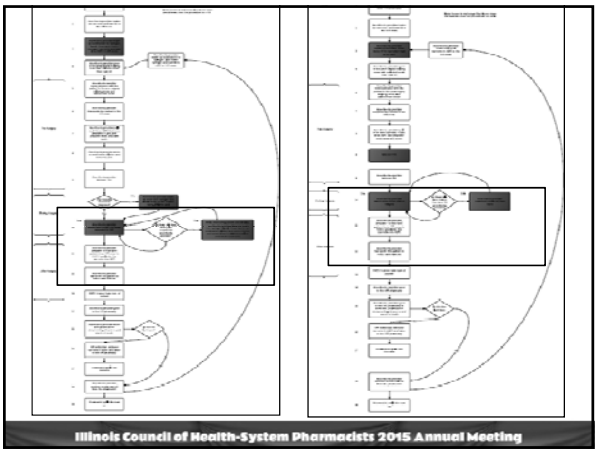
- **Located in Charleston, SC**
- **709-bed academic medical center**
- **Level 1 Trauma Center**
- **Operating Room Suites**
  - Medical University Hospital Main OR
  - Ashley River Tower OR
  - Rutledge Tower Ambulatory OR
- **23,550 cases/year**
- **3 OR Pharmacies**
  - 6 FTE pharmacists
  - 3.2 FTE pharmacy technicians
  - 0.4 FTE pharmacy students



Methods

- **Work system analysis observing general surgery cases**
  - Self-filled syringes
  - Pre-filled syringes
- **Identify system vulnerabilities/process map**
- **Anesthesia clinician proactive risk assessment**
  - Occurrence
  - Severity
  - Disruptiveness to workflow





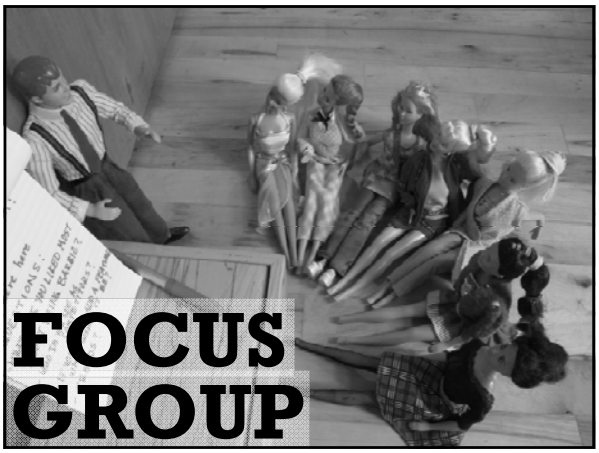
What are "system vulnerabilities"?

An activity or event that has the potential to reduce safety, efficiency, and/or provider workflow

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

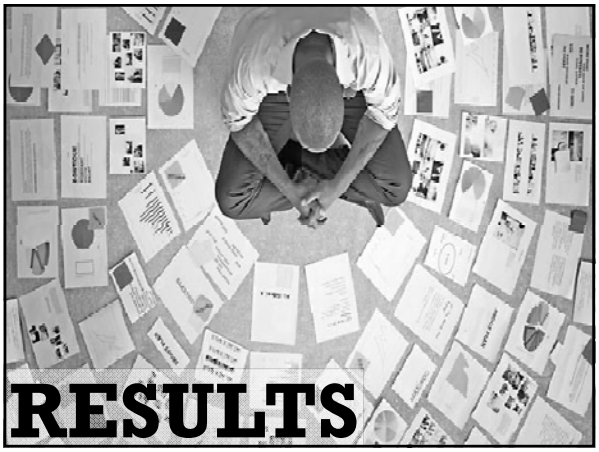
SV#	Steps in WFA	SV Description	Possible Effects	Additional Notes	Occurrence	Severity on Patient	Disruptiveness to Workflow	Discussion
1	3(E) 2(F) 2(G); 10a (D); (E) Anesthesia provider draws up medication, places sticker on syringes and labels syringes	Anesthesia provider completes the process in an incorrect sequence: placing medication sticker first, then drawing-up medication, and finally labeling self filled syringes.	This SV could lead to the potential for **incorrect labeling** of medication, and **incorrect medication administration**, especially if completed in distracting environment.	As required by the Joint Commission, medications should be drawn-up first, and then a sticker should be placed and a label created. This SV violates the TJC standard.				
2	3 (G); 10a (F) Anesthesia provider labels the syringe by signing initials, date and time of the draw-up, and the concentration of the med.	Anesthesia provider forgets to label, or purposely does not label, or inappropriately labels post-immediate administered medication.	This SV could lead to the potential for **incorrect medication administration**.	The Joint Commission requires that self-prepared medications must be appropriately labeled with the drug name, strength, amount, expiration date, MD/CRNA initials, and date and time of when it was drawn up. This SV is a violation of the TJC standard.				
3	3 (H) Anesthesia provider prepares syringes in a pink, bin in the top drawer of ADC and then goes to the pre-surgery holding room	When preparation is complete, anesthesia provider leaves syringes on the ADC counter surface, instead of storing them in the drawer of ADC.	Leaving syringes on counter, increases the exposure time to air, causing **sterility problems**. Also, it increases the risk that these medications can be tampered with or taken by inappropriate personnel.	N/A				

SV#	Steps in WFA	SV Description	Possible Effects	Additional Notes	Occurrence	Severity on Patient	Disruptiveness to Workflow	Discussion
1	1 Anesthesia provider organizes needed medications and stores PPS cassette/ narc kit in ADC	Anesthesia provider stores cassette / narc kit in ADC directly without working on necessary preparation and organization for current case.	Not organizing PPS prior to the case could create **workflow delays** when patient arrives to the OR.	N/A				
2	3 (A); 4; 5 10a (B) Anesthesia provider organizes medications by quickly looking at medication name and dose	Although Tall-Man lettering (e.g., Succ vs. Vec) is used, similarly colored packaging is used for completely different medications.	This similar packaging creates the opportunity for **an incorrect medication** to be selected and then administered to patient.	The potential impact of this SV is magnified during hectic situations when extra medications are needed.				
3	2; 7; 10a Anesthesia provider pulls medication in the ADC top drawer and prepares work area by placing PPS on ADC counter surface.	Each anesthesia provider organizes syringes on ADC surface based on personal preferences, such as grouping similar types of syringes together (e.g., emergency, induction, muscle relaxation, etc.).	This SV could increase the opportunity for a **medication administration error**, especially when other providers take over shifts because the new provider may not be familiar with the previous provider's method of organization.	There is no national best practice for this process standardization.				
4	9; 10a Anesthesia provider prepares and administers medication	Multiple teaching methods by attending anesthesiologists result in different medication delivery styles and administration quality by residents	This SV could impact the **quality of medication administration** of anesthesia medications.	The teaching process should be standardized.				



Focus Group

Ratings	Occurrence	Severity on Patient	Disruptiveness to Workflow
1	This SV **rarely** occurs (e.g. 0-3 times per year)	This SV results in **no injury** to the patient.	This SV has **no influence** on provider's workflow
2	This SV **sometimes** occurs (e.g. roughly 1-2 times per month)	This SV results in **moderate injury** to the patient	This SV results in a **slight but recoverable disruption** to provider's workflow
3	This SV **often** occurs (e.g. daily/weekly)	This SV results in **major but recoverable injury** to the patient	This SV results in a **moderate but recoverable disruption** to provider's workflow
4	This SV **always** occurs (e.g. 1-3 times per case)	This SV results in **permanent loss of function or catastrophic death** of the patient	This SV results in an **severe and unrecoverable disruption** providers' workflow



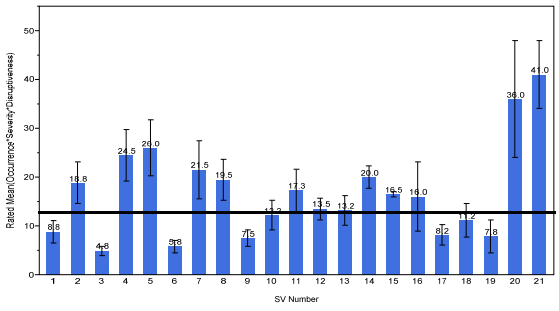
Results

	SELF-FILLED SYRINGES	PRE-FILLED SYRINGES
Number of cases	8	9
Process steps	21	19
System vulnerabilities	21	8
Medications administered per case	9.6	10.3

System Vulnerabilities - SFS

- **Complexity of the preparation and administration process**
- **Variability of task risks to sterility**
- **Lack of standardization of labeling**
- **Usability concerns of packaging**
- **Significant waste after administration**

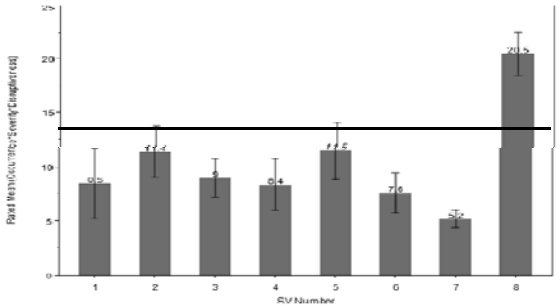
System Vulnerabilities - SFS



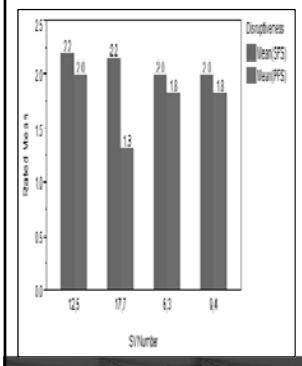
System Vulnerabilities - PFS

- **Variability of task completion**
- **Usability concerns of packaging**
- **Amount of wasted medications**

System Vulnerabilities - PFS

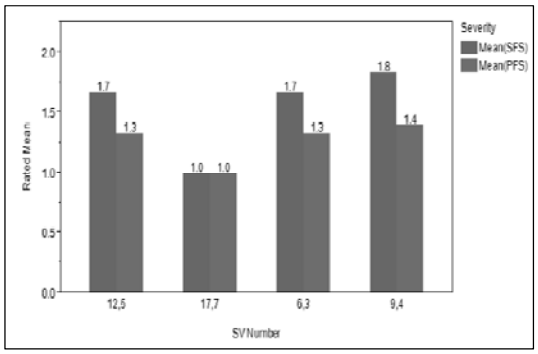


Disruptiveness



- **Obtaining syringes**
- **Syringe organization**
- **Variable delivery styles**
- **Product waste**

Severity



Severity - SFS

- **11 SV had severity score above 16**
  - Pharmacists management product vial changes (drug shortages)
  - Difficulties to ensure the correct medication name on the vial packaging
  - Complex medication preparation process during surgery

Study Conclusions

- **Reduced risk with use of PFS**
- **Highest severity SV for SFS are completely removed with the use of PFS**
- **Most of SV for PFS can be reduced through training and user-centered re-design**
  - Working with anesthesia clinicians on 8 system vulnerabilities
  - Consider the addition of barcode scanning in the OR
- **Make anesthesia providers aware of USP 797 immediate use regulations**

Drug Waste

61%

TOTAL WASTE REDUCTION WITH THE USE OF PFS

Waste Reduction Summary

	Phase I (baseline)	Phase II (PFS)
Days	10	10
Cases	154	171
Case w/ waste	110 (71%)	66 (38%)
Drug waste (mL)	3284.2 mL	1266.3 mL
Avg. waste per case	21.3 mL	7.4 mL

Clinician Satisfaction Survey

% of Respondents (n=24)	Survey Question
79.3 %	Clinicians felt that less drug was wasted when they used PFS
91%	Clinicians felt that using PFS saved them time in preparing syringe for procedure
74%	Clinicians felt that using PFS increased their confidence in integrity of the preparations

* 24 respondents including attending anesthesiologists, resident/fellow anesthesiologists, CRNA, and anesthesia technicians

Clinician Satisfaction Survey

Time saved with the use of PFS	
Estimated time saved	**% of respondents (n=24)**
5 to 6 minutes	42%
3 to 4 minutes	29%
7 to 9 minutes	8%
1 to 2 minutes	4%

* 4 clinicians did not respond to this survey question

Clinician Satisfaction Survey

Most beneficial features of PFS
1. Labeling
2. Reduced risk of contamination
3. No need for reconstitution
4. Tamper evident
5. Diluted
6. Expiration based upon real-time stability
7. Sterility testing

Conclusion

- **System Vulnerabilities can be identified**
- **More system vulnerabilities identified with self-filled vs prefilled syringes**
  - Prefilled syringes have the potential to improve medication safety through enhanced labeling, standardization, and extended beyond use dating.
  - Use of prefilled syringes show a decrease in drug waste vs self-filled syringes

Thinking Like an Engineer

POST-TEST QUESTIONS - FORTIER

1. The Institute of Medicine is against Human Factors Engineering as a way to improve systems and performance.
    a. True
    b. False

2. Human Factors Engineering helps to improve
    a. Quality
    b. Satisfaction
    c. Efficiency
    d. Comfort
    e. All of the Above

3. Which of the following are human factors engineering principles were utilize in this study?
    a. Proactive risk assessment
    b. Work system analysis
    c. Identify system vulnerabilities
    d. All of the Above

4. The proactive risk assessment determined the severity of the following system vulnerabilities, except?
    a. Disruptiveness
    b. Provider error
    c. Occurrence
    d. Severity to patient

5. The implementation of pre-filled medications syringes improved human factors medication safety in the OR by:
    a. Reducing the number of workflow steps around the administration of medications in the OR
    b. Increasing the number of workflow steps around the administration of medications in the OR
    c. Significantly reducing the severity of system vulnerabilities within the medication use process in the OR
    d. A and C
    e. None of the above

Hot Topics: Provider Status, Workforce and Accreditation Update

Janet A. Silvester, Pharm.D., MBA, FASHP
Vice-President, Accreditation Services
ASHP

Conflicts of Interest

I have no conflicts of interest to disclose

Overall Learning Objectives for Pharmacists

- Explain provider status and steps required for grassroots activities to impact legislation.
- Describe the results of the 2014 National Pharmacy Workforce Study and the priorities of the Pharmacy Workforce Center.
- Address issues related to accreditation of both pharmacy residency programs and the new collaboration between ASHP and ACPE for accredited technician education and training programs.
- Review new resources available for implementation of the new PGY1 residency standards.
- Discuss the alignment of the PTCB 2020 policies with ASHP policies and the goals of the ASHP/ACPE collaboration on technician education and training.

Overall Learning Objectives for Pharmacy Technicians

- Describe what provider status is.
- Describe the results of the 2014 National Pharmacy Workforce Study and the priorities of the Pharmacy Workforce Center.
- Address issues related to accreditation of both pharmacy residency programs and the new collaboration between ASHP and ACPE for accredited technician education and training programs.
- Discuss the alignment of the PTCB 2020 policies with ASHP policies and the goals of the ASHP/ACPE collaboration on technician education and training.
- Review key requirements in the technician program standards.

PROVIDER STATUS

Discussion Points

- Describe what provider status is.
- Describe why amending the Social Security Act to recognize pharmacists as Medicare Part B providers is important for patients.
- Explain current legislation, and the efforts of ASHP and the Patient Access to Pharmacists' Care Coalition to facilitate amending the Social Security Act to recognize pharmacists as Medicare Part B providers.
- Describe grassroots efforts that individual pharmacists and ASHP state affiliates need to take to achieve recognition as Medicare Part B providers in the Social Security Act.

Provider Status is About Patients

Achieving provider status is about giving patients access to care that improves:

- Patient safety
- Healthcare quality
- Outcomes
- Decreases costs

Who Has Provider Status?

- Physicians
- Nurse practitioners
- Physician assistants
- Certified nurse midwives
- Psychologists
- Clinical social workers
- Certified nurse anesthetists
- Speech-language pathologists
- Audiologists
- Registered dietitians
- Physical therapists

What is Provider Status?

- Being listed in section 1842 or 1861 of the Social Security Act as a supplier of medical and other health services.
- Becoming a "provider" in the Social Security Act means:

  Pharmacists can participate in Part B of the Medicare program and bill Medicare for services that are within their state scope of practice to perform.

Why is provider status important for pharmacists?

- Pharmacists are not recognized under the Social Security Act as health care providers
- New payment systems emphasize quality and outcomes
  - Accountable Care Organizations
  - Medical Homes
- Social Security Act determines eligibility

What is H.R. 592/S. 314?

- A bipartisan bill that would amend the Social Security Act to recognize pharmacist services to patients under Medicare Part B in medically underserved communities
  - Applies to licensed pharmacists working within their state's scope of practice laws
  - Establishes a mechanism of pay for pharmacist provider services under Medicare Part B
  - Reintroduction of H.R. 4190, a bill which was introduced by Representatives Guthrie (R-KY), Butterfield (D-NC) and Young (R-IN) in the House of Representatives on March 11, 2014
  - That bill had 123 bipartisan cosponsors include two physicians: Reps. Roe (R-TN) and Bera (D-CA).

H.R. 592/S. 314 Specifics

- Amends Section 1861(s)(2) of the Social Security Act to include:
  - Pharmacists services furnished by a pharmacist licensed by State law
    - *Which the pharmacist is legally authorized to perform in the State*
  - In setting located in/for and defined in federal law:
    - *Medically underserved area*
    - *Medically underserved population*
    - *Health professional shortage area*

Why does H.R. 592/S. 314 only cover medically underserved communities?

- Help meet unmet health care needs
  - Increase access
  - Improve quality
  - Decrease costs
- Follow similar successful paths taken by other health care professionals to gain provider status

What are medically underserved communities?

- Medically Underserved Areas
- Medically Underserved Populations
- Health Professional Shortage Areas

Medically Underserved Communities, a Closer Look

- Medically Underserved Areas:
  - Medically Underserved Areas (MUAs) may be a whole county or a group of contiguous counties, a group of county or civil divisions or a group of urban census tracts in which residents have a shortage of personal health services.

Medically Underserved Areas, MUA

- Medically Underserved Areas, how are they calculated?
  - Uses Index of Medical Underservice (IMU), scale 0-100; 62 or less is MUA
  - Uses 4 variables to calculate:
    - *Ratio of primary care physicians per 1,000 people*
    - *Infant mortality rate*
    - *Percent of population below poverty*
    - *Percent of population 65 or older*

Medically Underserved Populations, MUP

- Medically Underserved Populations
  - Uses same IMU but applies it to population groups
  - Medically Underserved Populations (MUPs) may include groups of persons who face economic, cultural or linguistic barriers to health care
  - Typically low income or Medicaid eligible

Exceptional Designations

- May not fit the criteria of MUA/MUP
- Governor can make the request for an exception
- Based upon “unusual Local Conditions”

Patient Access to Pharmacists' Care Coalition (PAPCC)

- Formed January 2014
- Group of 30 organizations representing patients, pharmacists, pharmacies and other interested stakeholders
- Drafted H.R. 4190 to expand medically-underserved patients' access to pharmacist services consistent with state scope of practice
- Facilitated reintroduction

Patient Access to Pharmacists' Care Coalition (PAPCC)

Current Members

- ASHP
- APhA
- AACP
- ASCP
- HLC
- IACP
- HOPA
- NCPA
- NACDS
- NASPA
- Walgreens

Current Members

- Albertson's
- Amerisource Bergen
- Bi-Lo Pharmacy
- Cardinal Health
- CVS Caremark
- Food Marketing Institute
- Fred's Pharmacy
- Fruth Pharmacy
- Kroger
- National Center for Farmworker Health
- Omnicell
- Rite Aid
- Safeway Inc.
- SuperValu Pharmacies
- Target
- Thrifty White Pharmacy
- WalMart
- Winn-Dixie

Why Do Pharmacists Want Provider Status When Fee-For-Service is Going Away?

- Over the next 5 or more years traditional fee-for-service will be phased out and replaced with new payment systems that emphasize quality, outcomes, and team-based patient care.
- Pharmacists recognize that traditional fee-for-service is not the model of the future, and we view ourselves as members of interprofessional teams collaborating with physicians, nurses, and others throughout the continuum of care.
- However, the Social Security Act (SSA) remains the *reference point* for which practitioners are eligible to participate in current, new, and emerging delivery systems and payment models (see ACO example).
- Therefore, for pharmacists to fully participate in current and emerging delivery and payment systems, pharmacists need to be listed in the SSA along with other providers.

State Scope of Practice

- Provider status at the federal level will only allow a pharmacist to participate in the Medicare program and to bill for services that are within their state scope of practice to perform (the same is true for physicians and other providers)
- State scope of practice will determine what pharmacists can actually do in terms of the provision of service
- As provider status at the federal level is achieved continued efforts by states to ensure scope of practice for pharmacists is sufficiently robust will be vital

Status Update

- As mentioned earlier, HR 4190 had 123 cosponsors at the end of the 113 Congress
  - Reintroduced in 2015 as H.R. 592/S. 314.
  - The strategy for 2014, late in the Congressional session, was to build support for this legislation by getting as many cosponsors as possible, for quick re-introduction in 2015
  - 2015 will see Coalition pushing for cosponsors; House and Senate hearings and committee consideration

Status Update

- H.R. 592 Co-Sponsors (as of August 11, 2015)
  - 185
- SB 314
  - 28

ASHP Students Visit Capitol Hill

Questions (both House and Senate)

- How qualified are pharmacists to provide these services?
  - Pharmacists are very well-qualified to provide these services.
  - The legislation would enable pharmacists to provide services they already are authorized to provide under state law, and prepared to provide through their extensive professional education.
- What will this cost Medicare?
  - We believe that pharmacist provided patient care will lead to better health outcomes and in many cases reduce costs – care transitions is a good example
  - However, we also know that the Congressional Budget Office often does not score (assign a price tag) bills with offsets

Questions (both House and Senate)

- Who decides what services pharmacists could provide?
  - The services pharmacist can provide would still be set by state scope of practice laws and regulations, just as is done today. This bill does nothing to change such regulations; it simply permits Medicare to pay pharmacists for delivering care to patients that fits within the regulations of each state.
- Is there precedence for this type of legislation?
  - Yes. Longstanding law has enabled nurse practitioners and physician assistants to be reimbursed by Medicare for providing Part B services. The law originally limited such reimbursement to cases when delivered to underserved rural populations, but such restrictions were removed in the late 1990s.

Questions (both House and Senate)

- Does this proposal seek to have pharmacists fill the role of doctors?
  - No. It simply seeks to have pharmacists help address acute shortages and to be eligible for payment for services they are already allowed to provide under their respective state licenses.
  - The intention is not to displace doctors; rather it is to help doctors in medically underserved communities so physicians can focus their time and attention on those patients who need it most.
  - Just like NPs, PAs and others are part of the large healthcare ecosystem and seen as part of the interdisciplinary care team, so to should be pharmacists.
  - To date, no physician groups have come out opposed to the bill
- Is this collaborative?
  - Yes, full ACO, medical home or other integrated effort can only be achieved with provider status—all roads lead back to being listed

Does H.R. 592/S. 314 require pharmacists to be residency trained, Board certified, or possess other credentials?

A: No, just like other health care professionals who are recognized as providers, H.R. 592/S. 314 requires pharmacists to be licensed by a state, and the state legislature and board of pharmacy, health care organizations, and private health plans determine what credentials are required to perform certain services (e.g., CA: "Advanced Practice Pharmacist" NM: "Pharmacist Clinician").

Most hospitals and health systems have a process to credential and privilege pharmacists based on the type and level of patient care services they provide.

Why isn't ASHP calling for credentialing requirements given that ASHP started pharmacy residencies and supports Board certification?

A: ASHP supports these concepts, but they do not belong in federal law.

Instead, credentialing and privileging requirements are for states and organizations to decide through state pharmacy practice acts, private health plan requirements, and credentialing and privileging requirements by hospitals and health systems.

Key Takeaways

- Key Takeaway #1
  - H.R. 592/S. 314 would grant provider status to pharmacists practicing in medically underserved areas, or populations
- Key Takeaway #2
  - Virtually all of the pharmacy profession is on board
- Key Takeaway #3
  - Must continue pushing, addressing the cost questions and grow the coalition

The Path Forward

- Reintroduction of the House bill in 2015
- Introduction in Senate
- Ramp up grassroots efforts
- Secure additional cosponsors
- Push for committee hearings
- Grow the coalition
- Educate the public on value of pharmacists' care

Keys to Success

- Pharmacy must maintain unified stance
- Grassroots efforts must be robust
  - 270,000 licensed pharmacists in the U.S. can have a huge impact
- Focusing on the unmet need, new Medicare enrollees
- Election results do not change our message

How can you support H.R. 592/S. 314?

- Ask your legislators to cosponsor the bill
- Encourage colleagues to get involved.

http://www.ashp.org/menu/Advocacy/GrassrootsNetwork

- Participate in the ASHP PAC

http://www.ashp.org/menu/Advocacy/ASHPPAC

Specific State Affiliate and Individual Actions

- Recruit individual health system support of H.R. 592/S. 314
- Solicit other state-level health profession organization support of H.R. 592/S. 314:
  - Medical specialties
  - Nurse practitioners
  - Physician assistants
- Visit elected officials/staff in Washington DC or district office

State Provider Status

- ASHP to work with state affiliates to move state legislation to recognize pharmacists as providers
- Expanding state scope of practice so pharmacists can practice at the top of their license
- State Medicaid, private payers

Recent Report

The Expanding Role of Pharmacists in a Transformed Health Care System

National Governors Association

January 13, 2015

http://www.nga.org/files/live/sites/NGA/files/pdf/2015/1501TheExpandingRoleOfPharmacists.pdf

Conclusions

- The patients we serve will benefit greatly when pharmacists are recognized by Medicare.
- Pharmacy is better positioned and closer than ever to being federally recognized as providers.

Conclusions

- It will take unprecedented levels of grassroots engagement by individual pharmacists and state affiliates to make it happen.
- Students can and should play a major role
- ASHP is here to help you every step of the way.

True or False

- **True or False**: Being listed in the Social Security Act as Medicare Part B providers will expand pharmacists' scope of practice.
- **True or False**: Medically underserved areas include both urban and rural parts of the United States.
- **True or False**: The Pharmacy and Medically Underserved Areas Enhancement Act (H.R. 592 and S. 314) prohibits states, health insurers, and healthcare organizations from requiring pharmacists to have additional training or credentials such as residency training and/or Board certification.
- **True or False**: A key goal of The Pharmacy and Medically Underserved Areas Enhancement Act (H.R. 592 and S. 314) is to help fulfill and unmet need in the healthcare delivery system.
- **True or False**: The healthcare payment system is moving to a value-based (pay for outcomes and performance) versus volume-based (fee-for-service) model.

National Pharmacist Workforce Study 2014

Discussion Points

- Describe the priorities of the Pharmacy Workforce Center
- Describe the results of the 2014 National Pharmacy Workforce Study
- Recognize trends presented in patient care and pharmacists activities

Pharmacy Workforce Center, Inc.

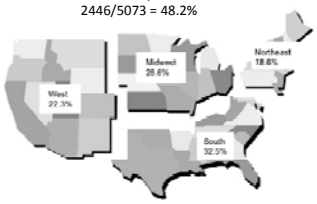
- American Association of Colleges of Pharmacy (AACP)
- American College of Clinical Pharmacy (ACCP)
- American Pharmacists Association (APhA)
- American Society of Health-System Pharmacists (ASHP)
- Board of Pharmacy Specialties (BPS)
- Bureau of Health Workforce (BHW)
- National Alliance of State Pharmacy Associations (NASPA)
- National Association of Boards of Pharmacy (NABP)
- National Association of Chain Drug Stores (NACDS) Foundation
- National Community Pharmacists Association (NCPA),
- Pharmacy Technician Certification Board (PTCB)

Presentation Overview

- Overview of the National Pharmacist Workforce Studies
- Results of the 2014 National Pharmacist Workforce Study
- Trends in Patient Care and Other Activity Pharmacists
- Conclusions

Response Distribution by Region

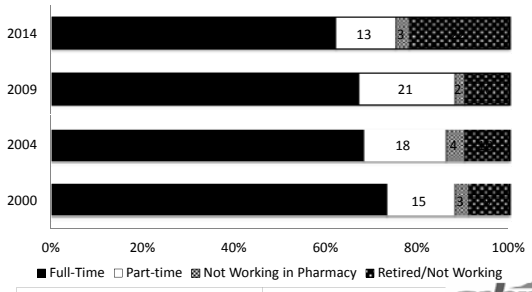
Overall Response Rate:
2446/5073 = 48.2%



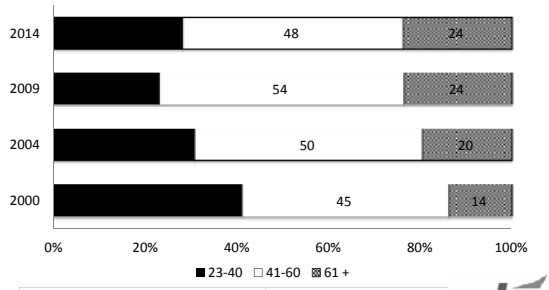
Respondents
Northeast (n=458)
South (n=793)
Midwest (n=649)
West (n=546)

Non-Respondents
Northeast (n=536)
South (n=963)
Midwest (n=553)
West (n=578)

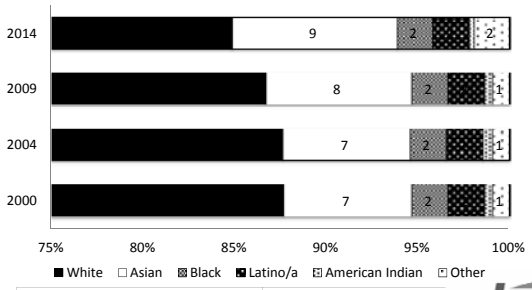
Work Status of Licensed Pharmacists



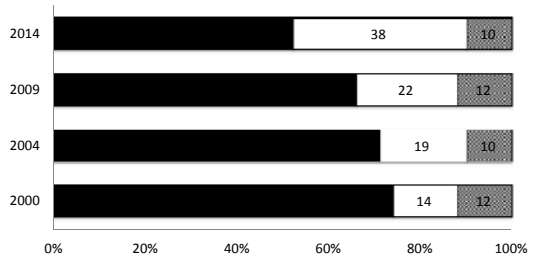
Age of Licensed Pharmacists



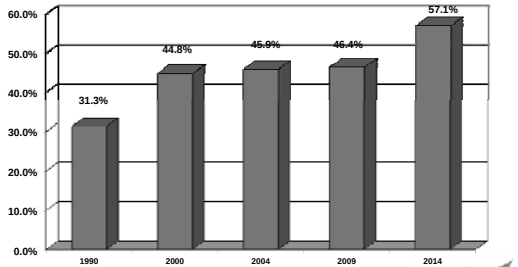
Race/Ethnicity of Licensed Pharmacists



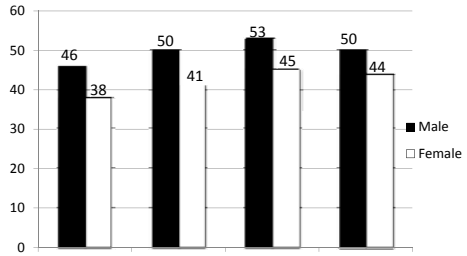
Highest Degree Earned by Licensed Pharmacists



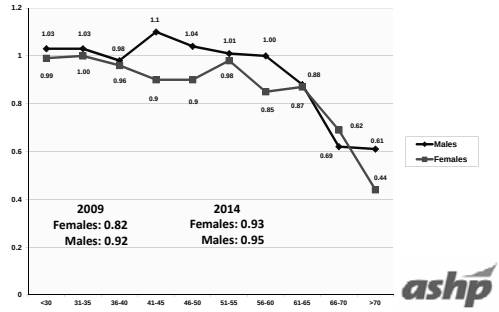
Percent of Actively Practicing Pharmacists that are Female: 1990-2014



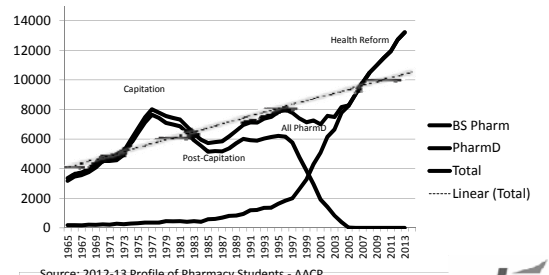
Mean Age by Gender: 2000-2014



Mean Full-Time Equivalent (FTE) Contributions by Age & Gender



Pharmacy Degrees Conferred as First Professional Degree (1965 – 2013)



Source: 2012-13 Profile of Pharmacy Students - AACP

Practice Settings

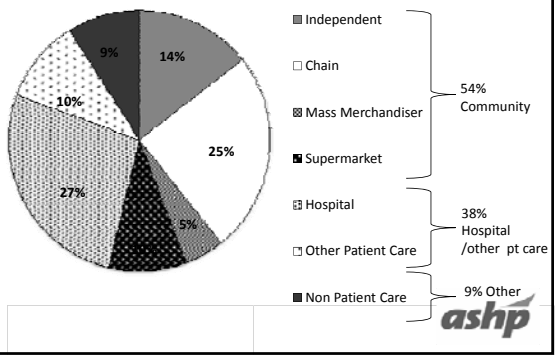
Community: Independent, Chain, Mass Merchandiser, Supermarket

Hospital: In-patient or out-patient hospital settings

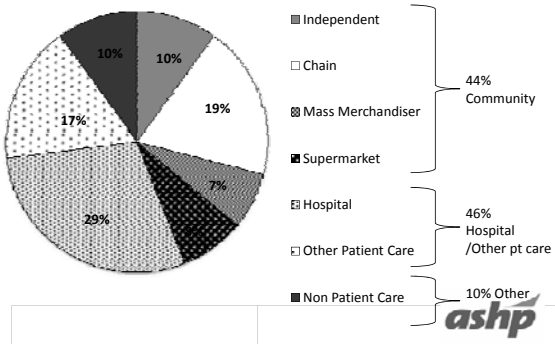
Other Patient Care Settings: nursing home, long term care, HMO, nuclear, clinic-based, mail service, central fill, home health/infusion, and specialty pharmacies

Other Non-Patient Care Settings: pharmacy benefit administration, academic, government administration, pharmaceutical industry, consulting, professional associations, and other organizations that were not licensed as a pharmacy

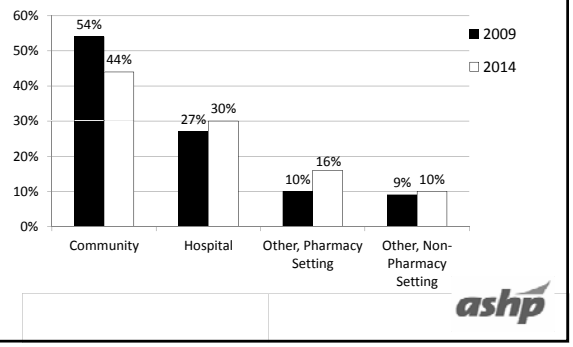
Actively Practicing Pharmacists' Employment Setting: 2009



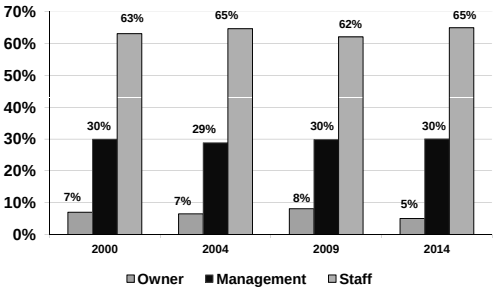
Actively Practicing Pharmacists' Employment Setting: 2014



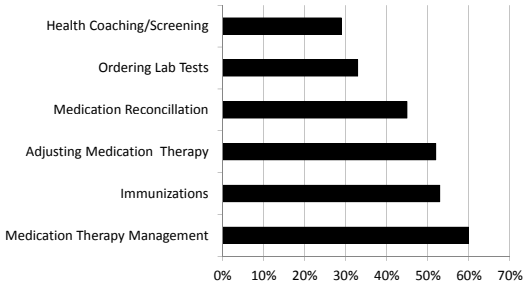
Practice Settings 2009 and 2014



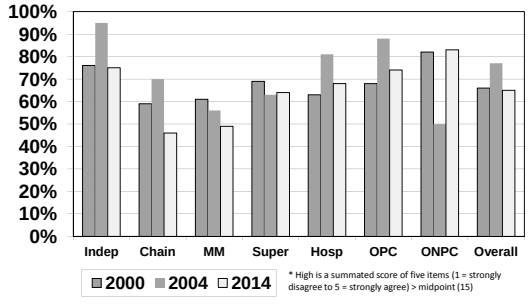
Position Type 2000, 2004, 2009,2014



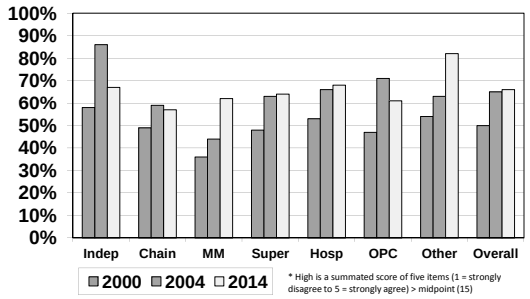
Services Offered At Practice Site: 2014



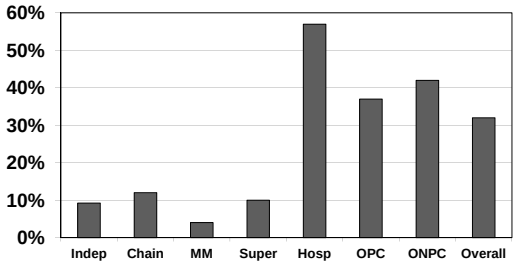
Proportion of Full-time Pharmacists with High* Job Satisfaction by Practice Setting: 2000, 2004, & 2014



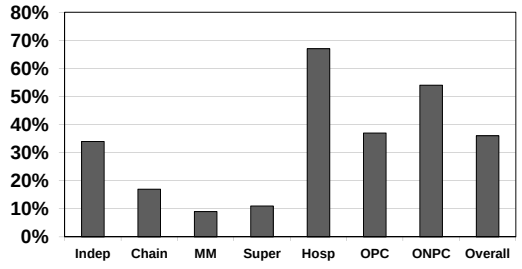
Proportion of Full-time Pharmacists with High* Professional Commitment by Practice Setting: 2000, 2004 & 2014



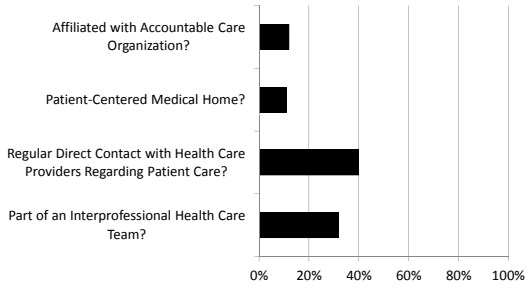
Proportion of Pharmacists Who Are Part of an Interprofessional Health Care Team Providing Patient Care by Practice Site: 2014



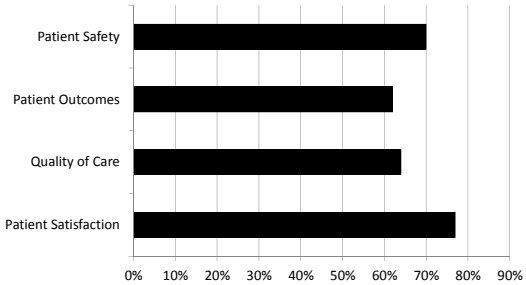
Proportion of With Regular Direct Contact with Other Health Care Providers Regarding Patient Care Activities by Practice Site: 2014



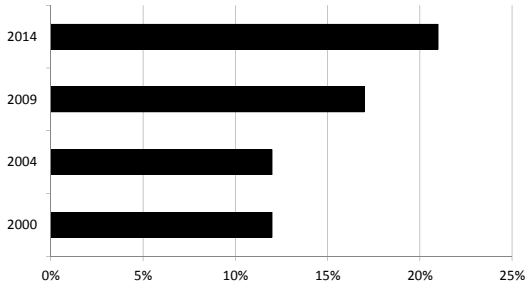
Participation in Contemporary Healthcare Activities 2014 (all pharmacy settings)



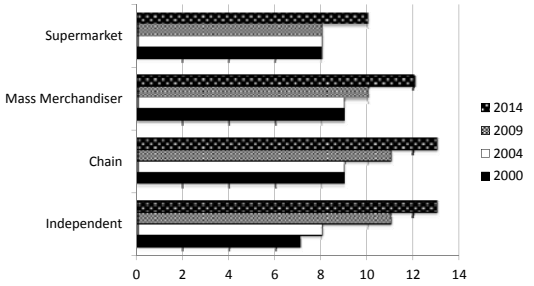
Activities Monitored or Evaluated in Your Work Place 2014



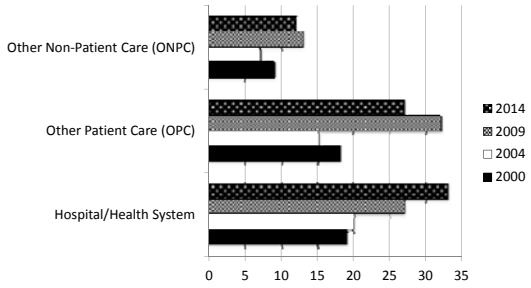
Percent Time Spent in Patient Care: 2014



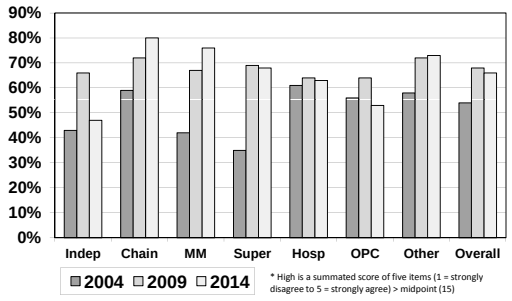
Percentage of Time Spent in Patient Care by Community Pharmacists: 2000-2014



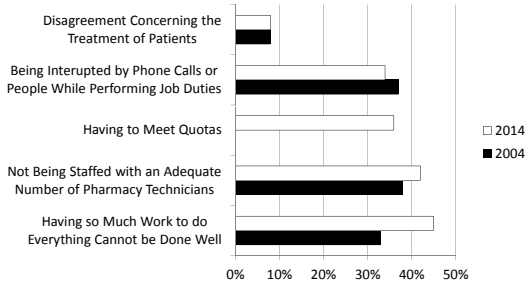
Percentage of Time Spent in Patient Care Activities by Hospital, Other Patient Care and Non-Patient Pharmacists: 2000-2014



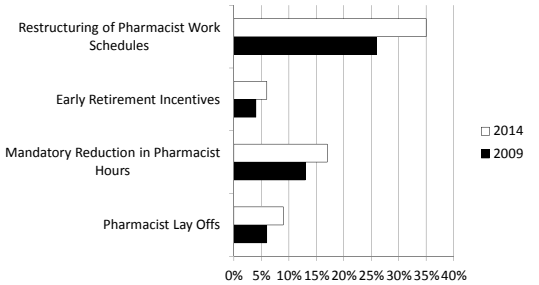
Ratings of Workload as High or Excessively High* by Work Setting: 2004, 2009 & 2014



Pharmacists' Ratings of Highly Stressful Events: 2004 & 2014



Workplace Labor Reductions: 2009 & 2014



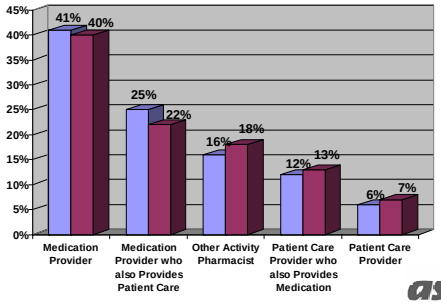
Work Activities

- **Patient Care Services Not Associated with Medication Provision**: assessing and evaluating patient medication-related needs, monitoring and adjusting patients' treatments to attain desired outcome, and other services designed for patient care management

- **Patient Care Services Associated with Medication Provision**: preparing, distributing, and administering medication products, including associated consultation, interacting with patients about selection and use of over-the-counter products, and interactions with other professionals during the medication dispensing process

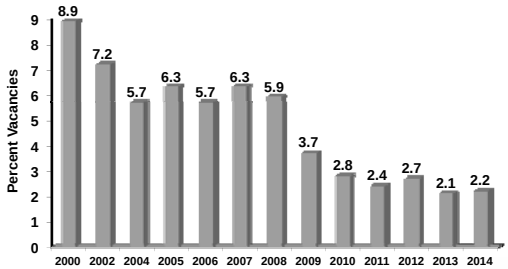
ashp

Proportion of U.S. Pharmacists by Segment in Descending Size
(2009 data in lighter tone and 2014 data in darker tone)



Hospital Pharmacist Vacancy Rates

ASHP Surveys show peak pharmacist shortage in 2000, with decline in vacancy rates since

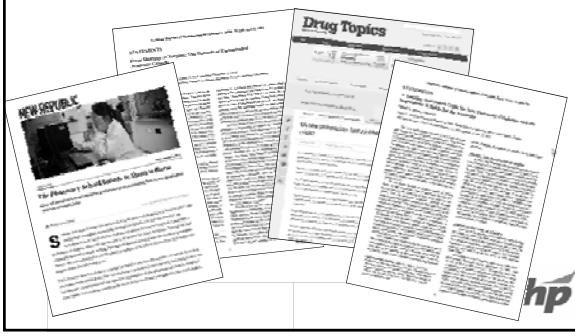


Pharmacy Director perceptions of availability

Type of Staff	*2014*		*2008*
Management			
Shortage	68%		90%
Balanced	29%		9%
Excess	3%		1%
Clinical Coordinator			
Shortage	44%		72%
Balanced	46%		23%
Excess	10%		5%
Clinical Specialist			
Shortage	37%		70%
Balanced	45%		23%
Excess	18%		7%
Entry-level Frontline R.Ph.			
Shortage	10%		75%
Balanced	35%		23%
Excess	55%		2%
Experienced Frontline R.Ph.			
Shortage	41%		89%
Balanced	40%		10%
Excess	19%		1%

2008-2014 ASHP National Survey

A lot of press on possible surplus of pharmacists



National Center for Health Workforce Analysis

Health Workforce Projection: Pharmacists

- Released December 2014
- Uses HRSA Health Workforce Simulation Model
- Accounts for changes in supply (new entrants, retirement, hours worked patterns)
- Accounts for changes in demand (ACA Rx coverage, population demographics, demand for prescription medications)
- Does not account for future growth in patient care services/roles of pharmacists, provider status, changes in part D coverage

HRSA Health Resources and Services Administration

Projected Supply for Pharmacists: 2012-2025

FACTOR	SUPPLY
Estimated supply in 2012	264,100
Total supply growth	2012-2025: 91,200 (35%)
New entrants	160,500
Changing work patterns	(61,340)
Attrition	7,960
Projected supply, 2025	355,300

Health Workforce Projections: Pharmacists; National Center for Health Work Force Analysis: May 2015

Projected Demand for Pharmacists: 2012-2025

FACTOR	DEMAND
Estimated demand, 2012	264,100
Total demand growth 2012-2025	42,300 (16%)
Changing demographics impact	35,800 (14%)
ACA insurance coverage impact	6,500 (2%)
Projected demand, 2025	306,400
Adequacy of supply, 2025	355,300 - 306,400 = **+48,900**

Health Workforce Projections: Pharmacists; National Center for Health Work Force Analysis: May 2015

Factors influencing the "supply"

- The number of pharmacy graduates (big, long term)
- State of the economy (big, short term)
  - ❖ Impact on the number of pharmacists retiring
  - ❖ Impact on part time to full time shift
- The gender mix (slowly growing)
- The number of international pharmacy graduates (minimal)

Factors influencing the "demand"

- The demand by employers
  - ❖ State of the economy
  - ❖ Prescription volume
  - ❖ NEW roles of pharmacists
  - ❖ Changing role of pharmacists
  - ❖ Changing role of pharmacy technicians
  - ❖ Impact of automation and technology

Conclusions

- We are living in dynamic times as a health care profession
- Pharmacists have taken a larger role in health care delivery by increasing access for patients through provision of expanded service offerings
- But, how do we determine the appropriate supply of and demand for pharmacists?
- Continued monitoring of the pharmacist workforce is crucial so the pharmacy profession is able respond to the rapidly changing landscape

ASHP Accreditation Update

Discussion Points

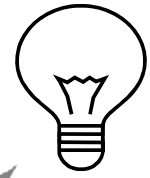
- Identify key changes in the revised PGY1 residency standard
- Review new resources available for implementation of the new PGY1 residency standards
- Describe the 2014 residency match statistics and results

New PGY1 Standards: Background

- New PGY1 Standards approved 2014
- Major goals of revision:

  Update and streamline while maintaining quality

Highlights



Same purpose statement for all PGY1 residency programs

From the Standard

PGY1 Program Purpose:

PGY1 pharmacy residency programs build on Doctor of Pharmacy (Pharm.D.) education and outcomes to contribute to the development of clinical pharmacists responsible for medication-related care of patients with a wide range of conditions, eligible for board certification, and eligible for postgraduate year two (PGY2) pharmacy residency training.

Goals and objectives streamlined and reduced in number

	2005	2014
❖ **Competency areas / Outcomes**	**6**	**4**
❖ **Goals**	**23**	**9**
❖ **Objectives**	**66**	**33**

RPD may delegate some authority

- ❖ 1.1: The RPD or designee must evaluate qualification of applicants…
- ❖ 3.4.a.(2): The results of residents' initial assessments must be document by the program director or designee in each resident's development plan…
- ❖ 3.4.d.(1) Each resident must have a resident development plan documented by the RPD or designee.
- ❖ 3.4.d.(2) On a quarterly basis, the RPD or designee must assess residents' progress and determine if the…plan needs to be adjusted.
- ❖ 3.5.b: The RPD or designee must develop and implement program improvement activities…
- ❖ 4.1.c: The RPD may delegate, with oversight, to one or more individuals…administrative duties/activities for the conduct of the residency program.

Preceptor qualifications include more options and include teaching and precepting skills

4.8 Preceptor Qualifications

- 4.8.a. Ability to precept residents… by use of clinical teaching roles…
- 4.8.b. Ability to assess residents' performance

Preceptor-in-training role added

4.9.a. Pharmacists new to precepting who do not meet the qualifications for residency preceptors…must:

(1) be assigned an advisor or coach who is a qualified preceptor; and,

(2) have a documented preceptor development plan to meet the qualifications for becoming a residency preceptor within two years.

New Training Update: *Residency Program Design and Conduct*

- ***New online recorded webinars***
- ***New workshops***

NEW! Recorded Webinars Available Online

- Recorded webinars:
  - **Design of PGY1 residency programs**
    - **PGY1 residency program purpose**
    - **PGY1 competency areas, goals, and objectives**
    - **Residency program structure**
    - **Learning experience descriptions**
  - **The four preceptor roles**
  - **Evaluation**
  - **Residents' development plans**
  - **Continuous residency program improvement**

New workshops: National Pharmacy Preceptors Conference and the Midyear

- Residency Program Design and Conduct (RPDC) Workshops
  - **Instructors answer your questions**
  - **Apply information to your program**
  - **Bring your program's materials for individualized feedback**
  - **Peer sharing**

More-see Accreditation webpage "Additional Accreditation Resources," "Accreditation-Related Online Education":

- Resident's Learning Activities: Understanding Learning Taxonomies and Levels - New (2014) Standards
- Customizing the Resident Training Plan (2005 Standard)
- All About Purpose Statements (2005 Standard)
- Anatomy of the Outcomes, Goals and Objectives (2005 Standard)
- Level With Your Resident: Learning Taxonomies and Levels (2005 Standard)
- Starring Roles: The Four Preceptor Roles and When to Use Them (2005 Standard)
- Responding to an ASHP Accreditation Survey Report

Coming soon:
Additional programs on the new standards

AJHP: Residents Edition

- Expands publication opportunities for residents
- Further engages residents, preceptors and residency program directors in *AJHP* and ASHP

AJHP: Residents Edition

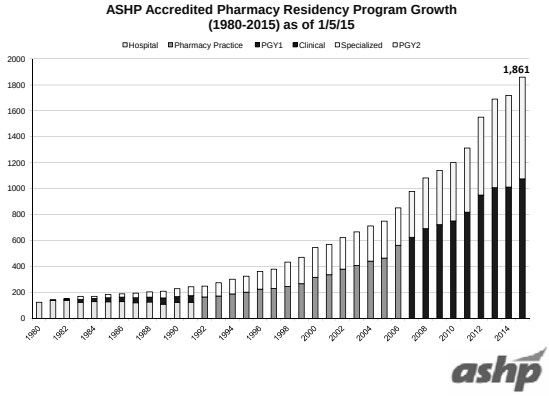
- Quarterly, online supplement to *AJHP*
- Member benefit
- Founders Bryan McCarthy and David Reardon to become *AJHP* contributing editors, pharmacy resident publications
- Coming … June 2015

ASHP Match 2015

Pharmacy Residencies

MATCH

pharmacists advancing healthcare

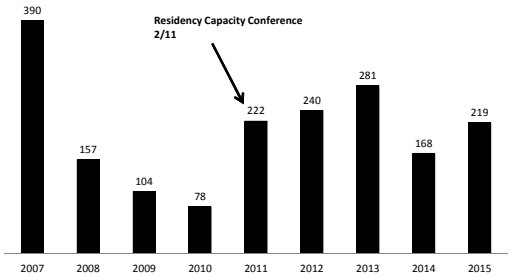


Program Count by Category as of 7/2015

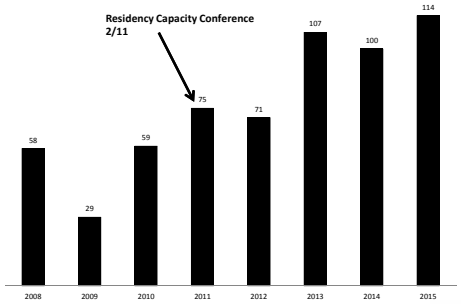
Category	Sub Category	Programs
PGY1		
	Pharmacy	926
	Community Pharmacy	122
	Managed Care Pharmacy	45
PGY1 & PGY2 Combined		
	PGY1 Pharmacy & PGY2 Health-System Pharmacy Administration/MS	37
	PGY1 Pharmacy & PGY2 Pharmacotherapy	12
	PGY1 Pharmacy & PGY2 Health System Pharmacy Administration	7
	PGY1 Pharmacy & PGY2 Pharmacy Informatics	1
	PGY1 Community Pharmacy & PGY2 Community Pharmacy Administration/MS	1
	Pharmacotherapy	1
	PGY1 Pharmacy & PGY2 Specialty Pharmacy	1
	PGY1 Pharmacy & PGY2 Specialized Area: Medication Systems & Operations	1

PGY2	Critical Care Pharmacy	116
	Ambulatory Care Pharmacy	102
	Oncology Pharmacy	88
	Infectious Diseases Pharmacy	72
	Psychiatric Pharmacy	51
	Pediatric Pharmacy	47
	Solid Organ Transplant Pharmacy	35
	Internal Medicine Pharmacy	34
	Health-System Pharmacy Administration	33
	Emergency Medicine Pharmacy	29
	Cardiology Pharmacy	28
	Pharmacy Informatics	20
	Geriatric Pharmacy	18
	Drug Information	13
	Palliative Care/Pain Management Pharmacy	11
	Medication-Use Safety	9
	Pharmacotherapy	5
	Pharmacy Outcomes/Healthcare Analytics	4
	Transitions of Care	4
	Pharmacogenetics	3
	HIV Pharmacy	3
	Nutrition Support Pharmacy	2
	Neurology	1
	Nephrology Pharmacy	1
	Nuclear Pharmacy	1
	Family Medicine	1
	Health System Corporate Pharmacy Administration	1
	Corporate Pharmacy Leadership	1

PGY1 positions added to Match each year



PGY2 positions added to Match each year



2015 versus 2014 match

- 5% increase in PGY1 applicants
- 6.5% increase in # of filled PGY1 positions

  (total = 2,640 PGY1 positions filled)

- 7% increase in PGY2 applicants
- 12.5% increase in filled PGY2 positions

  (total = 794 PGY2 positions filled - includes 297 early commits)

Applicants view on March 20, 2015

3,308 applicants match day

2811 PGY1 matched

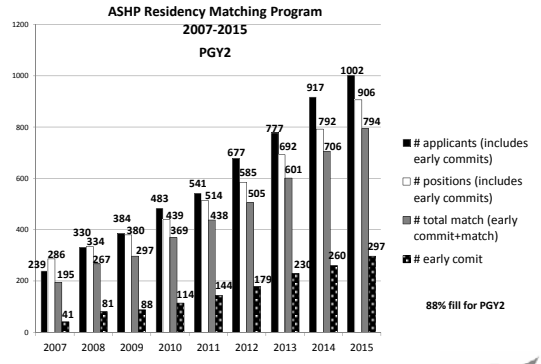
497 PGY2 match & 297 Early Commit = 794 PGY2

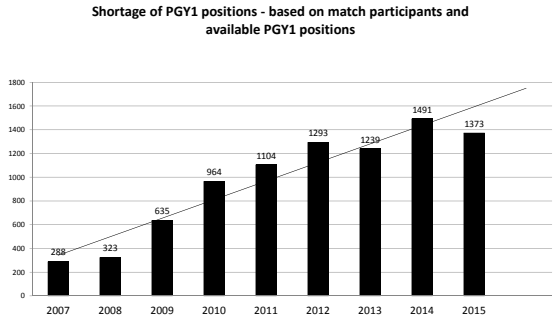
1,755 applicants unmatched

1,547 PGY1 & 208 PGY2

382 unfilled positions

ashp pharmacists advancing healthcare





Percentage of Graduates seeking Residency

Year	Graduates	Participants in PGY1 Match	Percentage of Grads in Match
2006	10,199	1,356	13.3%
2007	10,282	1,898	18.5%
2008	11,127	2,092	18.8%
2009	11,516	2,501	21.7%
2010	11,487	2,898	25.2%
2011	12,346	3,257	26.4%
2012	13,163	3,706	28.2%
2013	13,207	3,933	30%
2014	13,838	4,142	30%
2015 (Knapp, et al)	13,856		
2016	14,923	**3,925 (26%), 4,477 (30%)**	

We will need to grow positions by 56% or by 1,615 positions by 2016

What is ASHP doing to address shortage?

- 2/11 Capacity Conference
- Highlighting programs with expansion at Meetings
- New training programs – including web based
  - How To Start a Residency
  - How To Expand Existing Residencies
- National Pharmacy Preceptors Conference (NPPC)Yearly
- Preceptor Skills Resource Page
- On line education about accreditation standard
- PR – Video
- New streamlined Accreditation Standards
- Guidance documents for PGY1 standard
- New AJHP residents edition for journal

Pharmacy Technician Program Accreditation

Discussion Points

- Describe the new collaboration between ASHP and ACPE for accredited technician education and training programs
- Review key requirements in the technician program standards
- Discuss the alignment of the PTCB 2020 policies with ASHP policies and the goals of the ASHP/ACPE collaboration on technician education and training

Pharmacy Technician Accreditation Commission (PTAC)

- Formed through ASHP/ACPE collaboration
- PTAC recommendations require approval of both ASHP and ACPE Boards
- Transition occurred in 2014 and joint accreditation decision recommendations to ASHP and ACPE Boards began in June 2015
- PTAC adopted newly approved ASHP standards, guidelines, procedures
- Programs now transitioning from ASHP-accredited to ASHP/ACPE accredited status

Pharmacy Technician Accreditation Commission

- Angela Cassano, PharmD, BCPS, FASHP – President Pharmfusion Consulting, LLC, Midlothian, VA
- Michael Diamond, MSc – President World Resources Chicago Evanston, IL
- Jacqueline Hall, RPh, MBA – Pharmacy Manager Walgreens, New Orleans, LA
- Jan Keresztes, PharmD – South Suburban College, South Holland, IL
- Barbara Lacher, BS, RPhTech, CPhT – North Dakota State College of Science Wahpeton, ND
- Douglas Scribner, CPhT, Med –Central New Mexico Community College, Albuquerque, NM
- John Smith, EdD – Corinthian Colleges, Inc., Santa Ana, CA
- Donna Wall, PharmD – Indiana University Hospital, Indianapolis, IN
- LiAnne (Webster) Brown, CPhT – Richland College, Dallas, TX
- Lisa Lifshin, B.S.Pharm, ASHP, Secretary
- Board Liaisons

  Anthony Provenzano, PharmD – ACPE Board Liaison, New Albertson's, Inc. Chicago, IL

  Kelly Smith, PharmD – ASHP Board Liaison, University of Kentucky College of Pharmacy, Lexington, KY

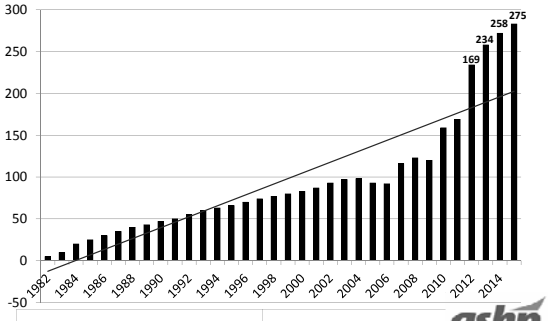
Functions of PTAC

- **Reviewing applications** for accreditation and **evaluations** of pharmacy technician education and training programs,
- Recommending accreditation actions to the **ASHP** Board of Directors and the **ACPE** Board of Directors
- Making recommendations to the Boards regarding standards, policies and procedures, and other matters related to PTAC's activities and services
- Assisting in **strategic planning** in matters related to pharmacy technician education and training accreditation.

Functions of PTAC cont.

- Identifying potential activities and collaborative opportunities
- Soliciting and receiving input and advice from other stakeholders to obtain broad perspectives to help assure the quality, validity and improvement of PTAC's accreditation standards, activities and services.

ASHP-Accredited Pharmacy Technician Training Programs



Ultimate Goal of ASHP-ACPE Collaboration

→ A better **qualified** and trained workforce

→ Improved patient **safety**

→ Greater **consistency** in technician workforce

→ Accreditation standards updated as needed to stay consistent with expanding roles and responsibilities of technicians

→ Greater ability to **delegate** technical tasks from pharmacists to technicians

→ Less turnover in pharmacy technician positions

Accreditation Standards for Pharmacy Technician Training Programs

- New accreditation standards approved by ASHP and ACPE
  - ❖ Six components to new standard:
    Administration, Program Faculty, Education & Training, Students, Evaluation & Assessment, Graduation & Certificate
  - ❖ Knowledge areas mapped to PTCB task analysis
  - ❖ Changes to program director/experiential site requirements
  - ❖ Hours requirement revised

Faculty (Standard 2)

Program Director

- Must be Pharmacist or Pharmacy Technician
- Pharmacy Technician
  - ❖ Minimum – working on Associates Degree or State Teaching Certificate

Experiential Site coordinator

- Individual working at the experiential training site, coordinating activities
- Liaison to Program Director

Std. 3.6: Education and Training Goals (n= 45)

- Personal/Interpersonal Knowledge and Skills (n=7)
- Foundational Professional Knowledge and Skills (n=9)
- Processing and Handling of Medications and Medication Orders (n=11)
- Sterile and Non-Sterile Compounding (n=3)
- Procurement, Billing, Reimbursement and Inventory Management (n=4)
- Patient- and Medication-Safety (n=6)
- Technology and Informatics (n=1)
- Regulatory Issues (n=2)
- Quality assurance (n=2)

Students - Qualifications of Candidates (Standard 4)

- In High School, or HS graduate or equivalent
- English Proficiency
- Math Proficiency
- Age Requirements (state dependent)
- Illicit drug use and criminal background
  - ❖ Assessed prior to acceptance

Related Materials

- **Guidance document**

http://www.ashp.org/DocLibrary/Accreditation/Guidance-Document.pdf

- **Model curriculum**

http://www.ashp.org/DocLibrary/Accreditation/Model-Curriculum.pdf

- **Regulations**

http://www.ashp.org/DocLibrary/Accreditation/Regulations-on-Accreditation-of-Pharmacy-Technician-Education.pdf

Program Composition Standard: Knowledge Areas

Technician Accreditation Standard		PTCB Blueprint
Personal/Interpersonal Knowledge & skills	--------	
Foundation Professional Knowledge & skills	↔	Pharmacology
Processing & Handling of Medication Orders	↔	Medication Order Entry and Fill Process
Sterile & Non-Sterile Compounding	↔	Sterile and Non-Sterile Compounding
Procurement, Billing, Reimbursement &	↔	Pharmacy Billing & Reimbursement
Inventory Management	↔	Pharmacy Inventory Management
Patient and Medication Safety	↔	Medication Safety
Technology & Informatics	↔	Rx Information System Usage/Application
Regulatory Issues	↔	Pharmacy Law & Regulations
Quality Assurance	↔	Pharmacy Quality Assurance

45 total goals

About PTCB

Mission Statement

PTCB develops, maintains, promotes and administers a nationally accredited certification program for pharmacy technicians to enable the most effective support of pharmacists to advance patient safety.

Certification Program Changes

New PTCB requirements:

- **2015:** PTCB only accepting **technician-specific CE**
- **2020:** Complete an **ACPE/ASHP-accredited education** program - *Pharmacy Technician Accreditation Commission (PTAC)*

Advanced Certification Programs in Development

- Task force met in **May** for sterile compounding

Why 2020?

- Changing pharmacy roles
  - ❖ Pharmacist
  - ❖ Technician
  - ❖ Clerk
- National pharmacy organization input
  - ❖ ASHP PPMI
  - ❖ NABP Task Force on Technician Education
- CREST Summit

PTCE Updated Blueprint

- 2011 job analysis
- Evolution of technician responsibilities
- Knowledge domains
- Revising the PTCE
  - ❖Blueprint and item mapping
  - ❖Gap analysis and new item development
  - ❖Standard setting

Going in the Same Direction

- Pharmacist provider status
- Increased pharmacist access = increased care
  - ❖ Telepharmacy, clinical team, immunizations
- Increased clinical tasks
  - ❖ Flu test, strep test, MTM
- All non-clinical tasks
  - ❖ Tech-check-tech
- National standard for pharmacy technicians
  - ❖ Defines minimally competent technician

Conclusions

- PTCB requirements and ASHP Technician Training Program Standards are closely aligned
- Still have 4 ½ years to grow technician training programs
- Currently ASHP, ACPE and PTCB working with Chains to support training program development to meet the standards
- We all support standardized education, training and certification of technicians and we will all have to work together to get there

Self-assessment Questions

1. In the new PGY1 residency standard, the number of goals and objectives has been
   a. Reduced
   b. Increased
   c. Left the same
2. The number of graduates from pharmacy school is growing as fast as the number of residency programs
   a. True
   b. False
3. There are currently about _____ Accredited Technician Training Programs
   a. 350
   b. 275
   c. 425
   d. 500

Self-assessment Questions

1. The new PTAC commission is a collaboration between ASHP and
   a. ACCP
   b. APhA
   c. ACPE
   d. PTCB
2. To sit for the PTCB exam in 2020, a technician will have to have what?
   a. Worked in a pharmacy for 2 years
   b. Completed and ASHP/ACPE accredited training program
   c. Pay a fee of $200
   d. Must be 18 years old

Questions?

Lost in Translation: Improving Med Rec Through Collaboration

Heather Harper, Pharm.D., BCPS
Karin Terry, Pharm.D.

Conflict of Interest

- We have no actual or potential conflict of interest in relation to this activity.

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Pharmacist Objectives

- Describe key metrics to evaluate the effectiveness of a Discharge Medication Review program.
- Identify opportunities to optimize the Electronic Health Record to improve efficiency of a Pharmacist Discharge Medication Review program.
- Explain the "life-cycle" of an order and how other facilities and/or encounters are impacted by transitions of care into or out of an acute care setting.

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Technician Objectives

- Define the difference between performing discharge medication reconciliation and discharge medication review.
- Recognize common defects when a patient experiences a transition of care.
- Explain the "life-cycle" of an order and how other facilities and/or encounters are impacted by transitions of care into or out of an acute care setting.

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

OSF Saint Francis Medical Center

- 616 bed tertiary care medical center located in Peoria, Illinois
  - 124 beds in Children's Hospital of Illinois
  - Midwest St. Jude affiliate
- Teaching affiliate of the University of Illinois College of Medicine at Peoria
- Level 1 Adult and Pediatric Trauma Center
- Currently 80+ pharmacists on staff

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Medication Reconciliation[1]

- A formal process for identifying and correcting unintended medication discrepancies across transitions in care

1. Pronovost P, Weast B, Schwarz M, Wyskiel RM, Prow D, Milanovich SN, Berenholtz S, Dorman T, Lipsett P. Medication reconciliation: a practical tool to reduce the risk of medication errors. J Crit Care. 2003 Dec;18(4):201-5.

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Medication Reconciliation: Why is it important? [1]

- Up to 67% of patients admitted to hospitals have unintentional medication discrepancies
- Reported rates of discrepancies having the potential to harm are as high as 59%

1. Kwan JL, Lo L, Sampson M, Shojania KG. Medication reconciliation during transitions of care as a patient safety strategy: a systematic review. Ann Intern Med. 2013 Mar 5;158(5 Pt 2):397-403.

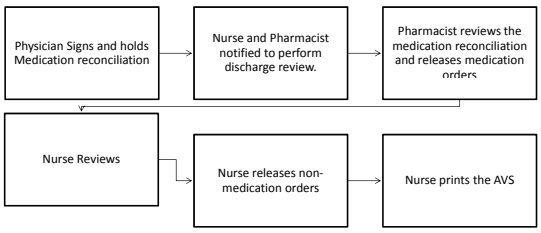
The Circle of Med Rec Life

- Discrepancies on PTA med list become discrepancies on inpatient list
- Discrepancies on inpatient list become discrepancies on outpatient list
- Changes made after leaving the facility do not always get resolved in our EMR
- These changes may become discrepancies on PTA med list next time

Medication Reconciliation vs. Medication Review at OSF

- Medication Reconciliation
  - Provider function
  - Process of determining what meds to order from PTA med list and other meds at a transition of care
- Medication Review
  - Performed by a pharmacist prior to patient discharge
  - Review appropriateness of provider order choices

Discharge Order Workflow



Discharge Med Rec Review at SFMC

- Centralized area where pharmacists perform reviews
- Auto-consult is sent to pharmacy in-box with each order in the discharge workflow
- Pharmacists work out of in-box in the order the consults are received

Case Study

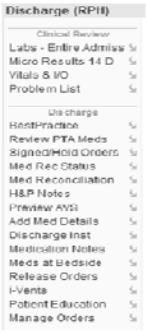
Pharmacist Discharge Procedure

- RPh Discharge Navigator
- Checklist
- Documentation

Discharge Medication Review Workflow

- Pharmacist performs the discharge medication review
  - Will review the patient's discharge after visit summary (AVS) for any medication discrepancies
    - In addition will review:
      - Prior-to-admission (PTA) medication list
      - Inpatient medication list
      - Culture results
      - Lab results
      - Vital signs
      - Progress notes

RPh Discharge Navigator



Pharmacy Discharge Review Checklist

Discharge Med Review Consult Checklist: / /

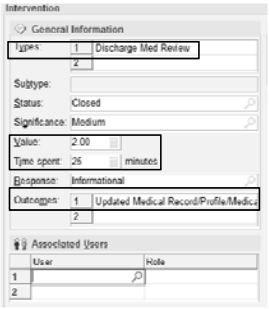
Patient Name		Patient Name	
	Is Med Rec Complete?		Is Med Rec Complete?
	✓AVS including instructions		✓AVS including instructions
	Review D/C Med Rec		Review D/C Med Rec
	Release D/C Meds		Release D/C Meds
	Send NUR 1113 order		Send NUR 1113 order
	Create i Vent		Create i Vent
	Complete Consult		Complete Consult
	Done in-basket message		Done in-basket message

Discharge Medication Review Documentation

- Pharmacist documents completion of discharge medication review
- Documents interventions made on discrepancies of critical or high severity

Intervention Documentation

- Example of discharge medication review with defects
- Because there were defects, additional documentation is needed if they are critical or high severity



Metrics – What We Measure

- Time
  - Average time per review
  - Average time review in queue
- System Score card
  - % Patients reviewed prior to discharge
  - % Defect free reviews
- SFMC
  - % High and Critical Interventions
  - Average # defects per review requiring intervention

Collaborating with Nurses

- Pharmacists found medication discrepancies at discharge that originated on admission
- Determined that nurses were not documenting the PTA med list in a consistent way
  - Confirmed with Simulation Exercise
- Established a new position called "Medication History Specialist (MHS)" Nurse
  - Responsible for timely completion of PTA med list and allergy documentation

Collaborating with Nurses

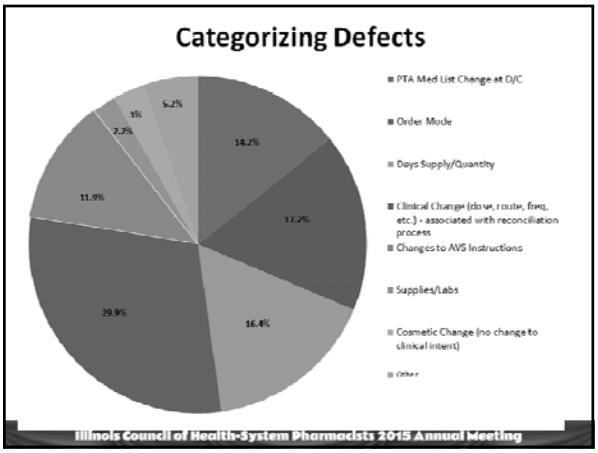
- MHS nurses were trained with 2 hour "in the seat" training sessions
  - Pharmacist assisted with training
  - Didactic as well as hands-on
  - Patient scenarios with real-life examples
- Mechanism created to allow documentation of events related to inaccurate PTA medication lists
- Pharmacists met with MHS managers to discuss events and learning opportunities

Collaborating with Nurses

- Eight different "tip sheets" created to assist MHS nurses
- Pharmacists also given updated training and tip sheets for updating PTA medication lists
- Collaborated with nurses on presentation to Magnet surveyors

Collaboration with Providers

- Individual phone calls
- Medication event follow up with Med Staff events
- UHATS/Hospitalist scorecard
  - Department meeting education created
- QSB / System feedback
- Education for Medical Residents and Attendings



Collaborating with Other Facilities

- Local LTACH was finding discrepancies on their admissions from our facility
- Worked with the hospitalists to find a process to resolve issues
- LTACH pharmacists called our Med Rec Office for every admission
- After 3 months of collaboration, phone calls no longer needed

Collaborating with Other Facilities

- Within our own system, we recognized that our data was not comparable from facility to facility
- Facilities reviewed different information during a review
- Facilities "counted" different things as defects
- As a system, we didn't know where to focus our efforts with the non-standard data
- A survey was created in order to establish a baseline

Difference in Defect Definitions

Incorrect quantity or days supply	68.75%	11
Incorrect/improper dose, route, and frequency of a prescription medication	100.00%	16
Incorrect start date	68.75%	11
Incorrect Order mode (escribe, normal, fax, OTC, etc)	31.25%	5
Missing dose or tablet size on OTC	31.25%	5
Non-ideal product selection (no change in clinical intent; ie.change in tablet size, neb consolidation, etc)	50.00%	8
Presence of multiple prescriptions when only one is needed as outpatient (ie. steroid taper, warfarin different doses, etc)	68.75%	11
Lack of order for follow labs (ie. INR, Vanco level, etc)	50.00%	8
Updates to the typed discharge instructions on the AVS	50.00%	8
Dug-drug mismatch	50.00%	8
Medication discrepancy at discharge that is caused by a discrepancy on the PTA med list	100.00%	16
Lack of supplies ordered (ie. New diabetes diagnosis without needles, lancets, etc)	18.75%	3
Un-reconciled inpatient orders at discharge (ie. Maintenance fluids in a patient going home)	75.00%	12
Incorrect pharmacy chosen for the E-scribe/Fax	25.00%	4
Other (please specify)	25.00%	4

Responses

Collaborating With Other Facilities

- We worked with the CNOs and CMOs of each of our system facilities
- Recognized needs for standard definition of a defect
  - Establish a new baseline
  - Determine which portion of the process to allocate resources

Lessons Learned

- Logistics considerations
  - When resources are needed
  - What resources are available
  - Where discharge med review occurs
- Documentation
  - Justification of service
  - Process improvements
  - Scorecard/Outcomes data

Lessons Learned

- Collaboration
  - Do it early and often
  - Include all players who touch medication reconciliation, inpatient and outpatient
  - Include the C-Suite
- Medication reconciliation is a fluid process
  - Process improvement should not be done in a silo

Question 1

- What is the difference between discharge medication reconciliation and discharge medication review?
  - A. Discharge medication reconciliation is a pharmacist function
  - B. Discharge medication review is performed by a panel of providers when issues are identified post-discharge
  - C. Discharge medication reconciliation is a provider function to determine discharge medications and pharmacists review their actions taken during discharge medication review
  - D. Discharge medication reconciliation and discharge medication review are synonymous terms

Question 2

- Which of the following are common defects identified when a patient experiences a transition in care?
  - A. Inappropriate medication frequency
  - B. Medication duplication
  - C. Medication omission
  - D. All of the above

Question 3

- Which of the following key metrics can be used to evaluate the effectiveness of a discharge medication review service?
  - A. HCAHPS scores
  - B. % of defect free discharge medication reviews
  - C. Average # of meds reviewed per discharge
  - D. Average time to perform a discharge medication review

Question 4

- Discharge medication review workflow was streamlined at OSF by addition of which of the following?
  - A. Collaborative practice agreement for pharmacists to reconcile medications
  - B. RPh discharge navigator in the EHR
  - C. Pharmacy Technicians obtaining medication histories
  - D. Patients having complete and up-to-date medication lists

Question 5

- Which of the following is correct for the "Life Cycle" of a medication order?
  - A. Inpatient and outpatient medication lists are exclusive to reduce potential discrepancies
  - B. Patients' medication lists change little after discharge, and a medication history is not needed for a bounce back re-admission
  - C. When not identified and corrected, medication discrepancies will flow from the outpatient to the inpatient setting
  - D. Medication discrepancies are infrequent

What questions do you have for us?

Isn't All of Pharmacy "Special"? Developing Specialty Pharmacy Services

Presented to: 2015 ICHP Annual Meeting
Presented on: September 10, 2015
Presented by: Lana Gerzenshtein, Pharm.D., BCPS
The speaker has no conflicts of interest to disclose in relation to this presentation.

Learning Objectives

- Explain the unique benefits of an integrated health system specialty pharmacy program
- Identify operational and clinical metrics of a specialty pharmacy program
- Describe how certified pharmacy technicians play a role in delivering specialty pharmacy services
- Describe roles associated with the specialty pharmacy back office

Specialty Pharmacy Definition

"specialty pharmacy is a unique class of professional pharmacy practice that includes a comprehensive and coordinated model of care for patients with chronic illnesses and complex medical conditions. Specialty pharmacies provide expert therapy management services, coupled with patient education and counseling, that collectively drive adherence, compliance, and persistence, manage dosing, and monitor appropriate medication use. This unparalleled, patient-centric model is organized to dispense/distribute typically high cost, injectable/infusible/oral and other hard-to-manage therapies within a collaborative framework designed to achieve superior clinical, humanistic, and economic outcomes."

The Specialty Pharmacy Association of America (SPAARx)

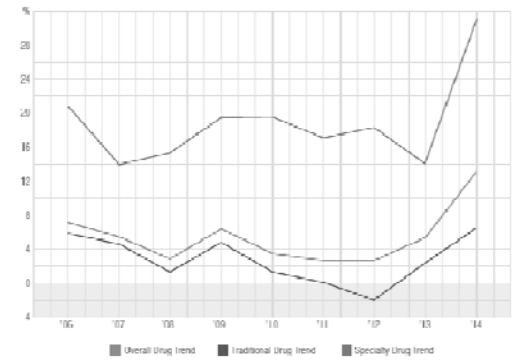
Specialty Pharmaceutical	Specialty Pharmacy
Treats complex, chronic illnesses	Patient education Therapy Management Services
High cost	Adherence coaching/monitoring
Special storage/administration requirements	Benefits Investigation Prior Authorization
Require ongoing efficacy/toxicity monitoring	Enrollment in patient assistance programs
Risk Evaluation and Mitigation Strategy (REMS)	Refill reminders and shipping coordination
Oral, injectable, infusible	24/7 access to pharmacist
Limited distribution	Ongoing treatment monitoring

Specialty Pharmacy Spend & Patient Factors

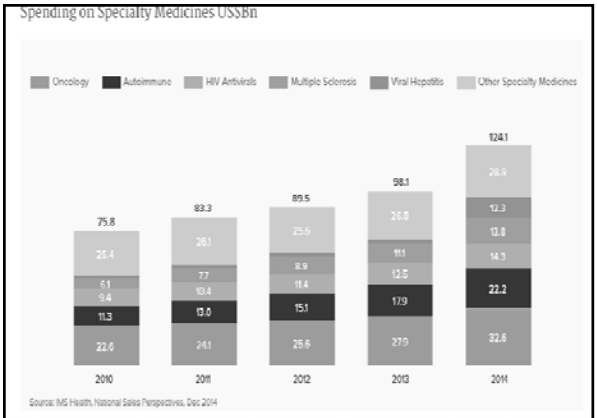
Specialty Pharmaceuticals

- Account for ~33% of spend in 2014
  - $124.1Bn (up from 23% ~5 years ago)
  - $54Bn increase in 5 years (73% overall spend)
- Medicare specialty spend increased 45.9%
  - biggest drivers were oncology, multiple sclerosis and hepatitis C (57.8% of total specialty spend)
- Represent 42% of late-stage pipeline drugs

1. IMS: Medicines Use and Spending Shifts. Available at http://www.imshealth.com/portal/site/imshealth. Accessed July 28th, 2015.
2. The Express Scripts Drug Trend Report 2014. Available at http://lab.express-scripts.com/drug-trend-report. Accessed July 28th, 2015.



Source: The Express Scripts 2014 Drug Trend Report



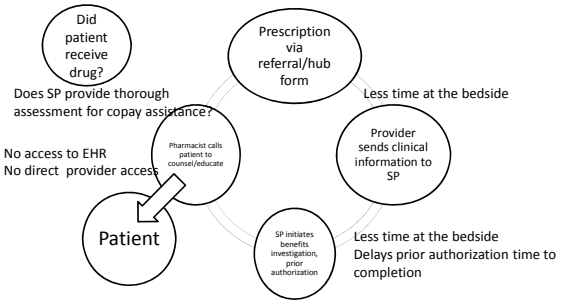
Ecosystem of Patient Care

Focus: Quality, Cost, Access
Goal: Total Patient Care

- Provider
- Hospital
- Health Plan
- Pharmacy Benefit Manager
- Specialty Pharmacy
- Retail Pharmacy
- Urgent Care Clinic / Retail Care Clinic
- Infusion Center
- Nurse – Case Management

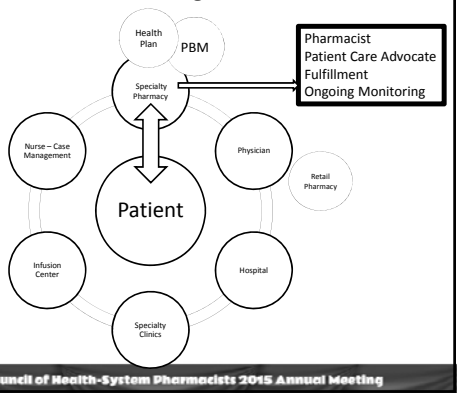
Ecosystem of Patient Care

Fragmented Model



Ecosystem of Patient Care

Patient Centric Integrated Model



Patient Case: Fragmented Care

- Patient with breast cancer prescribed lapatinib and capecitabine for treatment.
  - Health Plan is BCBS IL and PBM is Prime Therapeutics
  - Prime Therapeutics Specialty Pharmacy unable to fill lapatinib (limited distribution; no access to medication)
  - Patient directed to go to Walgreen's Specialty Pharmacy for lapatinib and Prime Therapeutics Specialty Pharmacy for capecitabine
  - Patient has to coordinate with 2 mail order pharmacies for her oncology medications
- ***Benefits of a Health-System Specialty Pharmacy***
  - *NM Specialty Pharmacy would have been able to provide seamless transition from clinic to home for this patient.*
  - *As an NCI designated center, NM Specialty Pharmacy has access to both lapatinib and capecitabine*

Patient Case: Coordinated Care

- Avoiding treatment discontinuation
  - during follow-up phone call for new HIV therapy, patient c/o rash since starting regimen but denied any other concerning symptoms
  - component of regimen known to cause rash-usually benign
  - Timely discussion with prescriber: pharmacist called patient and instructed to continue ART with symptomatic relief from an OTC product
  - Able to get an appointment with provider for the next day to assess rash: ***AVOIDED DISRUPTION IN THERAPY IN PATIENT WITH INCREASED RISK OF PROGRESSING TO AIDS***

Benefits Of A Health System Specialty Pharmacy

Patient Perspective

Benefits of a Health-System Specialty Pharmacy

- Coordination of care
  - 24/7 access to pharmacist
- Access to high cost medication
  - Prior authorization, appeals
  - Copay assistance enrollment
- Ongoing monitoring for safety/efficacy
- Adherence coaching
- Documentation in the health-record
  - Timely communication with team

Health System Perspective

Benefits of a Health-System Specialty Pharmacy

- Improve quality of care
  - Hanson et al. (UI Health)
  - Barada et al. (NMH)
- New revenue opportunity
  - ~$1000/prescription
- Managing your "own" patient
  - Outcomes data
- Building relationships
  - Providers
  - Patients
- Improved customer satisfaction

3. Colgan K. et al. Importance of specialty pharmacy to your system. Am J Health-Syst Pharm. 2015; 72:753-6
4. Hanson et al. J Manag Care Pharm. 2013;19(1):49-67
5. Barada et al. Pending poster presentation at ID Week; October 7-11, 2015 San Diego Convention Center

Opportunities to Optimize Care

- Collaboration!
- Continuity of care
- Adherence
- Side effect management
- Drug-drug interaction potential
- Access
  - Prior Authorization/Patient Assistance Programs
- Documentation (health record)

Development & Implementation Considerations

Big Picture Overview

☑Pharmacists performing medication management in specialty clinics
☑Staff to provide benefits investigation, prior authorization and payment assistance services
☑Payer contracts
☑24/7 access for patients
☑Space for fulfillment and shipping
☑Accreditation as a future goal

Current State/Opportunities

- Fulfillment services already in place vs establishing completely new infrastructure
- Meet with clinical staff within specialty clinics
  - What works currently, what are their needs?
- Assess number of prescriptions within each clinic
  - Payer mix?
  - Revenue potential?

Northwestern Medicine (NM) Specialty Pharmacy

Business Plan/Goals brought to Growth Committee:

Offer NM patients specialty pharmacy services through a closed door setting
- Improved continuum of care
- Improved medication safety and patient outcomes
- Improved patient and provider satisfaction

Rationale

- Providing specialty pharmacy services can improve the continuity of care in the health system. It can also improve health outcomes through safe and effective medication use through a closed loop system.

NM Specialty Pharmacy

Mission:
To help patients with complex or chronic diseases receive exceptional care by delivering specialty pharmacy services in a safe and efficient manner at an affordable cost.

Starting From Scratch!

External Involvement	Intra/Inter-departmental Involvement
•Group purchasing organization •Healthcare furniture •Manufacturer accounts •Packaging •Pharmacy Management System: ScriptPro® •Shipping: FedEx®,UPS®, Courier Service •Wholesaler accounts	•Clinic Administration •Environmental Services •Facilities •Finance •Human Resources •Informatics •Information Technology •Internal Audit •Managed Care •Marketing •Materials Management •Physician and Nurse Leaders •Revenue Cycle •Telecommunications •Treasury

Planning

- •Kick off presentations describing new services to key stake holders
- •Hiring staff
- •Licensing → Out of state delivery patients?
- •Meetings with inter-department collaborators (Finance, Contracting, etc.)
- •Contracting → Consultant:
  - •Identify top 20 PBMs
  - •Obtain applications
- •Revenue cycle
  - •Work-flow between front and back end
- •Pharmacy Management System (ScriptPro®)
  - •Hardware installation
  - •Interface development
- •Clinical Care Plans
- •Case Management System

NM Specialty Pharmacy: Prescriptions Work-flow

Clinic pharmacist meets with patient to educate on new specialty medication

Pharmacist recommends use of NM Specialty Pharmacy and if pt agrees, prescription sent to NM Specialty Pharmacy

Rx can be filled: delivered to clinic or mailed to pt

Rx cannot be filled: NM Specialty Pharmacy facilitates transfer to appropriate pharmacy with documentation and call to patient

Call at 72 hours to confirm patient is taking and tolerating regimen

Call monthly to assess adherence, tolerability and need for refill

Specialty Pharmacy submits prior authorizations and/or helps to apply for patient assistance programs

Patient Care Advocates

Certified technicians engaged in direct patient care!

- Prescription fulfillment
- Prior authorization completion
- Copay assistance enrollment
- Monthly refill/adherence calls
- Documentation in clinical case management tool
- Documentation in EHR

New Opportunities: Back Office Roles

- Data Analyst
  - Metrics reporting (financial/clinical)
    - Value-based reimbursement
- Revenue Cycle/Finance
- Payer Contracting
- Communication with Pharma

Metrics

Operational

- Number of prescriptions filled
  - capture rate in each specialty clinic
- Number of prior authorizations completed
  - Rate of prior authorization approval
  - Time to prior authorization approval
- Time to first fill (prescription written to prescription filled)
- Number of enrollments into medication assistance programs
- Patient/provider satisfaction surveys

Metrics

Clinical

- Pharmacist interventions on:
  - prescribing errors (correct indication, drug, dose, schedule)
  - drug interactions
- Adherence
  - adherence (MPR/PDC)
- Patients educated
- Time to treatment
- *Number of re-admissions avoided*
- *Number of admissions avoided*
- *Number of ED visits avoided*

Specialty Pharmacy Networks

- *UHC Specialty Pharmacy Program*
- *Excelera™ Specialty Pharmacy Network*
- Gain access to limited distribution agents
- Gain access to payer contracts
- Data management

Why Choose NM Specialty Pharmacy?

Integrated specialty medication management

- Pharmacy staff integrated in clinic practice
- Face to face interaction with patient in clinic setting creating a seamless transition
- Experienced Clinical Pharmacists
  - Board certified pharmacists
  - Focused practice specialty area
- Educating future Clinical Pharmacists
  - Post graduate residency training in ID, Cancer, Transplant
- Access to EMR
  - Reduce time to obtain prior authorization
  - Communication and documentation of medication related issues in EMR
  - Research
  - Call Center
- Ongoing follow up and management of patients by pharmacy staff

Summary

- Health system specialty pharmacy can optimize patient care by facilitating access to medication and therapy management while at the same time generating a new revenue source
- Certified technicians can be utilized in advanced roles that allow for more direct patent care
- Specialty Pharmacy programs can provide metrics that support value based reimbursement

References

1. IMS: Medicines Use and Spending Shifts. Available at http://www.imshealth.com/portal/site/imshealth.
2. The Express Scripts Drug Trend Report 2014. Available at http://lab.express-scripts.com/drug-trend-report.
3. Colgan K., Beacher R. Importance of specialty pharmacy to your system. Am J Health-Syst Pharm. 2015; 72:753-6.
4. Hanson R L, Gannon M J, Khamo N, Sodhi M, Orr A M, Stubbings J. Improvement in Safety Monitoring of Biologic Response Modifiers After the Implementation of Clinical Care Guidelines by a Specialty Pharmacy Service in an Academic Health System. J Manag Care Pharm. 2013;19(1):49-67.
5. Barada, F. Identification of Patient Factors Associated with Hepatitis C Treatment Failure in a Pharmacist Managed Hepatitis C Program. Pending poster presentation at ID Week; October 7-11, 2015 San Diego Convention Center.

Isn't All of Pharmacy "Special"?

Lana Gerzenshtein

1. What are benefits of a health system based specialty pharmacy?
    A. Coordination of care, education for patients and ongoing treatment monitoring
    B. Pharmacy staff can send prior authorization paperwork back to providers
    C. Pharmacists and technicians have less direct communication with providers
    D. Pharmacists do not have access to the EHR

2. Which of the following is an *operational* metric that can be measured within specialty pharmacy services?
    A. Number of patients that achieved successful clinical outcomes with completion of Hepatitis C therapy
    B. Prescription capture rate within each specialty clinic
    C. Number of patients that were able to go back to work after starting therapy with a specialty medication
    D. Adherence rates

3. Which of the following can be performed by a certified pharmacy technician within specialty pharmacy?
    A. Verifying prescriptions
    B. Educating patients on new specialty medications
    C. Filling out and submitting prior authorizations
    D. Writing SOAP notes

4. Which of the following roles can be fulfilled within the specialty pharmacy back office?
    A. Data analyst
    B. Medical assistant obtaining patient vitals
    C. Prior authorization review
    D. Patient copay assistance enrollment

Maximizing the Role of GLP-1 Agonists in Our Patients with Type 2 Diabetes

128th Annual TPA Convention & Exposition – Murfreesboro – July 15
2015 ICHP Annual Meeting – Oakbrook Terrace – September 10
KSHP 2015 Fall Meeting – Louisville – October 1
NMSHP 2015 Balloon Fiesta Symposium – Albuquerque – October 4
GSHP Fall Meeting – Young Harris – October 17

Planned by ASHP Advantage and supported by educational grants from AstraZeneca and Lilly.

ashp Advantage

Maximizing the Role of GLP-1 Agonists in Our Patients with Type 2 Diabetes

Activity Overview

This educational activity will provide pharmacists with an overview of new and emerging GLP-1 based therapies. Important differences among the GLP-1 agonists will be reviewed, including preparation and administration technique required for the various agents.

Learning Objectives

After the conclusion of this application-based educational activity, participants should be able to

- Review the effect of GLP-1 on glucose metabolism.
- Compare pathophysiologic mechanisms of GLP-1 agonists to other diabetes medications.
- Discuss the differentiating characteristics of available GLP-1 agonists including long-term safety.
- Explain the importance of proper injection device technique in the preparation and administration of GLP-1 agonists in the management of type 2 diabetes.
- Strategize how to overcome barriers in GLP-1 agonist use.

Continuing Education Accreditation

The American Society of Health-System Pharmacists is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This activity provides 1.0 hour (0.1 CEU – no partial credit) of continuing pharmacy education credit (ACPE activity # 0204-0000-15-428-L01-P).

Participants will process CPE credit online at http://elearning.ashp.org/my-activities. CPE credit will be reported directly to CPE Monitor. Per ACPE, CPE credit must be claimed no later than 60 days from the date of the live activity or completion of a home study activity.

Additional Educational Activities on this Topic

- **On-Demand Activity:** "Case Studies in the Use of GLP-1 Agonists in Type 2 Diabetes Management: An Individualized Approach to Patient Care"—Coming in mid-August to www.leadingdiabetescare.org.

Activity Faculty

Susan Cornell, Pharm.D., CDE, FAPhA, FAADE
Assistant Director of Experiential Education
Associate Professor
Department of Pharmacy Practice
Midwestern University Chicago College of Pharmacy
Downers Grove, Illinois

Susan Cornell, Pharm.D., CDE, FAPhA, FAADE, is Assistant Director of Experiential Education and Associate Professor, Department of Pharmacy Practice at Midwestern University Chicago College of Pharmacy in Downers Grove, Illinois. Dr. Cornell is also a certified diabetes educator and clinical pharmacy consultant, specializing in community and ambulatory care practice.

Dr. Cornell has over 24 years of practice in community pharmacy where she has practiced as a clinical pharmacist, diabetes educator, and preceptor, as well as the inaugural coordinator of the American Diabetes Association (ADA)-recognized Dominick's Pharmacy Diabetes Self-Management Education program. Dr. Cornell's current clinical practice is with the Access Community Health Network, where she trains, educates, and supervises students from the colleges of medicine, pharmacy, and health sciences as they provide diabetes education classes for patients in underserved community clinics.

Dr. Cornell received her Bachelor of Science degree in pharmacy from the University of Illinois, College of Pharmacy in 1986 and her Doctor of Pharmacy degree from Midwestern University in 2002.

Dr. Cornell recently completed her term as President of the Illinois Pharmacists Association in October 2011. She has received numerous awards and recognitions, including the 2010 Teacher of the Year Award, the 2010 American Association of Colleges of Pharmacy Student Engaged Community Service Award, and the 2005 Midwestern University Golden Apple Teaching Award. In 2008, she received fellow recognition from the American Association of Diabetes Educators (AADE) and the American Pharmacists Association. She is an active member of the ADA, as well as the AADE, where she served on the board of directors from 2004 to 2007.

Dr. Cornell has served as an invited speaker nationally and internationally on diabetes and its related conditions and is recognized as a key opinion leader in the field of diabetes education. She has contributed to many peer-reviewed print and online publications in this field.

Maximizing the Role of GLP-1 Agonists in Our Patients with Type 2 Diabetes

Curtis L. Triplitt, Pharm.D., CDE
Associate Director, Diabetes Research Center, Texas Diabetes Institute
Associate Professor, Department of Medicine, Division of Diabetes
University of Texas Health Science Center at San Antonio
San Antonio, Texas

Curtis L. Triplitt, Pharm.D., CDE, is Associate Professor and Certified Diabetes Educator at the University of Texas Health Science Center at San Antonio (UTHSCSA) where he oversees many diabetes research projects. In addition, he clinically manages people with diabetes with an endocrinologist at the Texas Diabetes Institute.

Dr. Triplitt earned his Bachelor of Science degree in pharmacy from the University of Iowa and his Doctor of Pharmacy degree from the University of Texas at Austin and the Health Science Center at San Antonio. He completed a primary-care residency accredited by the American Society of Health-System Pharmacists at the William S. Middleton Veteran Administration's Hospital in Madison, Wisconsin.

Dr. Triplitt is well respected as a clinician, researcher, and author. He is an investigator in several ongoing research studies related to diabetes, and he has published several book chapters on diabetes, as well as articles in peer-reviewed journals, including *Diabetes Care, Diabetes Spectrum, Expert Review of Endocrinology & Metabolism, Pharmacotherapy, and Drugs*. Dr. Triplitt is currently Secretary of the Texas Diabetes Council (TDC), which is legislatively mandated to develop and implement a state plan for diabetes treatment, education, and training. The TDC's mission is also to develop standards of care for the prevention, identification, and treatment of patients with diabetes mellitus in Texas.

Disclosure Statement

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Improving Patient Outcomes

Maximizing the Role of the GLP-1 Based Therapies in Our Patients with Type 2 Diabetes

Maximizing the Role of GLP-1 Agonists in Our Patients with Type 2 Diabetes

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1.0 hr. CPE

Disclosures

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- All other faculty and planners report no financial relationships relevant to this activity.

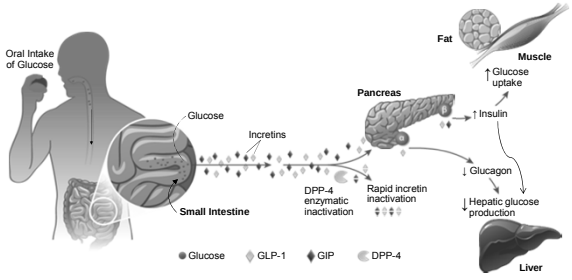
Objectives

- Review the effect of GLP-1 on glucose metabolism.
- Compare pathophysiologic mechanisms of GLP-1 agonists to other diabetes medications.
- Discuss the differentiating characteristics of available GLP-1 agonists including long-term safety.
- Explain the importance of proper injection device technique in the preparation and administration of GLP-1 agonists in the management of type 2 diabetes.
- Strategize how to overcome barriers in GLP-1 agonist use.

Objectives

- Review the effect of GLP-1 on glucose metabolism.

Incretin Glucose Regulation

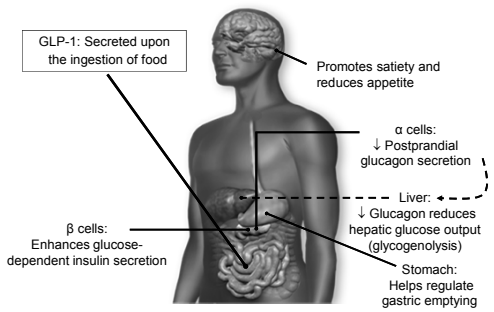


DPP=dipeptidyl peptidase, GLP=glucagon-like peptide, GIP=glucose-dependent insulinotropic polypeptide or gastric inhibitory polypeptide

Drucker DJ et al. *Lancet*. 2006; 368:1696-1705. Nauck MA. *Eur J Intern Med*. 2009; 20:S303-8. Kendal DM et al. *Am J Med*. 2009; 122:S37-50.

See enlargement, p. 17

GLP-1 Modulates Numerous Functions in Humans



Flint A et al. *J Clin Invest*. 1998; 101:515-20, Drucker DJ. *Diabetes*. 1998; 47:159-69.

See enlargement, p. 17

GLP-1 Agonists

- Actions:
  - Restore glucose-stimulated insulin secretion and first phase insulin
  - Suppress inappropriate glucagon secretion
  - Slow gastric emptying
  - Increase satiety
  - Resistant to DPP-4 enzyme
- Treatment options
  - Exenatide
    - Exenatide BID
    - Exenatide long-acting release (LAR) weekly
  - Liraglutide
  - Albiglutide
  - Dulaglutide

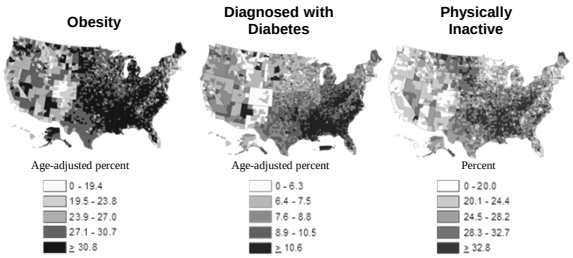
If we wanted to give a weekly GLP-1 agonist, what would be our choices?

a. Exenatide LAR
b. Albiglutide
c. Dulaglutide
d. All of the above

Objectives

- Compare pathophysiologic mechanisms of GLP-1 agonists to other diabetes medications.

The Diabesity Epidemic



Centers for Disease Control and Prevention: National Diabetes Surveillance System. www.cdc.gov/diabetes/data (accessed 2011 Jul 7)

See enlargement, p. 18

Insulin Resistance

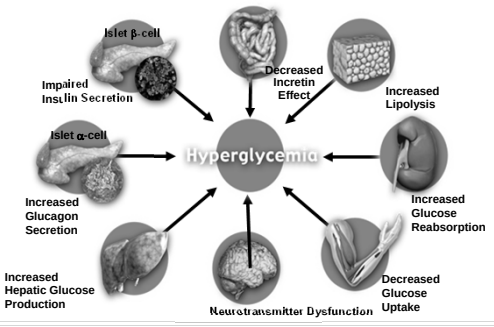
- Major defect in individuals with type 2 diabetes (T2DM)
- Reduced biological response to insulin
- Closely associated with obesity
- Associated with cardiovascular risk
- Type 1 diabetes patients can be insulin resistant as well

American Diabetes Association. *Diabetes Care* 1998; 21:310–14. Beck-Nielsen H et al. *J Clin Invest* 1994; 94:1714–21. Bloomgarden ZT. *Clin Ther* 1998; 20:216–31. Boden G. *Diabetes* 1997; 46:3–10.

Insulin Resistance

- Diet & Exercise
  - Additive effects: 3X higher improvement than diet or exercise alone
  - Even if a person cannot exercise, can improve insulin sensitivity with 5-10% weight loss
  - Calorie reduced diet of any composition is effective
  - Exercise typically 30-45 minutes moderate 3-5 times per week

Pathophysiologic Defects in Type 2 Diabetes: The Ominous Octet



DeFronzo RA. *Diabetes*. 2009; 58:773-95.

See enlargement, p. 18

12 Pharmacotherapy Options

Insulin

- Bolus insulin
  - Insulin lispro (Humalog)
  - Insulin aspart (Novolog)
  - Insulin glulisine (Apidra)
  - Insulin human inhaled (Afrezza)
  - Regular human insulin
    - (Humulin R)
    - (Novolin R)
- Basal insulin
  - Insulin NPH
    - (Humulin N)
    - (Novolin N)
  - Insulin detemir (Levemir)
  - Insulin glargine U100 (Lantus)
  - Insulin glargine U300 (Toujeo)

- Oral Medications
  - α-glucosidase inhibitors (AGI)
  - Biguanides
  - Bile acid sequestrants (BAS)
  - Dipeptidyl peptidase-4 (DPP-4) inhibitors (gliptins)
  - Dopamine agonists
  - Glinides
  - Sulfonylureas (SU)
  - Sodium Glucose Co-Transporter-2 inhibitors
  - Thiazolidinediones (TZDs or glitazones)
- Non-insulin injectable agents
  - Glucagon-like peptide-1 (GLP-1) agonists
  - Amylinomimetic

Cornell S et al. *Postgrad Med*. 2012;124:84-94. www.pdr.net (accessed 2015 Jan 30). www.pdr.net (accessed 2015 Mar 26).

Which dysfunctional organs do GLP-1 agonists target?

a. Brain and adipose fat
b. Muscle and adipose fat
c. Muscle, pancreas, and liver
d. Pancreas and liver
e. Pancreas, liver, brain, and GI tract

Glucose Lowering Comparison

Monotherapy	Route	Targets insulin resistance	Target Organs	Target Glucose: FPG or PPG	A1c Reduction %
Sulfonylurea	Oral	No	Pancreas	Both	1.5-2.0
Metformin	Oral	Yes	Liver	FPG	1.5
Glitazones	Oral	Yes	Muscle & adipose fat	Both	1.0-1.5
Meglitinides	Oral	No	Pancreas	PPG	0.5-2.0
AGIs	Oral	No	GI tract	PPG	0.5-1.0
DDP-4 inhibitors	Oral	No	Pancreas & liver	PPG	0.5-0.7
Bile acid sequestrant	Oral	No	GI tract	PPG	0.4
Dopamine agonists	Oral	No	Brain, possibly adipose fat	PPG	0.4
SGLT-2 inhibitors	Oral	Maybe	Kidney, possibly adipose fat	FPG	0.7 – 1.1
GLP-1 agonists	Injectable	No	Pancreas, liver, brain & GI tract	Short-acting—PPG Long-acting—Both	0.8-1.5
Amylin analogs	Injectable	No	Pancreas, liver, brain & GI tract	PPG	0.6
Insulin	Injectable	Yes (to a degree)		Basal - FPG Bolus – PPG	↓ as much as needed

FPG=fasting plasma glucose, PPG=postprandial glucose, GI=gastrointestinal.

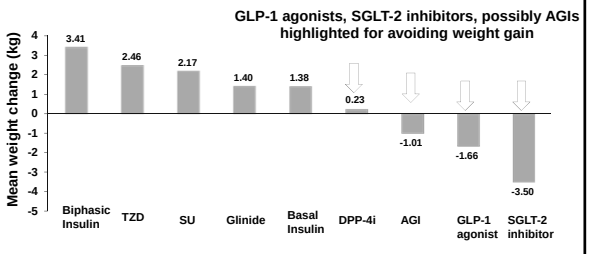
Unger J et al. *Postgrad Med*. 2010; 122:145-57. Cornell S et al. *Postgrad Med*. 2012; 124:84-94.

See enlargement, p. 19

Selection of Pharmacotherapy

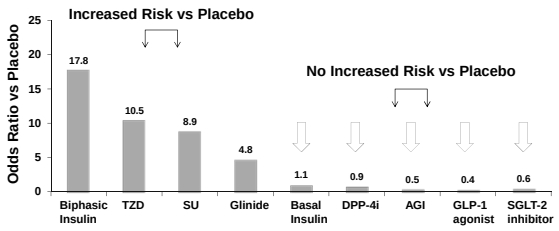
- Desired drug effects
  - Efficacious
  - Protect remaining β-cell function
  - Minimize hypoglycemic risks
  - Minimize weight gain
  - Minimize adverse effects and drug interactions
  - Cardiovascular benefit

Meta-Analysis: Weight Changes with Antihyperglycemic Agents Added to Metformin



Liu S et al. *Diabetes Obes Metab*. 2012; 14:810-20.

Hypoglycemic Risk of Antihyperglycemic Agents Added to Metformin



Liu S et al. Diabetes Obes Metab. 2012; 14:810-20.

GLP-1 Agonists

Short-acting GLP-1 agonists

- Exenatide BID (Byetta®)
  - 5 mcg & 10 mcg
  - Twice-daily dosing

Long-acting GLP-1 agonists

- Liraglutide (Victoza®)
  - 0.6 mg, 1.2 mg, & 1.8 mg
  - Once-daily dosing
- Exenatide LAR (Bydureon®)
  - 2 mg
  - Once-weekly dosing
- Albiglutide (Tanzeum®)
  - 30mg & 50mg
  - Once-weekly dosing
- Dulaglutide (Trulicity®)
  - 0.75 mg & 1.5 mg
  - Once-weekly dosing

GLP-1 Agonists

- Short-acting agonists lower postprandial glucose
  - Decreases A1c by 0.8% to 1.5% (~20-45 mg/dL; most postprandial)
- Long-acting agonists lower fasting and postprandial glucose
  - Decreases A1c by 0.8% to 1.8% (~20-50 mg/dL)
- Most common side effects
  - Weight loss
  - Stomach upset
  - Caution in patients at risk for pancreatitis

Cornell S et al. *Postgrad Med*. 2012; 124:84-94.

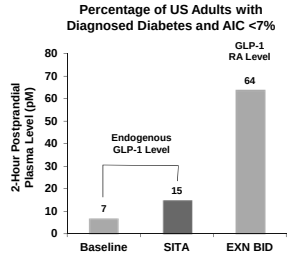
Comparison of Short-acting vs Long-acting GLP-1 Agonists

Parameter	Short-Acting	Long-Acting
HbA1c reduction	~0.5%-1.2%	~0.8%-1.9%
Body Weight Reduction	~1-4 kg	~1-4 kg
SBP Reduction	~3-4 mm Hg	Up to 6 mm Hg
Heart Rate Increase	No effect or small increase (0-2 beats/min)	2-4 beats/min
Lipids	Small improvement in some studies	Small improvement in some studies

Not head-to-head comparison
HbA1c=glycated hemoglobin, SBP=systolic blood pressure

Lund A et al. *Eur J Intern Med*. 2014; 25:407-14.

Comparing DPP-4 inhibitors and GLP-1 Agonists



- DPP-4 inhibitors (e.g., sitagliptin)
  - Oral administration
  - Block DPP-4 degradation of GLP-1
  - Increase endogenous GLP-1 levels ≈ 2-fold
- GLP-1 agonists
  - Subcutaneous administration
  - Add exogenous GLP-1 activity
  - Increase GLP-1 activity ≈ 9-fold
  - Greater A1c and weight effects than DPP-4 inhibitors

EXN BID=exenatide twice daily, SITA=sitagliptin

DeFronzo RA et al. *Curr Med Res Opin*. 2008; 24:2943-52. Inzucchi S et al. *Diabetes Care*. 2012; 35:1364-79.

Objectives

- Discuss the differentiating characteristics of available GLP-1 agonists including long-term safety.

Overview of Approved Incretin Therapies

Properties/Effects	Long Acting GLP-1 agonists	Short-acting GLP-1 agonists	DPP-4 inhibitors
Administration	SQ Daily or Weekly	SQ Twice Daily	Oral Daily
Glucose-dependent insulin increase	Yes	Yes	Yes
Glucose-dependent glucagon decrease	Yes	Yes	Yes
Slows Gastric Emptying	Yes	Yes	No
Lower hypoglycemia risk (in absence of SUs)	Yes	Yes	Yes
Effect on Body Weight	Loss	Loss	Neutral
Effect on A1c	High Efficacy	Moderate Efficacy	Moderate Efficacy
Effect on Fasting Plasma Glucose	Good	Modest	Modest
Major Adverse Effects	GI, nausea	GI, nausea	Well-tolerated
Adjustment/restriction in renal impairment	No, but GI SE in renally impaired patients - Caution	Yes, avoid in Severe/ ESRD	Yes, varies per medication

SQ=subcutaneous

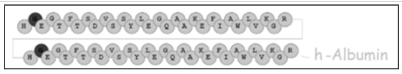
See enlargement, p. 19

Differences Between Incretin Mimetics

	Liraglutide	Exenatide*	Albiglutide	Dulaglutide
Dosing (SQ)	1.2-1.8 mg QD (after initial 0.6 mg QD x 7 days)	5-10 mcg within 60 min of AM/PM meals	30-50 mg weekly	0.75-1.5 mg weekly
Half-life	13 hr	2-4 hr	5 days	5 days
Max dose	1.8 mg QD	10 mcg BID	50 mg weekly	1.5 mg weekly
Renal elimination	No	Yes	No	No
Homology to GLP-1	97%	53%	97%	90%
Antibodies	8.6%	44%	2.5%	2%
Other effects	Less persistent nausea vs exenatide BID. Greater effects on FPG vs exenatide BID.	Exenatide BID - greater effects on PPG (*exenatide LAR has more effect on FPG, less nausea)	Nausea seems to be similar to other agents	No reconstitution Available as one-time use pens or pre-filled syringes

See enlargement, p. 20

Albiglutide



- Background
  - 97% homology to native GLP-1(7-36)
  - 2 copies of a modified GLP-1 fused to human albumin (C-terminus end of the modified GLP-1 sequence to the N-terminus of the human albumin)
  - Manufactured by rDNA technology - *Saccharomyces cerevisiae*
  - Resistant to DPP-4 metabolism - glycine replaces native GLP-1 alanine
  - Gives a half-life of 3.6 - 6.8 days

Tanzeum (albiglutide) prescribing information 2015 March.

Albiglutide

- Pharmacokinetics
  - Due to t1/2 - reaches steady state in 3-4 weeks
  - Distribution is not large due to albumin binding
  - Metabolism - ubiquitous proteolytic enzymes
- Dosing
  - 30 mg weekly
  - May increase to 50 mg weekly

Tanzeum (albiglutide) prescribing information 2015 March.

Albiglutide - Efficacy

- 3-year data, double-blind, placebo-controlled trial
  - Mean A1c 8.1%, Duration of diabetes 4 years
  - A1c reduction
    - Albiglutide 30 mg (n=30) -0.96%, SD 0.968
    - Albiglutide 50 mg (n=32) -1.07%, SD 0.887
    - Placebo (n=14) 0.61%, SD 0.644
- Albiglutide 50 mg weekly vs Liraglutide1.8 mg daily
  - At week 32 (n=422)
  - A1c - Albiglutide -0.78%, Liraglutide -0.99% (difference 0.21%; 0.08—0.34; non-inferiority p value=0.0846)
  - GI SE - Albiglutide 36%, Liraglutide 49%
  - Injection site reactions - Albiglutide 12.9%, Liraglutide 5.4%

ADA 74th Scientific Sessions, San Francisco, June 2014, P-959, P-1339. Pratley RE et al. Lancet Diabetes Endocrinol. 2014; 2:289-97.

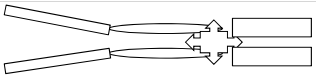
Albiglutide

- Side effect profile and warnings
- Similar to other long-acting GLP-1 agonists
  - MTC - 1 case of MTC with Albiglutide and 1 case in placebo
  - Warnings - similar to other long-acting GLP-1 agonists
    - Pancreatitis
    - Renal failure - do not use if eGFR <30 mL/min/1.73m^2
    - Hypoglycemia - if used with SU, glinide, or insulin
    - Hypersensitivity - mild injection site pruritus mostly, but 1 case of anaphylaxis in trials

MTC=medullary thyroid carcinoma

Tanzeum (albiglutide) prescribing information 2015 March.

Dulaglutide



- Recombinant GLP-1 Fc fusion protein linking GLP-1 analog to a human IgG4 Fc fragment
- Results in:
  - Prolonged t1/2: ~5 days
  - Once-weekly dosing
  - A solution - no reconstitution needed
  - Minimal renal clearance
  - Low immunogenicity risk

ADA 74th Scientific Sessions, San Francisco, June 2014, LB-110, P-979, P-962. Trulicity (dulaglutide) prescribing information. 20015 March.

Dulaglutide

Baseline (means)	D vs Lira AWARD-6	D vs Glar AWARD-2	D vs Glar AWARD-4
HbA1c (%)	8.1 vs 8.1	8.1 to 8.2	8.4 to 8.5
FPG (mg/dL)	167 vs 165	NR	150-157
Age (years)	56 vs 57	56-57	59-60
Weight (kg)	94 vs 94	85-88	91-92
Duration of diabetes (yr)	7 vs 7	~9	12-13
Background treatment	Metformin ~2 g/day	Maximum tolerated metformin and glimepiride	Poorly controlled on conventional insulin - added lispro TID to D or G

D=dulaglutide, Lira=liraglutide, Glar=glargine

ADA 74th Scientific Sessions, San Francisco, LB-110, P-979, P-962. Dungan K et al. *Lancet.* 2014; 384:1349-57.

Dulaglutide - Results

Outcomes (Means Reported)	D vs Lira AWARD-6 (26 week)		D vs Glar AWARD-2 (78 week)			D vs Glar AWARD-4 (52 week)		
Medication	D 1.5 mg	Lira 1.8 mg	D 0.75 mg	D 1.5 mg	G	D 0.75 mg	D 1.5 mg	G
HbA1c (%)	-1.42	-1.36	-0.62	-0.9	-0.59	-1.42	-1.48	-1.23
Weight change (kg)	-2.9	-3.6	-1.54	-1.96	1.28	1.6	0.6	3.7
TDD insulin	n/a		NR			97	93	132
% at goal <7%	68.3	67.9	NR			56	59	49
Other Info	All reported side effects comparable between treatments		PRO-less behavior & worry-hypoglycemia			Glargine ~64 units/day		

ADA 74th Scientific Sessions, San Francisco, LB-110, P-979, P-962. Dungan K et al. *Lancet.* 2014; 384:1349-57.

See enlargement, p. 20

Dulaglutide - Side Effects

Outcomes (%)	D vs Lira AWARD-6 (26 week)		D vs Glar AWARD-4 (@ 52 week)		
GI (%)	D 1.5 mg	Lira 1.8 mg	D 0.75 mg	D 1.5 mg	G
Nausea	20.4	8.0	17.7	25.8	3.4
Vomiting	7.3	8.3	10.6	12.2	1.7
Diarrhea	12.0	12.0	15.7	16.6	6.1
Injection site reaction	0.3	0.7	1.4	0.3	0.0
Hypoglycemia	≤70 mg/dL +/- Sx, Events/ pt/yr 0.34	0.52	Severe 1.7	2.1	3.7
			≤70 mg/dL 88.4	85.9	89.5
Other Info	D/C due to SE 6% in each group No pancreatitis or pancreatic cancer		No pancreatitis or pancreatic cancer reported		

ADA 74th Scientific Sessions, San Francisco, LB-110, P-979, P-962. Dungan K et al. *Lancet.* 2014; 384:1349-57.

See enlargement, p. 21

Head-to-Head Studies: HbA1c

Study Acronym	Drugs Comparison	HbA1c reduction (%)
DURATION-1	Exenatide BID	-1.5
	Exenatide LAR weekly	-1.9*
DURATION-5	Exenatide BID	-0.9
	Exenatide LAR weekly	-1.6*
DURATION-6	Exenatide LAR weekly	-1.28
	Liraglutide	-1.48*
LEAD-6	Exenatide BID	-0.79
	Liraglutide	-1.2*
GetGoal-X	Lixisenatide daily	-0.79
	Exenatide BID	-0.96

*Significant difference

Head-to-Head Studies: HbA1c

Study Acronym	Drugs Comparison	HbA1c reduction (%)
HARMONY-7	Albiglutide	-0.78
	Liraglutide	-0.99
AWARD-1	Dulaglutide 1.5 mg weekly	-1.51*
	Dulaglutide 0.75 mg weekly	-1.30*
	Exenatide BID	-0.99
AWARD-6	Dulaglutide	-1.42 (non-inferior)
	Liraglutide	-1.36

*Significant difference

Though all in the same class of medications, efficacy varies per product

Head-to-Head Studies: Weight

Study Acronym	Drugs Comparison	Weight Change (kg)
DURATION-1	Exenatide BID	-3.7
	Exenatide LAR weekly	-3.6
DURATION-5	Exenatide BID	Not Reported
	Exenatide LAR weekly	Not Reported
DURATION-6	Exenatide LAR weekly	-2.68
	Liraglutide	-3.57*
LEAD-6	Exenatide BID	-2.87
	Liraglutide	-3.24
GetGoal-X	Lixisenatide daily	-2.96
	Exenatide BID	-3.98

*Significant difference

Head-to-Head Studies: Weight

Study Acronym	Drugs Comparison	Weight Change (kg)
HARMONY-7	Albiglutide	-0.64
	Liraglutide	-2.16*
AWARD-1	Dulaglutide 1.5 mg weekly	-1.3
	Dulaglutide 0.75 mg weekly	-0.3
	Exenatide BID	-1.07
AWARD-6	Dulaglutide	-2.90
	Liraglutide	-3.61*

*Significant difference

Weight loss is slightly less with albiglutide and dulaglutide
Similar among other products

Side Effect Comparison

- DURATION-1 and DURATION-5
  - Exenatide BID more N/V vs exenatide LAR weekly
- DURATION-6
  - Liraglutide more nausea, vomiting, diarrhea vs exenatide LAR weekly
- LEAD-6
  - Adverse events less likely, but less severe with exenatide BID vs liraglutide
- GetGoal-X
  - Lixisenatide less side effects than exenatide BID
- HARMONY-7
  - More injection site reactions with albiglutide than liraglutide

Long-term Safety Concerns

- MTC/C-cell hyperplasia
  - Rodents - increase incidence
  - Humans - no increased incidence to date
  - Possible - GLP-1 receptors on C-cell tumors
- Pancreatitis
  - No causality, but continued association
  - Large observational studies do not show a risk
- Pancreatic cancer
  - No risk to date

Egan AG. *N Engl J Med*. 2014; 370:794-7. Geir B. *J Clin Endocrinol Metab*. 2012; 97:121-31.

Effect of GLP-1 Agonists on CVD Risk Factors

Lixisenatide press release-neutral for CV events

Risk Factor	Exenatide 10 mcg BID (3.5 years)[1]	Liraglutide 1.2 mg qd (26 weeks)[2]	Exenatide LAR 2.0 mg weekly (1 year)[3]	Albiglutide 30–50 mg weekly (32 weeks)[4]	Dulaglutide 1.5 mg weekly (26 weeks)[5]
SBP (mm Hg)	–3.5*	–6.7†	–6.2*	N/A	–1.7†
DBP (mm Hg)	–3.3*	–2.3	–2.8*	N/A	–0.4
TC (mg/dL)	–10.8*	–8.1	-7.9*	ND	–0.8 to –8.1‡
LDL-C (mg/dL)	–11.8*	–10.8†	–2.2	ND	–1.9 to –7.0‡
HDL-C (mg/dL)	8.5*	–1.2	N/A	ND	N/A
Triglycerides (mg/dL)	–44.4*	–14.7†	–40.0*	ND	–12.4 to –16.8

N/A=not available, ND=no difference vs placebo
*P <0.05 vs baseline, †P <0.005 vs placebo, ‡P <0.001 vs placebo

Klonoff DC et al. *Curr Med Res Opin*. 2008; 24:275–86. Zinman B et al. *Diabetes Care*. 2009; 32:1224–30. Bergenstal R et al. *Diabetes*. 2009; 58:165-OR. Pratley RE et al. *Lancet Diabetes Endocrinol.* 2014; 2:289–97. Nauck MA et al. *Diabetes Care*. 2014; 37:2149–58.

See enlargement, p. 21

Objectives

- Explain the importance of proper injection device technique in the preparation and administration of GLP-1 agonists in the management of type 2 diabetes.

Which statement regarding GLP-1 agonist pen administration is NOT true?

a. Prime before each use
b. Some devices will require "mixing"
c. Inject straight into the skin
d. Hold for 5 -10 seconds before removing the needle from skin

GLP-1 Agonist Comparison

GLP-1 Agent	Device	Mixing required	Pre injection waiting time	Refrigerated	Once Used (opened)
Exenatide BID Twice-daily dosing	Pen	No	No	Expiration Date	Do not refrigerate 30 days
Liraglutide Once-daily dosing	Pen	No	No	Expiration Date	Do not refrigerate 30 days
Exenatide LAR weekly Once-weekly dosing	Kit	Yes	No	Expiration Date	Can be stored at room temperature for 4 weeks
Exenatide LAR weekly Once-weekly dosing	Pen	Yes	No	Expiration Date	Can be stored at room temperature for 4 weeks
Albiglutide Once-weekly dosing	Pen	Yes	Yes (15-30 min)	Expiration Date	Can be stored at room temperature for 4 weeks
Dulaglutide Once-weekly dosing	Pen	No	No	Expiration Date	Can be stored at room temperature for 4 weeks

www.pdr.net (accessed 2015 April 20).

See enlargement, p. 22

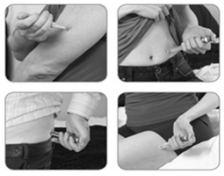
GLP-1 Agonist Delivery Systems

- Disposable pens (similar to insulin pens)
- Disposable single-use pen needles
  - 30 or 31 gauge pen for most
- Pen must be prepared before initial use;
  - priming not needed before each dose

Injection Technique

- Inject straight into the skin
  - Depress the button to release insulin into SQ tissue
- Hold for 5 to 10 seconds before removing the needle from skin
- Remove needle and dispose into sharps container
- Always have the patient demonstrate their technique
  - At first education of the device
  - At first follow-up visit
  - At frequent intervals thereafter

Inject "straight in" flush with skin



Exenatide BID (Byetta)

- Requires a one time priming of the device
- Subsequent doses can be given in the thigh, abdomen or back of the upper arms

- Starting position is →
- Pull knob until ↑ appears
- Rotate knob clockwise until 5 or 10 appears
- Pierce skin and press button down on knob for 5 seconds, ↑ will appear
- Rotate knob clockwise until → appears

Liraglutide (Victoza)

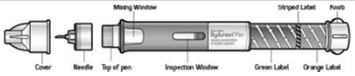
- Requires a one-time priming of the device
  - Dose is dialed to this marker and the button is pressed until a drop of solution is produced

- Subsequent doses can be given in the thigh, abdomen, or back of the upper arms
  - Button is held down for 6 seconds during administration

Exenatide LAR Weekly Kit (Bydureon)

- 4 parts (Single dose tray)
  - Needle
  - Vial Connector
  - Syringe (Diluent)
  - Vial (Powder)
- Complex preparation
- Dose can be given in the thigh, abdomen, or back of the upper arms
- Dose must be given immediately
- Push down on plunger until it stops

Exenatide LAR Weekly Pen Device (Bydureon)



- Same dosing, just new device-out "later this year"
- At least 15 minutes at room temperature prior to mixing steps

Major steps in preparation

- Twist until mix diluent with microspheres (audible click noted upon mixing)
- Gently move pen back and forth (oscillate) at least 80 times (about 1- 1 ½ minutes)
- Check Mixing Window for proper mixing-should see uniform grey color; If not - continue until uniform color seen in mixing window
- Twist until dosing plunger comes out of knob and will hear a second "click"
- Attach needle → ready for injection

Albiglutide (Tanzeum)

- Single reconstitutable pen
- Must be used within 8 hours of reconstitution

- Hold pen vertically with #1 visible
- Pen is turned clockwise until a click is heard and #2 appears
- Gently rock the pen side to side like a window wiper five times (0° to 180°)
- If 30 mg, let rest for 15 minutes and if 50 mg, let rest for 30 minutes upright
- After time has elapsed, rock the pen with similar technique five more times
- Solution should be yellow in appearance
- Attach the supplied needle and tap the pen gently to dislodge bubbles
- Turn the pen clockwise until #3 appears
- Inject into thigh, abdomen, or back of the upper arms
- Button is held down for 5 seconds during administration

Dulaglutide (Trulicity)

- Single prefilled syringe
- Can be injected into thigh, abdomen, or back of the upper arms

- Uncap the pen
- Place the pen on the desired injection area
- Turn the lock ring of the pen from the locked to unlocked position
- Press and hold the button down for 5 - 10 seconds
- The patient will hear a click when the button is pressed
- A second click will indicate the dose was administered

Patient Education

- What to expect
  - The most common side effects include
    - Headache
    - Nausea (usually mild to moderate)
    - Diarrhea
  - Tips to minimize/eliminate nausea
    - Eat smaller meals
    - Avoid overeating
    - Cut down on fatty foods
    - Wear comfortable clothes.
      - Tight waistbands can make you feel worse
  - If nausea is severe, call your health care professional

Objectives

- Strategize how to overcome barriers in GLP-1 agonist use.

Barriers to GLP-1 Agonist Use

Patient

- Unfamiliar with the drug
- Injectable
- Fear of side effects
- Cost

Prescriber

- Unfamiliar with the drug
- Unfamiliar with current treatment guidelines for hyperglycemia
- Injectable
- Fear of side effects
- Cost

Overcoming Barriers

- Education about benefits of GLP-1 agonist as monotherapy and in combination
  - Recognized as first and/or second choice in current guidelines (ADA/EASD and AACE/ACE)
- What is the reason for not wanting to try an injectable drug?
- Education and strategies for overcoming side effects
- Options for cost saving measures
  - Insurance plans
  - Patient assistance programs
  - 340B clinics

ADA/EASD=American Diabetes Assoc/European Assoc for the Study of Diabetes, AACE/ACE=American Assoc of Clinical Endocrinologists, and American College of Endocrinology

Inzucchi SE et al. *Diabetes Care*. 2015; 38:140-9. Handelsman Y et al. *Endocr Pract*. 2015; 21 (suppl 1):1-87.

Tips for Medication Adherence

- Education
  - What is the importance of this medication?
    - How does it work to help lower BG, BP, or decrease complications?
- Timing
  - When is the best time to take the medication to get the maximum benefit?
- Monitoring
  - When should the patient self-monitor blood glucose in order to know the medication is effective?
  - What are common adverse effects?

BG=blood glucose, BP=blood pressure

Patient JZ needs help with scheduling doses. Which GLP-1 agonist must be dosed prior to a meal?

a. Albiglutide
b. Dulaglutide
c. Exenatide BID
d. Liraglutide

Exenatide BID and Liraglutide

- Exenatide BID - good for postprandial control
  - Compliance - make sure taking evening dose
  - Space doses more away from meal for more satiety (up to 1-2 hours prior)
- Liraglutide - easy device to use
  - Compliance - Ask: Out of 7 injections in a week (once daily), how many are you usually able to take?

BG-Lowering Agents and the "Best" Time to Take Them

- Agents to be taken before meals
  - AGIs
  - Dopamine agonists
  - Glinides
  - Short-acting GLP-1 agonists
  - Bolus insulin
- Agents to be taken with or after meals
  - SU
  - Metformin
  - Bolus insulin
- Agents that can be taken with or without food
  - TZDs
  - DPP-4 inhibitors
  - Long-acting GLP-1 agonists
  - SGLT-2 inhibitors
  - Basal insulin

Cornell S et al. *Postgrad Med*. 2012; 124:84-94.

Six Key Questions to Ask Patients for EVERY Medication They Take

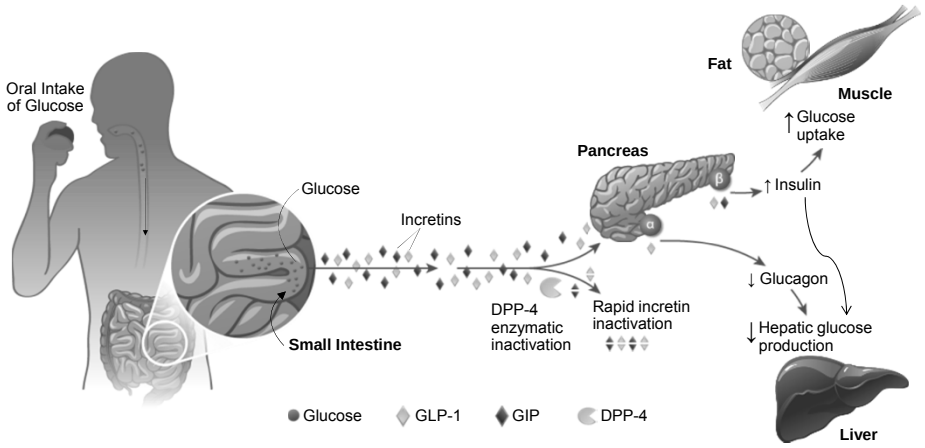
1. What are you taking this medication for?
2. How are you currently taking it?
3. What problems have you noticed since starting this medication?
4. What side effect concerns do you have about your medication?
5. What cost concerns do you have about your medications?
6. What days of the week do you NOT take your medication?
   - How often does this happen?

Cornell S et al. *Diabetes Trends*. 2009; 21(suppl A):3-11.

Summary

- T2DM is a result of 8 dysfunctional organs
  - Insulin resistance is a major contributor to T2DM
  - There is no single drug (when used as monotherapy) that fixes all 8 of the broken organs
- GLP-1 agonists fix 5 of the organs
  - Patient education can overcome barriers to use, enhance adherence and improve therapeutic outcomes
- Pharmacists should perform regular medication check-ups and routine assessment of device technique

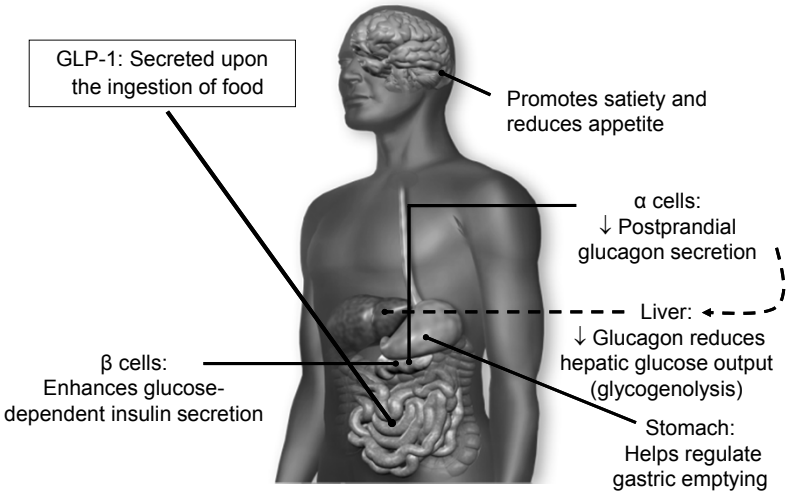
Incretin Glucose Regulation



DPP=dipeptidyl peptidase, GLP=glucagon-like peptide, GIP=glucose-dependent insulinotropic polypeptide or gastric inhibitory polypeptide

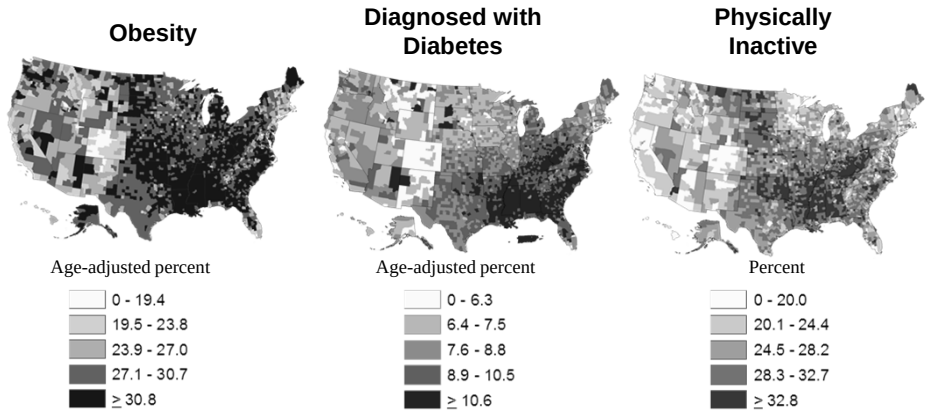
Drucker DJ et al. *Lancet*. 2006; 368:1696-1705. Nauck MA. *Eur J Intern Med*. 2009; 20:S303-8. Kendal DM et al. *Am J Med*. 2009; 122:S37-50.

GLP-1 Modulates Numerous Functions in Humans



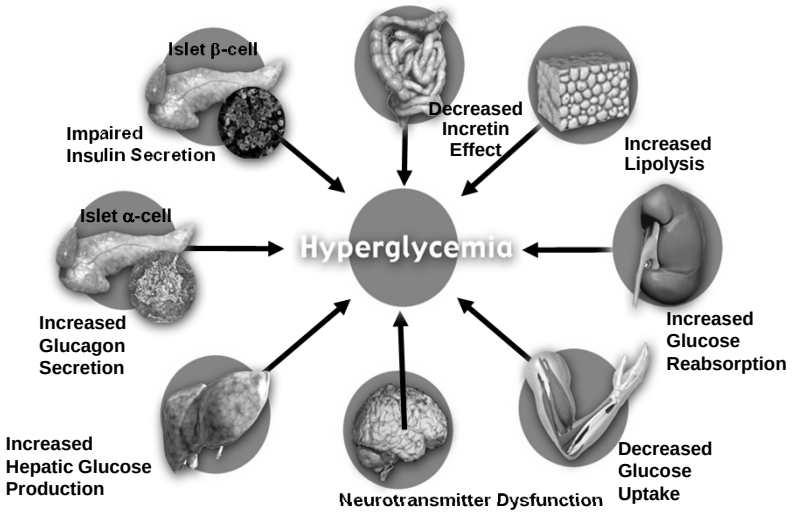
Flint A et al. *J Clin Invest*. 1998; 101:515-20, Drucker DJ. *Diabetes*. 1998; 47:159-69.

The Diabesity Epidemic



Centers for Disease Control and Prevention: National Diabetes Surveillance System. www.cdc.gov/diabetes/data (accessed 2011 Jul 7)

Pathophysiologic Defects in Type 2 Diabetes: The Ominous Octet



DeFronzo RA. *Diabetes*. 2009; 58:773-95.

Glucose Lowering Comparison

Monotherapy	Route	Targets insulin resistance	Target Organs	Target Glucose: FPG or PPG	A1c Reduction %
Sulfonylurea	Oral	No	Pancreas	Both	1.5-2.0
Metformin	Oral	Yes	Liver	FPG	1.5
Glitazones	Oral	Yes	Muscle & adipose fat	Both	1.0-1.5
Meglitinides	Oral	No	Pancreas	PPG	0.5-2.0
AGIs	Oral	No	GI tract	PPG	0.5-1.0
DDP-4 inhibitors	Oral	No	Pancreas & liver	PPG	0.5-0.7
Bile acid sequestrant	Oral	No	GI tract	PPG	0.4
Dopamine agonists	Oral	No	Brain, possibly adipose fat	PPG	0.4
SGLT-2 inhibitors	Oral	Maybe	Kidney, possibly adipose fat	FPG	0.7 – 1.1
GLP-1 agonists	Injectable	No	Pancreas, liver, brain & GI tract	Short-acting—PPG Long-acting—Both	0.8-1.5
Amylin analogs	Injectable	No	Pancreas, liver, brain & GI tract	PPG	0.6
Insulin	Injectable	Yes (to a degree)		Basal - FPG Bolus – PPG	↓ as much as needed

FPG=fasting plasma glucose, PPG=postprandial glucose, GI=gastrointestinal.

Unger J et al. *Postgrad Med*. 2010; 122:145-57. Cornell S et al. *Postgrad Med*. 2012; 124:84-94.

Overview of Approved Incretin Therapies

Properties/Effects	Long Acting GLP-1 agonists	Short-acting GLP-1 agonists	DPP-4 inhibitors
Administration	SQ Daily or Weekly	SQ Twice Daily	Oral Daily
Glucose-dependent insulin increase	Yes	Yes	Yes
Glucose-dependent glucagon decrease	Yes	Yes	Yes
Slows Gastric Emptying	Yes	Yes	No
Lower hypoglycemia risk (in absence of SUs)	Yes	Yes	Yes
Effect on Body Weight	Loss	Loss	Neutral
Effect on A1c	High Efficacy	Moderate Efficacy	Moderate Efficacy
Effect on Fasting Plasma Glucose	Good	Modest	Modest
Major Adverse Effects	GI, nausea	GI, nausea	Well-tolerated
Adjustment/restriction in renal impairment	No, but GI SE in renally impaired patients - Caution	Yes, avoid in Severe/ ESRD	Yes, varies per medication

SQ=subcutaneous

Differences Between Incretin Mimetics

	Liraglutide	Exenatide*	Albiglutide	Dulaglutide
Dosing (SQ)	1.2-1.8 mg QD (after initial 0.6mg QD x7 days)	5-10 mcg within 60 min of AM/PM meals	30-50 mg weekly	0.75-1.5 mg weekly
Half-life	13 hr	2-4 hr	5 days	5 days
Max dose	1.8 mg QD	10 mcg BID	50 mg weekly	1.5 mg weekly
Renal elimination	No	Yes	No	No
Homology to GLP-1	97%	53%	97%	90%
Antibodies	8.6%	44%	2.5%	2%
Other effects	Less persistent nausea vs exenatide BID. Greater effects on FPG vs exenatide BID.	Exenatide BID - greater effects on PPG (*exenatide LAR has more effect on FPG, less nausea)	Nausea seems to be similar to other agents	No reconstitution Available as one-time use pens or pre-filled syringes

Dulaglutide - Results

Outcomes (Means Reported)	D vs Lira AWARD-6 (26 week)		D vs Glar AWARD-2 (78 week)			D vs Glar AWARD-4 (52 week)		
Medication	D 1.5 mg	Lira 1.8 mg	D 0.75 mg	D 1.5 mg	G	D 0.75 mg	D 1.5 mg	G
HbA1c (%)	-1.42	-1.36	-0.62	-0.9	-0.59	-1.42	-1.48	-1.23
Weight change (kg)	-2.9	-3.6	-1.54	-1.96	1.28	1.6	0.6	3.7
TDD insulin	n/a		NR			97	93	132
% at goal <7%	68.3	67.9	NR			56	59	49
Other Info	All reported side effects comparable between treatments		PRO-less behavior & worry-hypoglycemia			Glargine ~64 units/day		

ADA 74th Scientific Sessions, San Francisco, LB-110, P-979, P-962. Dungan K et al. *Lancet*. 2014; 384:1349-57.

Dulaglutide - Side Effects

Outcomes (%)	D vs Lira AWARD-6 (26 week)		D vs Glar AWARD-4 (@ 52 week)		
GI (%)	D 1.5 mg	Lira 1.8 mg	D 0.75 mg	D 1.5 mg	G
Nausea	20.4	8.0	17.7	25.8	3.4
Vomiting	7.3	8.3	10.6	12.2	1.7
Diarrhea	12.0	12.0	15.7	16.6	6.1
Injection site reaction	0.3	0.7	1.4	0.3	0.0
Hypoglycemia	≤70 mg/dL +/- Sx, Events/ pt/yr		Severe		
	0.34	0.52	1.7	2.1	3.7
			≤70 mg/dL		
			88.4	85.9	89.5
Other Info	D/C due to SE 6% in each group No pancreatitis or pancreatic cancer		No pancreatitis or pancreatic cancer reported		

ADA 74th Scientific Sessions, San Francisco, LB-110, P-979, P-962. Dungan K et al. *Lancet*. 2014; 384:1349-57.

Effect of GLP-1 Agonists on CVD Risk Factors

Lixisenatide press release-neutral for CV events

Risk Factor	Exenatide 10 mcg BID (3.5 years)[1]	Liraglutide 1.2 mg qd (26 weeks)[2]	Exenatide LAR 2.0 mg weekly (1 year)[3]	Albiglutide 30–50 mg weekly (32 weeks)[4]	Dulaglutide 1.5 mg weekly (26 weeks)[5]
SBP (mm Hg)	–3.5*	–6.7†	–6.2*	N/A	–1.7†
DBP (mm Hg)	–3.3*	–2.3	–2.8*	N/A	–0.4
TC (mg/dL)	–10.8*	–8.1	-7.9*	ND	–0.8 to –8.1‡
LDL-C (mg/dL)	–11.8*	–10.8†	–2.2	ND	–1.9 to –7.0‡
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*P <0.05 vs baseline, †P <0.005 vs placebo, ‡P <0.001 vs placebo

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Albiglutide Once-weekly dosing	Pen	Yes	Yes (15-30 min)	Expiration Date	Can be stored at room temperature for 4 weeks
Dulaglutide Once-weekly dosing	Pen	No	No	Expiration Date	Can be stored at room temperature for 4 weeks

www.pdr.net (accessed 2015 April 20).

Self-Assessment Questions

The self-assessment questions included in this presentation are listed below for your review. You may wish to note the correct answers as you follow along with the speaker.

1. If we wanted to give a weekly GLP-1 agonist, what would be our choices?
    a. Exenatide LAR
    b. Albiglutide
    c. Dulaglutide
    d. All of the above

2. Which dysfunctional organs do GLP-1 agonists target?
    a. Brain and adipose fat
    b. Muscle and adipose fat
    c. Muscle, pancreas and liver
    d. Pancreas and liver
    e. Pancreas, liver, brain and GI tract

3. Which statement regarding GLP-1 agonist pen administration is NOT true?
    a. Prime before each use
    b. Some devices will require “mixing”
    c. Inject straight into the skin
    d. Hold for 5 -10 seconds before removing the needle from skin

4. Patient JZ needs help with scheduling doses. Which GLP-1 agonist must be dosed prior to a meal?
    a. Albiglutide
    b. Dulaglutide
    c. Exenatide BID
    d. Liraglutide

Instructions for Processing CE Credit with Enrollment Code

Claim CPE within 60 days

Pharmacists and Technicians:
Per ACPE, CPE credit must be claimed **no later than 60 days** from the date of the live activity or completion of a home study activity. All ACPE accredited activities which are processed on the eLearning site will be reported directly to CPE Monitor. To claim pharmacy credit, you must have your NABP e-Profile ID, birth month, and birth day. If you do not have an NABP e-Profile ID, go to www.MyCPEMonitor.net for information and application. Please follow the instructions below to process your CPE credit for this activity.

1. The **ASHP eLearning** site allows participants to obtain statements of continuing education credit conveniently and immediately using any computer with an internet connection. Type the following link into your web browser to access the e-Learning site: **http://elearning.ashp.org/my-activities**
2. If you already have an account registered with ASHP, log in using your username and password.

   If you have not logged in to any of the ASHP sites before and/or are not a member of ASHP, you will need to set up an account. Click on the **Register** link and follow the registration instructions.
3. Once logged in to the site, enter the enrollment code for this activity in the field provided and click **Redeem**.

   Note: The Enrollment Code was announced at the end of the live activity.
   Please record the Enrollment Code in the grid below for your records.
4. The title of this activity should now appear in a pop-up box on your screen. Click on the **Go** button or the **activity title.**
5. Complete all required elements. A green ✔ should appear as each required element is completed. You can now claim your credit.
6. Available credit(s) will appear beneath the completed required activities. Look for your profession in the list of available credits and click the appropriate **Claim** button. You might have to click to see more credit options if you don't see your profession listed.

   CPE Credit for Pharmacists and Technicians: To claim continuing pharmacy education (CPE) credit, you will need to enter your NABP e-Profile ID, birth month, and birth day. Once you have entered this information the first time, it will auto fill in the future. Please note: All CPE credit processed on the eLearning site will be reported directly to CPE Monitor.
7. Review the information for the credit you are claiming. If all information appears to be correct, check the box at the bottom and click **Claim**. You will see a message if there are any problems claiming your credit.
8. Your credit will be reported directly to CPE Monitor.

Date of Activity	Activity Title	Enrollment Code	Credit Hours
9/10/15	Maximizing the Role of GLP-1 Agonists in Our Patients with Type 2 Diabetes		1.0

NEED HELP? Contact **eLearning@ashp.org**.

Important Tips in the Management of Epilepsy

Deepika Pereira, Pharm.D, BCPS
Neuro/Spine Critical Care Pharmacist
Northwestern Memorial Hospital

No conflicts of interest to disclose

Learning Objectives for Pharmacists

- List treatment pearls for common issues related to the management of epilepsy in the hospital setting
- Describe alternative treatment options for epilepsy due to medication shortage issues in the hospital setting

Learning Objectives for Pharmacy Technicians

- Recognize the impact of drug shortages on the management of epilepsy in the hospital setting
- List the available dosage forms of the anti-epileptic medications discussed during this presentation

Epilepsy: Background

- Affects ~3 million people in the US each year
- 10% of Americans will experience a seizure sometime in their lives
- 3% will receive a diagnosis of epilepsy by age 80
- Encompasses different seizure types and syndromes
- Usually difficult to ascertain cause
- Idiopathic (unknown cause) vs symptomatic (secondary to an identifiable condition)

Epilepsy: Definitions

- Seizures: disordered, synchronous and rhythmic firing of neurons thought to arise from the cerebral cortex
- Epilepsy: disorder of brain function characterized by the periodic and unpredictable occurrence of seizures

Management of Epilepsy

- Medication management
  - First unprovoked seizure
  - Chronic epilepsy syndromes
  - Status epilepticus
- Surgery

Medication management challenges

- Timing of medication administration
- Evidence based literature includes mostly expert opinion
- Extensive drug-drug interactions, short term and long term adverse effects, therapeutic drug monitoring
- Pharmacoresistance
- Drug shortages
- Education of healthcare providers

Timing

- Status epilepticus (SE) is defined as 5 minutes or more of (i) continuous clinical and/or electrographic seizure activity or (ii) recurrent seizure activity without recovery between seizures
- "Animal data suggest that permanent neuronal injury and pharmacoresistance may occur before the traditional definition of 30 min of continuous seizure activity have passed"
- Control of SE should be achieved within 60 mintutes of onset
- Refractory SE is defined as those patients who have failed first 2 anti-epileptic drugs (AEDs) administered
  - Consider use of continuous infusions

Tips on timing

- No established intravenous access
  - Alternate routes of benzodiazepines
    - Rectal diazepam
    - Intramuscular (IM) midazolam
    - IM: 2 ml in the deltoid and thigh muscles, and up to 5 ml in the gluteus maximus
  - Fosphenytoin is not caustic
- Hemodynamically unstable patients
  - Use of fosphenytoin
  - Maximum rate: 150 mg/min

Evidence-based support

Treatment	Class/level of evidence	References
Emergent treatment		
Lorazepam	Class I, level A	[19, 30, 52, 83, 87–88]
Midazolam	Class I, level A	[84, 99–106]
Diazepam	Class IIa, level A	[30, 87, 90, 95, 97–105, 107, 109–114]
Phenytoin/fosphenytoin	Class IIb, level A	[30, 87, 94, 115–119]
Phenobarbital	Class IIb, level A	[30, 87, 114]
Valproate sodium	Class IIb, level A	[116, 117, 120–123]
Levetiracetam	Class IIb, level C	[119, 123–130]
Urgent treatment		
Valproate sodium	Class IIa, level A	[117, 120–122, 131–136]
Phenytoin/fosphenytoin	Class IIa, level B	[30, 87, 93, 107, 114, 115, 117, 119, 132, 133, 137]
Midazolam (continuous infusion)	Class IIb, level B	[106]
Phenobarbital	Class IIb, level C	[138, 139]
Levetiracetam	Class IIb, level C	[119, 123, 125–127, 129, 130, 140, 141]
Refractory treatment		
Midazolam	Class IIa, level B	[28, 106–108, 142–150]
Propofol	Class IIb, level B	[26, 36, 62, 66, 68, 104, 151–155]
Pentobarbital/thiopental	Class IIb, level B	[26, 27, 56, 58, 59, 62, 63, 66, 68, 107, 115, 139, 154, 156–158]
Valproate sodium	Class IIa, level B	[120, 121, 131, 136, 159–161]
Levetiracetam	Class IIb, level C	[37, 66, 125–127, 129, 140, 141, 159, 162–164]
Phenytoin/fosphenytoin	Class IIb, level C	[57, 165]

Evidence-based support

Table 4. Summary of studies and level of evidence for each seizure type and epilepsy syndrome

Seizure type or epilepsy syndrome	Class I studies	Class II studies	Class III studies	Level of efficacy and effectiveness evidence (in alphabetical order)
Adults with partial-onset seizures	4	1	34	Level A: CBZ, LEV, PHT, ZNS Level B: VPA Level C: GBP, LTG, OXC, PB, TPM, VGB Level D: CZP, PRM
Children with partial-onset seizures	1	0	19	Level A: OXC Level B: None Level C: CBZ, PB, PHT, TPM, VPA, VGB Level D: CLB, CZP, LTG, ZNS
Elderly adults with partial-onset seizures	1	1	5	Level A: GBP, LTG Level B: None Level C: CBZ Level D: TPM, VPA
Adults with generalized onset tonic-clonic seizures	0	0	27	Level A: None Level B: None Level C: CBZ, LTG, OXC, PB, PHT, TPM, VPA Level D: GBP, LEV, VGB
Children with genetic (and unknown) onset tonic-clonic seizures	0	0	14	Level A: None Level B: None Level C: CBZ, PB, PHT, TPM, VPA Level D: OXC
Children with absence seizures	1	0	7	Level A: ESM, VPA Level B: None Level C: LTG Level D: None
Benign epilepsy with centrotemporal spikes (BECTS)	0	0	3	Level A: None Level B: None Level C: CBZ, VPA Level D: GBP, LEV, OXC, STM
Juvenile myoclonic epilepsy (JME)	0	0	1	Level A: None Level B: None Level C: None Level D: TPH, VPA

Evidence-based support

- SE guidelines include recommendations made from the results of an international survey and expert opinion
- International League Against Epilepsy updated review concluded that existing randomized controlled trials researching adult generalized tonic-clonic epilepsy are methodologically flawed and not adequate to answer important clinical questions

Medication profiles

Drug	Metabolism	Half-life (hours)	Therapeutic drug monitoring	ADE	Dosage forms	Comments
Fosphenytoin	rapidly converted via hydrolysis to phenytoin	**Conversion half-life: 15 minutes**	Free phenytoin level: 1-2 Total phenytoin level: 10-20	Arrhythmias	IV: 50 mg PE/ml	**Preferred use in hemodynamically unstable patients or those with inadequate IV access**
Lacosamide	40% unchanged 30% O-desmthyl-LCM (CYP2C19)	13	None	PR prolongation	Oral: 50 mg, 100 mg, 150 mg, 200 mg tablets and 10 mg/ml solution IV: 10 mg/ml	**Reduce dose in severe liver cirrhosis** 50% supplemental dose after dialysis
Levetiracetam	66% excreted unchanged 24% hydrolyzed	7		Well tolerated	Oral (IR): 250 mg, 500 mg, 750 mg, 1000 mg and 100 mg/ml solution Oral (ER): 500 mg and 750 mg IV: 100 mg/ml	Renal dose adjustment Supplemental dose adjustments after dialysis
Lorazepam	Glucuronidation 75% of metabolite excreted in urine	14-18	None	Hypotension Respiratory depression	Oral: 0.5 mg, 1mg, 2 mg tablets and 2 mg/ml solution IV: 2 mg/ml and 4 mg/ml	**Contains propylene glycol**

Drug	Metabolism	Half-life (hours)	Therapeutic drug monitoring	ADE	Dosage forms	Comments
Pentobarbital	Hydroxylated and then glucuronidated	15-50	5-20 mcg/ml	Respiratory depression Cardiac depression Paralytic ileus	IV: 50 mg/ml	**Can mimic brain death** Must be mechanically ventilated
Phenobarbital	50% hydroxylated, 25% glucuronidated 25% excreted unchanged	80-100	10-40 mcg/ml	Sedation Hypotension Respiratory depression	Oral: 20 mg/5ml solution 15 mg, 16.2 mg, 32.4 mg, 60 mg, 64.8 mg, 97.2 mg and 100 mg tablets IV: 65 mg/ml and 130 mg/ml	**Sequential loading if hypotensive**
Phenytoin	70% hydroxylated, then glucuronidated	20-60	Free phenytoin level: 1-2 Total phenytoin level: 10-20	Arrhythmias Hypotension Purple glove syndrome	Oral: 50 mg chew tabs, 30 mg and 100 mg ER capsules, 125 mg/ml solution IV: 50 mg/ml	**Saturable pharmacokinetics** **Unpredictable levels in uremia**
Valproate sodium	50% glucuronidated 50% multiple other pathways including beta-oxidation	9-16	Total valproate levels: 50-150 mcg/ml	Hyperammonemia Hepatotoxicity Thrombocytopenia	Oral: 125 mg sprinkle capsules, 250 mg and 500 mg ER tablets, 125mg, 250 mg and 500 mg DR tablets 250 mg IR capsules 250 mg/5 ml solution IV: 100 mg/ml	Preferred in anoxic brain injury Many formulations

Pharmacoresistance

- Failure of adequate trials of two tolerated, appropriately chosen and administered antiepileptic drugs (whether as monotherapy or in combination) to achieve seizure freedom
- Likelihood of successful treatment with other drugs of different class diminishes

Pharmacoresistance

- Alternative treatment options:
  - Combination medication therapy
  - Newer agents: eslicarbazepine and perampanel
  - Ketogenic diet
  - Rapid cooling
  - Herbal: ginger, ginseng, ginkgo biloba, kava kava, marijuana, melatonin, St. John's wort, valerian

Drug shortages

- Defined as a supply issue that affects how the pharmacy prepares or dispenses a drug product or influences patient care when prescribers must use an alternative when prescribers must use an alternative agent

Current Shortages

Drug Name	Shortage date	Reason
Divalproex sodium tablets	June 8, 2015	Product discontinued, manufacturer delay, on allocation
Levetiracetam injection	July 22, 2015	Manufacturer delay, increased demand
Lorazepam injection	July 16, 2015	Product discontinued, increased demand
Valproate sodium injection	August 11, 2015	Manufacturer delay

Resolved Shortages

Drug Name	Date resolved
Diazepam injection	October 4, 2013
Fosphenytoin injection	April 2, 2015
Ketamine injection	October 23, 2014
Midazolam injection	August 6, 2015
Phenobarbital injection and tablets	October 19, 2011 and May 8, 2014
Phenytoin injection and oral	January 23, 2015 and Octiber 4, 2011
Propofol injection	January 19, 2014
Topiramate capsules	August 10, 2011
Topiramate sprinkle capsules	April 23, 2014

Alternative treatment options

- Evidence based literature

Treatment	Class/level of evidence	References
Emergent treatment		
Lorazepam	Class I, level A	[10, 30, 52, 83, 87–90]
Midazolam	Class I, level A	[84, 99–108]
Diazepam	Class IIa, level A	[30, 87, 90, 95, 97–105, 107, 109–114]
Phenytoin/fosphenytoin	Class IIb, level A	[30, 87, 94, 115–119]
Phenobarbital	Class IIb, level A	[30, 87, 114]
Valproate sodium	Class IIb, level A	[116, 117, 120–122]
Levetiracetam	Class IIb, level C	[119, 123–130]
Urgent treatment		
Valproate sodium	Class IIa, level A	[117, 120–122, 131–136]
Phenytoin/fosphenytoin	Class IIa, level B	[30, 87, 97, 107, 114, 115, 117, 119, 132, 133, 137]
Midazolam (continuous infusion)	Class IIb, level B	[106]
Phenobarbital	Class IIb, level C	[138, 139]
Levetiracetam	Class IIb, level C	[119, 123, 125–127, 129, 133, 140, 141]
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Pentobarbital/thiopental	Class IIb, level B	[26, 27, 56, 58, 59, 62, 63, 66, 68, 107, 115, 139, 154, 156–158]
Valproate sodium	Class IIa, level B	[120, 121, 131, 136, 159–161]
Levetiracetam	Class IIb, level C	[37, 66, 175–177, 179, 140, 141, 159, 167–164]
Phenytoin/fosphenytoin	Class IIb, level C	[57, 165]

Alternative treatment options

- Use different agents within the same class
  - Benzodiazepines
  - Barbiturates
  - Phenytoin versus fosphenytoin

Alternative treatment options

- Use different dosage forms
  - Oral loading: phenytoin
    - Maximum absorption= 400 mg
  - Switch from oral solutions to tablets or capsules
    - dose based on drug delivery of formulation

Alternative treatment options

- Use agents with similar mechanism of action

Drug Name	Sodium channel	Calcium channel	GABA
Benzodiazepines			++
Carbamazepine	++	+	
Lacosamide	++		
*Lamotrigine	++	+	
Levetiracetam		+	
Oxcarbazepine	++	+	
Phenobarbital			++
Phenytoin	++		
*Topiramate	+	+	+
*Valproate	+	+	+

*Broad spectrum

Summary

- Management of epilepsy is complex and challenging
- No established guideline or literature to support the use of one AED over another
  - guidelines exist for the treatment of status epilepticus
- Pharmacists and technicians can make an impact in assisting healthcare providers with alternatives in the setting of drug shortages.

CW is a 20 year old female who presents to the emergency department after a generalized tonic-clonic seizure and brief loss of consciousness. She is alert and oriented currently and able to tell you that she has never had a seizure before and she has been very stressed lately with finals. She has been pulling consecutive all nighters and consuming 2 pots of coffee each day.

How would you treat CW?

A. Initiate phenytoin 15 mg/kg loading dose and 100 mg PO TID
B. Do not initiate any medication at this time
C. Administer lorazepam 2 mg IV push and send CW home
D. Initiate midazolam infusion

The guidelines for the management of status epilepticus includes:

A. Only Class I, level A evidence based recommendations
B. Only expert opinion
C. Some expert opinion and some Class I, level A evidence
D. Evidence that cannot be interpreted

A patient is noted to have status epilepticus on electroencephalogram (EEG) monitoring but has lost IV access and the physician would like to administer medication to break the seizure now.

What medication could you provide?

A. Rectal diazepam 0.2 mg/kg
B. Rectal midazolam 0.2 mg/kg
C. Intramuscular diazepam 0.15 mg/kg
D. Phenytoin oral loading dose 15 mg/kg

Pharmacoresistance is a prevalent issue in managing epilepsy. What alternative treatment option is recommended to overcome pharmacoresistance?

A. Herbal supplements
B. Electroconvulsive therapy
C. Combining AEDs with differing mechanisms of action
D. Warming

Valproate sodium injection is on short supply. A patient has been on 500 mg IV infusion every 6 hours and needs to be converted to an oral formulation. What dosing would be equivalent?

A. Divalproex sodium 500 mg DR PO twice a day
B. Divalproex sodium 1500 mg ER PO once daily
C. Divalproex sodium 500 mg DR PO every 6 hours
D. Valproic acid oral solution 500 mg PO every 6 hours

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Establishing a Patient Care Ritual: Pharmacists' Patient Care Process

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Audience Polling: Are you familiar with the new Pharmacists' Patient Care Process (PPCP)?

1. Yes
2. No

Audience Polling: Have you utilized or taught the pharmacists' patient care process in your practice?

1. Yes
2. No

Learning Objectives (Pharmacists and Technicians)

1. Describe how a standardized patient care process has been defined by national pharmacy organizations.
2. Explain the rationale for using a standardized patient care process.
3. Devise a care plan using the standardized patient care process.
4. Apply factors to consider, including health information technology, when implementing a standardized patient care process in various practice settings.
5. Identify how to obtain resources and tools for implementing a standardized patient care process.

Self-Assessment Question #1

The pharmacists' patient care process was created to:

1. promote consistency across the profession.
2. document immunizations in the community.
3. make pharmacy practice more challenging.
4. serve only the didactic needs of Colleges of Pharmacy.

Self-Assessment Question #2

The pharmacists' patient care process is:

1. pharmacist centric.
2. meant to be implemented independently by the pharmacist.
3. a five-step process: collect, assess, plan, implement, follow-up: monitor and evaluate.
4. a totally new process.

Self-Assessment Question #3

The pharmacists' patient care process identifies three key roles that transcends all steps. They are:

1. communicate, measure, and report.
2. interview, assess, and coordinate.
3. medication reconciliation, counseling, and document.
4. collaborate, communicate, and document.

Self-Assessment Question #4

In order to implement the PPCP in your practice:

1. an action plan should be developed to evaluate existing services.
2. education of colleagues and other health care providers will be necessary.
3. continuous quality improvement should be used.
4. All of the above.

Self-Assessment Question #5

Key national organizations are developing strategies to implement the PPCP.

1. True
2. False

Joint Commission of Pharmacy Practitioners (JCPP)

JCPP Vision:

- Patients achieve optimal health and medication outcomes with pharmacists as essential and accountable providers within patient-centered, team-based healthcare.

Pharmacists' Patient Care Process

JCPP Strategic Plan: **Consistent patient care process** identified as a key driver for achieving the JCPP vision

- Supports the profession's provider status activities
- Needed to meet demands of evolving health care system
  - Movement towards outcomes-based payment

Collaboration of national pharmacy organizations working to develop a standardized pharmacist patient care process

- Purpose: to stimulate consistency, predictability, and measurability in pharmacists' service delivery

Need for Consistency, Predictability, and Measurability

- Outcomes based payment
- Objective comparisons between individual and groups of pharmacists
- Consistent expectations for diverse stakeholders
  - Patients, other healthcare providers, payers, regulatory bodies, government
- Comparative effectiveness research

JCPP Pharmacists' Patient Care Process Workgroup

Activities: January 2012-May 2014

- Workgroup meetings
- Environmental scan
- Testing among clinicians
- Organizational feedback

Pharmacists' Patient Care Process Development

Review of key resources

- Pharmaceutical care – Strand & Cipolle
- Profession's MTM definition and MTM Core Elements
- PCPCC Medication Management Resource Guide
- ACA language
- Nurse Practitioner's Practice Standards

Pharmacists' Patient Care Process Development

Should apply to the wide variety of patient care services provided by pharmacists AND the pharmacist's medication expertise

- Level of intensity varies depending on the service
- One pharmacist (or technician) might be responsible for all the steps in some settings where in others more than one pharmacist may be involved at different stages of the process.

Goals

*Pharmacists' patient care process created to:

- promote consistency across the profession.
- provide a framework for delivering patient care in any practice setting.
- be a contemporary and comprehensive approach to patient-centered care delivered in collaboration with other members of the health care team.
- apply to a variety of patient care services delivered by pharmacists, including medication management.

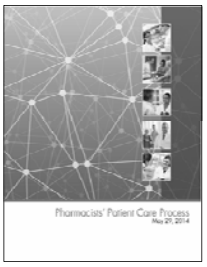
Pharmacists' Patient Care Process

Foundational Components:

- Establishment of patient-pharmacist relationship
- Engagement and effective communication with patient, family, caregivers
- Continually collaborate, document, and communicate with physicians and other health care providers
- Process enhanced by interoperable information technology systems that facilitate effective and efficient communication

Pharmacists' Patient Care Process

- Approved by JCPP organizations in May 2014
- Supported by 13 national pharmacy organizations



http://www.pharmacist.com/sites/default/files/PatientCareProcess.pdf

Pharmacists' Patient Care Process

COLLECT

Necessary subjective and objective information about the patient in order to understand the relevant medical/medication history and clinical status of the patient.

Information may be gathered and verified from multiple sources.

Collect:

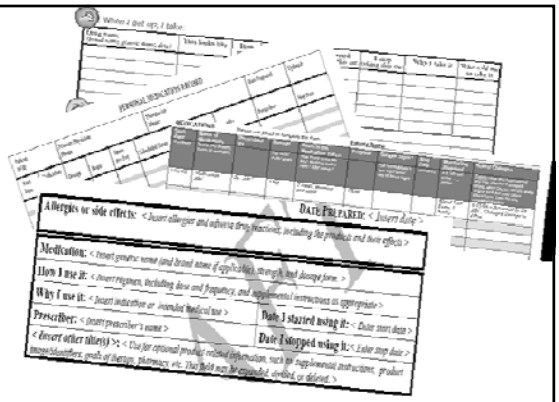
1. A current medication list and medication use history for prescription and nonprescription medications, herbal products, and other dietary supplements
2. Relevant health data that may include medical history, health and wellness information, biometric test results, and physical assessment findings
3. Patient lifestyle habits, preferences and beliefs, health and functional goals, and socioeconomic factors that impact access to medications and other aspects of care

Collect: 1. Medication List

Fundamental role

"current" "complete" "active"

Medication reconciliation



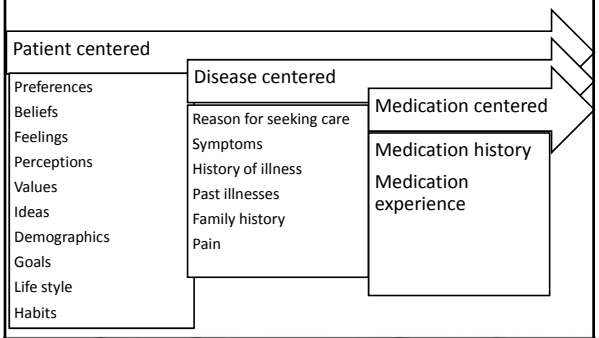
Medication List- Components to Consider

Patient Information ▪ **Patient name** ▪ **Patient contact information** ▪ **Patient date of birth**	▪ **Medical record number** ▪ **Emergency contact**
List For Each Current or Active Medication (Rx, OTC, herbals, etc)	
▪ **Indication** ▪ **Generic and trade name** ▪ **Strength of ordered tablet, capsule, inhaler, etc.** ▪ **Current dose (# of tablets, capsules, etc., that equal that dose)** ▪ **Frequency of administration** ▪ **Route of administration**	▪ Special instructions ▪ Optimal time to take medication ▪ Description of medication or picture ▪ Other as needed (i.e., side effects, goals, special instructions, etc.) ▪ Date medication was started ▪ Prescribing provider ▪ Refill date
Additional Content ▪ **Allergies** ▪ **Source of current list, who created list)** ▪ **Date it was created**	▪ Providers (including pharmacies) and their contact information ▪ Medication past history, reason medication was stopped, and date stopped

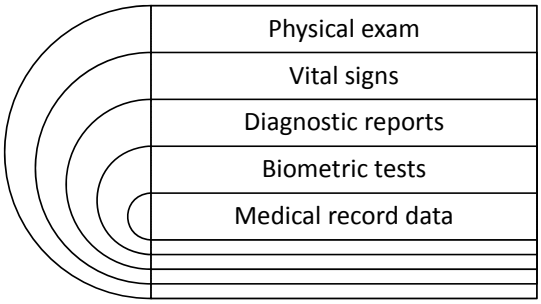
Collect:
2. Relevant Health Data

- Depth and breadth of services requested
- Location of services
- Complexity of patient

Subjective Patient Data



Objective Patient Data



Challenges

Pharmacist factors
- Knowledge
- Communication skills

Patient factors
- Accuracy as a historian
- Cognitive abilities
- Communication skills

System factors
- Efficiency
- Access
- Time

29

Patient Case: Mr. W.A.

68 year old Caucasian male referred to pharmacy services because of three hospital admissions for exacerbation of heart failure in the past year.

What information do you want to collect?

Patient Case: Mr. W.A. EMR data

CC: 68 yo presented with increasing shortness of breath and bilateral leg swelling

HPI: On vacation in Key West and noticed in airport on his way home he had to stop to catch his breath.
Legs have been swelling so took some extra furosemide and swelling improved but persistent SOB. Unable to put shoes on today.
States he was very active in Florida.
Since home has had low energy and stamina
No palpitations, fever, chills, cough
More lightheaded and dizzy than usual

ROS: 15 lb weight gain on trip with 7 lb weight loss since furosemide
Dyspnea on exertion

PMH: HTN, atrial fib with failed cardioversion x2, CAD, S/P CABG single vessel RCA; hyperlipidemia, GERD osteoarthritis, BPH, stage 3 CKD

Patient Case: Mr. W.A. EMR data

FH: both parents with HTN
SH: non-smoker occ alcohol
Allergies: Zolpidem
Medications:

- Warfarin 3mg daily
- Pravastatin 40mg daily
- Metoprolol XL 25mg daily
- Amlodipine 5mg daily
- Lisinopril 10mg daily
- Furosemide 40mg daily
- KCl 20mEq daily
- Omeprazole 20mg daily (OTC)

Patient Case: Mr. W.A. EMR data

PE/Vitals
HR 67, BP 119/70 RR 20 Ht 74 inches, 129.5 kg (285 lbs) BMI- 36.5
Cardio: Mild JVD ireg ireg rhythm
Lungs bilateral rales
Extremities: visit 2-3+ bilateral edema
Labs
H/H 14.8/44.8, WBC 6.2
Na 138, K 4.0 BUN/Cr 23/1.88
Troponin 0.02 CK 80 CK-MB 1.1 INR 2.5
Lipids: TC 240 LDL 115 HDL 35
Other tests
O2 sat 97%
EFR 40%
EKG – atrial fib

You are ready to visit the patient. What additional information do you want to collect?

1. A current and complete medication list and medication use history

2. Relevant health data
   - medical history
   - health and wellness information
   - biometric test results
   - physical assessment findings

3. Lifestyle habits, preferences and beliefs, health and functional goals, and socioeconomic factors that impact access to medications and other aspects of care

Patient Case: Mr. W.A. interview

S: Since retired travels for pleasure 4-5 times a year with friends

Diet: Goes out to eat frequently, especially when on vacation, likes McDonalds hamburgers, does not add salt, cannot eat greens so pretty much meat and potatoes

Exercise: Plays golf at least 2-3 times per week with cart

Occasionally weighs himself. Does not understand why he is supposed to weigh himself daily. Tough to do when traveling

Medications: rarely misses medications, easy for him to take except furosemide which he there is something he is doing in the morning he does not take

zolpidem allergy - felt fuzzy in the head

Other: has had insomnia for years for which he takes diazepam

SH: Retired VP of a high tech firm

Patient Case: Mr. W.A. interview

Additional Medications
- Diazepam 5 mg prn sleep – uses regularly
- Vitamin D 2000 units daily
- Vitamin C 500 units daily
- Centrum silver daily
- Celebrex 200 mg as needed for aches and pain especially after golfing
- Tadalafil 2.5 mg when needed
- Acetaminophen 325 mg as needed

ASSESS

The pharmacist assesses the information collected and analyzes the clinical effects of the patient's therapy in the context of the patient's overall health goals in order to identify and prioritize problems and achieve optimal care.

Assess:
- Each medication for **appropriateness, effectiveness, safety**, and patient **adherence**
- Health and functional status, risk factors, health data, cultural factors, health literacy, and access to medications or other aspects of care
- Immunization status and the need for preventive care and other health care services, where appropriate

'Assess' Components

- **Medication assessment**
  - Appropriateness
  - Effectiveness
  - Safety
  - Adherence
- Patient history and risk assessment
- Preventive care assessment

Knowledge and Problem Solving Skills

Patients medical and medication history

Clinical practice guidelines

Evidence based medicine

Disease state risk factors

Medication Assessment

Medication Appropriateness
- Are there any disease states or indications for which the patient does not currently have a medication but a medication may be beneficial?
- Is the patient taking a medication for no medically valid indication?
- Does each prescribed medication have a current and valid indication? Do some medications have duplicate indications pertaining to the patient?

Mr. W.A.

HTN, atrial fib, HF, CAD, S/P CABG single vessel RCA
Warfarin 3mg daily
Metoprolol XL 25mg daily
Amlodipine 5mg daily
Lisinopril 10mg daily
Furosemide 40mg daily
KCl 20 mEq daily

Hyperlipidemia
Pravastatin 40mg daily

GERD
Omeprazole 20mg daily (OTC)

Osteoarthritis
Celebrex 200 mg as needed

Insomnia
Diazepam 5 mg prn sleep – uses regularly

ED
Tadalafil 2.5 mg when needed

BPH

Stage 3 CKD

Other
Vitamin D 2000 units daily
Vitamin C 500 units daily
Centrum silver daily
Acetaminophen 325 mg as needed

Medication Assessment

Medication Effectiveness

- Is the medication working? Achieving desired therapeutic goals?
- Is the medication the optimal choice for the indication being treated?
- Is the patient on the correct (adequate) dose of medication?
- Are monitoring parameters in place to evaluate medication effectiveness and safety?
- Do results of medication monitoring indicate continued use of this medication?

Mr. W.A.

HTN, atrial fib, HF, CAD, S/P CABG single vessel RCA
Warfarin 3mg dail
Metoprolol XL 25r
Amlodipine 5mg d
Lisinopril 10mg da
Furosemide 40mg daily
KCl 20mEq daily

HF target doses
Spironolactone?

NSAIDs contraindicated

Hyperlipidemia
Pravastatin 40mg daily

Diazepam high risk in the elderly

GERD
Omeprazole 20mg daily (O

Osteoarthritis
Celebrex 200 mg as needed

Insomnia
Diazepam 5 mg prn sleep

PE
BP 120/69 HR 65 irreg-irreg, RR
15, wt 127 kg (280 lbs)
ilaterally
edema bilat
Est CrCl – 53 ml/min
ASCVD – 21.5%
0 BUN/Cr 23/1.88
INR 2.5
0 LDL 115 HDL 35

Medication Assessment

Medication Safety

- Is the dose of medication higher than the usual recommended dose for its indication?
- Is the patient experiencing signs or symptoms of adverse medication effects?
- Is the patient experiencing a side effect or issue that decreases patient safety that may be a result of a drug–drug, drug–food, or drug–laboratory test interaction?
- Do results of medication monitoring indicate a need for intervention?

Medication Assessment

Medication Adherence

- Is the patient taking the medication too frequently or too much at one time?
- Is the patient not meeting clinical goals or measures based on not receiving or taking the medication as prescribed?
- Can the patient afford the medications? Is cost affecting medication adherence?
- Are there alternative therapies that could be used for an indication that would decrease patient cost burden?
- Are there therapies that may be unnecessary and would decrease cost if discontinued?
- Does the patient have a medical problem that is the result of not receiving a medication because of economic, psychological, sociological, or pharmaceutical reasons?

Mr. W.A.

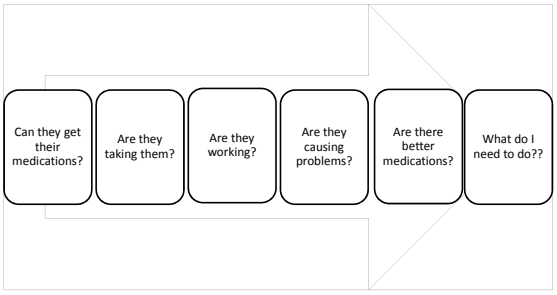
Safety

- Diazepam
- NSAID

Adherence

- Furosemide

Patient History and Risk Assessment- Thought Process



Preventative Care Assessment

- Immunizations
- Self-examinations
- Screenings

- Based on collected data- medical history, family history, lab values, current disease states, environmental factors

Mr. W.A.

Risk assessment

- ASCVD
  - 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults. Available at http://circ.ahajournals.org
- Aspirin
  - 2013 ACC/AHA Guideline on the assessment of Cardiovascular Risk. JACC 2014;63:2935-59
  - AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients with Coronary and Other Atherosclerotic Vascular Disease: 2011 Update. Available at http://circ.ahajournals.org

Preventative Care

- Immunizations- CDC

PLAN

The pharmacist develops an individualized patient-centered care plan, in collaboration with other health care professionals and the patient or caregiver that is evidence-based and cost-effective.

The plan:

- Addresses medication-related problems and optimizes medication therapy
- Sets goals of therapy for achieving clinical outcomes in the context of the patient's overall health care goals and access to care
- Engages the patient through education, empowerment, and self-management
- Supports care continuity, including follow-up and transitions of care as appropriate

Medication Related Problems and Optimizing Therapy

Rules to abide by

- Evidence Based
- Cost Effective
- Best achieve desired outcomes
- In collaboration with the patient
- In collaboration with the team
- Coordination of care

Setting Goals of Therapy

S	• Specific
M	• Measurable
A	• Action-oriented
R	• Realistic
T	• Time-specific

Setting Goals of Therapy

- Based on evidenced-based guidelines
- ie. Laboratory values (A1C, blood pressure), safety parameters (side effects, drug interactions), adherence (refills)

What would you like to do for Mr. W.A.?

Plan: Mr. W.A.

Heart failure: Goals decrease hospitalization, relieve symptoms, no side effects to medications

Medications:

- Increase Lisinopril to 20 mg daily (potentially 40 mg)
  - **monitor BP, K+, Cr**
- Consider adding spironolactone 12.5 mg daily
  - **monitor K+, Cr**
- Stop amlodipine if needed to maintain BP

Education:

- Heart failure medications and how they work
- Diet – restricted sodium intake and fluid management
- Daily weights
- Optimal use of furosemide
- Exercise and weight loss

Plan: Mr. W.A.

Atrial fibrillation: Goal INR at goal range, no side effects or stroke

- Continue Warfarin 3 mg daily
  - **Monitor INR monthly, consider self management**
  - **Educate as needed**

Hyperlipidemia: Goal current recommendations, no side effects

- Switch to atorvastatin 80 mg daily
  - **Monitor if tolerated in 7-14 days**

GERD: Goal control of symptoms

- Continue present management

Osteoarthritis: adequate pain control, stable renal function

- Evaluate use and need for NSAID
- Educate on reasons NSAID not recommended

Insomnia: adequate sleep, appropriate therapy

- Recommend and refer sleep study and OSA evaluation
- Educate on diazepam concerns

IMPLEMENT

The pharmacist implements the care plan in collaboration with other health care professionals and the patient or caregiver.

The pharmacist:

- Addresses medication- and health-related problems, and engages in preventive care strategies, including vaccine administration
- Initiates, modifies, discontinues, or administers medication therapy as authorized
- Provides education and self-management training to the patient or caregiver
- Contributes to coordination of care, including the referral or transition of the patient to another health care professional
- Schedules follow-up care as needed to achieve goals of therapy

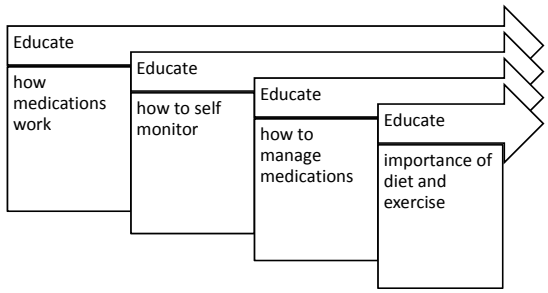
Tips for implementing the plan

- Prioritize medication related problems
- Consider number and order of therapy changes
- Personalize education to patient needs and abilities
- Coordinate care with health team members
- Determining reasonable follow up
- Document

Communication Tips

S • Situation	S • Subjective
B • Background	O • Objective
A • Assessment	A • Assessment
R • Recommendation	P • Plan

Implementation with Mr. W.A.



FOLLOW-UP: MONITOR AND EVALUATE

The pharmacist monitors and evaluates the effectiveness of the care plan and modifies the plan in collaboration with other health care professionals and the patient or caregiver as needed.

Monitor and evaluate:

- Medication appropriateness, effectiveness, and safety and patient adherence through available health data, biometric test results and patient feedback
- Clinical endpoints that contribute to the patient's overall health
- Outcomes of care, including progress toward or the achievement of goals of therapy

Measuring Outcomes

Mandated

- ACO
- Star measures
- HEDIS
- CAHPS scores

Measure sources

- Pharmacy Quality Alliance
- National Quality Measures Clearinghouse
- National Quality Forum (NQF)
- National Committee for Quality Assurance (NCQA)

Measuring Outcomes- Examples

Clinical Measures	Humanistic Measures	Economic
• Blood pressure • A1c • Medication problem resolution • Adverse drug events • Adherence	• Patient medication knowledge • Patient functioning • Self-management capability • Satisfaction	• Hospitalizations • Emergency department visits • Medication Costs

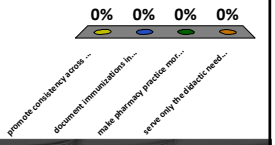
Restarting the Wheel

- Is the patient making progress toward therapeutic goals?
- Are previous problems resolved?
- Have any new problems emerged?
- What are the results of treatment changes?
- What are the results of any referrals?

Self-Assessment Question #1:

The pharmacists' patient care process was created to:

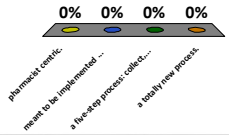
1. promote consistency across the profession.
2. document immunizations in the community.
3. make pharmacy practice more challenging.
4. serve only the didactic needs of Colleges of Pharmacy.



Self-Assessment Question #2:

The pharmacists' patient care process is:

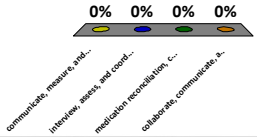
1. pharmacist centric.
2. meant to be implemented independently by the pharmacist.
3. a five-step process: collect, assess, plan, implement, follow-up: monitor and evaluate.
4. a totally new process.



Self-Assessment Question #3:

The pharmacists' patient care process identifies three key roles that transcends all steps. They are:

1. communicate, measure, and report.
2. interview, assess, and coordinate.
3. medication reconciliation, counseling, and document.
4. collaborate, communicate, and document.

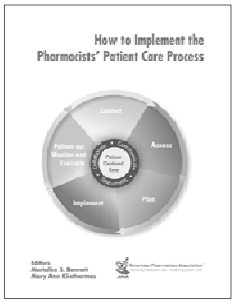


Applying and Implementing the PPCP

National Implementation

Current strategies underway:	Outreach: Press release, presentations
	Communications plan, toolkit, practice-setting specific case examples, and other materials under development through JCPP
	ACPE has incorporated the patient care process in PharmD standards 2016.
	Pharmacy HIT Collaborative is using the process as a framework to develop structured patient care documents to be used electronically via the electronic health record (EHR).
	The Pharmacy Quality Alliance (PQA) is considering the process in developing quality measures.
	Projects: Patient care process is being used in a national patient safety organization project to identify gaps in care.
	Training: The Alliance for Integrated Medication Management (AIMM) Collaborative, several Center for Medicare and Medicaid Innovation (CMMI) grantees, CE providers incorporating the process into education and training.

Resources



http://www.pharmacist.com/sites/default/files/PatientCareProcess.pdf

Step 1: Practice. Apply the process to patient case studies

Collect	List the necessary subjective and objective information you need to collect.
Assess	Analyze the information in the context of the patient's overall goals, and identify and prioritize the problems.
Plan	Develop an individualized patient-centered care that is both evidence based and cost effective.
Implement	Execute the care plan in collaboration with other health care professionals and the patient or caregiver.
Follow-up: Monitor and Evaluate	List monitoring and evaluation parameters.

Application Examples: Service/Setting

- Comprehensive medication review and follow-up
- Pharmacist consult in hospital
- IV to oral anticoagulant dosing
- Medication reconciliation during a care transition
- Diabetes management
- Immunization

Step 2: Evaluate existing services, develop strategies, and implement the process

Create Action Plan

- What patient care service?
- How to apply the process?
- Staff development?
- Anticipated impact?

Evaluate Existing Services

Patient Care Service	Collect	Assess	Plan	Implement	Follow up: Monitor & Evaluate
Comprehensive Medication Reviews	2	3	1	2	1

Rate the current delivery of each service-line for alignment with each step in the PPCP:

Alignment: Low = 1, Medium = 2, High = 3

Evaluating Existing Services

Patient Care Process Step	Quality Improvement Strategy	Implementation Timeline
Collect	1. Develop a protocol to standardize collection process 2. Design and implement standard patient intake form in EHR	1. One month 2. Three months
Assess		
Plan		
Implement		
Follow-up: Monitor and Evaluate		

Step 3: Advocate, Educate, and Promote

- Identify those associated with your practice
  - Colleagues
  - Other healthcare providers
  - Payers
  - Residents/Students
- Create a plan
  - Action item
  - Desired Outcome
  - Timeline

Step 4: Use Continuous Quality Improvement

- Reassess services on a periodic basis for alignment with the PPCP.
- Develop strategies and implementation plans for areas with low alignment.
- (see Step 2)

Key Points

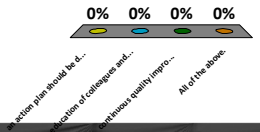
- Consistency, predictability, and measurability
- Across all practice sites and disease states
- Patient-centered
- Team based care
- Patient Care Process
  - Collect
  - Assess
  - Plan
  - Implement
  - Follow up: Monitor and Evaluate

Pharmacists' Patient Care Process

Self-Assessment Question #4:

In order to implement the PPCP in your practice:

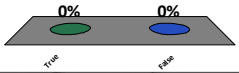
1. an action plan should be developed to evaluate existing services.
2. education of colleagues and other health care providers will be necessary.
3. continuous quality improvement should be used.
4. All of the above.



Self-Assessment Question #5:

Key national organizations are developing strategies to implement the PPCP.

1. True
2. False



Self-Assessment Question #6:

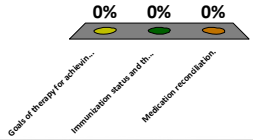
ACPE has incorporated the pharmacists' patient care process into PharmD Standards for 2016.

1. True
2. False

Self-Assessment Question #7:

Which of the following are considered during the 'Plan' step of the PPCP?

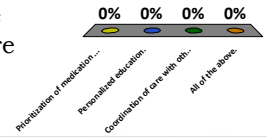
1. Goals of therapy for achieving clinical outcomes.
2. Immunization status and the need for preventative care.
3. Medication reconciliation.



Self-Assessment Question #8:

The 'Implementation' step of the PPCP should include:

1. Prioritization of medication related problems.
2. Personalized education.
3. Coordination of care with other healthcare providers.
4. All of the above.



Self-Assessment Question #9:

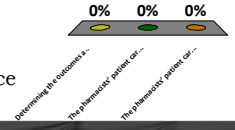
The need for consistency, predictability, and measurability in pharmacy practice is driven in part by the movement towards outcomes based payment.

1. True
2. False

Self-Assessment Question #10:

Choose the most correct answer related to the pharmacists' patient care process:

1. Determining the outcomes and value of pharmacists' services requires a consistent process of care.
2. The pharmacists' patient care process is only applicable to the ambulatory/community pharmacy setting.
3. The pharmacists' patient care process requires the use of collaborative practice agreements.



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Interprofessional Practice: Start at the Grassroots

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Disclosures

Reid Blackwelder & Brian Cross declare no conflicts of interest, and have no financial interests, arrangements or affiliations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Disclosure Statement of Unapproved/Investigative Use

Reid Blackwelder and Brian Cross, DO NOT anticipate discussing the unapproved/investigative use of a commercial product/device during this activity or presentation

Learning Objectives for Pharmacists and Pharmacy Technicians

1. Describe payer, including CMS, programs that incentivize health care professionals to improve patient outcomes.
2. Discuss effective strategies for incorporating pharmacists as part of health care teams.
3. Describe roles and responsibilities of pharmacists as part of the healthcare team.
4. Explain how pharmacists and pharmacy technicians bring value to the health care team and contribute to meeting patient outcomes as part of team-based care.

All of the following are examples of changing issues within the US healthcare system EXCEPT:

1. PCMH
2. ACO
3. PMPM
4. IPTM

The process of medication reconciliation should include:

1. Assurance that the current medication list represents what the patient is actually taking (Rx, OTC, natural medicines, vitamins)
2. Documentation of all potential medication-related problems and potential interventions to remedy them
3. Use of evidence-based medicine principles to create and individualize pharmacotherapy regimens for each patient
4. All of the above

Which of the following represent potential barriers to creating collaborative team-based practices?

1. Fractured communication
2. Historical perceptions of siloed responsibilities
3. Health record inter-operabilities
4. All of the above

Why we are here

- ***Stories from Reid***
  - Medicine
  - NHSC
  - Quillen COM
- ***Stories from Brian***
  - Pharmacy
  - IHS
  - Gatton COP

Realities

- Old "Healthcare" System broken
- ACA "process" crippled
- Fee for Service consequences
- Siloed, fragmented care
- Poor patient outcomes, poor satisfaction, high cost

"Patient-Centered"

- Not so much!
- Practice / Practitioner centered instead
- The latest catch-phrase is Team-Based Care

Current "Team"

- No record inter-operability
- Reinforced silos
- Employed status changes relationships
- Faxes, Pas, insurance divert healthy, professionally engaging interactions
  - - - as well as
  - **DIRECT CARE**
- **PCMH MODEL OF CARE**

SOUNDS LIKE A GOOD IDEA, I THINK….

Community-based Care

- ***Trenton***
- ***San Carlos***
- ***Kingsport***

Example: "Community" Pharmacy

- Only place with "complete" medication list….
  - ……..maybe
- Need Provider(s) records
- AND……. patient's real medicine cabinet
- The EMR reconcile button is provider-centered

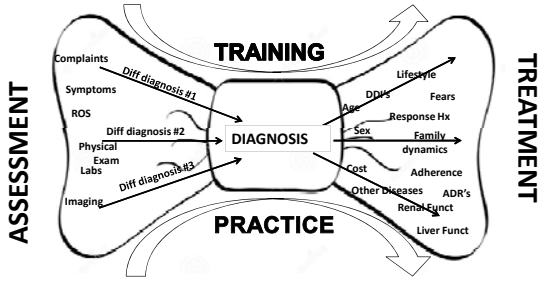
RECONCILE

- REMEMBER: EVERY PRACTICE HAS A COMMUNITY TO BE SERVED

Transformation

- ***Delivery models are changing***
  - PCMH, ACO's, Retail clinics, telemedicine
- ***Payment models are changing***
  - Pay for value *(instead of volume)*
  - Chronic Care Management
  - PMPM
  - Trends toward models for **teams** being responsible for **care AND outcomes**

The Bowtie Phenomenon



Natural Team Members

- Education & implementation for providers
- Lots of variables from undifferentiated process
- **TO "AN ANSWER"**
- Education & implementation for pharmacists
- Move out from a differentiated process to lots of variables to be considered

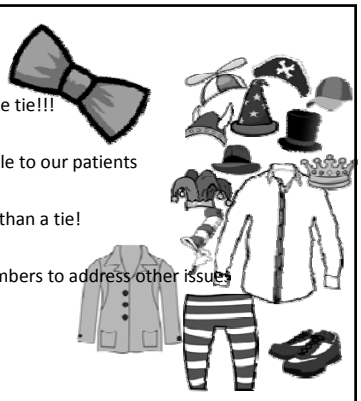
Example

- Acute & chronic issues almost always involved
- ***Reid*** – "I focus on keeping variables in mind"
- Medications often connect all team members
- ***Brian*** – "I ensure true medication reconciliation"

Relationships

- "Assume good intent!"
- Miscommunication is easy
- How can we talk more readily, respectfully
- Recognize we are all here to help **PATIENTS**

BUT…..



- The patient **WEARS** the tie!!!
- We are ALL accountable to our patients
- And…. we need more than a tie!
- Many other team members to address other issues

Communication Styles

Instead….

Changes needed - Practice

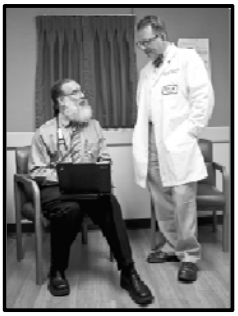
- Change from student/employee mentality….
  - …..to that of a professional
- To accept the call to service
- MUST be **involved** **WHERE** change is happening so we can impact **WHAT** change happens
  - **CARE DELIVERY & PAYMENT MODELS**
  - **DEFINE YOUR COMMUNITY**
  - **INDENTIFY WHAT YOUR PATIENTS NEED**
- **Relationships** allow big systems to work better
- Most aisles are more narrow than they look – reach across them

Changes needed - Training

- We should be training **WITH EACH OTHER**
  - **NOT BESIDE EACH OTHER**
- **IPE** – two or more professions learning **with**, **from**, & **about each other** to improve ***collaboration*** and the ***quality of care***
- If silos are minimized during training, maybe they won't be so obvious in practice
- Let's create a **different pavlovian conditioning** in our professions

BECAUSE

It's ALL about Relationships



- Based on trust, respect
- And especially on improving patient care!
- And it can be up to you! (No memo needed)

And Remember….

- It is **NOT patient-centered** until the **patient says** it is **patient-centered**
- The **PATIENT** wears the **TIE**

Action

- What relationships do you need?
- What is one thing you can do personally to build a stronger relationship?
- What tools do you need?

Key Points

- Delivery & payment models for care are being transformed with increasing focus on team-based, outcomes-based care
- The training & skills of ALL team members are symbiotic when combined in the patient care arena
- Changes must occur both in training & practice areas to ensure relationships can be optimized in a team-based approach to patient care

Ultimate Goal….

- **PATIENTS DESERVE:**
  - The Right Care
  - In the Right Place
  - From the Right Team Members
  - At the Right Time!

All of the following are examples of changing issues within the US healthcare system EXCEPT:

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3. PMPM
4. IPTM

The process of medication reconciliation should include:

1. Assurance that the current medication list represents what the patient is actually taking (Rx, OTC, natural medicines, vitamins)
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4. All of the above

Which of the following represent potential barriers to creating collaborative team-based practices?

1. Fractured communication
2. Historical perceptions of siloed responsibilities
3. Health record inter-operabilities
4. All of the above

How to turn a regular tie into a bow tie

- http://binged.it/1ApXZgk
- http://binged.it/1xrkMqO

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Informatics Pearls

Learning Objectives for Pharmacists and Pharmacy Technicians

1. Describe an automated system that can be used to track drug recalls.
2. Explain the roles available to pharmacy technicians in the informatics space.
3. Identify a method for reporting near-miss errors.
4. Illustrate an automated workflow for restocking a used pharmacy kit.
5. Describe strategies that can be employed to overcome alert fatigue.

Informatics Pearls - Battling Alert Fatigue

Michelle Geurink, RPh
OSF Healthcare System

No Conflict of Interest

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Know Your Alerts

- Drug-Drug
  - Severity
  - Documentation
  - Management Code
- Allergy
  - Inert Ingredients
  - Cross Allergens
- Precautions
  - Pregnancy
  - Lactation

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Know Your Alerts

- Duplicate Medication
  - Route
  - Status (PRN)
- Duplicate Therapy
  - Categories
  - Status
- Dose
  - Minimum/Maximum
  - Dose/Day

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Low Hanging Fruit

- Duplicate Therapy Allowances
- Suppression in Order Sets
  - Pregnancy Alerts in OB order sets
    - 0.4 warnings/100 orders= 2851 alerts
    - 0.2 warnings/100 orders= 1398 alerts
  - Duplicates (Heparin load, bolus, infusion)
    - 823 alerts/month (August 2014)
    - 0 alerts/month (April 2015)

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Know Your Options

- Example: Drug-Drug Interaction

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Know Your Options

- Example: Duplicate Therapy

Enlist the Experts

- Workgroup
  - Review Optimization Report
  - Drug-Drug Interactions
    - Management Code
  - Duplicate Therapy
    - What meds are included

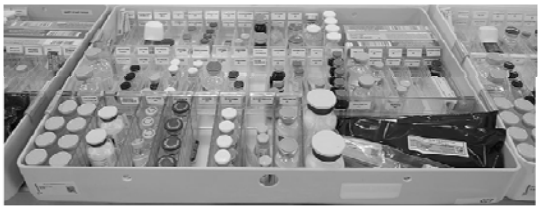
Next Steps

- Workgroup
  - Evaluate Changes
  - Review Optimization Report
  - Drug-Drug
- User Filtered Alerts
  - Drug-Drug
  - Pregnancy/Lactation (order sets)
  - Others Already Filtered (e.g. Drug-Food)

Automated Pharmacy Kit Replenishment Solutions

Joshua Hartman, PharmD, MS
Sinai Health System
Clinical Informatics Specialist
No actual or potential conflicts of interest

One Tray Many Drugs



Polling Question

- Does your institution use an automated pharmacy kit replenishment solution?
  - A. Yes
  - B. No

Available Solutions

- Kit Check
- MedEx Tray Safe

Keeping your numbers straight

- Utilizes RFID technology and/or 3D barcoding to ensure accuracy of tray contents
- Monitor usage, expiration, and lot number information for recalls
- Enables advanced reporting
- Potential for reduction of stock

Operational Considerations

- Tray Turnover
- Number of items in rotation
- Space Considerations
- Technical requirements

Self-Assessment Question

An automated pharmacy kit replenishment solution has the potential to reduce the time spent checking kits by how much?

A. > 25%
B. >40%
C. >50%
D. >75%

Informatics Pearls – The Role of the Technician in Informatics

Heather Horton, PharmD, M.S.
Pharmacy Technician Program
South Suburban College

Speaker has no conflict to disclose.

Objective

- Explain the roles available to pharmacy technicians in the informatics space

Questions

- What is a Pharmacy Technician Informaticist (PTI)?
- In what setting(s) are PTIs employed?

Pharmacy Technician Informaticists

- Manage pharmacy IT processes
  - Automation and technology systems management
  - Project management
  - Training and education
  - Policy and governance
  - Customer service
  - Reporting

Inpatient Pharmacy Informatics

- Barcode Medication Administration
- Automated Dispensing Systems
- Inventory
- Computerized Physician Order Entry
- Electronic Health Record

Community Pharmacy Informatics

- Software evaluation and implementation
- Documentation strategies
- Billing and reimbursement
- End user training
- Maintenance and support

Other Settings

- Long Term Care
- Specialty Pharmacy
- Mail Order
- Software Vendors
- Third Party Payers
- Education

Review Questions

- What is a Pharmacy Technician Informaticist (PTI)?
- In what setting(s) are PTIs employed?

References

- ASHP statement on the pharmacy technician's role in pharmacy informatics. Available at: http://www.ashp.org/DocLibrary/BestPractices/AutoITStPTRolePharmInform.aspx. Accessed Aug 10, 2015
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- Dumitru, D. *The Pharmacy Informatics Primer*. Bethesda, Md: American Society of Health-System Pharmacists. 2008

Informatics Pearls – Near-Miss Error Reporting

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Adjunct Clinical Instructor
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Disclosure

- The speaker has no actual or potential conflict of interest to disclose in relation to this presentation.

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Outline

- Background
- Good-Catch Medication Error Reporting Program Overview
- Results of the Program
- Conclusion

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Poll the Audience

How many near-miss medication errors occur monthly at your institution?

a. <10

b. 10-50

c. 50-100

d. >100

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

BACKGROUND

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The Good-Catch Program

- Under-reporting identified during a mock Joint Commission Survey at Hospital Sisters Health System (HSHS) St. Elizabeth's Hospital
- Goals of the Program:
  - Increase error reporting
  - Identify clusters of events
  - Identify processes to target for improvement

Cure L, et al. J Biomed Inform. 2011

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Hospital Sisters Health System

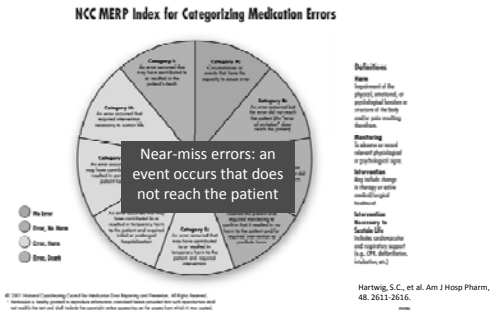
- Multi-institutional health care system comprised of 14 hospitals across Illinois and Wisconsin

Hospital Sisters HEALTH SYSTEM

HSHS St. Elizabeth's Hospital

- 303 bed community teaching hospital
- Located in Belleville, IL

Defining Medication Errors



Hartwig, S.C., et al. Am J Hosp Pharm, 48. 2611-2616.

GOOD-CATCH MEDICATION ERROR PROGRAM OVERVIEW

Prior to Implementation

- All medication error events were reported through a third party tool, Peminic®
- Average number of errors reported:11 per month
- Computerized Provider Order Entry (CPOE): 80.9%/month

Limitations to Reporting Through Peminic®

- Time consuming
- Number of clicks/screens to navigate
- Limited information collected by system
- Web based application
  - Interrupts pharmacist's workflow

Implementation of the Good-Catch Routine Entry

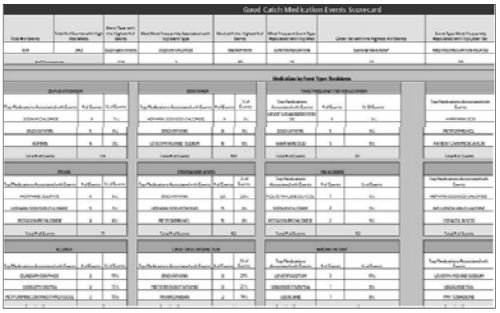
- Image removed due to possible proprietary restriction

RESULTS

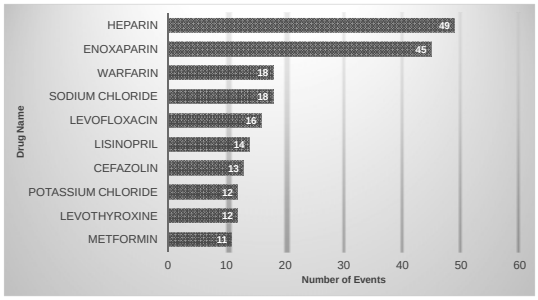
6 Months Post – Implementation

- September 2014-February 2015:
  - Total number of events = 654
    - Average number per month: 109
    - **891% increase in reporting**
  - Total number of events with high-alert medications = 280
    - 42% of total errors
- Flat file utilized to directly send data to be uploaded into Peminic®

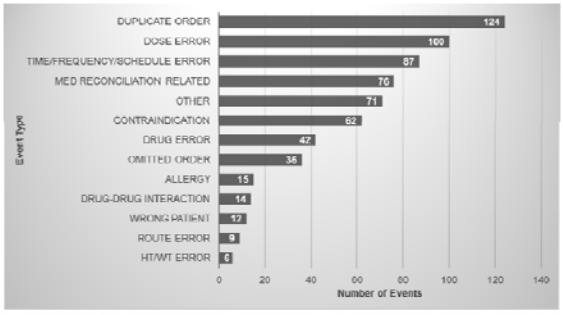
Scorecard



Number of Events by Medication



Number of Events by Event Type



Conclusion

- Strengths
  - Program increased reporting
  - Captured a large enough sample to analyze data
- Limitations
  - Likely not catching all near-miss errors
  - Entry is subjective, based on pharmacist's perception

Self-Assessment Question

Which factors must be taken into consideration when developing a process or tool to report medication errors?

A. Sustainability of the process
B. Ease of use of the reporting tool
C. Ability to track events reported through the tool
D. All of the above

Acknowledgements

- Michael Randazzo, PharmD
- Joshua Schmees, PharmD
- Julia Schimmelpfennig, PharmD, MS, BCPS, CDE
- Maggie Wong, PharmD, BCPS

References

1. Hartwig, S.C., Denger, S.D., & Schneider, P.J. (1991) Severity-indexed, incident report-based medication error-reporting program. Am J Hosp Pharm, 48. 2611-2616.
2. Cure L, Zayas-Castro J, Fabri P. Clustering-based methodology for analyzing near-miss reports and identifying risks in healthcare delivery. J Biomed Inform. 2011 Oct;44(5):738-48. doi: 10.1016/j.jbi.2011.03.012. Epub 2011 Apr 1.

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Drug Recall Tracking

Jeff Thiel, PharmD, MS
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The speaker has no conflicts of interest to disclose in relation to this presentation

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Recall Management

1. Recalls continue to be grow
   - Exponential growth since 2008[1]
2. Several challenges to Recall Management[2]
   - Source of truth
   - Response rate
   - Volume of recalls
   - Storage of information
   - Liability

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NorthShore University HealthSystem

- Integrated healthcare delivery system
- 4 Acute Care Hospitals
- 70+ Medical Group offices

How do we manage recalls for medications, devices, food, and equipment?

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Electronic Management

- Information feeds from FDA and Manufacturers
- Coordinator delegates to buyers
- Buyers are responsible follow up
- Comprehensive location to store follow up information
- Covers scope of all FDA recalls

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	Q3 Closed alerts	Q3 AVG Days to Close	% Closed Alerts Q3	Remaining Open Alerts Q3	Total Closed FY15	Total Open Alerts FY15
Biologics	11	3	100%	0	11	0
Biomedical Devices	231	10.1	87.5%	33	760	77
Blood Products	0	0	100%	0	0	0
Children's Products	16	1	100%	0	72	0
Engineering & Facilities	68	4.7	100%	0	360	0
Food	96	5.1	99%	4	488	4
Information Systems	0	0	100%	0	28	0
Lab Products	412	2.6	96.2%	16	1192	16
Med Supplies	350	1.6	100%	0	1130	0
OR Products	800	3.5	99.9%	1	2113	5
Pharmaceuticals	2672	7.4	97.6%	66	9098	110
Radiology Products	238	16.1	85%	42	771	109
Tissue	0	0	100%	0	0	0
Veterinary Products	1	23	100%	0	12	0
Total Alerts	4895	6.4	96.8%	162	16635	316

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What it doesn't solve

- People doing their job
- Getting 100% of all information
- Confusing updates
- Friday afternoon scramble
- "Track and Trace"

Self-Assessment Question

Which of the following is a benefit to having an automated or electronic medication recall system

A. Automatically removes recalled products from the storage areas
B. Provides a comprehensive electronic location to store follow up information that is easily retrievable
C. Sends recall information to patients
D. Fulfills all requirements of "Track and Trace" legislation

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1. Eckels, R. "Centralizing Drug Recall Management" Pharmacy and Purchasing Magazine. 2013; 10,11:4. Available at www.ppmag.com. Accessed August 1, 2015.
2. Food and Drug Administration. Drug Recalls. Available at: www.fda.gov/Drugs/drugsafety/DrugRecalls/default.htm. Accessed August 1, 2015.
3. RASMUS, Noblis. Availab at: http://info.rasmas.noblis.org/

Pathways to Informatics

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Clinical Informatics Specialist
No actual or potential conflicts of interest

Goals and Objectives

- Compare and contrast formal education options available to pharmacists and technicians wishing to pursue a career in pharmacy informatics.
- Describe career path options available for pharmacists and technicians interested in specializing in pharmacy informatics.

Health Informatics vs. Health Information Management (HIM)

- Health Informatics – "An evolving specialization that links information technology, communications, and healthcare to improve the quality and safety of patient care. Though the concept of health IT includes the use of technology in the healthcare field, health informatics is not synonymous with health IT…"
- HIM – "The practice of acquiring, analyzing, and protecting digital and traditional medical information…"

Polling Question

How much do you agree with the following statement, "I utilize informatics in every aspect of my current position."

A. Strongly Agree
B. Somewhat Agree
C. Somewhat Disagree
D. Strongly Disagree

So what would you say you do here, really?

Job Responsibilities

- Manage drug dictionary
- Build order sets
- Manage and support automated dispensing cabinets
- Support ancillary systems
- Triage Help Desk problems
- Formulary Service Vendor
- Attend departmental meetings
- Act as liaison between Pharmacy, IS, Network Operations, etc.

First a PharmD, an Informaticist Second

- Patient care is the first priority
- Within that framework must determine how to reach institutional goals mandated by pharmacy and IS

Pursuing a career in Pharmacy Informatics

Residency Programs

- Offer targeted learning experiences building upon established skills
- Accredited residency programs ensure common standards are met across programs
- ASHP accredited residencies (http://www.ashp.org/doclibrary/membercenter/sopit/informaticsspecialtyprogrammatrix.aspx)

Post Graduate Education

- Masters in Health Informatics
- Health Informatics Certificate Program
- Accredited by the CAHIIM
- Directory of accredited programs can be found at http://cahiim.org/

Professional Organizations

ICHP

HIMSS transforming healthcare through IT

AMIA

ashp

AHIMA American Health Information Management Association®

Don't Wait, Get Involved NOW

- Opportunities are everywhere
- Operational improvement relies heavily on innovation via informatics
- Reach out to coworkers in your own department as well as outside
- Be willing to go above and beyond

Networking

- "Pharmacy is a small world"
- Seek out experts
- Reach out to others with similar interests
- Find a mentor (e.g. ASHP Mentor Exchange program)
- Reach out to classmates or instructors from technician certification programs
- Chat while you wait

Many Paths to a Single Destination

- There is no right/wrong answer
- Have a plan, but be flexible
- Seize the opportunities presented to you, especially the ones that make you uncomfortable
- Don't be afraid to ask for help

Self-Assessment Question

- Health informatics and Health Information Management are interchangeable terms?

A. True

B. False

Self-Assessment Question

Which of the following organizations does NOT have resources for aspiring informaticists?

A. ASHP
B. ICHP
C. FDA
D. HIMSS

Self-Assessment Question

Which of following can assist in the pursuit of a career in pharmacy informatics?

A. Residency
B. Bachelors/Post Graduate Education
C. Networking
D. All of the above

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- ASHP Publications. "Pharmacy Informatics Specialist or Tech-savvy Generalist?" *ASHP Member Center*. ASHP, n.d. Web. 17 Aug. 2015.
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Optimizing Care through Clinical Surveillance

Overall Learning Objectives for Pharmacists and Pharmacy Technicians

1. Identify the prerequisites necessary for implementing a Clinical Surveillance system.
2. Articulate the benefits of using clinical surveillance tools in the pharmacy workflow.
3. Compare and contrast the features available with different systems in the marketplace.
4. Describe how a clinical surveillance system can improve clinical workflow.

Overview

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PGY-1 Resident, Non-Traditional
Northwestern Memorial Hospital

The speaker has no conflicts of interest to disclose in relation to this presentation.

Technology in Healthcare

- Increased adoption of electronic health records (EHRs)
  - Technological trend
  - American Recovery and Reinvestment Act
- Increased adoption of supportive technologies
- All providing potentially relevant clinical data

Technology in Healthcare

- Data overload
- Goals:
  - Present relevant data
  - Timing
  - Prevent fatigue

Clinical Decision Support

"**…** is a process for enhancing health-related decisions and actions with pertinent, organized clinical knowledge and patient information to improve health and healthcare delivery."

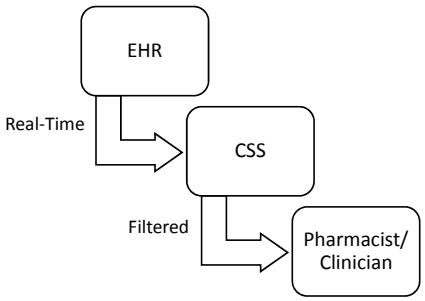
- Examples:
  - Order strings
  - Order sets
  - Alerts
  - Clinical surveillance

Improving outcomes with clinical decision support: an implementer's guide. Second Edition. HIMSS. 2011 (in press).

Clinical Surveillance Systems (CSS)

- Process clinical data in real-time
- Goals:
  - Systematically filter data
  - Actionable
  - Timing
  - Efficiency
  - Safety!

Clinical Surveillance



CSS Capabilities

- Real-time EHR data feed
- Alerts and rules
  - Custom vs pre-built
- Reporting
- Documentation
- Intervention tracking

CSS Applications

- Antimicrobial stewardship programs
- Infection control
- Communication
  - Daily rounding
- Intervention reporting

CSS Vendors

- CareFusion – MedMined®
- Cerner
- Epic
- ICNet
- Premier – TheraDoc™
- Truven
- VigiLanz™
- Walters Kluwer – Sentri7®

Takeaway Points

- CSS provides a systematic filter to real-time data
- Potential to increase efficiency
- Provides actionable data in a timely fashion
- Enables intervention tracking

Q1: What do you need to establish a CSS?

A. Electronic health record
B. Point-person to maintain
C. Staff buy-in
D. All of the above

Q2: What are the benefits of a CSS?

A. Alerts and rules
B. Reporting
C. Documentation
D. All of the above
E. Options B and C

Optimizing Care Through Clinical Surveillance – Theradoc

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Disclosure

- The speaker has no actual or potential conflict of interest to disclose in relation to this presentation.

Outline

- Background
- Overview of Theradoc
- Tools within Theradoc utilized by the Pharmacy Department

Poll The Audience

Who uses Theradoc currently or has used it in the past?

BACKGROUND

Hospital Sisters Health System

- Multi-institutional health care system comprised of 14 hospitals across Illinois and Wisconsin

Hospital Sisters HEALTH SYSTEM

HSHS St. Elizabeth's Hospital

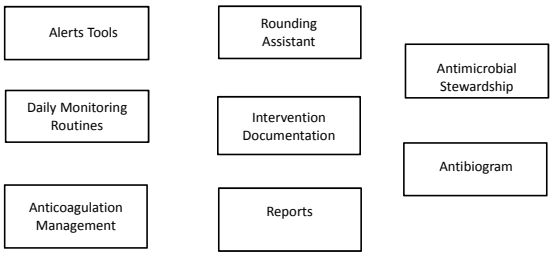
- 303 bed community teaching hospital located in Belleville, IL
  - St. Louis Metro area
- Theradoc utilized by the Pharmacy Department, Infection Prevention, and Emergency Department Nurses

OVERVIEW

Theradoc

- Standalone system that interfaces with the electronic medical record
- Originated as an infection prevention tool

What is in Theradoc?



Use within the Pharmacy Department

- Queries are written to identify patients
  - Daily monitoring and real-time alerting
  - Intervention documentation
- Integrated into daily workflow of pharmacists

TOOLS WITHIN THERADOC

Alerts

- "EZ Alerts"
  - Created by pharmacists
  - Image removed due to possible proprietary restriction

Theradoc©

Alerts for Daily Monitoring Routines

- Anticoagulation Daily Monitoring
  - Warfarin
  - Rivaroxaban
  - Apixaban
- Pharmacy-to-Dose Protocols
  - Vancomycin
  - Aminoglycosides
  - Warfarin

Real-Time Alerts

- Renal dosing
  - Piperacillin-Tazobactam CrCl >40 ml/min
- IV-to-PO conversions
  - Famotidine
- Core measures
  - Heart failure and myocardial infarction
- Antibiotic stewardship
  - Culture results
  - Broad spectrum antibacterial de-escalation
  - Redundant beta-lactam therapy

Viewing Alerts

- Floor alerts
  - Shows all alerts by location
- Alerts by type
  - Renal dosing
  - IV to PO conversion
  - Anticoagulation
  - Core Measures
  - Antibiotic Stewardship

Floor Alert View

Image removed due to possible proprietary restriction

Intervention Documentation

- Image removed due to possible proprietary restriction

Theradoc©

Intervention Subcategories

Mobile Device Alerts

- Image removed due to possible proprietary restriction

Theradoc©

Reports

- Report filters:
  - By alert
  - By alert status (active or dismissed)
  - By patient location
  - By patient population
  - By institution
- Report data columns can be customized

Self-Assessment Question

Tools for pharmacy within Theradoc include which of the following?

A. Real-time alerting
B. Intervention documentation
C. Rounding assistant
D. A and C
E. All of the above

Self-Assessment Question

Interventions within Theradoc are:

A. Associated with cost-savings
B. Categorized by type of intervention
C. Unable to be viewed by colleagues
D. A and B
E. All of the above

Acknowledgements

- Joshua Schmees, PharmD
- Maggie Wong, PharmD, BCPS

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Optimizing Care through Clinical Surveillance

VigiLanz ™

Rupal Patel, Pharm.D.

Anne & Robert H. Lurie Children's Hospital of Chicago

The speaker has no conflicts of interest to disclose in relation to this presentation

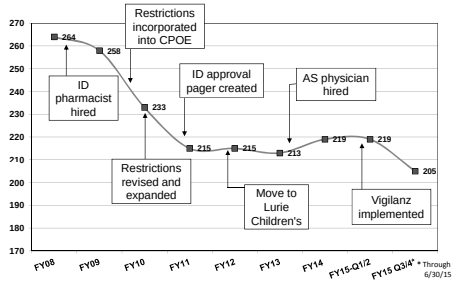
Ann & Robert H. Lurie Children's Hospital of Chicago

- 288 beds (capacity to increase to 313)
- 40 bed NICU
- 40 bed PICU
- 40 bed CCU

Antimicrobial Stewardship

- Formulary Restriction
  - amikacin, cefotaxime, ceftriaxone, ceftazidime, ciprofloxacin, meropenem, levoflocaxin, vancomycin, linezolid, oxacillin, micafungin, voriconazole, amphotericin
  - all non-Formulary anti-infectives
- Prospective Audit and Feedback

Targeted Antibiotics* DOT/1000 PD



* Includes: meropenem, piperacillin-tazobactam, ceftriaxone, cefotaxime, ceftazidime, cefepime, ciprofloxacin, levofloxacin, amikacin, tobramycin, linezolid, vancomycin IV

VigiLanz Dynamic Monitoring Suite™

- Web based
- Multiple interfaces
- Rules-guided software
- Real-time decision support
- High alert notification
- Data mining
- Antibiogram
- Software as a Service

VigiLanz™- Pharmacy Surveillance

- Antimicrobial stewardship
- 113 custom rules for real time alerting
  - New order for restricted antibiotic
  - Any antibiotic > 7 days and >14 days
  - Abnormal CSF parameters and NOT on appropriate antibiotic
  - De-escalation opportunities
  - Duplicate therapy (antifungal, anti-anaerobic, double gram negative)
  - Inappropriate antibiotic started based on diagnosis code
  - Organism-antibiotic mismatch
  - All positive CSF and blood cultures
  - Lab monitoring needed (vancomycin, aminoglycosides, voriconazole)
  - Alerts for antibiotics ordered that are on shortage

VigiLanz™- Pharmacy Surveillance

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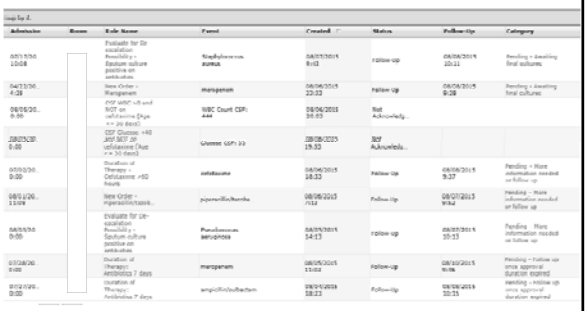
VigiLanz™- Pharmacy Surveillance



VigiLanz™- Pharmacy Surveillance

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VigiLanz™- Pharmacy Surveillance

- Image removed due to possible proprietary restriction

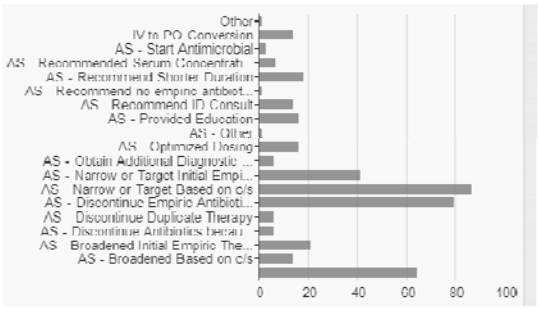
Data Collection-Interventions

	Accepted	Rejected
November	19	2
December	19	0
January	23	1
February	29	3
March	53	5
April	47	2
May	43	4
June	50	5
July	**75**	**5**

Data Collection-Interventions

RuleInterventionCategory	2015 July	2015 June	2015 May	2015 April	2015 March
A8 - Broadened Based on c/s	4	4	1	2	1
A3 - Broadened Initial Empiric Therapy	11		1	2	2
A8 - Discontinue Antibiotics because Therapy is Finished	1	2	2		1
A6 - Discontinue Duplicate Therapy		2	2	1	1
A5 - Discontinue Empiric Antibiotics	14	5	7	9	15
A9 - Narrow or Target Based on c/s	12	10	12	12	17
A3 - Narrow or Target Initial Empiric Therapy	9	12	5	6	3
A4 - Obtain Additional Diagnostic Tests	2	1		2	1
A3 - Optimized Dosing	5	7		1	1
A3 - Other			1		
A3 - Provided Education	7	1	4	2	1
A8 - Recommend ID Consult	7	2	1	3	1
A5 - Recommend no empiric antibiotics	1				
A3 - Recommend Shorter Duration	1	1	5	3	2
A3 - Recommended Serum Concentration Monitoring	3	2	1		1
A8 - Start Antimicrobial	2			1	
IV to PO Conversion		3	4	4	2
Therapy Optimization - Antimicrobial - Culture Mismatch					

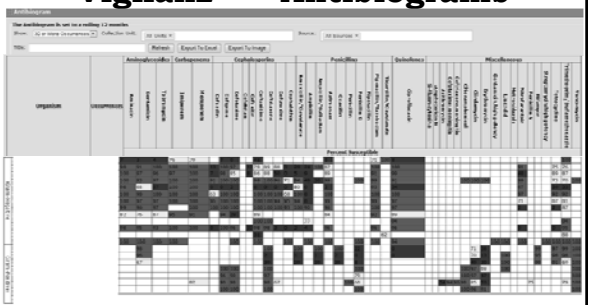
Data Collection-Interventions



Vigilanz™ - Antibiograms

- Rolling
- On demand
- Option to exclude <30 isolates
- Unit specific
- Source specific
- Exporting
  - Excel
  - Image

Vigilanz™ - Antibiograms



Tracking Drug Utilization

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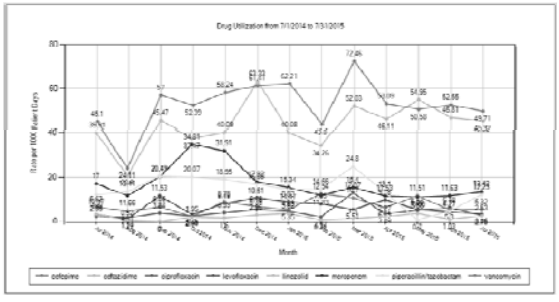
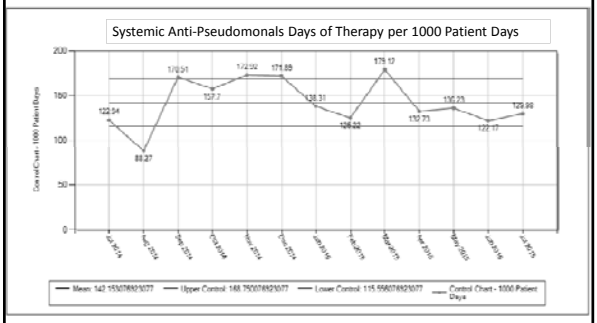
Tracking Drug Utilization



Tracking Drug Utilization



Avoiding Adverse Events

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- Septic shock in PICU; Scr doubled since admit
- Vanc initiated at1550mg q6h with plan to check the trough after 4 doses
- Vigilanz alert- vanc + norepinephrine ordered
- Discontinued vancomycin order after one dose
- 9 hour level-17mcg/ml
- Acute renal insufficiency averted

Challenges

- Rate limiting factor: custom rule build
- Alerts based on diagnosis
- Noise reduction
  - Three-tiered noise reduction feature
  - Layered alerts
- Data collection- validation
- Real time challenges
- Data retrieval for daily chart review
- Interventions not in EPIC

Self-assessment question

Computer decision support surveillance software can enhance the productivity of an Antimicrobial Stewardship Program by:

A. Reporting real time organism-antibiotic mismatches.
B. Alerting clinicians to potential toxicity from antimicrobials.
C. Providing on demand data mining capability to provide information on antibiotic utilization on a specific inpatient floor.
D. All of the above.

Optimizing Care Through Clinical Surveillance

CareFusion Medmined®

Zahra Khudeira, PharmD, BCPS, CPPS
Sinai Health System
Medication Safety Officer

September 11, 2015

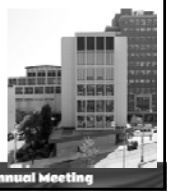
The speaker has no conflicts of interest

Discussion Points

- Explain the potential impact of clinical decision support systems (CDSS) on patient safety, clinical outcomes, and cost savings
- Describe how CDSS can enhance an antimicrobial stewardship program and improve patient care

Mount Sinai Hospital (MSH)

- 320-bed community teaching hospital in Chicago, IL
- Level I Trauma Center
- Level III NICU
- Implemented Medmined in October 2013
  - Infection Control
  - Pharmacy



Clinical Decision Support System (CDSS)

- Software that integrates order information, patient information, and clinical practice guidelines into computer-system logic to provide feedback to clinicians
- Program identifies opportunities for pharmacists to optimize drug therapy and prevent an adverse drug event

CareFusion MedMined®

- Web based surveillance software program interfaces with the hospital's electronic medical record
  - Filters pertinent patient data
  - Packages data as real-time alerts
  - Identifies opportunities for targeted clinical interventions
- Robust system that optimizes and prioritizes patient related events by generating alerts for the pharmacist
  - Provides opportunity for early intervention
  - Promotes patient safety by identifying potential adverse drug events

CareFusion MedMined®

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MSH Current Alerts

- Anticoagulation
- Antimicrobial
- Laboratory

Anticoagulation Alerts

- No VTE prophylaxis
- Thrombocytopenia with anticoagulants
- High INR values >3.5

Antimicrobial Alerts

- De-escalation
- Infection marker without treatment
- Bug-drug mismatch

Laboratory Alerts

- Potassium level less than 3 meq/L
- Renal dosing of low molecular weight heparin
- Drug induced hyperkalemia

Patient Event Advisor

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Alerts

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Labs

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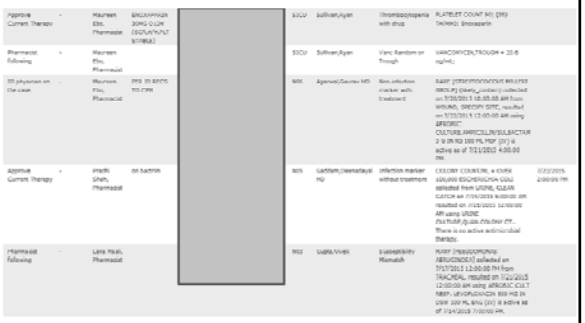

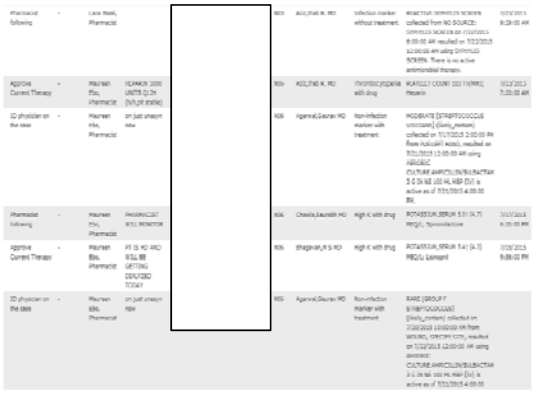

Intervention Types

- Pharmacist following: pharmacist aware
- Accepted intervention: made a recommendation or contacted prescriber for therapy change
- Approve current therapy: accepted intervention but no change made
- Rejected intervention

Intervention Types	User Comment	Alert Type	Alert Detail
Pharmacist Following	Antibiotic changed to ampicillin	Bug-drug mismatch	Few enterococcus faecalis collected on 5/22/2015 from aerobic culture of paracolic abscess and resulted on 5/27/2015. Ceftriaxone 2G Vial (IV) is active as of 5/27/2015
Accepted Intervention	Suggested 1 mEq/kg potassium rider for a pediatric patient	K less than 3	K = (2.6 meq/L). Dropped from 7.2 on 5/27/2015 to 2.6 on 5/31/2015
Approve Current Therapy	Hold chemical prophylaxis secondary to GI bleed	No VTE prophylaxis	No active VTE prophylaxis
Rejected Intervention	Pt with Acute Kidney Injury	High BNP and no ACE-I	BNP 611 and no active ACE-inhibitor

Thrombocytopenia Example

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Electrolyte Example

Medication Alerts

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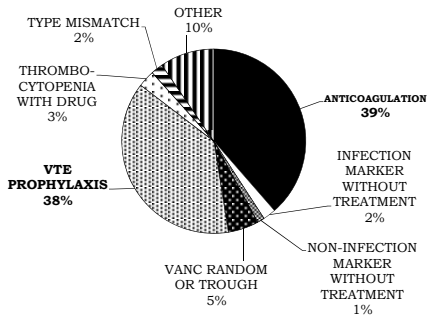
MSH Medmined Alerts

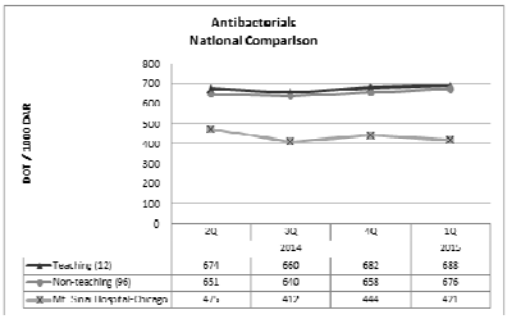
July 2014-July 2015



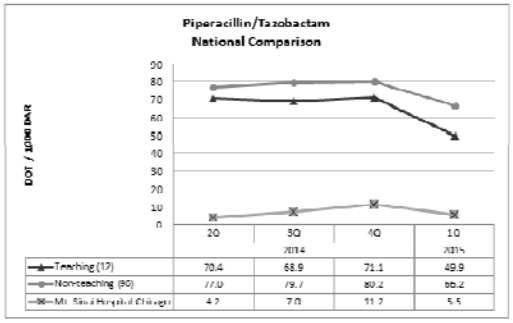
Antimicrobial Stewardship Program (ASPs)

- ASPs improve patient safety, quality of care, and significantly reduce the rate of hospital-acquired infections like *Clostridium difficile* infection (CDI).
- ASPs are endorsed by the CDC, IDSA, ASHP, and the Joint Commission.

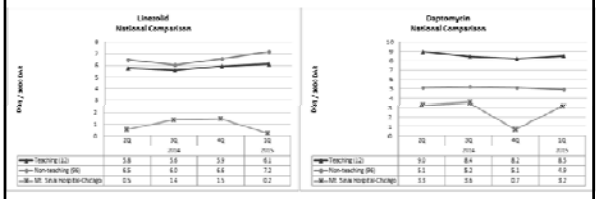
Benchmarking



Benchmarking



Benchmarking



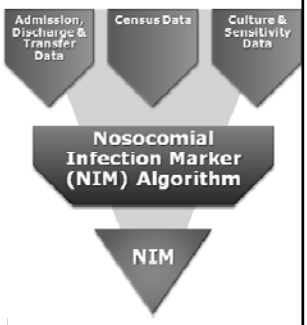
NIM Evaluation Process

Every positive isolate is evaluated

The NIM algorithm screens for:
- Community-acquired pathogens
- Contaminants and colonization
- Duplicate isolates
- Present on admission

The result is an objective, consisten reproducible marker for HAI case finding

Published, peer-reviewed sensitivity (86%) and specificity (98%),*



*Brossette S, et al. A Laboratory –Based, Hospital-Wide, Electronic Marker for Nosocomial Infection. American Journal of Clinical Pathology. 2006; 125: 34-39

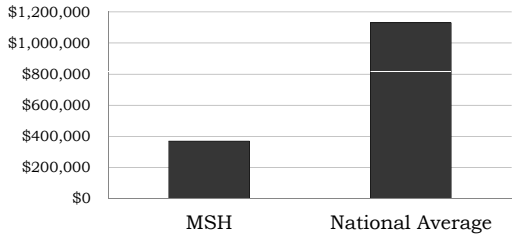
NIM Rates vs National Averages*

NIM Source	% of Admissions	National Average	National Comparison
Patient NIMs	2.38%	4.51%	47.2% lower
Total NIMs	3.17%	5.75%	44.9% lower
Blood NIMs	0.41%	0.68%	39.2% lower
Resp NIMs	0.91%	1.18%	22.7% lower
Urine NIMs	0.99%	1.93%	48.8% lower
Wound NIMs	0.50%	0.91%	44.8% lower
Stool NIMs	0.10%	0.56%	81.7% lower
Other NIMs	0.25%	0.49%	49.3% lower

* Based on CareFusion analysis of .67M inpatient admissions from Academic facilities during 2Q14-1Q15.

Benchmarking - CDI

Total CDI Cost



Audience Participation

1. Which of the following alerts would be most beneficial to a hospital pharmacist?

A. Bug-drug mismatch
B. Thrombocytopenia with anticoagulants
C. Drug induced hyperkalemia
D. No VTE prophylaxis
E. All of the above

Audience Participation

2. The goal of CDSS is to help:

A. Alert the physician on what labs to order
B. Alert the pharmacist about patients at potential risk of harm
C. Inform the pharmacy technician on what medications to fill
D. Generate drug interaction reports

Audience Participation

3. How do the alerts from CDSS contribute to patient care?

A. Help enhance patient safety
B. Increase medication compliance
C. Decrease lab errors
D. Monitor drug administration times

Summary

- CDSS is a promising application that focuses pharmacist's attention, manages information, and provides patient-specific information management.

Questions?

Optimizing Care Through Clinical Surveillance

Epic Antimicrobial Stewardship

Michelle Geurink, RPH
OSF Healthcare System
No Conflicts of Interest

Plan Your Surveillance

- Bug-Drug
- IV to PO
- Targeted Drugs
- De-Escalation
- Duplicate Therapy

Scoring System—Find It

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Find It- Example: Bug-Drug

- General Mismatch
- MIC
- Fluconazole/Candida Sputum
- Vanco/VRE

Document It

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Document-Closer View

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Intervention/Note

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Barriers

- Resources
  - Build of Scoring
  - Implementation
- System
  - Finding Patients
    - Large Lists Load Slow
  - Knowing Lab Processes

Next Steps

- Pharmacy Acuity System
- Total Score Columns
  - General Pharmacy Scoring
    - Exists; being optimized
    - IV/PO, High INR, Decreasing CrCl, ADE
  - Antimicrobial Stewardship Scoring
  - Anti-thrombosis Scoring (future)
  - Others

Top Things to Know About Five Commonly Encountered Diseases

Top Things to Know about Hepatitis C Virus Now

Michelle T. Martin, PharmD, BCPS, BCACP

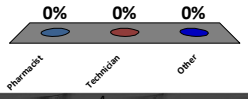
Appointments and Disclosures

- Clinical Pharmacist
  - Bobby and Marvin Fink Family Liver Clinic
  - University of Illinois Hospital and Health Sciences System
- Clinical Assistant Professor
  - University of Illinois at Chicago College of Pharmacy

- I hold shares of Gilead stock. I have no other financial conflicts of interest related to the content of this presentation. Conflicts were resolved through peer review
- I will discuss off-label use of medications, and medications that are not yet FDA-approved.

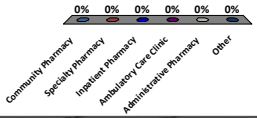
What is your role?

A. Pharmacist
B. Technician
C. Other



What is your primary practice site?

A. Community Pharmacy
B. Specialty Pharmacy
C. Hospital Pharmacy
D. Ambulatory Care Clinic
E. Administrative Pharmacy
F. Other



Learning Objectives

1) Describe critical therapeutic concepts for commonly encountered disease states
2) Identify clinical information that can be applied to your work setting
3) List potential future developments for commonly encountered disease states

Do you work with hepatitis C virus treatment?

A. Yes
B. No

Learning Objective 1

- Describe critical therapeutic concepts for hepatitis C virus (HCV)
  - Guidelines for HCV management
  - Recent medication approvals

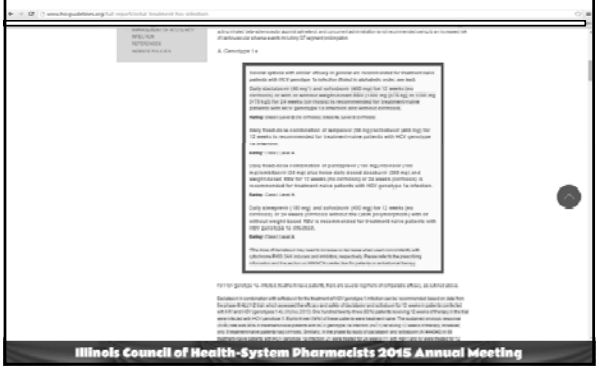
Starting HCV Treatment

- To ensure correct HCV agent and length of treatment, you need to know (at minimum):
  - Genotype
  - Previous treatment history
  - Presence/absence of cirrhosis
- Concomitant comorbidities (renal impairment)
- Check concomitant medications to avoid DDIs
- Use guidelines to select proper agent

HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

- First published online 1/29/2014, updated several times since: http://www.hcvguidelines.org/

Sample from Guidelines



HCV Medication Class Suffixes

- -previr = NS3/4A protease inhibitors (PI)
  - simeprevir, paritaprevir
- -asvir = NS5A replication complex inhibitors
  - ledipasvir, ombitasvir, daclatasvir
- -buvir = NS5B inhibitors
  - sofosbuvir, dasabuvir

PrOD (PTV/r/OBV+DSV) (Viekira Pak™) Pearls

- FDA approved for treatment of HCV GT 1
  - Treatment naïve, treatment experienced, cirrhotic, and non-cirrhotic patients
- ADRs: asthenia, fatigue, nausea, insomnia, anemia
- Dosing: x 12 or 24 weeks
  - 2 tablets once daily (OBV 12.5mg, PTR 75mg, ritonavir 50mg) with food
  - 1 tablet twice daily (DSV 250mg) with food
  - +/- ribavirin (RBV)
  - Up to 10 pills daily
  - Ensure patient can verbalize understanding of administration / importance of adherence

http://www.hepmag.com/articles/abbvie_viekira_pak_2501_26610.shtml

PTV/r/OBV (Technivie™) + RBV Pearls

- FDA approved for treatment of HCV GT 4
  - Treatment naïve, treatment experienced, and non-cirrhotic patients
- ADRs: asthenia, fatigue, nausea, insomnia, anemia with RBV
- Dosing: x 12 weeks
  - 2 tablets once daily (OBV 12.5mg, PTR 75mg, ritonavir 50mg) with food
  - + ribavirin (RBV)
  - Ensure patient can verbalize understanding of administration / importance of adherence
  - Up to 8 pills daily

http://www.medscape.com/viewarticle/848090

PTV/r/OBV +/- DSV Pearls

- Drug-drug interaction considerations
  - Paritaprevir: inhibitor of OATP1B1,OATP1B3, BCRP, and P-gp; substrate of CYP3A4
  - Ritonavir: inhibitor of CYP3A4, BCRP, and P-gp, substrate of CYP3A4
  - Strong CYP3A4 and CYP2C8 inducers may decrease efficacy of PrO+/-D)
  - CYP2C8 inhibitors (may increase DSV levels and risk of QT prolongation)
- Examples of contraindicated concurrent medications
  - Combined oral contraceptives
  - Carbamazepine, phenytoin, phenobarbital
  - Efavirenz, simvastatin, sildenafil for PAH
- Cyclosporine and tacrolimus doses must be adjusted

http://www.hepatitisc.uw.edu/page/treatment/drugs/3d

Ledipasvir (LDV)/Sofosbuvir (SOF) (Harvoni™) Pearls

- FDA-approved for treatment of HCV GT 1
  - Treatment naïve, treatment experienced, cirrhotic, and non-cirrhotic patients
- Dosing: x 8, 12, or 24 weeks
  - 1 combination tablet (LDV 90mg / SOF 400mg) once daily
- ADRs: fatigue, headache, nausea, diarrhea
- Drug-drug interactions
  - Substrate of P-gp
    - Contraindications with phenytoin, carbamazepine, etc
  - Requires acidic environment for absorption
    - Timing with PPIs, H2RAs, antacids

http://www.empr.com/harvoni/drug/34390/

SOF + Daclatasvir (DCV) (Daklinza™) Pearls

- FDA approved for treatment of HCV GT 3
  - Treatment naïve, treatment experienced patients
    - ALLY-3: 90% in TN, 86% in TE, 63% SVR in cirrhotics, 96% in non-cirrhotics
- ADRs: fatigue, headache, nausea, diarrhea
- Dosing: x 12 weeks
  - 2 tablets once daily (DCV 60mg + SOF 400mg) x 12 weeks → 2 copays
- Drug-drug interactions
  - DCV is a substrate of CYP-3A4
    - Decrease dose to 30mg daily with strong inhibitors, increase dose to 90mg daily with moderate inducers
  - Substrate and inhibitor of P-gp
    - Contraindications with phenytoin, carbamazepine

http://www.egyreg.com/2015/04/sovaldi-plus-daklinza-effective-for.html

SOF + RBV Pearls

- FDA approved for treatment of HCV GT 2
  - Treatment naïve, treatment experienced; cirrhotic and non-cirrhotic patients
- ADRs: fatigue, headache, nausea, diarrhea
- Dosing
  - 1 tablet once daily (SOF 400mg) x 12-16 weeks
  - + RBV
  - Up to 7 tablets daily
- Monitor hgb and CrCl during treatment

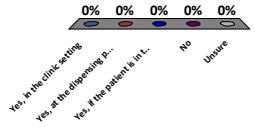
http://www.forbes.com/sites/theapothecary/2014/08/18/uk-says-sovaldi-is-worth-it-we-should-listen/

Learning Objective 2

- Identify clinical information that can be applied to your work setting
  - Role of pharmacists in different settings
  - Insurance restrictions
  - Patient assistance programs

Does a pharmacist interact with HCV patients on treatment at your institution? (even if it is not you)

A. Yes, in the clinic setting
B. Yes, at the dispensing pharmacy
C. Yes, if the patient is in the hospital
D. No
E. Unsure



Ambulatory Care HCV Management Pearls

- Aid in medication selection
  - Use guidelines to confirm/select regimen
- DDI screening and management
- Pt management
  - Clinic visits
  - Provide education – ADRs, dosing, adherence
  - Monitor labs
- Liaison for medication assistance programs
- Recommend screening, team involvement

Community / Specialty HCV Management Pearls

- Verify medication selection and length of treatment / refills
- Work with payors and patient assistance programs to ensure coverage
- Patient education - counsel on:
  - Adherence
  - Coadministration with food (PrO +/- D)
  - DDIs and coadministration with other medications
- Refill management

Inpatient HCV Management Pearls

- Prevent interruption in HCV treatment (unless team stops treatment)
  - Family or friend to bring pt's HCV medication to hospital
- Counsel on adherence
- DDI screening
- Ensure appropriate labs are drawn
- HCV screening

Payors

- Want to prevent treatment failure and encourage successful treatment
- Prioritization of patients for treatment
- Some insurance plans cover only one course of HCV treatment

Examples of Payor Requirements

Select Insurance Plan Requirements for HCV Medication Coverage (as of 8/10/15)

Insurance Plan	Documentation of sobriety (EtOH and illicits)	Documentation of treatment adherence and counseling	Metavir Fibrosis Score Covered	HCV RNA required in the last:	Additional Lab Testing
Aetna Better Health	12 months – in MD note + Tox Screen	letter signed by pt	F4 only	3 months	Not required
Cigna Health Spring Medicaid	12 months - EtOH/Tox screen in last 15 days	letter signed by pt - commitment to treatment plan	F4 only	3 months	Negative pregnacy test
County Care	6 months – in MD note	must be documented by MD in clinic note	F3/F4	6 months	HIV Ab test in last 6 months and Hep B serologies
IHFS (Illinois Medicaid)	12 months – in MD note + Tox Screen in last 15 days	letter signed by pt	F4 only	3 months	Not required

Patient Assistance Programs

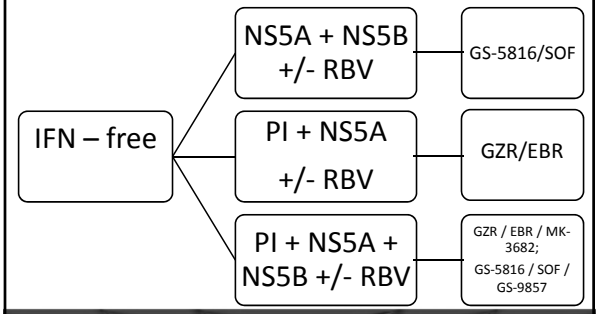
	My Support Path (Gilead)	ProCeed (AbbVie)	(Bristol-Myers Squibb)
Medications Covered	sofosbuvir, ledipasvir / sofosbuvir	paritaprevir/ ritonavir/ombitasvir, +/- dasabuvir; ribavirin	daclatasvir
Website	http://www.mysupportpath.com/	https://www.viekira.com/proceed-support	http://www.bms.com/products/Pages/programs.aspx
Phone	1-855-7-MYPATH (855-769-7284)	1-844-2PROCEED (844-277-6233)	1-844-44-CONNECT (844-442-6663)

Learning Objective 3

- List potential future developments for HCV
  - Guidelines – continual updates
  - Medications in the pipeline

http://www.hcvadvocate.org/hepatitis/hepC/HCVDrugs.html

Select HCV Pipeline Combinations



Grazoprevir/Elbasvir FDC

- NDA filed on 5/28/2015 for GT 1, 4, 6
  - Breakthrough status
    - for renal impairment and GT 4
  - PDUFA date in 12/2015
- Future plans for triple DAA (GZR/EBR with MK-3682 in a FDC)

Grazoprevir/Elbasvir Phase III

Trial Name	Patient Population	Regimen	SVR
C-EDGE TN	N=316 Treatment Naïve, GT 1,4,6, 22% cirrhotics	12 weeks GZR/EBR	95%
C-EDGE TE	N=420 Treatment Experienced, GT 1,4,6, 35% cirrhotics	12 wks GZR/EBR 12 wks GZR/EBR + RBV 16 wks GZR/EBR 16 wks GZR/EBR + RBV	92% 94% 92% 97%
C-EDGE CO-INFXN	N= 218 HIV/HCV pts, GT 1,4	12 weeks GZR/EBR	95%
C-SURFER	N=224 GT 1,4,6; CrCl <30mL/min, 75% on dialysis	12 wks GZR/EBR	94%

GS-5816 100mg / SOF 400mg FDC

- Pangenotypic
- ADRs: fatigue, headache, nausea, insomnia (anemia with RBV)
- Phase III data forthcoming in 11/2015 (ASTRAL-1, -2, -3 trials)
- Future plans for triple DAA (GS-5816 / SOF / GS-9857 in a FDC); shorter duration?

Summary

- HCV is a major public health concern
- Online guidelines are updated regularly
- HCV treatment is advancing rapidly; approval of more pipeline agents is anticipated in late 2015 and 2016
- Pharmacists have an important role in educating patients and providers about HCV medications
- DDIs and insurance coverage will continue to complicate HCV treatment

Top Things to Know about Hepatitis C Virus Now

Michelle Martin

1. Which of the following direct acting antiviral combinations was recently FDA-approved for HCV Genotype 4?

    A. Paritaprevir / Ritonavir / Ombitasvir + Ribavirin

    B. Paritaprevir / Ritonavir / Ombitasvir + Dasabuvir

    C. Sofosbuvir + Daclatasvir

    D. Sofosbuvir + Simeprevir

Heart Failure

Christie Schumacher, PharmD, BCPS, BCACP, BC-ADM, CDE
Associate Professor, Pharmacy Practice
Midwestern University Chicago College of Pharmacy
Clinical Pharmacist, Advocate Medical Group

The speaker has no conflicts of interest to disclose in relation to this presentation

What Is Heart Failure?

- Structural or functional impairment of ventricular filling or ejection of blood

Classification	EF (%)	Description
Heart failure with reduced ejection fraction (HFrEF)	≤ 40	Also referred to as systolic heart failure Randomized control trials have demonstrated efficacious therapy options
Heart failure with preserved ejection fraction (HFpEF)	≥ 50	Also referred to as diastolic heart failure Lack of evidence supporting benefit of medication therapy

J Am Coll Cardiol. 2013;62:e147–239.

ACC/AHA Classification Table			NYHA Functional Class	
Stage	Description	Examples	Class	Description
A	High risk of developing HF. No identified structural or functional abnormalities. No signs or symptoms	HTN, CAD, DM, h/o alcohol abuse, h/o rheumatic fever, FH of CMP	No comparable functional class	
B	Developed structural heart disease, but have never shown s/sx of HF	LV hypertrophy or fibrosis; asymptomatic vavlular heart disease; previous MI	I	No limitation of physical activity
C	Current or prior symptoms of HF associated with underlying structural heart disease	Dyspnea or fatigue due to left ventricular systolic dysfunction; asymptomatic patients who are undergoing treatment for prior symptoms of HF	I	No limitation of physical activity
			II	Comfortable at rest, but ordinary physical activity results in symptoms of heart failure
			III	Marked limitation of physical activity. Comfortable at rest but less than ordinary activity causes symptoms of HF
			IV	Unable to complete any physical activity without discomfort and symptoms at rest
D	Advanced structural heart disease and marked symptoms of HF at rest despite max med therapy	Frequently hospitalized for HF; at home receiving continuous IV support for symptom relief or supported with a mechanical circulatory assist device	IV	Unable to complete any physical activity without discomfort and symptoms at rest

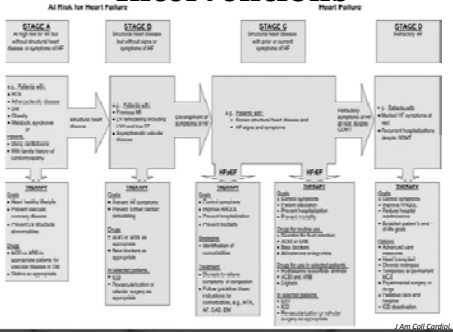
J Am Coll Cardiol. 2013;62:e147–239.

Nonpharmacological Interventions

- Self-care is an important component
  - Daily weights
  - Sodium restriction
  - Fluid restriction
  - CPAP use
  - Physical activity/cardiac rehab

J Am Coll Cardiol. 2013;62:e147–239.

HFrEF Pharmacological Interventions



J Am Coll Cardiol. 2013;62:e147–239.

Clinical Question

A 52 yo Caucasian male with idiopathic dilated cardiomyopathy presents to clinic today for medication management. A recent ECHO shows an EF of 25-30%. His medication regimen includes furosemide 40 mg twice daily, lisinopril 20 mg daily, and metoprolol succinate 150 mg daily. Vital signs include BP 138/86 mmHg and HR 56 bpm. Laboratory values include Scr 1.3 mg/dL and K+ 4.3 mEq/L. Which of the following recommendations is the most appropriate at this time?

a) Increase metoprolol succinate to 200 mg daily
b) Initiate hydralazine 25 mg three times daily and isosorbide dinitrate 10 mg three times daily
c) Initiate spironolactone 25 mg daily
d) Increase lisinopril to 40 mg daily

Recently Approved Medications for HFrEF

- Sacubitril/valsartan (Entresto™)
  - LCZ696 (PARADIGM-HF)
- Ivabradine (Corlanor®)

Sacubitril/Valsartan

- Sacubitril – neprilysin inhibitor
  - Neprilysin is an endopeptidase that degrades natriuretic peptides, bradykinin and adrenomedullin
  - Counteract neurohormonal activation
    - → vasoconstriction, sodium retention and remodeling
- Combination of ACEI and neprilysin inhibitors has been associated with severe angioedema

Entresto(TM) [package insert]. East Hanover, New Jersey: Novartis Pharmaceuticals Corporation; 2015.

Sacubitril/Valsartan

- Dosing:
  - Sacubitril 49 mg and valsartan 51 mg twice daily
  - Double dose every 2 – 4 weeks
  - Target dose: sacubitril 97 mg and valsartan 103 mg twice daily
  - Concomitant use of ACEI is CI
    - Allow 36 hour washout period when switching
  - Initiate sacubitril 24 mg and valsartan 26 mg twice daily in patients previously taking ACEI or ARB or in patients with eGFR < 30 mL/min/1.73m^2

Entresto(TM) [package insert]. East Hanover, New Jersey: Novartis Pharmaceuticals Corporation; 2015.

PARADIGM-HF

- 8442 patients
  - Class II, III, IV HF with EF ≤ 40% (≤ 35%)
- Received sacubitril/valsartan (LCZ696) 200 mg twice daily or enalapril 10 mg twice daily
- Primary outcome:
  - Composite death from cardiovascular causes or hospitalizations for heart failure
- All patients on ACEI/ARB prior to trial
- At randomization:
  - Diuretics (80%), BB (93%), AA (54,57%), Digitalis (29,31%)

N Engl J Med. 2014;371:993-1004.

PARADIGM-HF

- Trial stopped early at median follow-up of 27 months

Primary outcome	LCZ696 (N = 4187)	Enalapril (N = 4212)	Hazard Ratio (95% CI)	P-value	NNT
Death from cardiovascular causes or first hospitalization for worsening heart failure	914 (21.8)	1117 (26.5)	0.80 (0.73 – 0.87)	< 0.001	21
Death from cardiac causes	558 (13.3)	693 (16.5)	0.80 (0.71 – 0.89)	< 0.001	31
First hospitalization for worsening heart failure	537 (12.8)	658 (15.6)	0.79 (0.71 – 0.89)	< 0.001	36

N Engl J Med. 2014;371:993-1004.

PARADIGM- HF

- Secondary outcomes:
  - LCZ696 decreased death from any cause ($p < 0.001$)
  - Decreased symptoms and physical limitations of heart failure ($p = 0.001$)
- Adverse events with LCZ696:
  - Higher risk of hypotension and angioedema
  - Lower risk of renal impairment, hyperkalemia and cough

N Engl J Med. 2014;371:993-1004.

Ivabradine

- ↓ HR via direct sinus node inhibition
  - No direct effects on myocardial contractility and intracardiac conduction
- Shown to reduce hospitalizations but not death in patients receiving HF standards of care

Lancet. 2010;376(9744):875-885.

Ivabradine

- Indicated in patients with LVEF ≤ 35% in sinus rhythm with resting HR ≥ 70 bpm
- Use in patients who are taking max dose beta-blocker or have CI to beta-blocker

Lancet. 2010;376(9744):875-885.

Heart Failure Preserved Ejection Fraction (HFpEF)

- 50% of all HF diagnosis
- Morbidity and mortality rate similar to HFrEF
- Diagnosis of exclusion
  - Presence of clinical HF with preserved LVEF
  - Rule out other causes
    - Valvular disease, COPD, pulmonary HTN, etc.
- Lack of evidence supporting benefits of medication therapy

Pharmacotherapy. 2015;35(4):351-360.

Heart Failure Preserved Ejection Fraction (HFpEF)

- Acute therapy similar for both HFrEF and HFpEF
  - Diuretics to reduce volume overload and improve dyspnea
- Chronic management
  - Treat precipitating conditions
    - E.g. Atrial fibrillation, HTN
  - Control symptoms with diuretics
  - Counsel patients on nonpharm measures
- Risk factors for exacerbation similar
  - Nonadherence
  - Excessive sodium or fluid intake
  - Atrial fibrillation, HTN, MI
  - NSAIDs and other medications which cause Na+/H2O retention

Pharmacotherapy. 2015;35(4):351-360.

Heart Failure Preserved Ejection Fraction (HFpEF)

- Pharmacotherapy Literature Review
  - ARBs
    - CHARM-Preserved and I-PRESERVE
      - No significant difference in CV death or HF hospitalization
  - ACEIs
    - PEP-CHF
      - No significant difference in all-cause mortality or HF hospitalization at the end of follow-up
  - Beta-blockers
  - Aldosterone Antagonists
    - TOPCAT
      - Primary outcome – composite of CV death, HF hospitalization, or aborted cardiac arrest not significant
      - Spironolactone reduced HF hospitalizations in secondary outcomes HR 0.89 (95% CI 0.69 – 0.99)

Lancet. 2003;362:777–81.
N Engl J Med. 2008;359:2456–67.
Eur Heart J. 2006;27:2338–45.
N Engl J Med. 2014;370:1383–92.

Clinical Question

A 55yo male patient presents to clinic with worsening edema and dyspnea on exertion. His PMH is significant for HTN and Type 2 DM. A recent ECHO shows an EF of 60-65% and grade III diastolic dysfunction with moderate tricuspid valve regurgitation. Pertinent vitals and labs include: BP 160/85 mmHg, HR 68 bpm, Scr 0.9 mg/dL, and K^+ 4.3 mEq/L. His current weight is 10 lbs above baseline and he is currently taking aspirin 81 mg daily and atorvastatin 10mg daily. Which of the following recommendations is the most appropriate at this time?

a. Initiate candesartan and furosemide
b. Initiate candesartan and carvedilol
c. Initiate carvedilol and furosemide
d. Initiate furosemide

Transitions of Care

Recommended for all heart failure patients	Exacerbating factors addressed
	Near optimal volume status observed
	Transition from IV to oral diuretics completed
	Patient and family education completed, including clear discharge instructions
	LVEF documented
	Smoking cessation counseling initiated
	Near optimal pharmacologic therapy achieved (e.g. ACEI, BB)
	Follow-up clinic visit scheduled within 7-10 days
Should be considered for patients with advanced HF or recurrent admissions for HF	Oral medication regimen stable for 24 hours
	No IV vasodilator or ionotropic agent for 24 hours
	Ambulation before discharge to assess functional capacity after therapy
	Plans for post-discharge management (scale, visiting nurse, scheduled telephone call 3 days after discharge)
	Referral for other disease state management

J Card Fail. 2010;16:e1-194.

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Top 5 things to know about heart failure

Christie Schumacher2

Self-assessment questions:

1. The cardiologist in your clinic would like to switch a patient from enalapril 10 mg twice daily to sacubitril-valsartan 24-26 mg twice daily. He would like for you to counsel the patient on the new medication and when to start. How long should you counsel the patient to wait before he/she starts the sacubitril-valsartan prescription after discontinuing enalapril?
    a. 12 hours
    b. 24 hours
    c. 36 hours
    d. 48 hours

2. Which of the following patients would be a candidate for ivabradine?
    a. A 55 year old patient in sinus rhythm with a LVEF of 25% and a pulse of 74 bpm on a max dose beta-blocker, ACEI, spironolactone and furosemide
    b. A 55 year old patient in atrial fibrillation with a LVEF of 25% and a pulse of 74 bpm on a low dose beta-blocker, ACEI, spironolactone and furosemide
    c. A 55 year old patient in sinus rhythm with a LVEF of 55% and a pulse of 64 bpm on a max dose beta-blocker, ACEI, spironolactone and furosemide
    d. A 55 year old patient in sinus rhythm with a LVEF of 25% and a pulse of 64 bpm on a low dose beta-blocker, ACEI, spironolactone and furosemide

The Top 5 Things Pharmacists Can **Do** for Patients with COPD

Lori Wilken, PharmD

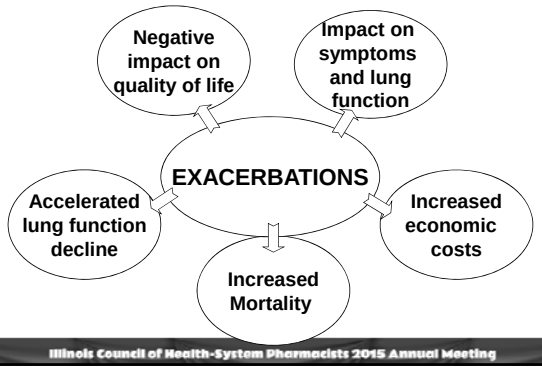
Disclosure

- Grant money was received in the past year from Pfizer. All conflicts were resolved through peer review.
- I will be discussing "off label" uses of the following medications:
  - Nicotine replacement patch, gum, inhaler, nasal spray and lozenge
  - Bupropion SR and Varenicline

Top 5: Number 5

USE CORTICOSTEROIDS CAUTIOUSLY

Consequences Of COPD Exacerbations



GOLD Category	COPD SEVERITY		Exacerbations in the past 12 months
4 3	C	D	≥2 or any COPD related hospitalizations
2 1	A	B	1 or less and not leading to hospitalization
	CAT <10 Few symptoms	**CAT ≥10** Many symptoms	

COPD Severity Grade

goldcopd.org 5

GOLD Category	COPD SEVERITY		Exacerbations in the past 12 months
4 3	LAMA or ICS/LABA	LAMA and/or ICS/LABA	≥2 or any COPD related hospitalizations
2 1	SAMA or SABA	LAMA or LABA	1 or less and not leading to hospitalization
	CAT <10 Few symptoms	**CAT ≥10** Many symptoms	

COPD Severity Grade

goldcopd.org 6

Pneumonia and Inhaled Corticosteroids

	Mortality	Exacerbation	Pneumonia
Placebo	15.2%	1.13	12.3%
Salmeterol	13.5%	0.97 (P<0.001)	13.3%
Fluticasone	**16%**	0.93 (P<0.001)	18.3% (P<0.001)
Combo	12.6% (P=0.052)	0.85 (P<0.001)	19.6% (P<0.001)

N Engl J Med 2007 356;775-789

7

Combination ICS and Long-Acting Bronchodilator

- Clinical Use
  - Severe COPD
  - Repeated exacerbations
    - *2 or more exacerbations in the past year or*
    - *1 COPD hospitalization*
  - **Patient has asthma and COPD**

http://www.goldcopd.org/

8

Acute COPD Exacerbation

- Prednisone 40mg for **5 days**
  - Improves spirometry, ABGs, and symptoms
  - Reduced relapse rates at 30 days and prolonged time to relapse

goldcopd.org

9

Withdrawal of ICS?

- 12 month, double blind, parallel-group
- Randomized to withdrawal fluticasone over 12 weeks
- 2485 patients with history of COPD exacerbations
- Triple therapy (tiotropium + salmeterol +fluticasone)

Magnussen H. N Engl J Med 2014; 371:1285-1294.

Withdrawal of ICS?

- Time to first exacerbation
  - 110 days in withdrawal group
  - 107 days in the continuation group
- Loss of lung function **worse in withdrawal group**
- QOL and safety similar at 52 weeks

Top 5: Number 4

CHECK ADHERENCE TO LONG-ACTING INHALERS

↓ Exacerbations and/or Hospitalizations

Medication Class	Generic
LAMA	Tiotropium Aclidinium
LABA	Formoterol Indacaterol Salmeterol
ICS/LABA	Budesonide/formoterol Fluticasone/salmeterol Fluticasone/vilanterol
Phosphodiesterase 4 Inhibitor	Roflumilast

New Inhalers

Generic	Brand	MOA	Indication	Picture
Fluticasone furoate and Vilanterol 100/25 mcg 200/25 mcg	Breo Ellipta	ICS LAMA	COPD and Asthma ≥ 18	
Umeclidinium and Vilanterol 62.5/25 mcg	Anoro Ellipta	LAMA LABA	COPD	
Umeclidinium 62.5 mcg	Incruse Ellipta	LAMA	COPD	
Tiotropium 2.5 mcg	Spiriva Respimat	LAMA	COPD	
Olodaterol 2.5 mcg	Striverdi Respimat	LABA	COPD	
Tiotropium and Olodaterol 2.5 mcg	Stiolto Respimat	LAMA LABA	COPD	
Albuterol 90 mcg	ProAir Respiclick	SABA	Asthma ≥ 12	

Top 5: Number 3

WATCH INHALER TECHNIQUE

Every Visit
Every Inhaler

http://use-inhalers.com/

70% of people use inhalers incorrectly!

Top 5: Number 2

SCREEN AND PROVIDE IMMUNIZATIONS

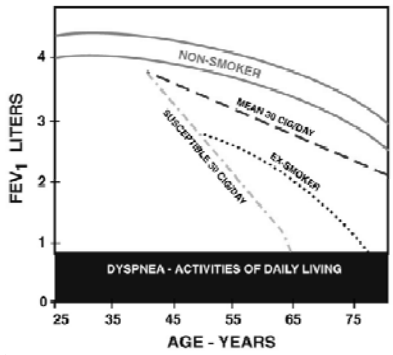
Immunizations

- Influenza vaccine
  - Reduces serious illness and death by **50% in COPD patients**
  - Intramuscularly
  - Annually (October-March)

Top 5: Number 1

ASSIST WITH TOBACCO DEPENDENCE

Relationship of FEV_1, age and smoking



BMJ 1977;1:1645

20

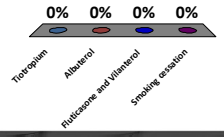
Treatment of Tobacco Dependence

- Nicotine Replacement Therapy (NRT)
  - Transdermal patches
  - Gum
  - Nasal Spray
  - Inhaler
  - Lozenges
- Bupropion SR
- Varenicline
- Combination therapy

21

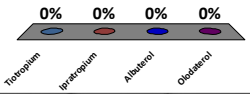
Which of the following treatments has been shown to slow the decline in lung function for patients with COPD?

A. Tiotropium
B. Albuterol
C. Fluticasone and Vilanterol
D. Smoking cessation



Which of the following medications has demonstrated decreased COPD exacerbations and hospitalizations?

A. Tiotropium
B. Ipratropium
C. Albuterol
D. Olodaterol



FUTURE DEVELOPMENTS

Pipeline for COPD

Drug Entity	MOA	Study Phase	Company
Indacaterol Glycopyronnium	LABA/LAMA	Expected launch 2016	Novartis
Glycopyrronium	LAMA	Expected launch 2016	Novartis
Fluticasone Umeclidinium Vilanterol	ICS/LAMA/LABA	Expected launch 2019	GSK
Aclidinium formoterol	LAMA/LABA	Phase 3	Astra Zeneca
Benralizumab	Biologic IL-5 antibody	Phase 3	Astra Zeneca
Mepolizumab	Biologic IL-5 antibody	Phase 3	GSK
TD-4208	LAMA nebulized soln daily	Phase 3	Theravance Biopharma/Mylan
Losmapimod	p38-kinase inhibitor	Phase 2	Pfizer

Pipeline Drug for Tobacco Dependence

"

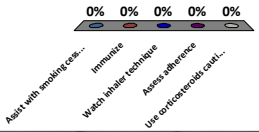
- "A New Strategy for Smoking Cessation: Characterization of a Bacterial Enzyme for the Degradation of Nicotine"
  - Xue S, Schlosburg JE, Janda KD. *Journal of the American Chemical Society*, 2015

Summary

1. Assist with **stopping smoking**!
2. Screen and provide (or recommend) **influenza vaccine**
3. ***Watch*** inhaler technique
4. Check **adherence** to long-acting inhalers
5. Use corticosteroids cautiously

What do you plan to do when you return to work to help patients with COPD?

A. Assist with smoking cessation
B. Immunize
C. Watch inhaler technique
D. Assess adherence
E. Use corticosteroids cautiously



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Top Things to Know About Community-acquired Pneumonia

John Esterly, PharmD, BCPS AQ-ID
Chicago State University COP
Northwestern Memorial Hospital

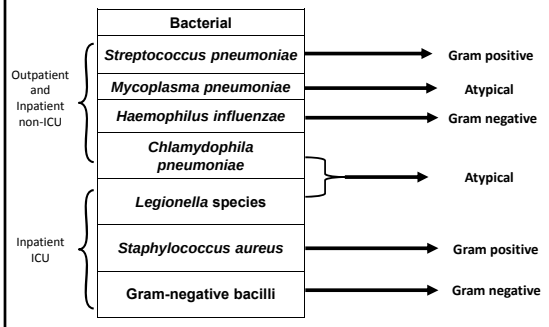
Disclosures

- The speaker has served on an Advisory Board for BioCryst Pharmaceuticals, Inc. (10/2014)
- All conflicts resolved through peer review

What is CAP?

- Pneumonia (lower respiratory track infection) in a patient who otherwise does not have risk factors for exposure to "nosocomial" pathogens
  - Diagnosis plus rule out of HCAP, HAP, VAP qualifying criteria
  - Essentially limits scope of pathogens and expected resistance profiles requiring empiric coverage

Etiology of CAP - Review



How to Decide Who Gets What Therapy?

- **Pneumonia severity scoring guides treatment location and pathogen risk**
  - CURB-65, PORT index
- **Risk factors requiring *Pseudomonas* coverage for CAP**
  - Advanced COPD w/ steroids, structural lung disease (brochiectasis), +++ antibiotic exposures
- **HCAP (so CAP rule-out) qualifiers**
  - Hospitalization w/in 90 days, nursing home/long-term care, recent antibiotics or IV chemo or wound care, visited hemodialysis clinic past 30 days

Mandell L et al. *Clin Infect Dis.* 2007; 44(suppl 2):S27-S72.

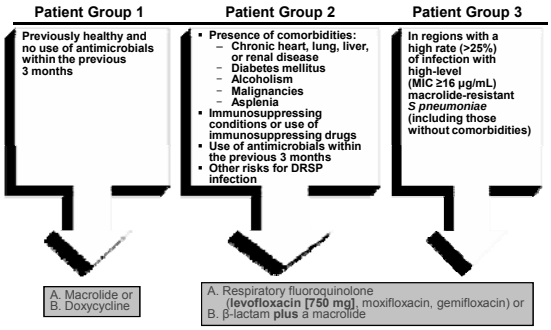
CAP Severity Assessment: CURB-65

- British Thoracic Society Scoring Tool
- Score: 0–5, with 1 point for each of the following
  - **C**onfusion
  - B**U**N >19.6 mg/dL
  - **R**R ≥30 breaths/min
  - S**B**P <90 mm Hg or D**B**P ≤60 mm Hg
  - Age ≥**65** yr
- 2 points - consider hospital admission
- ≥3 points - consider ICU admission

CURB-65 Score	Mortality Risk	Disposition
0	Low (0.6%)	Outpatient
1	Low (2.7%)	Outpatient
2	Moderate (6.8%)	Out/Inpatient
3	Significant (14.0%)	Inpatient
4	High (27.8%)	Inpatient/ICU
5	High (27.8%)	Inpatient/ICU

Adapted from Mandell LA et al. *Clin Infect Dis.* 2007;44(suppl 2):S27-S72.

Outpatient Treatment Recommendations for CAP



Adapted from Mandell LA et al. *Clin Infect Dis.* 2007;44(suppl 2):S27-S72.

Inpatient Treatment Recommendations for CAP

Non-ICU
β-lactam + Macrolide
Antipneumococcal Quinolone
β-lactam + Doxycycline
Tigecycline

Non-ICU with Pseudomonal Risk
Antipseudomonal β-lactam + Antipseudomonal Quinolone
Antipseudomonal β-lactam + Aminoglycoside + Quinolone
Antipseudomonal β-lactam + Aminoglycoside + Macrolide

ICU
β-lactam + Macrolide
β-lactam + Quinolone
β-lactam + Aminoglycoside + Macrolide
β-lactam + Aminoglycoside + Quinolone

Adapted from Mandell LA et al. *Clin Infect Dis.* 2007;44(suppl 2):S27-S72.

Other New/Emerging CAP Treatment Options?

With Current FDA Approval

- Linezolid (2000)
  - Option with anti-MRSA activity
  - MRSA causes <1% of CAP in studies
  - Level III recommendation in current guidelines
- Ceftaroline (2010)
  - Approved for CABP
  - Too recent to make last guideline iteration (2007)

Investigational Drugs currently in Phase 3 Trials

- Ceftobiprole
  - Broad IV cephalosporin
- Cethromycin, Solithromycin
  - Oral/IV ketolide antibiotics
- Faropenem
  - Oral carbapenem
- Nemonoxacin
  - Oral quinoline (non-FQ)

Data from www.clinicaltrials.gov using search terms "Community-acquired neumonia, bacterial" and limited to "Phase 3".

Ceftaroline CABP Data

- FOCUS 1 & 2
  - Identical Phase 3, randomized, multinational studies
- Compared 5-7 days of ceftaroline 600 mg i.v. every 12 hrs vs. ceftriaxone 1 g i.v. every day
- Hospitalized patients with PORT risk class III & IV
- Primary outcome was non-inferiority in clinical cure rates for clinical efficacy and modified intent-to-treat efficacy

File TM et al. *Clin Infect Dis.* 2010; 51:1395-1405.

Pooled Results from FOCUS 1 & 2

Clinical Cure Rates by Study Population at the Test-of-Cure Visit.

Variable	CE	MITTE	ME	mMITTE
FOCUS 1				
Ceftaroline	194/224 (86.6)	244/291 (83.8)	62/69 (89.9)	66/75 (88.0)
Ceftriaxone	163/234 (78.2)	233/300 (77.7)	54/71 (76.1)	60/80 (75.0)
Difference, % (95% CI)	8.4 (1.4–15.4)	6.2 (−0.2 to 12.6)	13.8 (1.3–26.4)	13.0 (0.7–25.2)
FOCUS 2				
Ceftaroline	199/235 (84.7)	235/289 (81.3)	68/85 (81.2)	72/90 (80.0)
Ceftriaxone	166/215 (77.2)	209/273 (75.5)	57/76 (75.0)	66/88 (75.0)
Difference, % (95% CI)	4.9 (−2.5 to 12.5)	5.9 (−1.0 to 12.7)	6.2 (−6.7 to 19.2)	5.0 (−7.4 to 17.4)
Integrated FOCUS				
Ceftaroline	387/459 (84.3)	479/580 (82.6)	131/154 (85.1)	138/165 (83.6)
Ceftriaxone	349/449 (77.7)	439/573 (76.6)	111/147 (75.5)	126/168 (75.0)
Weighted treatment difference, % (95% CI)	6.7 (1.6–11.8)	6.0 (1.4–10.7)	9.7 (0.7–18.8)	8.7 (−0.6 to 17.4)

NOTE. Data are proportion (%) of patients, unless otherwise indicated. CE, clinically evaluable population; CI, confidence interval; FOCUS, Ceftaroline Community Acquired Pneumonia Trial versus Ceftriaxone in Hospitalized Patients; ME, microbiologically evaluable population; MITTE, modified intent-to-treat efficacy population; mMITTE, microbiological modified intent-to-treat efficacy population.

File TM et al. *Clin Infect Dis.* 2010; 51:1395-1405; by permission of Oxford University Press.

Pooled Results from FOCUS 1 & 2

Clinical Cure Rates by the Most Common Baseline Pathogens at Test-of-Cure Visit, Integrated Microbiological Modified Intent-to-Treat Efficacy Population.

	Proportion (%) of patients					
	FOCUS 1		FOCUS 2		Integrated FOCUS	
Variable	Ceftaroline (group)	Ceftriaxone (group)	Ceftaroline (group)	Ceftriaxone (group)	Ceftaroline (group)	Ceftriaxone (group)
Gram positive						
Streptococcus pneumoniae	24/27 (88.9)	20/30 (66.7)	35/42 (83.3)	28/40 (70.0)	59/69 (85.5)	48/70 (68.6)
MDRSP[a]	2/2 (100)	0/1 (0)	2/2 (100)	2/8 (25.0)	4/4 (100)	2/9 (22.2)
Staphylococcus aureus	9/10 (90.0)	9/14 (64.3)	10/15 (66.7)	9/16 (56.3)	19/25 (72.0)	18/30 (60.0)
MRSA[b]	NA	0/1 (0)	NA	1/1 (100)	NA	1/2 (50.0)
Gram negative						
Haemophilus influenzae	4/5 (80.0)	7/10 (70.0)	13/15 (86.7)	13/14 (92.9)	17/20 (85.0)	20/24 (83.3)
Haemophilus parainfluenzae	7/8 (87.5)	9/10 (90.0)	9/9 (100)	6/8 (75.0)	16/17 (94.1)	15/18 (83.3)
Klebsiella pneumoniae	7/8 (87.5)	3/5 (60.0)	7/7 (100)	7/8 (87.5)	14/15 (93.3)	10/13 (76.9)
Escherichia coli	8/8 (100)	5/7 (71.4)	2/4 (50.0)	4/6 (66.7)	10/12 (83.3)	9/13 (69.2)

NOTE. FOCUS, Ceftaroline Community Acquired Pneumonia Trial versus Ceftriaxone in Hospitalized Patients; MDRSP, multidrug-resistant *S. pneumoniae*; MRSA, methicillin-resistant *S. aureus*; NA, not applicable.

[a] MDRSP was defined in these studies as strains resistant to ≥2 antimicrobial classes of drugs, including penicillin, macrolides, tetracycline, fluoroquinolones, chloramphenicol, trimethoprim-sulfamethoxazole, and cephalosporins.

[b] Patients with confirmed or suspected community-acquired pneumonia caused by MRSA at baseline were excluded from the study.

File TM et al. *Clin Infect Dis.* 2010; 51:1395-1405; by permission of Oxford University Press.

Treatment Considerations - Ceftaroline?

- "Non-inferior" for CABP in 2 RCTs
  - Compared ceftaroline 600 mg IV q 12 hours with regimen of ceftriaxone 1 g IV daily x 5-7 days
- Higher response rates for *S. pneumoniae*?!?
  - 85.5% vs. 68.6% (n=~70 each arm)
  - Sub-group analysis was *post hoc* so results are underpowered
  - Too few multi-drug resistant strains to make an evaluation
- Too early to be guideline endorsed for either of FDA-approved indications!

CMS Measures for CAP

- Which of the following statements is correct regarding CMS reimbursement tied to pneumonia?
- A. Antibiotics must start with 4 hours
- B. Antibiotics must start with 8 hours
- C. Antibiotics must start with 24 hours
- D. There is no mandate to start therapy on a specific timeline

What Does CMS Care About?

Set Measure ID#	Measure Short Name
~~PN-3a~~	~~Blood Cultures Performed Within 24 Hours Prior to or 24 Hours After Hospital Arrival for Patients Who Were Transferred or Admitted to the ICU Within 24 Hours of Hospital Arrival~~
PN-3b	Blood Cultures Performed in the Emergency Department Prior to Initial Antibiotic Received in Hospital
~~PN-5c~~	~~Initial Antibiotic Within 6 hours of Arrival~~
PN-6	Initial Antibiotic Selection for Community-acquired pneumonia (CAP) in Immunocompetent Patient
PN-6a	Initial Antibiotic Selection for CAP in Immunocompetent – ICU Patient
PN-6b	Initial Antibiotic Selection for CAP Immunocompetent – Non ICU Patient

Centers for Medicare & Medicaid Services. The Joint Commission. Specifications manual for national hospital inpatient quality measures. (URL in ref list)

How Does CMS Evaluate You?

- Guideline concordant antibiotic therapy
  - Mandate to start antibiotics within a specific timeframe pushed out to 24 hours
  - Therapy choice must be consistent with current guidelines and inpatient location
- 30-day risk-standardized measures
  - Mortality
  - 30-day readmission
    - "Higher than expected" readmissions can lead to reduced reimbursement rates

Centers for Medicare & Medicaid Services. The Joint Commission. Specifications manual for national hospital inpatient quality measures. (URL in ref list).

How Can Stewardship Efforts Be Complimentary with CMS?

- Ensure appropriate use per guidelines
  - Implementation of CAP order sets!
- Avoid overuse of antibiotics
  - CMS allows "outs" for unsure diagnosis, antibiotics with previous 24 hours, transfer from other acute care facilities, pathogen-directed therapy, study enrollment, comfort care patients
- Clearly define the need for anti-pseudomonal therapy
  - Distinguish CAP vs. HCAP

Pneumonia ED Order Set Example

LAB		
If cultures are obtained, they should be collected prior to initiating antibiotics		
Choose Both BC orders for 2 sets		
Blood Culture	Stat, Add On = No	
Blood Culture	Stat, Add On = No	
Respiratory Culture s/Gram Stain	Stat, Once, Specimen type: Sputum	
A viral PCR test should ALWAYS be ordered with a rapid influenza test due to limited sensitivity of the rapid influenza test.		
Influenza Antigen Test, Direct	Stat, Specimen type: Nasopharyngeal	
Influenza A/B & RSV A/B Detection by PCR	Routine, Once, Specimen type: Nasopharyngeal	
The Streptococcal Pneumoniae Antigen test should be ordered in patients with suspected CAP.		
Strept Pneumoniae Antigen Test	Stat, Urine, Once	
Legionella Urine Antigen	Stat, Urine, Once	
CAP - ORAL TREATMENT		
Continue "ZPak" for 4 additional days		
azithromycin (Zithromax)	500 mg, DF: Tab, PO, Once	
or moxifloxacin 400 mg daily x 5 days		
moxifloxacin (Avelox)	400 mg, DF: Tab, PO, Once	
CAP - INPATIENT FLOOR ADMISSION		
Choose Both		
ceftriaxone (Rocephin)	1 g, IVPB, Once	Rate: 300 mL/Hr, Infuse Over: 20 Minutes
azithromycin (Zithromax)	500 mg, IVPB, Once	
or		
moxifloxacin (Avelox)	400 mg, IVPB, Once	Rate: 250 mL/Hr, Infuse Over: 60 Minutes

Pneumonia ED Order Set Example

CAP - ICU ADMISSION		
Choose Both		
ceftriaxone (Rocephin)	2 g, IVPB, Once	Rate: 300 mL/Hr, Infuse Over: 20 Minutes
moxifloxacin (Avelox)	400 mg, IVPB, Once	Rate: 250 mL/Hr, Infuse Over: 60 Minutes
Alternative to ceftriaxone if Beta-lactam allergy		
vancomycin	15 mg/Kg, IVPB, Once	Rate: 250 mL/Hr, Infuse Over: 60 Minutes
HEALTH-CARE ASSOCIATED PNEUMONIA (HCAP)		
Choose ALL 4 antibiotics		
cefepime	2g, IVPB, Once	
vancomycin	15 mg/Kg, IVPB, Once	Rate: 250 mL/Hr, Infuse Over: 60 Minutes
amikacin	15 mg/Kg, IVPB, Once	
azithromycin (Zithromax)	500 mg, IVPB, Once	
Alternative to cefepime if Beta-lactam allergy		
aztreonam (Azactam)	2 g, IVPB, Once	
LUNG ABSCESS		
Choose both amp-sulbactam and vancomycin		
ampicillin-sulbactam (Unasyn)	3 g, IVPB, Once	
vancomycin	15 mg/Kg, IVPB, Once	Rate: 250 mL/Hr, Infuse Over: 60 Minutes
Choose moxifloxacin for alternative to amp-sulbactam for Beta-lactam allergy		
moxifloxacin (Avelox)	400 mg, IVPB, Once	Rate: 250 mL/Hr, Infuse Over: 60 Minutes
SEVERE ACUTE EXACERBATION OF COPD		
azithromycin (Zithromax)	500 mg, IVPB, Once	
or		
moxifloxacin (Avelox)	400 mg, IVPB, Once	Rate: 250 mL/Hr, Infuse Over: 60 Minutes
INFLUENZA		
For outpatients, efficacy of treatment is only proven if started within 48 hours of symptom onset (Continue BID for 5 days)		
oseltamivir (Tamiflu)	75 mg, DF: Cap, PO, Once	

Antibiotic De-escalation Strategies

- Definitively confirm diagnosis of pneumonia
  - Radiology, oxygnation, cultures, other supporting labs (e.g. procalcitonin, CRP)
- Target antibiotics with single-drug therapy when possible
  - Cultures/susceptibilities, PCR, antigen testing results
- Convert to PO therapy when clinically stable
  - Can discharge as soon as able to take PO if no other medical problems and a safe transition environment

Mandell L et al. *Clin Infect Dis.* 2007; 44(suppl 2):S27-S72.

Optimizing Treatment Duration

- 5 days minimum recommended
  - Afebrile for 48-72 hours before discontinuation of therapy
  - ≤1 CAP-associated sign of clinical instability
  - No sign of extrapulmonary infection
- Shorter courses of therapy → reduced resistance, adverse events, and cost
  - Education!!!

Mandell L et al. *Clin Infect Dis.* 2007; 44(suppl 2):S27-S72.

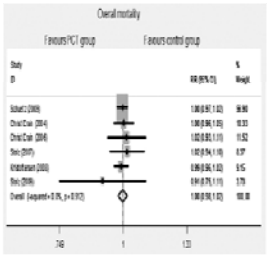
Procalcitonin (PCT)

- PCT is a pro-hormone of calcitonin
  - No known biological role
- Produced by cells in a wide range of organs and tissues in response to inflammation
- Conversion to calcitonin is inhibited by cytokines and bacterial endotoxins
- PCT levels are selectively elevated in patients with bacterial infections and a strong correlation exists

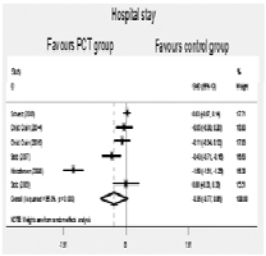
Scheutz, et al. Arch Intern Med. 2011 Aug 8;171(15):1322-31.

Meta-analysis of PCT in Respiratory Infections

Comparison of all-cause mortality between the PCT-guided antibiotic group and the control group



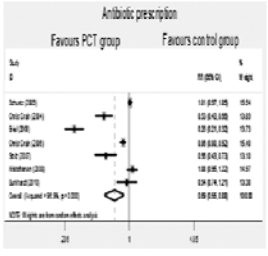
Forest plot for the weighted mean difference in length of hospital stay



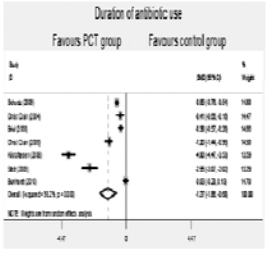
Li, et al. Antimicrob Agents Chemother. 2011 Dec;55(12):5900-6.

Meta-analysis of PCT in Respiratory Infections

Forest plot for odds ratio of antibiotic prescriptions in PCT-guided antibiotic treatment groups and control groups.



Forest plot for the weighted mean difference of duration of antibiotic use.



Li, et al. Antimicrob Agents Chemother. 2011 Dec;55(12):5900-6.

Clinical Role for PCT?

- PCT shows promise as another clinical tool to contribute to clinician evaluation of initiation and duration of antibiotic therapy
- Predominance of data comes from trials evaluating respiratory infections
- The most useful role for PCT may be to help guide discontinuation of antibiotic unnecessary antibiotic therapy

ACIP Updates for Pneumococcal Vaccination Recommendations

Prevnar-13® (PCV-13)

- 13-valent conjugate vaccine
- Improved response when given with PPSV-23
- Recommended for:
  - Routine use in adults ≥65 years
  - Use in adults >18 years with immunocompromising conditions, asplenia, CSF leak, cochlear implant
- ACIP Category A recommendation

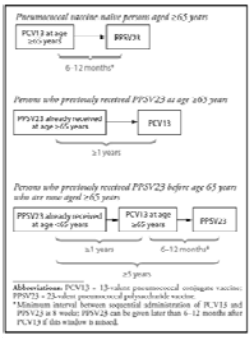
Pneumovax-23® (PPSV-23)

- 23-valent polysaccharide vaccine
- Recommendations for administration have not changed except to accommodate for inclusion of PCV-13

CDC. Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine Among Adults Aged ≥65 Years: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2014; 63:822-25.

PCV-13 and PPSV-23 Recommendations

- Both vaccines should be routinely given to patients ≥65
  - PCV-13 first, followed by PPSV-23 in 6-12 months
  - If PPSV-23 given, PCV-13 follows in 1 year
  - If PPSV-23 given prior to age 65, PCV-13 first, followed by PPSV-23 in 6-12 months after 5 year period



CDC. Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine Among Adults Aged ≥65 Ye
Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2014; 63:822-25.

Thank You for Your Attention!

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- Mandell LA, Wunderink RG, Anzeuto A, et al. Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults. *Clin Infect Dis.* 2007;44:S27-S72. (http://cid.oxfordjournals.org/content/44/Supplement_2/S27.full.pdf+html)
- File TM Jr, Wilcox MH, Stein GE. Summary of ceftaroline fosamil clinical trial studies and clinical safety. *Clin Infect Dis.* 2012 Sep;55 Suppl 3:S173-80.
- The Joint Commission Specifications Manual for National Hospital Inpatient Quality Measures. (http://www.jointcommission.org/specifications_manual_for_national_hospital_inpatient_quality_measures.aspx)

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- Li H, Luo YF, Blackwell TS, Xie CM. Meta-analysis and systematic review of procalcitonin-guided therapy in respiratory tract infections. *Antimicrob Agents Chemother.* 2011 Dec;55(12):5900-6.
- CDC. Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine Among Adults Aged ≥65 Years: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2014; 63:822-25. (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6337a4.htm)

Top Things to Know about Community-acquired Pneumonia

John Esterly

1. Which of the following statements is correct regarding CMS reimbursement tied to Community-acquired Pneumonia?
    A. Antibiotics must start with 4 hours
    B. Antibiotics must start with 8 hours
    C. Antibiotics must start with 24 hours
    D. There is no mandate to start therapy on a specific timeline

2. Which of the following newer antimicrobials was most recently approved for the treatment of Community-acquired Bacterial Pneumonia?
    A. Ceftaroline
    B. Cethromycin
    C. Tedizolid
    D. Nemonoxacin

Top Things to Know About Five Commonly Encountered Diseases: Chronic Kidney Disease

Ayesha Khan, PharmD, BCPS
Assistant Clinical Professor, Internal Medicine
Chicago State University College of Pharmacy
September 11, 2015

Conflicts of Interests

- No conflicts to disclose

CKD Discussion Points

Methods available to estimate renal function

⇩

Strengths/limitations of each estimation tool

⇩

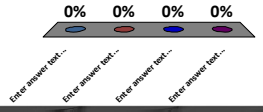
Patient care considerations for the pharmacist

⇩

Chronic hyperkalemia treatment options
• Current options & Pipeline drugs

Which of the following do you utilize most often to estimating renal function for drug dosing?

A. Modification of Diet in Renal Disease (MDRD)
B. Cockroft-Gault
C. Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)
D. Any of the above
E. None of the above



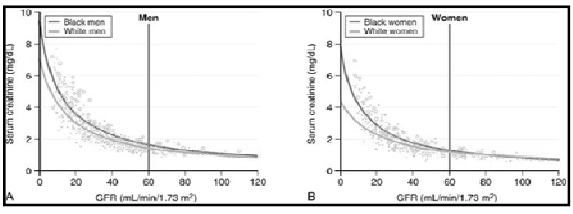
Glomerular Filtration Rate

- Indicator of overall kidney function
- Serum markers used to estimate GFR
  - Achieves stable plasma concentration
  - Inert, freely filtered by glomeruli
  - Not reabsorbed, secreted or metabolized
  - Gold standard: inulin, iothalamate, iohexol
  - Endogenous markers: serum creatinine, serum urea, serum cystatin C

Stevens LA, Corest J, Greene T, et al. *N Engl J Med.* 2006;354:2473-2483.

Serum Creatinine (SCr)

- Secreted by proximal tubule & filtered by glomerulus → clearance exceeds GFR
- Isolated use to assess renal function is not advised
- Inverse relation between GFR and SCr is nonlinear



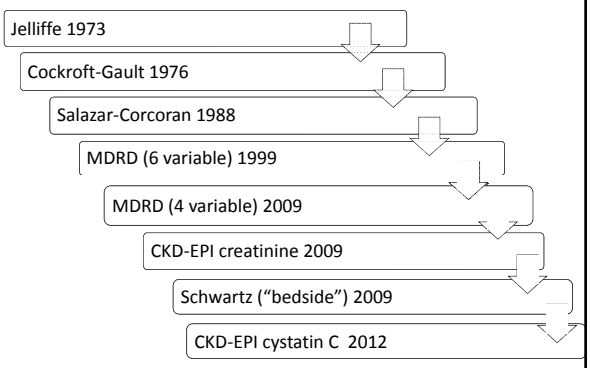
Levey AS, et al. *Ann Intern Med.*1999;130:461-470

Factors Affecting SCr

- Demographics
  - Aging ↓
  - Female gender ↓
  - Ethnicity
    - AA ↑, Hispanic ↓, Asian ↓
- Body Habitus
  - Muscular ↑
  - Malnourished/amputation ↓
- Medications
  - Cimetidine, trimethoprim, probenecid, K-sparing diuretics ↑

Levey AS. *Am J Kidney Dis.* 1993;22(1):207-214.

GFR Estimation Equations



Estimation of renal function

Cockroft-Gault (CG)

$$CrCl = \frac{(140 - age) \times (weight)}{72 \times SCr} \quad (X\ 0.85\ if\ female)$$

- Gold-standard
- 249 males with stable renal function
- Utilized ABW, suggest correction with ascites or obesity
- Adjustments in obesity (40%)

Cockroft DW, Gault MH. *Nephron.* 1976;16(1):3141.
Verhave JC, Fesler P, Ribstein J, et al. *Am J Kidney Dis.* 2005;46:233-241.

Estimation of renal function

Modification of Diet in Renal Disease (MDRD)

IDMS calibrated assays:
GFR= 175 x $SCr^{-1.154}$ x $age^{-0.203}$ x (0.742 if female) x (1.21 if AA)

Non-IDMS assays:
GFR= 186 x $SCr^{-1.154}$ x $age^{-0.203}$ x (0.742 if female) x (1.21 if AA)

- 6-variable equation simplified in 2 variations
- 1628 participants with CKD and mean GFR 40 ml/min/1.73 m^2
- More accurate than CG when using TBW
- Validated in GFR <60 ml/min/1.73 m^2 only

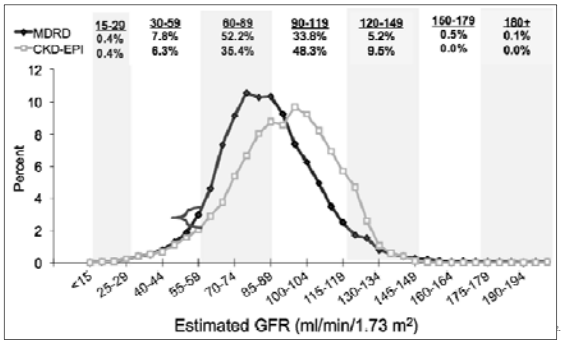
Level AS, Bosch JP, Lewis JB, et al. *Ann Intern Med.* 1999;130:461-470.
Froissart M, Rossert J, Jacquot C, et al. *J Am Soc Nephrol.* 2005;16:763-773

CG and MDRD Limitations

- Require stable SCr concentrations
  - Use cautiously in the critically ill, AKI
- SCr rounding in elderly patients
  - Rounding to 1.0 mg/dL may underestimate renal function
  - Percentage based correction
- Obesity
  - May lead to increased renal plasma flow and GFR
  - 2009 MDRD study
    - 999 overweight patients & 1039 obese patients
    - Tended to underestimate measured GFR
  - Use of adj. BW has been validated in aminoglycoside dosing
  - Use of lean body weight recommended by some experts

Pai MP, Paloucek FP. *Ann Pharmacother.* 2000;34(9):1066-9.
Lamb EJ, Webb MC, O'Riordan SE. *Age Ageing.* 2007; 36:689-692..

MDRD vs CKD-EPI



Levey AS, et al. *Ann Int Med.* 2009;150:604-612.

Estimation of renal function

Chronic Kidney Disease Epidemiology Collaboration (CKD- EPI)

GFR = 141 x min (Scr/k, 1)$^{\alpha}$ x max (Scr/k, 1)$^{-1.209}$ x 0.993^{Age} x 1.018[female] x 1.159 [if Black]

- F/u to MDRD equation to improve accuracy with GFR >60
- Validated retrospectively in 8,254 patients from 10 studies
- Renal failure patients excluded
- 45% women, 87% non-black patients

Levey AS, et al. *Ann Int Med.* 2009;150:604-612.

CKD-EPI Serum Cystatin C

- Freely filtered at the glomerulus, metabolized in the proximal tubule
- Generation is uniform across populations
- Produced by nucleated cells
  - Levels may differ in rapid cell turnover, uncontrolled thryoid, or corticosteroid use
- Cystatin C use may improve classification of GFR
- Screening beneficial in persons with:
  - Borderline estimated GFR (Cr based equation)
  - High risk of CKD
  - Conditions impacting creatinine sensitivity

Stevens LA, Coresh J, Schmid CH, et al. *Am J Kidney Dis.* 2008;51:395-406.
Shlipak MG, et al. *Am J Kidney Dis.* 2013;62(3):595-603.

Drug Dosing

- CG used in PK studies→ standard for drug dosing
- Insignificant translation into drug dosing (MDRD and CG)
  - CG more practical for bedside applicability
- MDRD or CG can be used to estimate kidney function for drug dosing
- Review package insert to determine body weight
  - Ex. rivaroxaban utilizes actual body weight

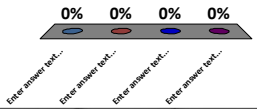
National Kidney Disease Education Program. Chronic Kidney Disease and Drug Dosing: Information for Providers. Available at http://www.nkdep.nih.gov/.../CKD_DrugDosing_508.pdf. Updated April 18, 2015. Accessed July 13, 2015.

Take Home Points

- All current eGFR methods have limitations
- Scr must be stable if used to for eGFR
- Estimate GFR from serum creatinine
  - MDRD and Cockroft-Gault
- Suggest use of CKD-EPI for general population
- Suggest use of cystatin C for confirmatory testing
- Renal function is a mosaic representation
  - Consider labs, clinical signs, symptoms in addition to renal function estimation equations

Patiromer is a new medication currently under FDA review for the treatment of:

A. Hypophosphatemia
B. Hypocalcemia
C. Hyperparathyroidism
D. Hyperkalemia



Hyperkalemia in CKD

- Hyperkalemia (>5 mmol/L) reported in up to 50% of CKD patients
  - Reported in 2-3% of general population
- Contributing risk factors in CKD
  - Dietary modifications
  - Blood transfusions
  - Kidney transplant
  - Diabetes (insulin deficiency and hypertonicity)
  - Cardiovascular disease (medications)
  - RAAS inhibitors (RAASi)

Weir MR, Rolfe M. *Clin J Am Soc Nephrol.* 2010;5:531-548.
Kovesdy CP. *Nat Rev Nephrol.* 2014;10(11):653-62.

Hyperkalemia Treatment

- Avoid NSAIDs, low-dose ACEi/ARB
- Thiazide or loop diuretics
- Sodium polystyrene sulfonate (SPS)
  - Na^+ cation exchange polymer
  - Approved in 1958 → *Prior to Kefauver-Harris Drug Amendments*
  - Limited efficacy data
    - 0.4 mEq/L drop in 23/30 patients in 24 hours
    - About 5mmol of K^+ delivered to colon per day
  - Colonic necrosis and mucosal injury of upper GI tract with long-term use

Scherr L, et al. *N Engl J Med.* 1961;264:115-119.
Parham WA, et al. *Tex Heart Inst J.* 2006;33(1):40-47.

Hyperkalemia: Pipeline Drugs

ZS-9

- Submitted for FDA approval in 2015
- Insoluble, non-absorbed zirconium silicate
- Inorganic cation exchanger with high selectivity for K^+
- Tasteless powder dissolvable in water
- HARMONIZE trial:
  - 2/3 of patients on RAASi therapy, 60% had CKD, 41% had heart failure, 58% had diabetes
  - 84% of patients normokalemic by 48 hours, maintained over the 28 day study period ($p<0.001$)
  - Safety: adverse events, including GI symptoms, similar to placebo group, edema (15mg group)

Packham DK, et al. N Engl J Med. 2015; 372:222-231.
Kosiborod M, et al. JAMA. 2014;312(21):2223-33.
Ingelfinger JR. N Engl J Med. 2015;372:275-277.

ZS-9

- Compound does not swell in the GI tract
  - Results in limited GI symptoms
- Very well tolerated
- Long-term safety and efficacy studies needed
- Potential for continuation of RAASi therapy
- Cost of therapy?

Patiromer

- Phase III study
- Non-absorbed polymer binds K^+ in exchange for Ca^+
- Predominantly binds in distal colon → K^+ level highest
- Oral suspension
- AMETHYST-DN trial:
  - 304 patients with stage 3-4 CKD
  - 76% (95% CI, 70-81) of patients normokalemic by at week 4
  - Safety: mild-moderate constipation (11%), hypokalemia (3%)

Bakris GL, et al. *JAMA.* 2015;314(2):151-161.
Weir WR, et al. *N Engl J Med.* 2015;372:211-221.

Patiromer

- Long-term safety and efficacy studies needed (>12 weeks)
- Decrease in K^+ appears to be gradual
  - Use in acute situation is unclear
- Potential for continuation of RAASi therapy
- Cost of therapy?

Managing Bleeding in Patients on Direct Oral Anticoagulants

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Disclosure

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  - Consultant/Clinical Investigator for Janssen
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- All conflicts resolved through peer review.

Objectives - Pharmacists

1. Compare bleeding risk among various patient populations receiving a direct oral anticoagulant
2. Review management strategies for reversal of the anticoagulant effect of direct oral anticoagulants
3. Describe drugs in the pipeline for management of bleeding associated with direct oral anticoagulant use

Objectives - Technicians

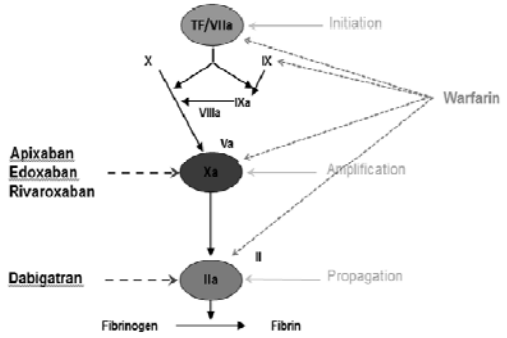
1. List the risks for bleeding among patients receiving a direct oral anticoagulant
2. Review methods to reverse the effects of direct oral anticoagulants
3. Describe drugs in the pipeline for management of bleeding associated with direct oral anticoagulant use

Nomenclature

- NOAC
  - New/Novel oral anticoagulants
  - NO anticoagulants
- NVKOA
  - Non vitamin K oral anticoagulants
- TSOAC
  - Target specific anticoagulants
- DOAC
  - Direct oral anticoagulants

Barnes G, et.al. J Thromb Haemost 2015; 13: 1154–60.

Mechanism of Action



Adapted from Weitz JI, et. al. J Thromb Haemost 2005; 3: 1843-53.

DOACs vs Warfarin

Advantages

- Rapid onset/offset
- Short T1/2
- Predictable PK / fixed dosing
- Fewer drug interactions
- No need for routine monitoring
- Convenience

Disadvantages

- Short T ½ = strict adherence
  - Monitoring adherence
- Drug accumulation in renal impairment
- No reliable, clinically available assay to determine levels
- Lack of dosing flexibility
- High acquisition cost
- Fewer approved indications
- No specific antidote

DOACs: US Indications and Dosage

FDA Indication / Dosage	Apixaban (Eliquis)	Dabigatran (Pradaxa)	Edoxaban (Savaysa)	Rivaroxaban (Xarelto)
Stroke Prevention in Atrial Fibrillation	✔	✔	✔	✔
VTE Treatment Acute Extended	✔ ✔	✔* ✔	✔* ✔	✔ -
Major Orthopedic Surgery (THA/TKA)	✔	-	-	✔
Available dose strengths	2.5mg; 5mg (tablets)	75mg; 150mg (capsules)	15mg; 30mg; 60mg (tablets)	10mg; 15mg; 20mg (tablets)

*Dabigatran and Edoxaban approved for acute VTE treatment only after an initial course of at least 5 days of a parenteral anticoagulant

Pharmacology of DOACs

	Apixaban	Dabigatran	Edoxaban	Rivaroxaban
Bioavailability	50%	3%-7%	62%	80%-100% [10-mg] 66% [20-mg]
Tmax	1-3 hours	1-3 hours	1-2 hours	2-4 hours
Onset of anticoagulant effect	Within 3 hours	Within 2 hours	Within 1- 2 hours	Within 4 hours
CYP metabolism	25% CYP3A4	No	CYP3A4 (minimal)	30% CYP3A4, CYP2J2
Renal excretion	25%	80%	50%	33%
Half-life	8-14 hours	12-17 hours	10-14 hours	6-9 hours; 12-13hrs elderly
Dialyzable	No	Yes	No	No
Dosing frequency	BID	BID	Once daily	Once daily

CYP=cytochrome P450; Tmax=time to maximum concentration

Segal D, et.al. Drug Discov Today. 2014;19(9):1465-1470; Greinacher A, et.al. Thromb Haemostasis. 2015;113(5):931-942.

Objectives

1. Compare bleeding risk among various patient populations receiving a direct oral anticoagulant
2. Review management strategies for reversal of the anticoagulant effect of direct oral anticoagulants
3. Describe drugs in the pipeline for management of bleeding associated with direct oral anticoagulant use

Definition of Bleeding

Severity	Definition
Major	• Involves major organ including central nervous system (intracranial or epidural), pericardial, intraocular, retroperitoneal, intra-articular, intramuscular with compartment syndrome • Clinically overt bleeding with a drop in hemoglobin at least 2g/dl • Requires transfusion of at least 2 units • Requires surgical correction • Requires intravascular vasoactive agents
NMCRB	Clinically overt bleeding that does not satisfy criteria for major bleeding but requires • Hospitalization or increased level of care, or • Prompt physician guided medical or surgical treatment, or • A change in antithrombotic therapy
Minor	• Self terminating • Does not require an office visit • No hospitalization of treatment by a health care professional

NMCRB: non-major clinically relevant bleeding

Kovacs et al. JACC 2015;65(13):1340-60.

Self-Assessment 1:

The following is true about the incidence of DOAC associated MB reported in Phase III clinical trials

A. MB is >4% in patients treated for SPAF
B. MB is <4% in patients treated for SPAF
C. MB is > 2% in patients treated for acute VTE
D. MB is < 2% in patients treated for acute VTE
E. Unsure

DOAC: Bleeding Profile in Treatment of Acute VTE

	Dabigatran		Rivaroxaban		Apixaban	Edoxaban
	RE-COVER	RE-COVER II	EINSTEIN DVT	EINSTEIN PE	AMPLIFY	Hokusai-VTE
Dose	150mg bid	150mg bid	15mg bid x 21 d then, 20mg od	15mg bid x 21 d then, 20mg od	10mg bid x 7d then, 5mg bid	60mg od[a]
Comparator	UFH/Warf	UFH/Warf	Enox/VKA	Enox/VKA	Enox/Warf	UFH/Warf
MB/NMCRB *DOAC vs Comparator (%)*	5.6 vs 8.8*	5.0 vs 7.9	8.1 vs 8.1	10.3 vs 11.4	4.3 vs 9.7*	8.5 vs 10.3*
MB *DOAC vs Comparator (%)*	1.6 vs 1.9	1.2 vs 1.7	0.8 vs 1.2	1.1 vs 2.2 *	0.6 vs 1.8*	1.4 vs 1.6
ICH (%)	0 vs 0.24	0.16 vs 0.16	0.12 vs 0.12	0.12 vs 0.46	0.11 vs 0.22	0.12 vs 0.44
GI (%)	0.7 vs 0.4	0.5 vs 0.8	0.06 vs 0.18	0 vs 0	0.26 vs 0.67	0.02 vs 0.05

[a] 30mg od in patients with creatinine clearance 30-50ml/min, body weight ≤ 60kg or receiving concomitant treatment with a potent p-glycoprotein inhibitor
bid, twice daily; GI; Gastrointestinal; ICH, intracranial; MB, Major bleeding; NMCRB, Non Major Clinically Relevant Bleeding, od, once daily; UFH, unfractionated heparin;
* p< 0.05

Schulman S, et al. N ENG J Med 2009;361:2342-52.; Schulman S, et al. Circulation 2014.; 129: 764–772; Prins MH, et al. Thromb J 2013; 11: 21.;The EINSTEIN Investigators. N Engl J Med 2010; 363: 2499–2510.; EINSTEIN–PE Inv .N Engl J Med 2012; 366: 1287–1297.; Agnelli G, et al. N Engl J Med 2013; 369: 799–808.; The Hokusai-VTE Investigators. N Engl J Med 2013; 369: 1406–1415.

DOAC: Bleeding Profile in Extended VTE Treatment

	Dabigatran		Rivaroxaban	Apixaban	
	RE-SONATE	RE-MEDY	EINSTEIN EXT	AMPLIFY-EXT	
Dose	150mg BID	150mg BID	20mg od	2.5mg BID	5mg BID
Comparator	Placebo	Warfarin	Placebo	Placebo	
MB/NMCRB *DOAC v Comparator* (%)	5.3 vs 1.8*	5.6 vs 10.2*	6.0 vs 1.2*	3.2 vs 2.7	4.3 vs 2.7
MB *DOAC v Comparator* (%)	0.3 vs 0	0.9 vs 1.8	0.7 vs 0	0.2 vs 0.5	0.1 vs 0.5

bid, twice daily; MB, Major bleeding; od, once daily; NMCRB, Non Major Clinically Relevant Bleeding, od, once daily
* p< 0.05

Schulman S, et al. N Engl J Med 2013; 368: 709–718.; The EINSTEIN Investigators. N Engl J Med 2010; 363: 2499–2510.; Agnelli G, et al. N Engl J Med 2013; 368: 699–708.

DOAC: Bleeding Profile in NVAF (vs Warfarin)

	Dabigatran		Rivaroxaban	Apixaban	Edoxaban	
	RE-LY		ROCKET AF	ARISTOLE	ENGAGE AF-TIMI 48	
Dose	110mg bid	150mg bid	20mg od[a]	5mg bid[b]	30mg od[c]	60mg od[c]
MB[d] *DOAC v W (%/yr)*	2.92 vs 3.61*	3.40 vs 3.61[e]	3.6 vs 3.4	2.13 vs 3.09*	1.61 vs 3.43*	2.75 vs 3.43*
ICH *DOAC v W (%/yr)*	0.23 vs 0.76*	0.32 vs 0.76*	0.50 vs 0.70*	0.33 vs 0.80*	0.26 vs 0.85*	0.39 vs0.85*
GI *DOAC v W (%/yr)*	1.15 vs 1.07	1.56 vs 1.07*	2.00 vs 1.24*	0.76 vs 0.86	0.82 vs 1.23*	1.51 vs 1.23*
Fatal *DOAC v W (%/yr)*	0.2 vs 0.3	0.2 vs 0.3*	0.2 vs 0.5*	34 vs 55 *patients*	0.13 vs 0.38*	0.21 vs 0.38*

[a] 15mg if CrCl 30-49ml/min, [b] 2.5mg bid in patients with two or more of the following; age ≥ 80 years, body weight ≤ 60kg or serum creatinine ≥ 1.5mg/dl; [c] dose was halved if any of the following characteristics were presented at randomization or during the study: estimated CrCL 30-50 ml/min, a body weight ≤ 60kg, or the concomitant use of verapamil or quinidine (potent P-glycoprotein inhibitors); [d] definitions of major bleeding varied between studies; bid, twice daily; DOAC, Direct Oral Anticoagulant; GI; Gastrointestinal; ICH, intracranial hemorrhage; MD, Major bleeding; od, once daily; * Statistically Significant, p< 0.05

Connolly SJ, et al. N Engl J Med 2009; 361: 1139–1151.; Connolly SJ, et al. N Engl J Med 2010; 363: 1875–1876.; Connolly SJ, et al. N Engl J Med 2014; 371:1464–1465.; Patel MR, et al. N Engl J Med 2011; 365: 883–891.; Nessel C, et al. Chest 2012; 142: 84A–84A.; Granger CB, et al. N Engl J Med 2011; 365: 981–992.; Giugliano RP, et al. N Engl J Med 2013; 369: 2093–2104.

Self Assessment - 2

Compared to results from Phase III randomized clinical trials, DOAC associated major bleeding in "real-world" observational studies is:

A. Higher
B. Lower
C. Similar
D. Unsure

DOAC: Bleeding Profiles in Published Real-World Studies

	DOACs	Setting	N	MB	Fatal	Other
Beyer-W (2014)	Rivaroxaban	VTE or AF	1,776	3.4%/yr	6.3%*	**NMCR:** 19.7%
Larsen (2014)	Dabigatran Warfarin	AF	33,945	**D150**: 2.1-2.2%/yr **W:** 2.6-3.7%/yr	**D150:** 0.2-0.3%/yr **W:** 0.4-0.5%/yr	***ICH:*** **D150:** 0.2-0.3%/yr **W:** 0.7-1.0%/yr
Hernand. (2015)	Dabigatran Warfarin	AF	9,404	**D:** 9.0% **W:** 5.9%	NR	***ICH:*** **D:** 0.6%; **W:** 1.8% ***GI:*** **D:** 17.4%; **W:** 10.0%
FDA (2014)(2015)	Dabigatran Warfarin	AF	>134,000	NR	NR	***ICH:*** **D:** 0.3%/yr **W:** 1.0%/yr ***GI:*** **D:** 3.4%/yr **W:** 2.7%/yr

D, Dabigatran; GI, gastrointestinal; ICH: Intracranial hemorrthage; NMCR: Non-major clinically relevant; NR, not reported; W, Warfarin
*at 90days in patients hospitalized for bleeding

Beyer-Westendorf J, et al. Blood 2014;124 955–962.; Larsen TB, et al. Am J Med 2014;127: 650–656; Hernandez I, et al. JAMA Intern Med 2015;175:18–24. Food and Drug Administration. Available at: http://www.fda.gov/Drugs/DrugSafety/ucm396470.htm. Graham DJ, et al. Circulation 2015; 131: 157–164.

Major Bleeding: Case Fatality Rates

	Warfarin		DOACs	
	N	%	N	%
ROCKET AF	55/386	14%	27/395	7%
Dabigatran systematic review	53/407*	13%	57/627*	9%
ARISTOTLE	55/462	12%	34/327	10%
ENGAGE AF-TIMI 48	59/524	11%	32/418 21/254	8% 8%

* Estimated from paper

Patel MR, et al. N Engl J Med 2011;365:883-891.; Majeed A, et al. Circulation 2013;128: 2325-2332.; Granger CB, et al. N Engl J Med 2011; 365:981-992.; Giugliano RP, et al. N Engl J Med 2013; 369:2093-2104.

Self Assessment - 3

In clinical practice, patients who develop DOAC associated major bleeding are treated with factor concentrates:

A. 100% of the time
B. 50% of the time
C. 25% of the time
D. < 10% of the time
E. Unsure

How are Bleeds Managed? Dresden DOAC^ Registry

Bleeding Events [1082 bleeds/762 patients*]	Conservative	Surgery	RBC	Vit K	FFP	PCC	rFVIIa
Minor (637; 58.9%)	637/637 (100%)	0	0	0	0	0	0
NMCRB (379; 35%)	328/379 (86.5%)	51/379 (13.5%)	0	0	0	0	0
Major (66; 6.1%)	41/66 (62.1%)	25/66 (37.9%)	40/66 (60.6%)	1/66 (1.5%)	6/66 (9.1%)	6/66 (9.1%)	0
Total	1006/1082 (93%)	76/1082 (7%)	40/1082 (3.7%)	1/1082 (0.1%)	6/1082 (0.6%)	6/1082 (0.6%)	0

NMCRB, Non-major clinically relevant bleeding
^Rivaroxaban
*Data in the "as treated population"

Beyer-Westendorf J et al. Blood 2014;124(6):955-62.

Who is at Risk and What is the Need for a Bleeding Reversal Solution?

- Real-world bleeding rates are mostly reflective of clinical trials
  - although variations in outcomes observed among studies /settings
- Patients experiencing major bleeding:
  - tend to be older
  - have more comorbidities
    - Hypertension
    - CAD
    - Heart failure
    - Renal disease
  - tend to receive transfusions but NOT clotting factors
- Major bleeding leads to fatal bleeding
- Rapid control of bleeding is expected to improve clinical outcomes
  - Benefits of prompt anticoagulant reversal have not yet been proven

Tamayo S et al. Clin Cardiol. 2014; 38(2):63-8.; Beyer-Westendorf et al. Blood 2014;125(6):955-62.

What are Clinical Parameters for Successful Bleeding Management?

- Mortality
  - 30 days post-bleed all-cause mortality
- Thrombosis
- Length of ICU admittance
- ICH hematoma expansion
- Hemoglobin status
- Resource utilization
  - Transfusions
  - Platelets
  - Coagulation factors

Majeed A et al. Circulation 2013;128(21):2325-32.

Objectives

1. Compare bleeding risk among various patient populations receiving a direct oral anticoagulant
2. Review management strategies for reversal of the anticoagulant effect of direct oral anticoagulants
3. Describe drugs in the pipeline for management of bleeding associated with direct oral anticoagulant use

Self-Assessment 4

A 62-year-old female on apixaban 2.5 mg PO BID for VTE prophylaxis after a total hip arthroplasty presents to the ED with mild hematuria. She is hemodynamically stable. When asked, she states she last took her apixaban yesterday morning, and missed her evening dose due to not feeling well.

What are options for managing her bleeding episode?

A. Hemodialysis to remove the apixaban
B. Oral activated charcoal to remove the apixaban
C. Concentrated factors (PCC, aPCC, rFVIIa) to reverse apixaban
D. Supportive care and investigate for source of the bleed
E. Unsure

What Parameters Guide the use of a Reversal Agent in the Acutely Bleeding Patient?

- Predictable reversibility
- Need to acutely reverse anticoagulant effect
  - emergency surgery
- Renal function
- Magnitude/risk of rebound anticoagulation
- Cost
- FDA indication considerations

Miyares M et al. Am J Health-Syst Pharm 2012l69(17):1473-84.

Reversal Strategies

	Strategy	Mechanism
Non-Specific	Activated charcoal	Decontamination
	Hemodialysis	Accelerated elimination (dabigatran only)
	FFP	Coagulation factors / proteins
	PCC PCC3 (Bebulin®/Profilnine®) PCC4 (KCentra®)	Replacement of coagulation factors FII, FIX, FX, Heparin* FII, FVII, FIX, FX, Proteins C&S, AT, Heparin
	rVIIa (Novo Seven®)	aFVII
	aPCC (Feiba® NF)	Activated coagulation factors FII, aFVII, FIX, FX, Protein C
Specific	Andexanet	Recombinant inactive factor-Xa
	Idarucizumab	Monoclonal antibody
	Ciraparantag (Aripazine;PER977)	Small synthetic molecule

*Bebulin only

Quality of Evidence

In vitro studies	Animal studies	Healthy volunteers
May not simulate in vivo biology	Animals may differ from humans	Healthy volunteers may differ from patients
Laboratory endpoints may not predict clinical outcomes	Artificial injury models may differ from clinical bleeding	Laboratory endpoints may not predict clinical outcomes

Clotting Factors for DOAC Reversal

- **Clinical outcomes data** on the efficacy of PCC, aPCC and rFVIIa for the reversal of DOACs are lacking
- Available evidence is limited (healthy human volunteers, animal models, in vitro studies) with conflicting results
- These agents may be considered in addition to maximum supportive measures in patients with severe/life-threatening bleeding
- The net clinical benefit should be considered in light of their prothrombotic potential (~ 1.4% for PCC; up to 10% with rFVIIa)

Siegal DM et al. Drug Discov Today. 2014;19(9):1465-70.

Published Ex Vivo Studies of Non-Specific Agents

Reversal strategy	Dabigatran-treated plasma [volunteer or patient]	Factor Xa inhibitor-treated plasma [volunteer or patient]
PCC	Corrected some TG indices[1] Corrected PT, aPTT, TT and some TG indices[2] No correction of Hemoclot assay[2]	R: Corrected PT[2] Variably corrected TG indices[1,2] No correction of anti-Xa activity[2] A: Partial effect [4-PCC][6]
aPCC	Corrected some TG indices[1] Corrected PT, aPTT, and some TG indices[2,3] No correction of Hemoclot assay[2]	R: Corrected PT[2] Corrected TG indices[1,2] No correction of anti-Xa activity[2] A: Normalized fibrin network, corrected latency and quantitative parameters (aPCC>4-PCC/rVIIa)[6] E: Partial reversal of PT, aPTT, anti-FXa[7]
rVIIa	Corrected some TG indices[1] No correction of PT, aPTT, TG indices[4,5] No correction of Hemoclot assay[4,5]	R: Corrected PT[2] Variably corrected TG indices[1] No correction of anti-Xa activity[2] A: Partial effect[6] E: Partial reversal of PT, aPTT, anti-FXa[7]

A, Apixaban; aPTT, activated partial thromboplastin time; aPCC, activated prothrombin complex concentrate; E, Edoxaban; R, Rivaroxaban; PCC, prothrombin complex concentrate; PT, prothrombin time; rVIIa, recombinant activated factor VII; TG, thrombin generation; TT, thrombin time;

1.Marlu R, et al. Thromb Haemost 2012;108(22):217-24; 2.Herrmann R, et al. Thromb Haemost 2014;111(5):989-95; 3.Khoo TL, et al. Int J Lab Hematol 2013;35(2):222–224; 4.Providencia R, et al. Thromb Res 2014;134(6):1253–64; 5.Larsen TB, et al. J Am Coll Cardiol 2013;61(22):2264–2273; 6. Martin AC, et al. J Thromb Haemost 2015;13(9):426-36; 7. Halim AB, et al. Thromb Res 2014;134:909-913.

Published Human Studies of Non-Specific Agents

Reversal Strategy	Dabigatran-treated Healthy volunteers	Factor Xa inhibitor-treated Healthy volunteers
PCC	No correction of aPTT, ECT, TT[1]	R: Corrected PT[1] Corrected PT (4-PCC > 3-PCC)[2] Corrected some TG indices (3-PCC>4-PCC)[2] No effect on aPTT, anti-Xa activity[2] E: Reversal of prolonged bleeding duration and bleeding volume after punch biopsy (4-PCC 50IU/kg) dose[3] A: Corrected PT, partially restored ETP (4-PCC 37.5/25IU/kg)[4]
aPCC	N/A	N/A
rVIIa	N/A	N/A

aPTT: activated partial thromboplastin time; aPCC, activated prothrombin complex concentrate; E, edoxaban; ECT, ecarin clotting time; ETP, endogenous thrombin potential; R, Rivaroxaban; PCC, prothrombin complex concentrate; PT, prothrombin time; rVIIa, recombinant activated factor VII; TG, thrombin generation ; TT, thrombin time;

1. Eerenberg ES, et al. Circulation 2011;124(14):1573–1579; 2. Levi M, et al. J Thromb Haemost 2014;12(9):1428–1436; 3. Zahir H, et al. Circulation 2015;131(1):82–90; 4. Cheung YW, et al. J Thromb Haemost 2015;Aug 13; epub ahead of print

Reversal Considerations for DOACs

- Supportive care
- Discontinuation of drug

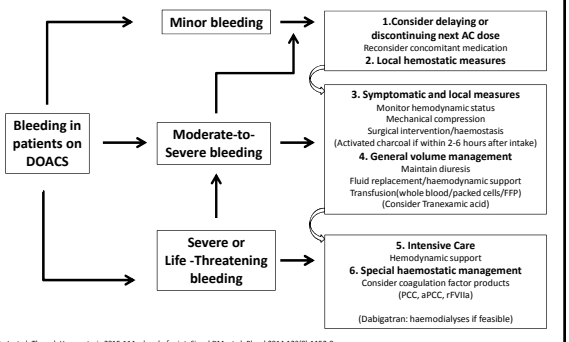
Likely sufficient for many patients

	Apixaban	Edoxaban	Dabigatran	Rivaroxaban
Oral activated charcoal	Yes	Unclear	Yes	Yes
Hemodialysis	No	No	Yes	No
FFP	No	No	No	No
Activated factor VII	Unclear	Unclear	Unclear	Unclear
3-factor PCC	Unclear	Unclear	Unclear	Unclear
4-factor PCC	Possible	Possible	Possible	Possible

Clotting Factors: Real-World Considerations

- No agents are currently approved to reverse the anticoagulant effects of DOACs in cases of active bleeding
- Efficacy data for reversal of F-Xa inhibitors with PCCs in this setting are limited
- The need to be able to quickly reverse the anticoagulant effect of DOACs is an ongoing concern
- Until a specific reversal agent becomes available for clinical use, hemostatic resuscitation remains the mainstay of treatment in the event of hemorrhagic complications

Management of DOAC Associated Bleeding



Weitz J, et al. Thromb Haemostasis 2015;114; ahead of print; Siegal DM, et al. Blood 2014;123(8):1152-8.

Reversal Agent	Dose(s) for Reversal of Specific Anticoagulant		
	Warfarin	**Dabigatran**	**F-Xa Inhibitors**
PCC3	25-50 units/kg	…	50 units/kg
PCC4	25-50 units/kg	25-50 units/kg	25-50 units/kg
rFVIIa	17.7-53.4 µg/kg	20-120 µg/kg	20-120 µg/kg
aPCC		Up to 25 units/kg initially with subsequent doses based on response;	Up to 25 units/kg initially; no data available in patients with active bleeding;
Building of PCC4	PCC3 50 units/kg + rFVIIa 1mg; if rFVIIa not available, addition of small dose FFP (1-2 units) could be considered	No data available; possibly extrapolate doses from warfarin reversal	No data available; possibly extrapolate doses from warfarin reversal

Nutescu EA, et al. Am J Health Syst Pharm. 2013;70(21):1914-29

Objectives

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3. Describe drugs in the pipeline for management of bleeding associated with direct oral anticoagulant use

Self-Assessment 5

A 56-year-old female on dabigatran 150mg mg PO BID for SPAF presents to the ED with major head trauma and needs emergent surgery. She took her last dabigatran dose 2 hours ago.

Which specific antidote is a good option to rapidly reverse the anticoagulant effect of dabigatran

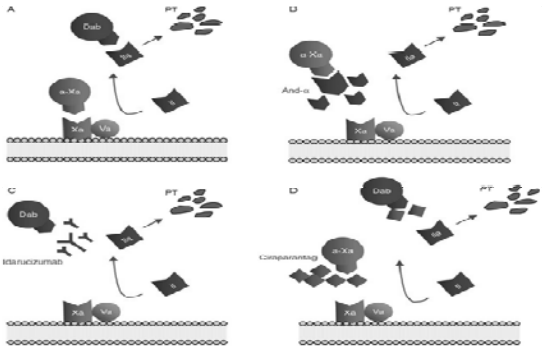
A. Andexanet alfa
B. Ciraparantag
C. Idarucizumab
D. A and B
E. B and C

Specific Reversal Agents in Development for DOACs

Agent	Target	Structure	Mechanism
Idarucizumab Boehringer Ingelheim	Dabigatran	Humanized antibody fragment	Non-competitive binding to Dabigatran with 350 times greater than thrombin
Andexanet alfa Portola	FXa Inhibitors	Recombinant human FXa analogue, catalytically inactive	Binds competitively to direct FXa inhibitors
Ciraparantag Perosphere	Universal Dabigatran, FXa inhibitors, heparins, fondaparinux	Small synthetic molecule	Binds through non covalent hydrogen bonding and charge–charge interactions

Crowther M, et al. Blood 2013;122:A3636; Crowther M, et al. J Thromb Haemost 2013;11:AS20.1; Crowther M, et al. J Thromb Haemost 2013;12:ACOA01; Crowther M, et al. Circulation 2014;130:A2116; Gold MA, et al. J Am Coll Cardiol 2015;65:A23; Glund S, et al. Circulation 2013;128:A17765; Glund S, et al. Blood 2014;124:344

Specific Reversal Agents: MOA



Andres Enriquez et al. Europace 2015;europace.euv030 (with permission)

Specific Reversal Agents: Animal and *In vitro* Studies

Agent	Animal Models	*In vitro* Studies
Idarucizumab	Reduction in blood loss and mortality in a porcine liver trauma model	Reversal of prolonged clotting time induced by Dabigatran
Andexanet alfa	Reduced blood loss induced by Rivaroxaban in mouse (tail transection) and rabbit (liver laceration) models	Complete and dose-dependent reversal of Apixaban and Rivaroxaban in human plasma
Ciraparantag	Reversed anticoagulation/decreased bleeding in a rat-tail transection model with all DOACs	Complete reversal of anti-Xa activity of Apixaban, Edoxban and Rivaroxaban

Andres Enriquez et al. Europace 2015;europace.euv030

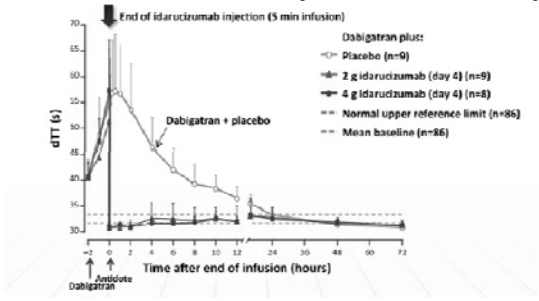
Specific Reversal Agents: Clinical Trials

Treatment	Study	Status	Population	N
Idarucizumab	**RE-VERSE-AD** [Dabigatran]	Phase III Ongoing *[prelim data NEJM2015]*	Life-threatening bleeding[a] Emergency surgery/ invasive procedure[b]	300* 90**
Andexanet alfa	**ANNEXA-A** [Apixaban]	Phase III-Part 1&2 completed	Healthy volunteers	33
	ANNEXA-R [Rivaroxaban]	Phase III-Part1 completed/Part2 ongoing	Healthy volunteers	41
	ANNEXA-E [Edoxaban]	Phase II ongoing/ Phase III planned		
Ciraparantag	**[Edoxaban]**	Phase I complete Phase II ongoing	Healthy volunteers	80

* Total estimated number of enrollment.; ** number of cases included in interim analysis.; a, GroupA.; b, Group B;

Crowther M. American Heart Association Scientific Sessions; Nov. 15-19, 2014; Crowther M, et al. ISTH 2015;13(Suppl 2): LB004.
Gold AM, et al. *J Am Coll Cardiol*. 2015;doi:10.1016/S0735-1097(15)60023-7, Pollack et al. N Engl J Med 2015;373:511-20; Ansell JE, et al. N Engl J Med 2014; 371:2141-2142.

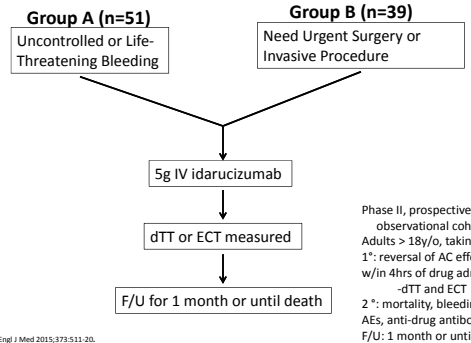
Idarucizumab: Healthy Volunteer Study



Glund et al. AHA 2013

Immediate, complete and sustained reversal of dabigatran

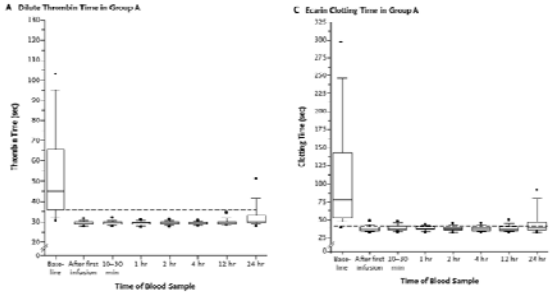
Idarucizumab: RE-VERSE-AD Study Design



Phase II, prospective, observational cohort
Adults > 18y/o, taking Dabi
1°: reversal of AC effect w/in 4hrs of drug admin -dTT and ECT
2 °: mortality, bleeding status, AEs, anti-drug antibodies
F/U: 1 month or until death

Pollack et al. N Engl J Med 2015;373:511-20.

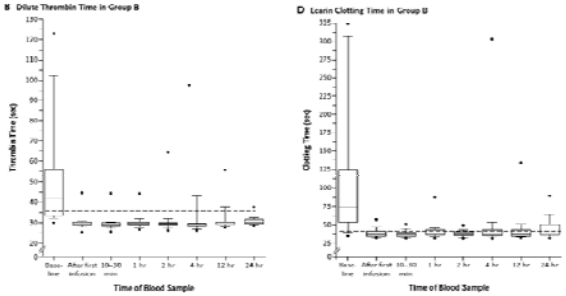
Idarucizumab: REVERSE-AD Results Group A



- median maximum percentage reversal was 100%
- 98% had normalized dTT; 89% had normalized ECT; effect w/in minutes
- no apparent toxic effects or rebound hypercoagulable state

Pollack et al. N Engl J Med 2015;373:511-20.

Idarucizumab: REVERSE-AD Results Group B



- median maximum percentage reversal was 100%; NL hemostasis in 92% who had procedure
- 93% had normalized dTT; 88% had normalized ECT; effect w/in minutes
- no apparent toxic effects or rebound hypercoagulable state

Pollack et al. N Engl J Med 2015;373:511-20.

Andexanet alfa: ANNEXA-A Part 1

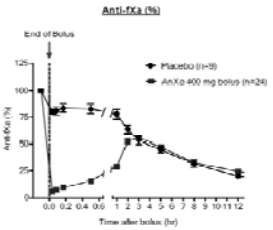
Healthy Volunteers (n=33)

Apixaban 5mg BID x 4d

Randomized

Andexanet alfa 400mg IV bolus (n=24)

Placebo (n=9)



- Rapid normalization of anti-Xa activity and thrombin levels with peak effect few minutes after bolus
- All treated subjects achieved ≥90% reversal; effect lasted 1-2 hrs

Crowther M. Circulation 2014;130:2105-26.

Andexanet alfa: ANNEXA-A Part2

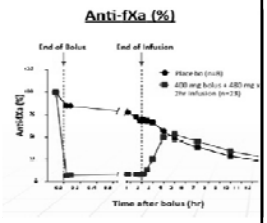
Healthy Volunteers (n=31)

Apixaban 5mg BID x 4d

Randomized

Andexanet alfa 400mg IV bolus + infusion 4mg/min x 120min (n=23)

Placebo (n=8)



- Rapid reversal of AC effect, sustained for duration of infusion
- Following bolus, anti-Xa activity reversed by 93.5% (p<0.001)
- After 2h infusion, anti-Xa activity remained reversed by 92.7% (p<0.001)

Crowther M et al. ISTH 2015;13(Suppl 2): LB004

Andexanet alfa: ANNEXA-R

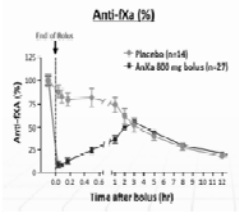
Healthy Volunteers (n=41)

Rivaroxaban 20mg od x 4d

Randomized

Andexanet alfa 800mg IV bolus (n=27)

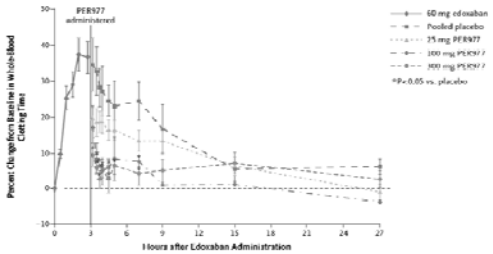
Placebo (n=14)



- 26 of 27 patients had a 90 percent or greater reduction in anti-Xa activity (p<0.001)
- Phase 2 ongoing: infusion 8mg/min x 120min

Gold AM, et al. *J Am Coll Cardiol*. 2015;doi:10.1016/S0735-1097(15)60023-7.

Ciraparantag: Edoxaban (Part1)



- Double blind, placebo-controlled; N=80 healthy subjects;
- Single oral 60-mg dose of edoxaban, followed 3 hours later by single IV dose of 25 mg, 100 mg, or 300 mg of Ciraparantag (PER977)or placebo
- Hemostasis restored w/in 10-30 min after 100-300mg Ciraparantag admin/maintained 24hrs
- No evidence of procoagulant activity; AE: mild/transient (flushing, dysgeusia)

Ansell JE, et al. N Engl J Med 2014; 371:2141-2142

Summary

- DOACs are associated with reduced rates of major, fatal and intracranial bleeding compared to warfarin
- Maximum supportive measures are the mainstay of managing bleeding
- Additional studies are needed to assess the safety and efficacy of non-specific agents
- Specific antidotes are on the horizon

"Nonprescription Drug Interactions with Prescription Drugs"
Illinois Council of Health System Pharmacists Conference
Drury Lane Conference Center
Oakbrook Terrace
September 12, 2015

Nicholas G. Popovich, Ph.D., R. Ph.*
Professor and Associate Dean for Professional Development
University of Illinois at Chicago
College of Pharmacy

Session Objectives:

After participating in the session entitled, "Nonprescription Drug Interactions with Prescription Drugs," the pharmacy technician will be able to:

1. Define nonprescription drugs.
2. Describe the various ways nonprescription drugs interact with prescription drugs.
3. Provide typical examples of nonprescription drugs which interact with prescription drugs.
4. Provide typical prescription drugs which interact with nonprescription drugs.
5. Name an example of a nonprescription drug-prescription drug interaction for each way nonprescription drugs interact with prescription drugs

Format/Overview of this session:

Page 2 is for your convenience and note taking. It allows you to jot down some notes and any questions you have to clarify (a) point(s) you did not understand.

Pages 3-7 of this handout contain tables to illustrate the various ways nonprescription drugs can interact with prescription drugs and diagnostic tests.

Page 8 is for your personal assessment of the session.

1. What are the "take away" points which you can employ in my practice after this session?
2. If there was something in this presentation which "surprised me," it was.....

Page 9 demonstrates a glossary for your understanding and Page 10 provides 2 figures to clarify important points which will be made during the presentation.

Page 11 allows you to suggest how to improve future presentations of this topic.

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*The presenter is grateful to Ms. Clara Gary, Certified Pharmacy Technician II, CPhT, Ambulatory Pharmacy Services, PCC Pharmacy, University of Illinois at Chicago Hospital, for her guidance in creating this presentation.

"Nonprescription Drug Interactions with Prescription Drugs"
Nicholas G. Popovich, Ph.D., R. Ph.

Notes:

Questions to ask:

Table I. Common mechanisms for drug-drug interactions with representative examples (R_X and OTC)

A. Drugs which act additively or synergistically when administered with other drugs

Drug (Category)	Interactant	Effect
Aspirin	Coumarin anticoagulants	Increased International Normalized Ratio [INR]. Oral warfarin and oral ASA increase the risk of side effects and cause bleeding or bruising. The need for simultaneous use of low-dose aspirin and warfarin are common for patients with cardiovascular disease; your doctor will monitor you closely.
	Nonsteroidal anti-inflammatory drugs (NSAIDs); e.g. Motrin, Naprosyn	Increased risk of gastroduodenal ulcers and bleeding; ASA should be taken at least 30 minutes before or 8 hours after ibuprofen;
Bulk Laxative (e.g., Psyllium Powder in Metamucil, Fiberall)	Anticholinergics (e.g. Pro-Banthine), Tricyclic Antidepressents [syn TCADs] (e.g., Elavil), and Phenothiazines (e.g., Thorazine)	Possible intestinal obstruction
Bismuth Subsalicylate (in Pepto-Bismol, KaoPectate)	Aspirin	Salicylate Toxicity (e.g., ringing, buzzing, or fullness in ears) if taken in high doses
Diphenhydramine HBr; Doxylamine succinate; in OTC Sleep Aids	Alcohol (as a beverage or a vehicle in medicinal products)	Additive CNS depression, e.g., sleepiness.
Fish Oils	Coumadin, e.g., Warfarin Sodium	Increased anticoagulant effect, i.e., ↑INR
Pseudoephedrine HCl in Cold-Decongestant Products, (e.g., Sudafed)	TCADs, Methyldopa	Increased blood pressure
Potassium chloride (salt substitutes, e.g. No-Salt)	Potassium Supplements (e.g., K-Lyte, Slow-K) Potassium-sparing diuretics (e.g. Aldactone, Midamor)	Possible hyperkalemia, i.e., increased serum potassium

B. Drugs which enhance or diminish the absorption of another drug from the GI tract.

Drug (category)	Interactant	Effect
Antacids	Anticoagulants, antidyskinetics, ketoconazole, antiretrovirals (e.g. atazanavir, indinavir)	Decreased absorption of interactant
Antacids, sucralfate, or large doses of zinc	Antibiotics (tetracyclines, oral quinolones [ciprofloxacin, norfloxacin, and ofloxacin], azithromycin)	Decreased absorption of interactant
Antacids or H_2 receptor antagonists (e.g., famotidine)	Ketoconazole, itraconazole, indinavir, iron salts	An acidic medium required for adequate dissolution and absorption. Thus, decreased absorption of the interactant.
Bismuth Subsalicylate (in Pepto-Bismol)	Tetracycline HCl and other tetracyclines	Decreased tetracycline absorption
Bulk Laxatives	Antibiotics, digoxin, salicylates	Decreased absorption of the interactants
Cholestryamine or Colestipol	Multiple interactants; check prescribing information	Decreased absorption of the interactants, administer 1 to 4 hours before or 4 to 6 hours after the drug
Iron Supplements (e.g., Feosol, Mol-Iron, Fergon)	Tetracycline antibiotics; oral quinolone antibiotics	Decreased antibiotic absorption
	Antacids, bulk laxatives	Decreased iron absorption
Magnesium-Aluminum Hydroxide Gel (e.g., Maalox, Kolantyl, Mylanta)	Tetracyclines, digoxin, phenytoin	Decreased absorption of interactants
Mineral Oil	Fat-soluble vitamins	Chronic mineral oil use can decrease the absorption of fat-soluble vitamins

C. Drugs which alter the distribution (e.g. plasma protein binding) of other drugs.

Drug (category)	Interactant	Effect
Aspirin (e.g. Bayer, Anacin)	Coumadin (Sodium Warfarin), Valproic Acid	Displacement of drug plasma binding sites resulting in an increased pharmacological response
Salicylates	Carbonic Anhydrase Inhibitors (e.g., Acetazolamide, methazolamide)	Displacement of CAIs from plasma protein binding sites resulting in lethargy, confusion, fatigue, anorexia, urinary incontinence, and hyperchloremic metabolic acidosis
Ibuprofen	Phenytoin	Displacement from protein-binding sites. Monitor free phenytoin levels; Adjust dosage or consider naproxen

D. Drugs which alter the renal excretion or effectiveness of another drug.

Drug (category)	Interactant	Effect
Ammonium Chloride (menstrual products, e.g., Aqua-Ban)	Weakly basic drugs dependent upon urinary excretion (e.g., TCAD's Quinidine)	Urinary acidification would enhance excretion of these drugs
Aspirin	Methotrexate	Competes for renal tubular secretion decreasing elimination of interactant
Sodium Bicarbonate (Antacid products, e.g., Alka Seltzer)	Weakly basic drugs dependent upon urinary excretion (e.g., amphetamine, quinidine)	Urinary alkalinization would diminish excretion of these interactants, possibly leading to toxicity
	Methenamine mandelate	Urinary alkalinization prevents conversion to methenamine to the active formaldehyde in urine
	Nitrofurantoin	Urinary alkalinization decreases the bactericidal effects of nitrofurantoin
	Pseudoephedrine HCl	Urinary alkalinization decreased renal excretion of psuedoephedrine
	Lithium	Sodium intake enhances lithium excretion
NSAIDs (e.g., Motrin)	Lithium	Serum lithium levels increase (N/V, diarrhea, anorexia, coarse tremor, slurred speech, confusion); Monitor for toxicity
	Methotrexate	Serum methotrexate levels increase (fever, mucosal ulcerations, severe nausea, diarrhea, gi bleeding); Monitor for toxicity

E. Drugs which decrease or increase the biotransformation of another drug resulting in increased toxicity or no therapeutic effect.

Drug (category)	Interactant	Effect
Phenylephrine HCl, Pseudoephedrine HCl (Decongestant products)	Monoamine Oxidase (MAO) Inhibitors, St. John's Wort	MAO Inhibitors decrease biotransformation causing possible hypertensive crisis
Cimetidine	Warfarin, Phenytoin, Propranolol, Theophylline, Diazepam	Cimetidine reduces hepatic metabolism of these drugs, thereby delaying elimination and increasing serum levels
Acetaminophen	Erythromycin, Azithromycin	Concurrent use of other hepatotoxic medications with erythromycin and azithromycin may increase the potential for hepatotoxicity
St John's Wort	Warfarin	The herbal may induce the Cytocrome P450 enzymes responsible for warfarin metabolism resulting in an altered International Normalized ratio (INR) or through an unknown mechanism decreases the absorption of the drug.
	SSRI	Concomitant ingestion may result in additive central serotonin excess (i.e., serotonin syndrome). Symptoms include grogginess, N/V, weakness, agitation, confusion, hypothermia, diaphoresis, hyperreflexia, and muscle rigidity
	Protease Inhibitor	The herbal caused a 28% decrease in the peak serum concentrations and AUC of indinavir (i.e., Crixivan) when administered concomitantly
Ginkgo biloba, feverfew, pure licorice, ginger	Warfarin (Sodium Warfarin), Clopidogrel (Plavix)	Should be used cautiously in patients on anticoagulant therapy, with known coagulopathy, or prior to some surgical or dental procedures

F. Drugs which interfere with or affect the desired effect of another drug/diagnostic test.

Drug (category)	Interactant	Effect
Alcohol (Vehicle e.g., Nyquil Nighttime Cold Liquid Medicine); 10% V/V. Mouthwashes, e.g., 20% V/V	Metronidazole, Chlorpropamide, Disulfiram (Antabuse)	Antabuse Effect, i.e., Elements of this reaction may include any of the following: flushing, throbbing in the head and neck, headache, nausea, vomiting, sweating, thirst, chest pain, palpitations, dyspnea, hyperventilation, tachycardia, confusion, arrhythmias, and convulsions. Avoid mouthwashes, antiperspirants, colognes, etc.
Ascorbic Acid	Fecal occult blood tests, urinary blood and Glucose Tests	False-Negative test results for blood; False-Negative for glucose in urine
Aspirin	Probenecid, Sulfinpyrazone	Inhibition of the uricosuric effect of the probenecid or sulfinpyrazone
Ephedrine SO_4	Inhalation Anesthetics, MAO Inhibitors, Sympathomimetics	May enhance the arrhythmogenic (capable of inducing a cardiac arrhythmias)/hypertensive effects of interactants
Milk of Mangesia	Aspirin, bisacodyl (Dulcolax)	Premature release of these drugs from their enteric-coated tablet in stomach could result in stomach distress for the patient.
	Methenamine Mandelate, Calcium Polystyrene Sulfonate	May increase adverse drug events of the interactant. Use in conjunction with magnesium containing laxatives may increase risk of metabolic acidosis
Pyridoxine (Vitamin B_6)	Levodopa	Levadopa's antiparkinsonian effects are reversed by as little as 5mg of oral pyridoxine
Salicylates, Iron Products, Ibuprofen	Fecal Occult Blood Tests	False-Positive Result

"Nonprescription Drug Interactions with Prescription Drugs"
Nicholas G. Popovich, Ph.D., R. Ph.

1. What are the "take away" points which I can employ in my practice after this session?

2. If there was something in this presentation which "surprised me," it was.....

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Glossary

Page 3 OTC Drug, i.e., Fish Oils, can cause an increased anticoagulant effect. An anticoagulant effect is defined as acting to prevent or to retard coagulation of the blood.

Page 5 OTC Drug Class of Salicylates (e.g., aspirin, magnesium salicylate) can displace carbonic anhydrase inhibitors, such as acetazolamide, from plasma protein sites resulting in a number of adverse effects including hyperchloremic metabolic acidosis which is defined as a decrease in plasma bicarbonate concentration and an increase in the plasma chloride concentration. Note Figure 5.7 (Minimum Toxic Concentration).

Page #6 OTC Drug, i.e., phenylephrine, can cause a hypertensive crisis with some drugs. A hypertensive crisis is defined as a severe increase in blood pressure which can lead in some instances to a stroke

Page #6 OTC Drug, i.e., acetaminophen, which can cause liver damage, i.e., hepatotoxicity, when overused and/or if used with another drug which can cause liver damage, e.g., azithromycin.

Page #6 OTC Dietary Supplement, e.g., St. John's Wort, with protease inhibitors can increase serum concentrations and the area under the curve (AUC). Note Figure 5.4 and Figure 5.7. (Page 10)

Page #6 OTC Dietary Supplement, e.g., *Ginkgo biloba*, can cause coagulopathy. Coagulopathy (syn. clotting disorder, bleeding disorder) is a condition in which the blood's ability to clot (or coagulate) is impaired. This condition can cause prolonged or excessive bleeding which may occur spontaneously or following an injury or medical and/or dental procedures.

Page #7 A liquid product vehicle, i.e., Alcohol, can cause an antabuse effect when used concurrently with some medications, e.g., metronidazole. The Antabuse effect blocks the ability of the body to metabolize alcohol and can cause a bad reaction, e.g., flushing, fast heartbeats, nausea, thirst, chest pain, vertigo, and low blood pressure.

Page #7 OTC Drug, i.e., Aspirin, can inhibit the effectiveness of probenecid or sufinpyrazone to eliminate from the body uric acid. Uricosurics are often used in the treatment of gout, a disease in which uric acid crystals form deposits in the joints.

"Nonprescription Drug Interactions with Prescription Drugs"
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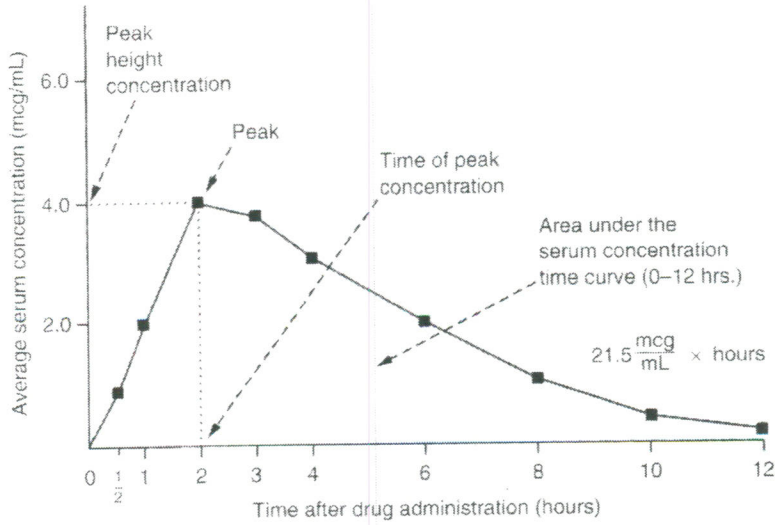


FIGURE 5.4 Serum concentration–time curve showing peak height concentration, time of peak concentration, and AUC. (Courtesy of D. J. Chodos and A. R. Disanto, Upjohn.)

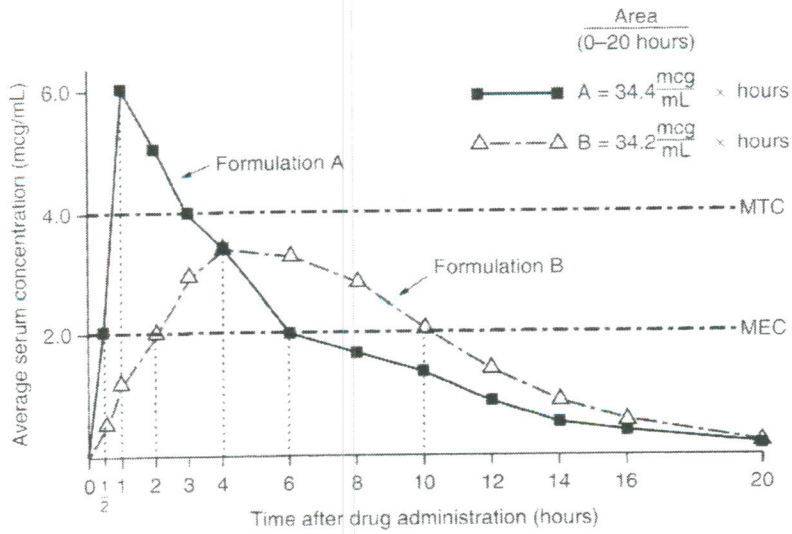


FIGURE 5.7 Serum concentration–time curve showing peak height concentrations, peak height times, times to reach MEC and areas under the curves for equal amounts of drug from two different formulations following oral administration. MEC, minimum effective concentration; MTC, minimum toxic concentration. (Courtesy of D. J. Chodos and A. R. Disanto, Upjohn.)

Allen LV, Popovich NG, Ansel HC. *Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems*, 9th edition, 2011, Lippincott Williams and Wilkins, Philadelphia PA, p 153 and 156.

"Nonprescription Drug Interactions with Prescription Drugs"
Nicholas G. Popovich, Ph.D., R. Ph.

Please answer the following question, remove this sheet from your handout, and turn this sheet into the session facilitator. Thank you very much.

My suggestion(s) to improve future presentations of this topic would include:

A. Drugs which act additively or synergistically when administered with other drugs

Drug (Category)	**Interactant**	**Effect**
Aspirin	Coumarin anticoagulants	Increased prothrombin time; bleeding
	Nonsteroidal anti-inflammatory drugs (NSAIDs); e.g. Motrin, Naprosyn	Increased potential lfor gastric upset; possible diminished activity for the NSAIDs
Bulk Laxative (e.g. Metamucil, Fiberall)	Anticholinergics (e.g. Pro-Banthine), Trricyclic Antidepressents (e.g. Elavil), and Phenothiazines (e.g. Thorazine)	Possible intestinal obstruction
Bismuth Subsalicylate (in Pepto-Bismol, KaoPectate)	Aspirin	Salicylate Toxicity (e.g. ringing, buzzing, or fullness in ears) if taken in high doses
Diphenhydramine (Sleep-Aid Products, e.g. Compoz, Nytol with DPH)	Alcohol (as a beverage or a vehicle in medicinal products)	Additive CNS depression
Fish Oils	Coumadin	Increased anticoagulant effect
Pseudoephedrine HCl in Cold-Decongestant Products, (e.g. Sudafed)	Theophylline	Monitor for increased CNS stimulation, e.g. restlessness, insomnia, irritablity
Potassium chloride (salt	Potassium Supplements (e.g. K-Lyte, Slow-K)	Possible hyperkalemia

substitutes, e.g. No-Salt)	Potassium-sparing diuretics (e.g. Aldactone, Midamor)	Possible hyperkalemia

B. Drugs which enhance or diminish the absorption of another drug from the GI tract.

Drug (category)	**Interactant**	**Effect**
Antacids	Anticoagulants, antidyskinetics, ketoconazole	Decreased absorption of interactant
Antacids, sucralfate, or large doses of zinc	Antibiotics (tetracyclines, oral quinolones [ciprofloxacin, norfloxacin, and ofloxacin])	Decreased absorption of interactant
Antacids or H2 receptor antagonist (e.g. cimetidine)	Ketoconazole	An acidic medium required for adequate ketoconazole dissolution and absorption. Thus, decreased absorption of ketoconazole
Bismuth Subsalicylate (in Pepto-Bismol)	Tetracycline HCl and other tetracyclines	Decreased tetracycline absorption
Bulk Laxatives	Antibiotics, digoxin, salicylates	Decreased absorption of the interactants
Cholestryamine or Colestipol	Multiple interactants; check prescribing information	Decreased absorption of the interactants, administer 1 to 4 hours before or 4 to 6 hours after the drug
Iron Supplements (e.g Feosol, Mol-Iron, Fergon)	Tetracycline antibiotics; oral quinolone antibiotics	Decreased antibiotic absorption
	Antacids, bulk laxatives	Decreased iron absorption

Magnesium-Aluminum Hydroxide Gel (e.g. Maalox, Kolantyl, Mylanta)	Tetracyclines, digoxin, phenytoin	decreased absorption of interactants
Mineral Oil	Fat-soluble vitamins	chronic mineral oil use can decrease the absorption of fat-soluble vitamins
C. Drugs which alter the distribution (e.g. plasma protein binding) of other drugs.		
Drug (category)	**Interactant**	**Effect**
Aspirin (e.g. Bayer, Anacin)	Coumadin, Diabinese, Valproic Acid	Displacement of drug plasma binding sites resultingin an increasedpharmacological response
Salicylates	Carbonic Anhydrase Inhibitors (e.g. Acetazolamide, methazolamide)	Displacement of CAIs from plasma protein binding sites resulting in lethargy, confusion, fatigue, anorexia, urinary incontinence, and hyperchloremic metabolic acidosis
D. Drugs which alter the renal excretion or effectiveness of another drug.		
Drug (category)	**Interactant**	**Effect**
Ammonium Chloride (menstrual products, e.g. Aqua-Ban)	Weakly basic drugs dependent upon urinary excretion (e.g. TCAD's Quinidine)	Urinary acidification would enhance excretion of these drugs
Aspirin (e.g Bayer, Anacin)	Methotrexate	Competes for renal tubular secretion decreasing elimination of interactant

Sodium Bicarbonate (Antacid products, e.g. Alka Seltzer)	Weakly basic drugs dependent upon urinary excretion (e.g amphetamine, quinidine)	urinary alkalinization would diminish excretion of these interactants, possibly leading to toxicity
	Methanamine mandelate	urinary alkalinization prevents conversion to methenamine to the active formaldehyde in urine
	Nitrofurantoin	Urinary alkalinization decreases the bactericidal effects of nitrofurantoin
	Lithium	sodium intake enhances lithium excretion
NSAIDs (e.g. Motrin)	Lithium	Serum lithium levels increase (N/V, diarrhea, anorexia, coarse tremor, slurred speech, confusion)
	Methotrexate	Serum Methotrexate levels increase (fever, mucosal ulcerations, severe nausea, diarrhea, gi bleeding)
E. Drugs which decrease or increase the biotransformation of another drug resulting in increased toxicity or no therapeutic e		
Drug (category)	**Interactant**	**Effect**
Phenylephrine, Pseudoephedrine HCL (Decongestant products)	Monoamine Oxidase (MAO) Inhibitors, St. John's Wort	MAO Inhibitors Decreae biotransformation with possible hypertensive crisis
Cimetidine	Warfarin, Phenytoin, Propranolol, Theophylline, Diazepam	Cimetidine reduces hepatic metabolism of these drugs, thereby delaying elimination and increasing serum levels
Acetaminophen	Erythromycin	Concurrent use of other hepatotoxic medications with erythromycin may increase the potential for hepatotoxicity

St John's Wort	Warfarin, SSRI, Protease Inhibitors	The herbal may induce the Cytocrome P450 enzymes responsible for warfarin metabolism resulting in an altered International Normalized ratio (INR) or through an unknown mechanism ecrease the absorption of the drug. Concomitant ingestion may result in additive central seratonin excess (i.e., serotonin syndrome). Symptoms inclue grogginess, N&V, weakness, agitation, confusion, hypothermia, diaphoresis, hyperreflexia, and muscle rigidity - The herbal caused a 28% decrease in the peak serum concentrations and AUC of indinavir (i.e., Crixivan) when administered concomitantly

F. Drugs which interfere with or affect the desired effect of another drug/diagnostic test.

Drug (category)	**Interactant**	**Effect**
Alcohol (Vehicle e.g., Nyquil Nighttime Cold Liquid Medicine)	Metronidazole, Chlorpropamide, Disulfiram	Antabuse Effect
Ascobic Acid	Fecal occult blood tests, urinary blood and Glucose Tests	False-Negative test results for blood; False-Negative for glucose in urine
Aspirin	Probenecid, Sulfinpyrazone	Inhibition of the uricosuric effect of the probenecid or sulfinpyrazone
Ephedrine SO4	Inhalation Anesthetics, MAO Inhibitors, Sympathomimetics	May enhance the arrhymogenic/hypertensive effects of interactants
Milk of Mangesia	Aspirin, Bisacodyl, Methenamine Mandelate, Calcium Polystyrene Sulfonate	Premature release of these drugs from their enteric-coated tablet in stomach coul result in stomach distress for the patient. --- Drug may increase adverse drug events of the interactant- Use in conjunction with magnesium containing laxatives may increase risk of metabolic acidosis

Pyridoxine (Vitamin B6)	Levodopa	Levadopa's antiparkinsonian effects are reversed by as little as 5mg of oral pyridoxine
Salicylates, Iron Products, Ibuprofen	Fecal Occult Blood Tests	False-Positive Result

"Nonprescription Drug Interactions with Prescription Drugs"
Illinois Council of Health System Pharmacists Conference
Drury Lane Conference Center
Oakbrook Terrace
September 12, 2015

Nicholas G. Popovich, Ph.D., R. Ph.
Professor and Associate Dean for Professional Development
University of Illinois at Chicago
College of Pharmacy

Assessment Questions

1. (Objective One) Define nonprescription drugs.

   All of the following are true about nonprescription drug products EXCEPT:

   A. Can be purchased over-the-counter at a pharmacy and/or retail outlet.
   B. These have a sufficient degree of safety for patient self care.
   C. With appropriate and clear directions can be used by the consuming public.
   D. Can be purchased without a doctor's prescription.
   E. Can be used to treat a long-term illness which can be self-diagnosed by the patient.

2. (Objective Two) Describe the various ways nonprescription drugs interact with prescription drugs.

   Intestinal obstruction can result when which of the following over-the-counter drugs is administered with a drug that slows down the gastrointestinal tract?

   A. Bismuth subsalicylate
   B. Calcium carbonate
   C. Famotidine
   D. Psyllium powder
   E. Zinc Ion

3. (Objective Three) Provide typical examples of nonprescription drugs which interact with prescription drugs.

   Antacids and H_2 receptor antagonists decrease the effectiveness of some drugs, e.g., antibiotics, digoxin, administered orally by:

   A. Displacing these drugs from plasma-protein binding sites.
   B. Causing increased metabolism of these drugs in the liver.
   C. By increasing stomach pH hinders prescription drug from dissolving.
   D. Altering the kidney excretion of these drugs.
   E. Adsorbing these drugs onto their surface.

4. (Objective Four) Provide typical prescription drugs which interact with nonprescription drugs.

   All prescription drugs have potential interactions with nonprescription drugs, but a few prescription drugs can lead to serious, life-threatening situations. An example of such a prescription drug would be:

   A. azithromycin
   B. metronidazole
   C. phenytoin
   D. propranolol
   E. sodium warfarin

5. (Objective Five) Name an example of a nonprescription drug-prescription drug interaction for each way nonprescription drugs interact with prescription drugs

   Which of the following combinations of a nonprescription drug administered with a prescription drug can cause organ damage?

   A. Acetaminophen-Azithromycin (Liver Toxicity)
   B. Ammonium chloride-Quinidine (Kidney Damage)
   C. Diphenyhydramine HBr-Alcohol (Brain Damage)
   D. Potassium chloride-Aldactone (Kidney Damage)
   E. Aspirin-Sodium Warfarin (Kidney Damage)

The Scope of Pharmacy Technician Practice

Sara Vander Ploeg, PharmD
Northwestern Memorial Hospital

The speaker has no actual or potential conflicts of interest as it relates to this presentation.

Objectives

- Discuss the scope of practice of a pharmacy technician and how this differs from a student pharmacist
- Outline the requirements for becoming a certified pharmacy technician in the state of Illinois
- Describe the Pharmacy Practice Model Initiative (PPMI)
- Explain how tech-check-tech falls within the law and expands the practice of pharmacy through PPMI

Pharmacy Technician

- Pharmacy technician is person who can assist in the practice of pharmacy under the supervision of the pharmacist
- In order to register and obtain a license
  - 16 years or older
  - "not engaged in conduct or behavior determined to be grounds for discipline"
  - Enrolled in or graduated from high school or comparable institution or received a high school equivalency certificate

225 ILCS 85- Pharmacy Practice Act

Role of a Technician

- Assisting in the practice of pharmacy, which includes:
  - Monitoring, evaluation and implementation of medication orders
  - Dispensing of medication orders
  - Drug selection and administration
  - Drug regimen review and counseling
  - Compounding and labeling of medications
- Functions of a technician:
  - Dispensing process
  - Offer to counsel
  - Receiving verbal prescription orders
  - Medication order clarification with the prescriber

225 ILCS 85- Pharmacy Practice Act

Technician Training

- Responsibility of pharmacy and pharmacist in charge to ensure the proper training of each pharmacy technician within 6 months of employment
  - Duties and responsibilities of both technician and pharmacist
  - Policies and procedures
  - Tasks required and ability to complete technical skills
  - Compounding, packaging, labeling and storage of medications
  - Record keeping that is necessary
  - Medical and pharmaceutical technology
  - Perform and apply arithmetic equations
- Keep a record of completed training

225 ILCS 85- Pharmacy Practice Act

Certification Requirements

- Starting January 1, 2010
  - Registered technicians must become certified within two years
  - Must successfully pass the Pharmacy Technician Certification Board (PTCB) exam or another technician exam approved by the board
    - Does not apply to technicians registered before January 1, 2008
- Must be at least 18 and of good moral character
- Must have completed training

225 ILCS 85- Pharmacy Practice Act

PTCB

- 2 hour exam with 90 multiple choice questions
  - 80 scored and 10 unscored
- Exam is organized into 9 knowledge domains
  - Each domain covers a number of knowledge areas
- Applications and testing fees = $130
- Passing scaled score of 1400 (range 1000-1600)

www.ptcb.org

Patient Counseling

- Communication between the pharmacist or student pharmacist and the patient about a medication or device in order to ensure proper use
  - Medication history
  - Allergies
  - Understanding of intended use of each medication
  - How to properly administer the medication
  - Side effects associated with the medication
  - Food-drug interactions
  - Importance of Adherence

225 ILCS 85- Pharmacy Practice Act

What can technicians do?

- Technicians can perform any aspect that does not require clinical interpretation
  - Medication history
  - Obtaining patient allergies and health conditions
  - Offer the receive counseling by a pharmacist or student pharmacist

225 ILCS 85- Pharmacy Practice Act

Student Pharmacist

- A registered technician who is enrolled in a school or college of pharmacy program
  - This also includes those who have graduated from a program in the last 18 months
- Excluded from the requirement of becoming certified
- May assist in all practices of pharmacy as designated by the pharmacist

225 ILCS 85- Pharmacy Practice Act

Self Assessment Question 1

Which of the follow activities does the law allow a student pharmacist to complete, but not a pharmacy technician?

A. Collection of a patient's allergies

B. Counseling on how atorvastatin works

C. Taking a medication history

D. Filling a medication order

Self Assessment Question 2

Susan became a registered pharmacy technician in May of 2013, which of the following must be true in order for her to become certified?

A. 18 years of age

B. Apply for and pass the PTCB exam

C. Enrolled in a college of pharmacy program

D. A & B

E. All of the above

Pharmacy Practice Model Initiative

- "The goal of this initiative is to significantly advance the health and well being of patients by supporting futuristic practice models that support the most effective use of pharmacists as direct patient care providers."
- Demand for high quality, safer care at a lower cost
- New practice model that is adapting with health care reform

http://www.ashpmedia.org/ppmi/rationale.html

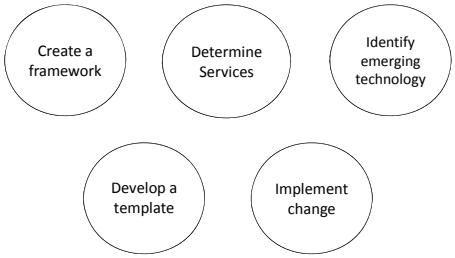
PPMI

Determination of what areas of practice need to evolve:

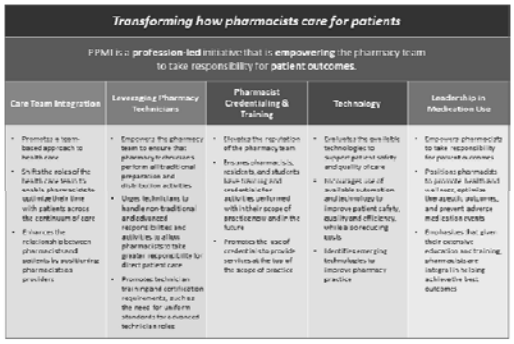
- Medication-use policies and the products being used
- Medication distribution
- Technology
- Clinical pharmacy practice
- Pharmacy technician roles
- Pharmacists' roles as organizational leaders
- Adherence to standards-based practice
- Medication-use safety quality and safety movements that are occurring across the nation

http://www.ashpmedia.org/ppmi/rationale.html

PPMI Objectives



http://www.ashpmedia.org/ppmi/rationale.html



Self Assessment Question 3

As hospitals look to implement PPMI into practice, in which of the following ways can we advance the practice of pharmacy technicians?

A. Creation of standard for training and certification

B. Utilization of technicians in all roles that do not require a pharmacist

C. Training of technicians in non-traditional or advanced roles

D. All of the above

WHAT ARE THE ADVANCEMENTS IN THE SCOPE OF TECHNICIAN PRACTICE?

Advanced Technician Roles

- Allows for pharmacists to practice at the top of their license, by allowing more time for clinical activities
- In order to do this we NEED:
  - Resources to invest in technician training and competency
  - Pharmacists who are committed to the development of technicians to succeed in these advanced roles
- Technicians should be equipped to perform any drug distribution function that does not require clinical judgment

Shane, R. Am J Health-Syst Pharm. 2011;68(19):1834-35

- Technician training standard
- Tech – Check – Tech
- Medication Histories
- Identification of patients who would benefit from pharmacist intervention
- Pharmacy Informatics

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Technician Training Standard

- There is currently no national standard by which technicians are educated, trained and certified
- Increased demands on pharmacists in patient care means increased need for well-trained technicians in many areas of practice
- American Society of Health-System Pharmacists and the American Pharmacy Associate are advocating for a single standard used nation-wide
  - Necessary for the practice of pharmacy to continue to advance
- If a national standard is created, programs can become accredited and technicians credentialing will become more uniform.

Manasse Jr HR and Menighan TE. Am J Health-Syst Pharm. 2010;67:348-49.
Manasse Jr HR and Menighan TE. Am J Health-Syst Pharm. 2011;68(10):869-870.

ASHP Standards

Administration	Program Faculty	Education/Training
Accredited when applicable by the appropriate agency Strategic plan reviewed annually Advisory Committee •Curriculum •Admission criteria •Successful completion	Director must be a pharmacist or technician with 5 years experience Instructors must have 3 yrs experience	Prepare for entry level pharmacy technician position 600 hours over 15 weeks •Didactic •Simulated •Experiential Set of goals for required knowledge and skills

Accreditation Standards for Pharmacy Technician Education and Training Programs. www.ashp.org 2013.
New ASHP Accreditation Standards for Pharmacy Technician Education and Training Programs Webinar. www.ashp.org

ASHP Standard continued

Students	Evaluation/Assessment	Graduation/Certificate
Policy stating •Financial obligations •Criminal record/background checks Minimum qualifications •Attending high school •English competency •Math competency	Assessment in each component of the program Ongoing performance evaluations Preparation for certification Ongoing faculty and program assessment	Documented graduation requirements Certificates only to students who successfully complete all components of the program

Accreditation Standards for Pharmacy Technician Education and Training Programs. www.ashp.org 2013.
New ASHP Accreditation Standards for Pharmacy Technician Education and Training Programs Webinar. www.ashp.org

9 Knowledge Areas

- Personal/Interpersonal Knowledge & skills
- Foundation Professional Knowledge & skills
- Processing & Handling of Medication Orders
- Sterile & Non-Sterile Compounding
- Procurement, Billing, Reimbursement & Inventory Management
- Patient and Medication Safety
- Technology & Informatics
- Regulatory Issues
- Quality Assurance

Accreditation Standards for Pharmacy Technician Education and Training Programs. www.ashp.org 2013.
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Tech Check Tech Programs

- Use of a specially trained technician to final check medication doses that were filled by another technician
- Training will vary by each institution, but should include topics:
  - Understand of the medication use process
  - Medication dosage forms
  - Review of look alike, sound alike medications
  - Labeling and medication safety
- Documentation of understanding (written and/or visual exam)
- Training with a pharmacist
- Validation of skill
- Annual competency

Reed et al. Am J Health-Syst Pharm. 2011;68:1820-23
Erickson AK. Pharmacy Today. 2012, Sept 1.

Validation

University of Wisconsin Hospitals and Clinics

- Ability of the technician to maintain 99.8% accuracy in checking >2500 consecutive doses
- Five separate audits occur over the course of 5 days
- The pharmacist will purposefully introduce at least 5 errors per 2500 doses
- All checked doses will be validated by the training pharmacist

Reed et al. Am J Health-Syst Pharm. 2011;68:1820-23

Ongoing validation

- Once technicians have been trained and validated, pharmacists continue to check at least 10% of the doses
  - Track accuracy rates by documentation of fill errors not detected by the technician
- At UWHC, implementation of a tech-check-tech program allowed for a daily reduction of 5 hours and 45 minutes of pharmacist time checking medication doses
- Of note: all doses being checked by a technician
  - Have already been verified by a pharmacist
  - Are subsequent doses in a regimen, the pharmacist checks all first fill medications

Reed et al. Am J Health-Syst Pharm. 2011;68:1820-23

How do you check a medication?

- Read the label
  - Medication name
    - Extended release vs. immediate release
    - 12 hour vs 24 hour sustained release
    - Tablet, chewable, oral disintegrating
  - Dose
- Check the medication label
  - Match medication name
  - Dose
- Are the correct number of tablets, size of container, etc present?
- Is the filled mediation expired?

Cooper et al. Am J Health-Syst Pharm. 2014;71:1567-74

Self Assessment Activity

1. Find a partner
2. First person, choose one of the packaged medications in front of you
3. "Fill the medication" by matching it to the appropriate label
4. Second person, you are the tech-check-tech
5. Explain to your partner how you are checking the accuracy of the fill
6. Switch roles with a new medication

- Technician training standard
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Medication Reconciliation

- Obtaining medication history from the patient
  - Getting the best possible and most up to date list of medications the patient is taking
- Challenges:
  - patient health literacy
  - knowledge of medications
  - time
- Accurate list of medication is necessary to complete medication reconciliation

Cooper et al. Am J Health-Syst Pharm. 2014;71:1567-74

Why is Med Rec important?

- There is no one healthcare professional that owns this task
  - Quality remains low
- Joint Commission has core measures for a number of disease states and compliance with these measures is linked to re-imbursement
- Proper medication reconciliation could have positive effects on reducing re-admissions

Cooper et al. Am J Health-Syst Pharm. 2014;71:1567-74

Success at Cone Health

Emergency Department

- Use of a blended model
  - Nurses for majority of histories
  - Pharmacy technicians for a double check if >10 meds
- Pharmacy technicians were given ownership of the process
- Creation of a standard form
  - Scheduled, as needed, short term and discontinued medications
- Currently have ~80 technicians who have completed the training and can conduct medication histories
- Improved compliance of physician med reconciliation at discharge

Cooper et al. Am J Health-Syst Pharm. 2014;71:1567-74

Technician Role

- Completion of a training program
  - Half day shadowing
  - 3-hour lecture
  - Half day of simulated medication histories with the pharmacist
  - 10 directly observed histories
- Trained technicians gather the medication list using
  - Structured patient interview
  - Standardized form
- Must have standardization and accountability on what meds to document

Cooper et al. Am J Health-Syst Pharm. 2014;71:1567-74

What are skills are necessary?

- Good communication skills
- Strong work ethic
- Time management
- Computer skills

Cooper et al. Am J Health-Syst Pharm. 2014;71:1567-74

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Postfracture Care

Kaiser Permanente Colorado

- As the areas in which a clinical pharmacist practices are increasing, we should be looking for ways to utilize technicians in these same areas
  - Allow for pharmacists to focus on clinical activities
- Quality of care is evaluated by the National Committee for Quality Assurance
  - Development of Healthcare Effectiveness Data and Information Set (HEDIS) for women ages 67 and older with a fracture within last 6 months
  - Patients who saw a clinical pharmacist post fracture were more likely to get a bone scan and start necessary medication

Irwin et al. Am J Health-Syst Pharm. 2014;71:2054-59

Role for Technicians

Kaiser Permanente Colorado

- Healthcare costs continue to rise, thus leaders have to be able to show increases in quality with expanded pharmacy services
- Under the supervision of a pharmacist, the technician
  - Assessed compliance with HEDIS measure and classify the patient into
    - In compliance (category 1)
    - Not in compliance, requires intervention (category 2)
    - Not in compliance, no intervention needed (category 3)
  - Reviewed and collected clinical information from the EHR
    - Completed subjective and objective information of a SOAP note

Irwin et al. Am J Health-Syst Pharm. 2014;71:2054-59

Endpoints

- Phase 1
  - Looking at accuracy of technician categorization and clinical information collected
  - Agreement with the pharmacist ~90% of the time
- Phase 2
  - Pharmacist time saved
  - Patients not requiring intervention
    - 5.0 vs 5.2 minutes
  - Patients requiring intervention
    - 13.5 vs. 18.2 min

Irwin et al. Am J Health-Syst Pharm. 2014;71:2054-59

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Informatics

"Interdisciplinary study of the design, development, adoption and application of IT-based innovations in healthcare services delivery, management and planning"

Pharmacy Informatics is "the use and integration of data, information, knowledge, technology, and automation in the medication use process for the purpose of improving health outcomes."

- Use of information to improve clinical practice, individual and public healthcare and research
- Potential of health information technology (HIT) to improve outcomes

ASHP Statement on the pharmacy technician's role in pharmacy informatics. AJHP. 2013; XX:18-20

Areas of practice

PTIs

- Automation and Systems Management
  - Understanding and assessment functionality
  - Maintenance and troubleshooting of machines
  - Resolve organizational and operational issues
- Project Management
  - Implementation and testing
- End-user Training
  - Education of staff on use of technology, promoting efficiency by integration into workflow

ASHP Statement on the pharmacy technician's role in pharmacy informatics. AJHP. 2013; XX:18-20

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Areas of Practice continued

PTIs

- Policy and Governance
  - Procedures for clinical data management
  - Compliance and best practice
- Customer Service
- Charge Integrity
  - Accuracy of patient and third-party billing
- Reporting

ASHP Statement on the pharmacy technician's role in pharmacy informatics. AJHP. 2013; XX:18-20

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Knowledge Requirements

Pharmacy Technicians as Informaticists

- Working under the supervision of a registered pharmacist, technicians will receive training and gain knowledge in:
- Information Technology Systems
  - Interfaces
  - Computer management
  - Problem resolution
  - Database maintenance
- Medication use and workflow
- Clinical practice at the institution, policies and procedures

ASHP Statement on the pharmacy technician's role in pharmacy informatics. AJHP. 2013; XX:18-20

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Conclusion

- Pharmacy technicians are an essential part of pharmacy practice
- The law allows technicians to assist in the practice of pharmacy
- The roles of technicians are expanding quickly!
- A need for standardization of programs and resources for technician training
- The opportunity for advanced training will continue to grow, as we strive to provide higher quality care for our patients

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Wrap-up

How many of you would be willing to undergo further training to expand the roles you were able to fill as a technician?

How many of you would be willing to train other technicians in areas where you are proficient in order to increase the quality/knowledge base of our staff?

Are there areas of pharmacy that you would like to be a part of, different from your current role?

What advanced practice areas are available to technicians at your institution?

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Paralyzing Danger:
Safety Strategies for Neuromuscular Blocking Agents

Peggy Bickham, PharmD
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University of Illinois Hospital
Chicago, IL

I have no conflict of interest to declare.

Which of the following drugs are neuromuscular blocking agents (NMBs)?

1. Cyclobenzaprine
2. Succinylcholine
3. Hydralazine
4. Clozepine
5. Carbamazepine

NMB Prototype: Curare

-Natural curare comes from a woody vine found in South America (Chondodendron tomentosum)
-First used by indigenous South American people as poison for arrow or dart tips
-Animals became paralyzed and died
-Not effective when orally ingested, so meat could be eaten safely

-Described in 1516 by Pietro Martire d 'Anghere in his book "De Orbo Novo"
-Spanish soldiers and explorers in Central and South America died when hit by poisoned arrows blown at them by natives
-Described by Sir Walter Raleigh in 1596
-Brought to Europe in 1745 by French explorers (Charles Marie de la Condamine) on scientific expedition to Ecuador
-Extensively studied and experimented with over the next 200 years

Booij , Leo . The history of neuromuscular blocking agents. Current Anaesthesia and Critical Care (2000) 11, 27-33.

How NMBs Work

- Acts at neuromuscular junction (motor endplate)
- Competitive antagonist of acetylcholine (ACh)
- Classified as
  - polarizing (succinylcholine)
  - nondepolarizing (everything else in clinical use today)

Historical Impact on Medicine

- Before NMBs were available, deep levels of anesthesia were required for intra-peritoneal surgeries
  - Caused cardiovascular and respiratory depression
  - High incidence of morbidity and mortality
- NMBs allowed development of "balanced anesthesia"
  - Lower, safer doses of anesthetic agents possible
- NMB as important to advancing the practice of anesthesia as ether, nitrous oxide, endotrachal intubation, and local anesthetics

Booij , Leo . The history of neuromuscular blocking agents. Current Anaesthesia and Critical Care (2000) 11, 27-33.

Clinical Use Today

- Produce skeletal muscle relaxation (including the diaphragm)
  - During surgery of intubated patient
  - During tracheal intubation
  - To facilitate mechanical ventilation of critically ill patients in ICU and decrease O2 requirement
- More rarely: to treat muscle spasms due to tetanus, epilepsy, drug overdose, black widow spider bite

Important FACTS!

- NMBs cause muscle paralysis ONLY!
- CNS is not affected
  - Consciousness and full awareness remain intact
  - Patient still senses pain

Therefore, it is essential to:

- **Intubate (artificial ventilation)**
- **Administer anesthesia**
- **Administer pain medication**

Meet the NMBs!

Ultra-Short-acting
- *Duration 4-6 minutes*
  - succinylcholine *

Short-acting
- *Duration 15-30 minutes*
  - mivacurium

Intermediate-acting
- *Duration 20-60 minutes*
  - vecuronium **
  - rocuronium
  - cisatracurium
  - atracurium

Long-acting
- *Duration 60-100 minutes*
  - pancuronium *

What's in a name?
*Similar to acetylcholine
**Similar to curare

Get To Know the NMBs!

...for the safety of our patients!

Generic Name	Brand Name	Confused Names
succinylcholine	Quelicin, Anectine	
vecuronium	Norcuran	Narcan (naloxone), vancomycin
rocuronium	Zemuron	
atracurium	Tracrium	Ativan
cisatracurium	Nimbex	
pancuronium	Pavulon	Peptavlon
mivacurium	Mivacron	

http://www.ismp.org/Tools/Confused-Drug-Names.aspx

Reports of Inadvertent Administration

- Pancuronium was misplaced among heparin flush stock…a nurse inadvertently administered 5ml to a non-intubated patient (recovered after 10 hours on ventilator). *2000*
- Verbal order for "Narcan" was misinterpreted by nurse to be 'Norcuron", obtained from cabinet and administered to patient, who experienced respiratory and cardiac arrest, was resuscitated, placed on ventilator and sent to ICU. *1998*
- ED physician mistakenly entered orders for midazolam and vecuronium for a trauma patient he was intubating into an oncology patient's record. Another ED nurse relieving for break administered to the patient, not realizing the patient must be intubated. She left the room and the patient arrested, could not be resuscitated. *2005*

Koczmara C, Jelincic V. Neuromuscular blocking agents: enhancing safety by reducing the Risk of accidental administration. ISMP Canada, 18 (1) Spring 2007. http://www.ismp.org/newsletters/acutecare/articles/20090226.asp accessed 8/7/2015.

Inadvertent Administration

- Atracurium was administered subcutaneously instead of hepatitis B vaccine to seven infants. Within 30 minutes all experienced respiratory distress. Five recovered, one sustained permanent injury, one died. Anesthesiologist had stored a vial in the refrigerator for convenience and it was similar in appearance to the vaccine vial. *2002*
- ED physician ordered NMB to sedate a combative patient. Nurse administered the drug too soon, before intubation. Patient arrested and suffered permanent anoxic injury.
- ED nurse prepared saline flush syringes each day. Left-over unlabeled vecuronium syringes from a trauma patient were inadvertently mixed in with the saline syringes. One was used to flush the line of a 3 year old child, who became flaccid and developed respiratory arrest. She was quickly intubated and ventilated and recovered. *2005*

Paralyzed by mistakes – preventing errors with neuromuscular blocking agents. ISMP Medication Safety Alert, Sept. 22, 2005. http://www.ismp.org/newsletters/acutecare/articles/20050922.asp accessed 7/11/2015

Predominant Medication Error Event Types Associated with NMB (n=120)

Event Type	Number	% of Total Reports (n=154)
Wrong drug	57	37%
Wrong dose / overdose	25	16.2%
Prescription / refill delayed	7	4.5%
Wrong technique	6	3.9%
Extra dose	6	3.9%
Other	19	12.3%

NMB: Reducing associated wrong-drug errors. PA Patient Safety Advisory 2009 Dec;6(4):109-14. http://patientsafetyauthority.org/ADVISORIES/AdvisoryLibrary/2009/Dec6(4)/Pages/109.aspx Accessed 8/4/2015.

Contributing Factors

- Unsafe storage or products
- Look-alike labeling and packaging
- Look-alike drug names
- Unlabeled syringes
- Inadequate knowledge of drug action
- Failure to ensure ventilator support
- Ordering errors

Paralyzed by mistakes: preventing errors with neuromuscular blocking agents. ISMP Medication Safety Alert. 2005;10(19).
NMB: Reducing associated wrong-drug errors. PA Patient Safety Advisory 2009 Dec;6(4):109-14.
http://patientsafetyauthority.org/ADVISORIES/AdvisoryLibrary/2009/Dec6(4)/Pages/109.aspx

Inattentional Blindness

A type of confirmation bias

- Failure to notice a fully visible but unexpected object because attention was engaged on another task, event, or object.
- The person performing the task fails to see what should have been plainly visible, and later, they cannot explain the lapse
- Vials and labels look similar to what we expect to see, so we tend to see what we expect

Inattentional blindness: What captures your attention? ISMP Medication Safety Alert, Feb. 26, 2009. https://www.ismp.org/newsletters/acutecare/articles/20090226.asp

Koczmara C, Jelincic V. Neuromuscular blocking agents: enhancing safety by reducing the risk of accidental administration. ISMP Canada, 18 (1) Spring 2007. www.ismp.org/newsletters/acutecare/articles/20090226.asp

Error Prevention Strategies

- Limit access
  - Allow floorstock only in OR, ED, critical care units where patients can be properly ventilated and monitored
- Segregate storage
  - Pharmacy should maintain a distinct sealed box with warnings affixed, in med area or refrigerator
- Warning labels
  - Affix fluorescent red labels on each vial, syringe, bag, and storage box

Error Prevention Strategies

- Safeguard storage in the pharmacy
  - Sequester NMB stored in the pharmacy
  - Affix warning labels to vials
- Standardize prescribing
  - Establish order sets and alerts to avoid misinterpretation
  - Include requirement or cross-checks for ventilator support and discontinuation after extubation
  - Do not allow "Resume previous meds" orders
  - Refer to as "paralyzing agents", not "muscle relaxants"
  - Do not allow "prn" orders

Paralyzed by mistakes: preventing errors with neuromuscular blocking agents. ISMP Medication Safety Alert. 2005;10(19).
NMB: Reducing associated wrong-drug errors. PA Patient Safety Advisory 2009 Dec;6(4):109-14.
http://patientsafetyauthority.org/ADVISORIES/AdvisoryLibrary/2009/Dec6(4)/Pages/109.aspx

Error Prevention Strategies

- Redundancies
  - Consider requiring independent double check before dispensing and administering
  - Double check against original order
- Require bedside attendance during initial administration
  - Licensed practitioner with experience in intubation and airway management

Error Prevention Strategies

- Prompt removal of discontinued products
  - Discard or sequester vials, IV bags, and syringes with NMB for immediate pharmacy pickup after discontinuation/ extubation
- Increase awareness
  - Educate staff about risks
  - Provide list of generic and brand names for all NMBs available at facility

In what areas do the errors involving NMBs most usually originate (in order of most-least)?

1. OR
2. ICU
3. ED
4. Pharmacy
5. Pediatrics

Predominant Care Areas Involved in Medication Errors Involving NMB (n=120)

Unit	Total	% of Total Reports
ED	21	13.6%
OR	19	12.3%
Pediatric ICU	15	9.7%
Anesthesia	15	9.7%
→ Pharmacy	10	6.5%
Med/Surg ICU	9	5.8%
Medical ICU	9	5.8%
Neonatal ICU	8	5.2%
Cardiac ICU	8	5.2%
Surgical ICU	6	3.9%

NMB: Reducing associated wrong-drug errors. PA Patient Safety Advisory 2009 Dec;6(4):109-14.
http://patientsafetyauthority.org/ADVISORIES/AdvisoryLibrary/2009/Dec6(4)/Pages/109.aspx

In which of the following scenarios might "inattentional blindness" have played a role?

Pharmacy Errors

1. Cisatracurium infusion prepared for a ventilated infant. Delivered by accident to adult unit with 3 bags of antibiotics. Nurse verified the 1st 3 bags of antibiotics, but was interrupted and did not check the 4th (cisatracurium). Label similar in color and so the bag was hung. Patient experienced respiratory arrest and required ventilation for several hours.
2. Pancuronium was misplaced among heparin flush stock…a nurse inadvertently administered 5ml to a non-intubated patient (recovered after 10 hours on ventilator).
3. Anesthesiologist ordered trial supply of mivacurium infusion from a drug rep. Product was delivered to pharmacy, was stocked next to metronidazole. Infusion was in foil wrapper like metronidazole. Tech labeled several bags as metronidazole, pharmacist did not catch, nurse did not catch, 4 patients received mivacurium. All arrested; two recovered, one suffered permanent harm, one died.

Paralyzed by mistakes: preventing errors with neuromuscular blocking agents. ISMP Medication Safety Alert. 2005;10(19).

Oregon hospital admits mistake led to patient death *

Sisters woman, 65, given paralyzing agent in ER

By Tara Bannow / The Bulletin / @tarabannow
Published **Dec 5, 2014** at 12:01AM / Updated Dec 5, 2014 at 06:31AM

An Oregon hospital' s flat-out admission that a medication error resulted in a 65-year-old woman's death this week serves as a reminder of hospitals' efforts to increase transparency and communication when such incidents occur.

The patient died Wednesday, two days after going to the hospital emergency room. She had been accidentally given a paralyzing agent, which caused her to go into cardiac arrest. Hospital officials have been forthcoming with the family about the mistake, asserting it's long been the health system's policy to do so.

The patient went to the emergency room Monday with anxiety and concerns about the medications she was taking after recent brain surgery at a different hospital. Staff members determined she needed an intravenous anti-seizure medication called fosphenytoin. Instead, she was given the wrong medication, a paralyzing agent called rocuronium, which caused her to stop breathing and go into cardiac arrest, leading to irreversible brain damage. The patient was on life support until Wednesday morning.

Three staff members involved in the patient's care are on administrative leave, and are receiving counseling through the hospital's caregiver assistance program. The Chief Clinical Officer declined to say what their jobs are but said they're "devastated by this."

* Edited to remove identifiers.

What Happened?

- Pharmacy received order for fosphenytoin for seizures
- Pharmacy prepared the IV solution, but accidentally added rocuronium instead of fosphenytoin
- The bag was dispensed labeled as fosphenytoin
- After the bag was hung, a code red was announced. The door to the patient room was closed to protect from fire.
- When the nurse re-entered, the patient was found in respiratory and cardiac arrest.

Tragic error with neuromuscular blocker should prompt risk assessment by all hospitals. ISMP Medication Safety Alert, Dec 14, 2014.
www.ismp.org/newsletters/acutecare/showarticle.aspx?id=97

Reflection:

How could this tragedy have been prevented?
Which of the strategies discussed might have made a difference?

ISMP Recommendations

- Limit neuromuscular blockers in formulary
- Segregate or eliminate storage from active pharmacy stock when possible
  - Highly visible storage container
  - Bright warning labels
- Regularly review storage areas to assess potential for mix-ups
- Thoroughly examine the entire pharmacy IV admixture process
  - Review ISMP IV Sterile Compounding Guidelines (www.ismp.org/sc?id=461)
  - Consider implementing IV workflow technologies

Tragic error with neuromuscular blocker should prompt risk assessment by all hospitals. ISMP Medication Safety Alert, Dec 14, 2014. www.ismp.org/newsletters/acutecare/showarticle.aspx?id=97

Consider implementing IV workflow technologies!!!

Future State (Why Not NOW?)

- IV workflow technologies utilize barcode scanning of products during IV admixture
- Double checks the accuracy of the ingredients of each compounded product (if utilized correctly)
- A number of systems are available on the market
- Potential to eliminate errors due to inattentional blindness

IV workflow systems "that utilize barcode scanning support can assure proper drug selection, but only if the systems are fully integrated with the pharmacy and hospital information systems. Without full integration between the IV workflow technology and the order entry system, errors can still be introduced into the process. Although some hospitals have chosen to limit use of these systems [IV workflow technology] *for focused areas like admixture of chemotherapy or high-alert drugs, there's no telling when someone might accidentally introduce a high-alert drug when preparing other drug classes that wouldn't ordinarily be scanned. Therefore, to be maximally effective, the system must be utilized for all compounded admixtures."*

Tragic error with neuromuscular blocker should prompt risk assessment by all hospitals. ISMP Medication Safety Alert, Dec 14, 2014. www.ismp.org/newsletters/acutecare/showarticle.aspx?id=97

What was the first department in the hospital to adopt barcode scanning?

1. The pharmacy
2. The operating room
3. Nursing – BCMA (bar code medication administration)
4. The gift shop

http://jerryfahrni.com/2015/01/a-missed-opportunity-for-safety-why-scanning-a-limited-formulary-in-the-i-v-room-is-a-mistake/ (Paraphrased from blog comment by Ray Vrabel)

Paralyzing Danger: Safety Strategies for Neuromuscular Blocking Agents

Post-Test Questions

1. Which of the following drug groups are all neuromuscular blocking agents (NMBs)?
    a. succinylcholine, rocuronium, Narcan
    b. Peptavlon, mivacurium, acetylcholine
    c. rocuronium, Nimbex, succinylcholine
    d. atracurium, vecuronium, cyclobenzaprine

2. List five error prevention strategies recommended by ISMP to reduce the risk of error with NMBs.
    a. _____
    b. _____
    c. _____
    d. _____
    e. _____

3. Which of the following technologies has the potential to eliminate wrong-ingredient errors in pharmacy sterile compounding if used properly?
    a. BCMA (bar code medication administration)
    b. Remote pharmacist verification of compounded sterile products utilizing cameras in the laminar airflow workstation (hood)
    c. IV workflow technology utilizing barcode scan verification only when chemotherapy and high alert drugs are compounded
    d. IV workflow technology utilizing barcode scan verification of all ingredients used in all sterile compounding

Keeping Kids Safe: Quality and Safety in the Pediatric Pharmacy

Daniel Hickman CPhT

OSF St. Francis Medical Center,
Children's Hospital of Illinois

The speaker has no conflicts of interest to disclose in relation to this presentation.

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Learning Objectives

1. Explain quality measures used in the Pediatric Pharmacy

2. Discuss safety practices to help reduce medication errors in the Pediatric Pharmacy

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

- As many as 1 in 10 hospitalized children are impacted by a medication error.[1,2]
- Up to 35% of these errors are serious or life threatening. [3]
- The goal is to learn from these events and to adopt effective strategies to prevent harmful errors from happening again.

- **References**

1) Takata GS, Mason W, Taketomo C, Logsdon T, Sharek PJ. Development, testing, and findings of a pediatric-focused trigger tool to identify medication-related harm in US children's hospitals. *Pediatrics.* 2008;121(4):927-35.

2) Takata GS, Taketomo CK, Waite S. California Pediatric Patient Safety Initiative. Characteristics of medication errors and adverse drug events in hospitals participating in the California Pediatric Patient Safety Initiative. *Am J Health Syst Pharm.* 2008;65(21):2036–44.

3) Tham E, Calmes HM, Poppy A, et al. Sustaining and spreading the reduction of adverse drug events in a multicenter collaborative. *Pediatrics.* 2011;128(2):438-45.gain.

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Children's Hospital of Illinois (CHOI)

- Established August 2010
- 126 bed hospital
- General Peds, PICU, PIC, NICU
- Pediatric Surgery
- St. Jude affiliate

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

CHOI Pharmacy

- Opened August 2010
- 16 Pharmacists
- 8 Technicians
- Averages 350 drawn up oral doses daily
- Averages 100 report IV doses daily

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Missing Medication Project

- Reduce the amount of missing meds in the CHOI Hospital
- Benchmarked at 12.08 missing meds per month
- Working with the Nursing Leaders of the floors to see how Nursing can help reduce missing meds

Missing Medication Scorecard

	FY14	oct	nov	dec	FY15 1Q	jan	feb	mar	FY15 2Q	apr	may	jun	FY15 3Q	FY15 YTD
Count	**198**	18	21	19	**58**	17	?	24	**41**	4	13	6	**23**	**122**
Target	**145**	12.08	12.08	12.08	**36.25**	12.08	12.08	12.08	**24.17**	12.08	12.08	12.08	**36.25**	**96.67**

What we have changed

- We have changed the General Peds report times to print twice a day
- DC'ed IV medications are retrieved during the next round of delivery to try and reuse them if possible
- Using the proper redispense reason in EPIC when investigating missing meds
- Investigating the missing med to find them or correct the problem of why they are missing

Wasted Medication Project

- Reduce oral medication waste from cart fill to decrease cost and increase efficiency in the pharmacy
- Split General Pediatric cart fill to twice a day
- Getting stop dates on IV's

Pediatric Pharmacy Medication Safety Committee

- PPMSC started in December 2012
- Committee looks at all medication error events, safety issues, and procedures within the Pediatric Pharmacy to increase patient safety

PPMSC Data

Event Range	Total Events Discussed	Changes Implemented	"Knowledge Deficit"	Reeducation
2013	66	32	19	5
2014	35	11	9	9
1-1-15/ 3-31-15	7	7	0	0
4-1-15/ 4-30-15	5	4	1	0
5-1-15/ 5-31-15	4	1	0	0
6-1-15/ 6-30-15	1	1	0	0
2015 YTD	17	13	1	0

Safety Coach Program

- Improve individual and team performance
- Recognize good behaviors
- Correct unsafe, unproductive behaviors

Safe Culture Through TRUST

- Safe environment to discuss safety concerns
- Non-punitive actions on safety issues
- Issues identified now have action items which allow closure
- Safety coach voice is heard, valued, and responded to

Goals of Observations

- Be the EYES of the unit regarding safety
- Provide 'real-time' feedback to co-workers
- Provide an effective feedback loop to increase awareness of proven safety practices
- Identify coaching/affirming opportunities
  - Use of TeamSTEPPS techniques (read back, clarifying questions, effective handoffs)
  - Identify strategy used
  - Highlighting opportunities for improvement
  - *Quality* of the coaching/affirmation vs. *Quantity* of Observations

Bottom Line:

- We all need to be aware of unsafe practices
- Being aware of the unsafe practices is the first step to eliminating them
- If you see something that is an "accident waiting to happen," tell someone
- Investigate "work arounds"

Conclusion

- Medication Errors happen
- Learn from your mistakes
- Make changes from the mistakes that are made

Question

What kind of Quality Measures are used in the CHOI Pharmacy?

A. Missing Medication Scorecard
B. Data from the Pediatric Pharmacy Medication Safety Committee
C. Taste testing of flavored medication
D. a and b

Question

The role of the Safety Coach is?

A. Improve individual and team performance.
B. Recognize good behaviors
C. Correct unsafe, unproductive behaviors
D. All of the above

Residency Project Pearls 2015

Evaluation of Opportunities for Pharmacist Integration into the Discharge Process

Thomas Yu, Pharm.D.
Outpatient Pharmacy Manager
Sinai Health System
ICHP Annual Meeting 2015
September 12, 2015

The speaker has no actual or potential conflict of interest in relation to this presentation

Learning Objectives

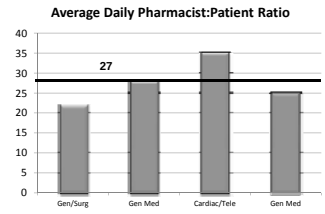
- Identify the transition of care where most medication discrepancies typically occur.
- Recognize the amount of time required to complete medication reconciliation at discharge.

Mount Sinai Hospital

- Part of Sinai Health System
- 319-bed urban teaching hospital on Chicago's west side
- Level I Trauma Center
- Safety Net Hospital
  - Emergency visits: 56,236
  - Outpatient visits: 207,728
  - > 700 health professionals trained annually

Mount Sinai Pharmacy Department

- Decentralized/centralized
  - 3 general medicine units
  - 1 general surgery units
  - ~1 APPE student/unit



Med History vs. Med Reconciliation

- Medication history (MH)
  - ***Initial list*** of medications obtained from the patient and other sources
- Medication reconciliation (MR)
  - ***Comparison*** of MH vs inpatient medications and ***error correction***

- An accurate MR cannot be obtained without an accurate MH

Br J Clin Pharmacol. 2009;67:671–675

Interpretation of the Medication Use Process

Admission
- Medication history
- Medication reconciliation

Inpatient
- Inpatient hospitalization (orders, transfers)

Discharge
- Medication reconciliation

Current Process at MSH

Current Medication Reconciliation Policy

Nurse or Physician

Admission
- Medication history
- Medication reconciliation

Inpatient
- Inpatient hospitalization (orders, transfers)

Physician

Physician

Discharge
- Medication reconciliation

Current Medication Reconciliation Policy

Nurse or Physician

Admission
- Medication history

Current Limitations

- **Documentation not standardized**
- **Med history quality variable**
- **Pharmacist involvement is suboptimal**

Physician

- Medication reconciliation

Audience Participation

What transition of care do most medication discrepancies typically occur?

A. Admission
B. ICU → Floor
C. ED → Floor
D. Discharge

Quality Improvement Project

Pharmacist Medication Reconciliation

Objectives of the Study

- Primary
  - Delineate role for pharmacists in the discharge process by identification of safety benefits derived from transition services
- Secondary
  - Identify drug classes and chronic disease states associated with medication discrepancies

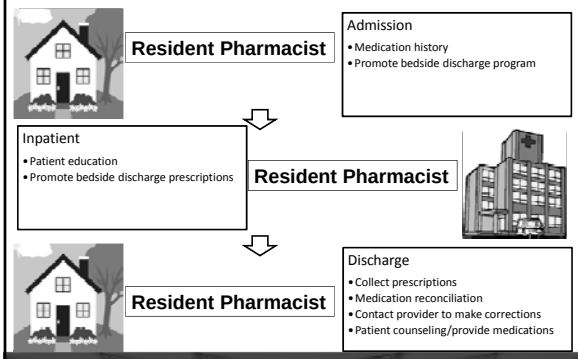
Methods

- Services provided during resident rotation on 3 adult medical units
  - December 8, 2014 to February 5, 2015
- Admission
  - Obtained complete medication history
  - Promoted bedside discharge services

Methods

- Discharge
  - Collected discharge prescriptions
  - Reviewed medication reconciliation performed by discharging physician
  - Contacted physician to correct any discrepancies on prescriptions prior to discharge
  - Counseled patients on new medication regimen

Methods



Methods

- Discrepancy definitions
  - Intended – Correct medication change due to disease/lab
  - Unintended – Incorrect medication change resulting in potential for ADR

Institute For Safe Medication Practices Arch Intern Med. 2005;165(16):1842-7

Methods

- Discrepancy classified by type
  - Omission (missing medication)
  - No indication for an ordered medication
  - Wrong dose and/or frequency
  - Wrong medication
  - Duplication (same drug or class)

Institute For Safe Medication Practices Arch Intern Med. 2005;165(16):1842-7

Methods

- Severity scale adapted from ISMP severity categories
  - No harm – No patient harm
  - Mild harm - Increased monitoring but no change in homeostasis
  - Moderate harm – Need for treatment/intervention or temporary harm
  - Critical harm – Prolonged hospitalization, near death or death

Institute For Safe Medication Practices Arch Intern Med. 2005;165(16):1842-7
ISMP = Institute of Safe Medication Practice

Methods

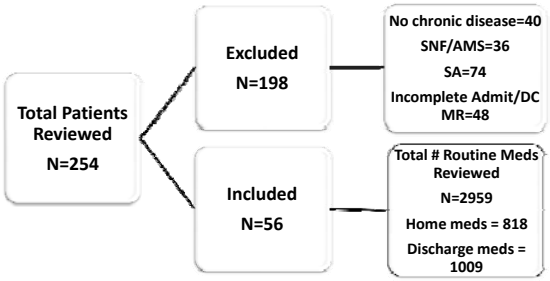
Inclusion

- Admitted to general medical unit
- History/new diagnosis ≥1 of the following chronic diseases
  - Chronic obstructive pulmonary disease (COPD)
  - Chronic heart failure (CHF)
  - Diabetes mellitus (DM)
  - Coronary artery disease (CAD)
  - Cerebrovascular accident (CVA)
  - Thromboembolism (VTE) requiring long term anticoagulation

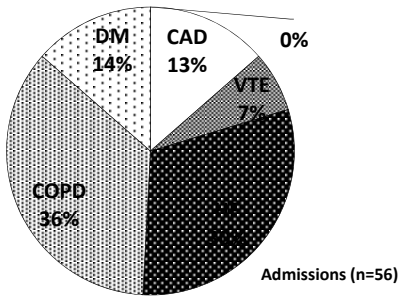
Exclusion

- Documented substance abuse (SA)
- Non-English speaking
- Admission from or discharge to skilled nursing facility (SNF)
- Diagnosis of dementia/altered mental status (AMS)
- Diagnosis of major schizoaffective disorder

Results



Baseline Demographics



Baseline Demographics

	Study (n=56)
Gender (F)	34 (61%)
Average Age	54.4 years
Length of Stay	4.6 days
Average # of Meds	11.2
Average # of Routine Meds	8.6
Number of Comorbidities	1: 9 (16%) 2: 13 (23%) 3: 23 (41%) 4: 8 (14%) 5: 3 (6%)
Insurance Status	**Medicaid 41 (75%)** Medicare 8 (14%) Self Pay 5 (8%) Insured 2 (3%)

Baseline Demographics

	Study (n=56)
Gender (F)	34 (61%)
Average Age	54.4 years
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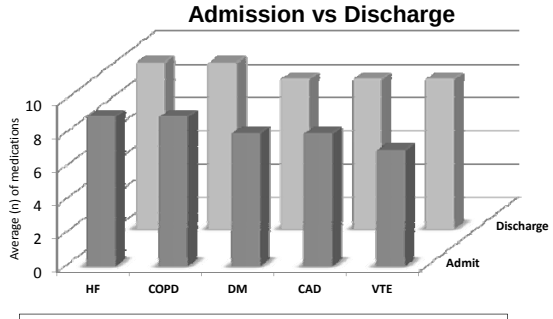
Average Number of Medications

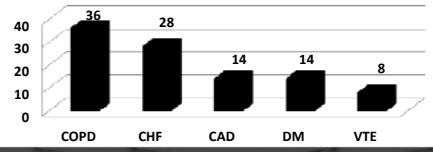


Average Number of Medications Increased at Discharge ~2.1

Discrepancies by Disease State

	COPD	CHF	DM	CAD	VTE	Sum
Total by Disease State	20	16	8	8	4	**56**
Average Per Patient	1.2	1.2	0.7	1	1	**1**
Percent of Total Discrepancies (%)	**36**	**28**	14	14	8	**100**

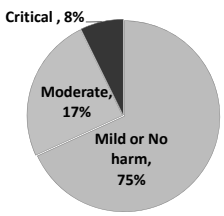
Percentage of Discrepancies



Discrepancies at Discharge by Type

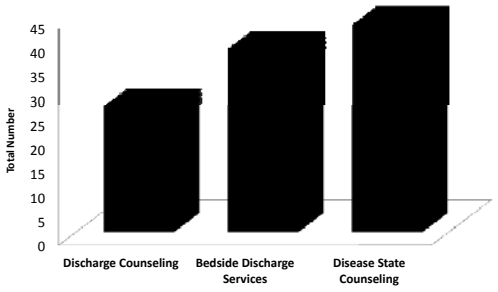
Type	Percent (%)	Example
Omission	57	Beta blocker for CHF Rescue inhaler for COPD
Wrong Dose	21	Insulin for DM
Duplication	11	2 statins for CAD
No Indication	8	PPI
Drug/Disease	3	Ibuprofen in CHF

Discrepancies at Discharge by Severity

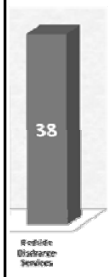


Severity	Type	Example	Disease State
Critical Harm	Wrong Dose Omission	Insulin Enoxaparin	DM VTE
Moderate harm	Omission Duplication	Beta blocker 2 statins	CHF COPD CAD

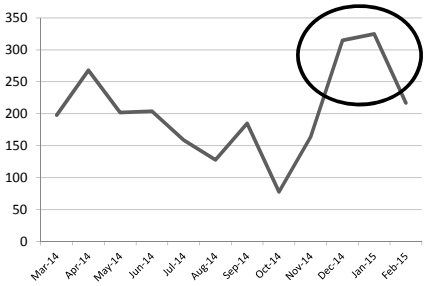
Resident Discharge Interventions Beyond Medication Reconciliation



Increase in Discharge Services



Bedside Discharge Rx Program



Result Highlights

- Safety benefits
  - Approximately 1 discrepancy per patient prevented
    - 25% of discrepancies critical or moderate
  - Prevented potential ADE

Result Highlights

- High Risk Disease States
  - CHF, COPD
    - Highest average number discharge medications (10)
    - Highest readmission rates
  - DM, VTE
    - Medications associated with highest potential for critical harm

Observations

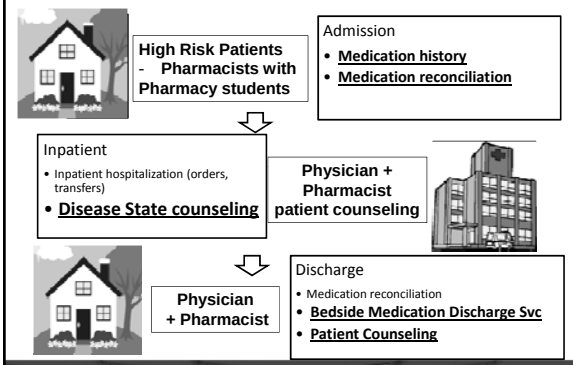
- Observed reduction in 30 day readmissions
- Analysis
  - Identified subset patients with readmissions (n=32)
  - ↓ 39%

Prior Admission	Resident Project 12/6/14 – 2/6/15	Post-Discharge

Limitations

- Small, retrospective, single center study limited to 2 months duration
- Unable to complete numerous Med Rec due to inadequate communication to pharmacist of discharge
- Resident categorized discrepancies by type and severity

Integration of Pharmacist in Discharge Process



Lessons Learned

- Need to start with admission med history
  - Cannot prevent discharge discrepancies without full knowledge of baseline medications
- More time spent with patient affects positive outcomes
- Bundled approach
  - A multiple layered approach has more significant impact than one dimensioned approach

Audience Participation

What patient populations would benefit from a pharmacist assisted medication reconciliation at discharge?

a. Patients with CHF
b. Patients with COPD
c. Patients on insulin
d. A and B only
e. All of the above

Acknowledgements

- Diane Cluxton, Pharm.D.
- Karen Trenkler, Pharm.D., BCPS
- Sameer Shah, Pharm.D., MHA
- Tejal Patel, Pharm.D., BCPS
- Mount Sinai Hospital General Medicine Pharmacists

Evaluation of Opportunities for Pharmacist Integration into the Discharge Process

Thomas Yu, Pharm.D.
Outpatient Pharmacy Manager
Sinai Health System
ICHP Annual Meeting 2015
September 12, 2015

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Evaluation of the Safety and Efficacy of Valganciclovir Twice Weekly Dosing in Kidney Transplant Patients with Impaired Graft Function

Great Lakes Resident Research
Presented by: Rachel Ralph, PharmD

The speaker has no actual or potential conflict of interest in relation to this presentation

Background

- Cytomegalovirus (CMV) is an opportunistic infection associated with significant morbidity and mortality in transplant recipients
- Incidence:
  - ~60% will have active infection (replicating virus)
  - >20% will have symptomatic disease
- Treatment options for CMV prevention in the post-transplant period include:
  - Intravenous (IV) ganciclovir
  - Valganciclovir (prodrug)

Cochrane AB. 2006;63:S17-21.
Cordero E, et al. 2012;44:694-700.

Valganciclovir

Adverse Effects

- Leukopenia/neutropenia [Black Box Warning (BBW)]
- Thrombocytopenia (BBW)
- Anemia (BBW)
- Renal insufficiency
- Liver function test (LFT) changes

Valcyte® [package insert].

Valganciclovir

Maintenance Dosing Recommendations

- CrCl ≥60 mL/min: 900 mg daily
- CrCl 40-59 mL/min: 450 mg daily
- CrCl 25-39 mL/min: 450 mg q2 days
- CrCl 10-24 mL/min: 450 mg twice weekly
- CrCl <10 mL/min or hemodialysis (HD): NOT RECOMMENDED

Valcyte® [package insert].

Valganciclovir vs. Ganciclovir

Maintenance Dosing Recommendations

Valganciclovir	Ganciclovir
• CrCl ≥60 mL/min: 900 mg daily	• CrCl ≥70 mL/min: 5 mg/kg/d
• CrCl 40-59 mL/min: 450 mg daily	• CrCl 50-69 mL/min: 2.5 mg/kg/d
• CrCl 25-39 mL/min: 450 mg q2 days	• CrCl 25-49 mL/min: 1.25 mg/kg/d
• CrCl 10-24 mL/min: 450 mg twice weekly	• CrCl 10-24 mL/min: 0.625 mg/kg/d
• CrCl <10 mL/min or HD: NOT RECOMMENDED	• CrCl <10 mL/min or HD: 0.625 mg/kg TIW

Valcyte® [package insert].
Ganciclovir. Lexicomp®.

Pharmacokinetic Studies

- Single dose 900 mg valganciclovir demonstrated:
  - 4-fold increase drug concentration in CrCl <10mL/min vs. 21-50 mL/min
- Similar systemic exposure between:
  - Valganciclovir 900 mg/day
  - IV ganciclovir 5 mg/kg/day
- Low-dose valganciclovir effective and relatively safe
  - Further dose decreases and discontinuation rate of ~20%

Czock D. 2002; 72:142-50.
Wiltshire H, et al. 2005;44:495-507.
Gabardi S, et al. 2004;24:1323-30.

Research Question

Is valganciclovir dosed 450 mg twice weekly both safe and effective in kidney transplant patients with slow graft function on HD or with CrCl <10 mL/min?

Outcome Measures

Primary Outcome

- Bone Marrow Suppression
  - Neutropenia
    - Composite: absolute neutrophil count (ANC) <1500 cells/ul
    - 500 < ANC < 1500 cells/ul
    - ANC <500 cells/ul (severe)
  - Thrombocytopenia
    - Platelet count <100 k/ul
  - Composite neutropenia and thrombocytopenia

Outcome Measures

Secondary Outcomes

- Use of growth colony stimulating factor (GCSF)
- CMV viremia: viral load >600 IU/mL

Study Design

- Retrospective case-control study
  - Matched 1:2 (study to control)
  - Matching criteria:
    - Transplant date within 1 calendar year
    - CMV serostatus
- This study was approved by the Northwestern University Institutional Review Board

Study Population

- Inclusion Criteria
  - Kidney transplant recipients
  - Alemtuzumab induction
  - Study: slow graft function (SGF) with CrCl <10 mL/min or necessitating HD
  - Control: CrCl >40 mL/min
- Exclusion Criteria
  - Simultaneous receipt of another organ
  - Rituximab desensitization
  - Antithymocyte globulin use
  - D-/R- CMV serostatus
  - HIV

Northwestern Memorial Hospital - Chicago, Illinois

Feinberg and Galter Pavilions

Prentice Women's Hospital

- 894-bed Academic Medical Center
- Primary teaching affiliate of Northwestern University Feinberg School of Medicine
- Fiscal Year 2014
  - 47,139 Inpatient Admissions
- Kovler Organ Transplantation Center
  - 220 kidney transplants annually
  - 122 living donor kidney transplants annually

My Role

- Designed study
- Obtained IRB approval
- Collected data
- Analyzed data

Data Analysis

- Continuous variables were analyzed with Student's t-test and Wilcoxan Rank-Sum test
- Categorical variables were analyzed with Chi-square and Fisher's Exact
- All data were analyzed with Epi-Info 7.1.3; Atlanta, GA

Study Population

SGF Patients

78 SGF Patients Identified

Excluded

- Basiliximab induction
- Receipt of
  - Rituximab
  - Antithymocyte globulin
- D-/R-
- No BIW dosing
- HIV
- Unable to find in medical record
- Duplicate entry

31 SGF Patients Included

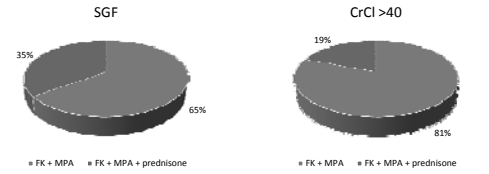
Baseline Demographics

	SGF (n=31)	CrCl >40 (n=62)	p-value
Age, yrs (mean, SD)	53.7 (11.6)	49.6 (14.7)	0.18
Gender, male (n,%)	25 (80.7%)	30 (48.4%)	<0.01
Race (n,%)			
White	9 (29%)	26 (41.9%)	0.23
Black	14 (45.2%)	10 (16.1%)	<0.01
Hispanic	4 (12.9%)	21 (33.9%)	0.05
Asian	3 (9.7%)	5 (8%)	0.99
Other	1 (3.2%)	0 (0%)	0.33

SGF patients:

- Median time BIW dosing: 55 days (IQR 24 to 167)
- Median time SGF: 14 days (IQR 6 to 17)

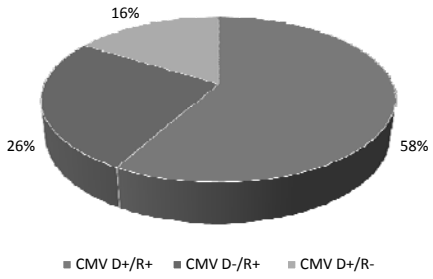
Immunosuppression



p=0.09

FK= tacrolimus; MPA= mycophenolic acid

CMV Serostatus



Primary Outcomes

Neutropenia			
	SGF (n=31)	CrCl >40 (n=62)	p-value
Neutropenia (Composite)	19 (61.3%)	32 (51.6%)	0.38
Neutropenia (500 < ANC < 1500)	14 (45.2%)	19 (30.7%)	0.17
Severe Neutropenia (ANC < 500)	5 (16.1%)	13 (21%)	0.58
Thrombocytopenia			
Thrombocytopenia (plts < 100)	12 (38.7%)	6 (9.7%)	<0.01
Composite Neutropenia and Thrombocytopenia			
ANC <1500 and/or plts <100	23 (74.2%)	33 (53.2%)	0.05

Secondary Outcomes

Use of GCSF			
	SGF (n=31)	CrCl >40 (n=62)	p-value
GCSF Use	10 (32.3%)	13 (21%)	0.24
CMV Viremia			
CMV Viremia	2 (6.9%)	0 (0%)	0.1

Subgroup Analysis

Impact of GCSF on ANC

GCSF Patients			
	SGF (n=10)	CrCl >40 (n=13)	p-value
Neutropenia (500 < ANC < 1500)	6 (60%)	1 (8%)	0.02
Severe Neutropenia (ANC < 500)	4 (40%)	12 (92%)	

Subgroup Analysis

Impact of HD versus reduced CrCl

SGF patients			
	HD (n=23)	Non HD (n=8)	p-value
Neutropenia (ANC <1500)	13 (56.5%)	6 (75%)	0.43
Thrombocytopenia (plts <100)	10 (43.5%)	2 (25%)	0.43
ANC <1500 and/or plts <100	16 (69.6%)	7 (87.5%)	0.64

Limitations

- Retrospective study design
- Sample size limited to patients during the protocol period
  - May not have been powered to detect significant differences
- Difficult to categorize time on HD
- Did not compare average MPA doses between groups

Summary and Conclusions

- Valganciclovir is renally eliminated necessitating dose adjustments
- Per labeling, valganciclovir is not recommended in CrCl <10 mL/min or HD
- Extrapolated valganciclovir dosing appears to be effective, however, was shown to lead to increased incidences of thrombocytopenia
  - Trend towards more neutropenia and GCSF use in the SGF group
- Prospective study may be warranted to further substantiate these findings and look for clinical significance

Future Directions

- Present results to P&T Committee
- Share data with the department of solid organ transplantation
- Submit abstract to American Transplant Congress (ATC) annual meeting for 2016
- Submit for publication

Question #1

Which of the following are adverse effects of valganciclovir?

A. Neutropenia
B. Eosinophilia
C. Thrombocytopenia
D. A & C only

Question #2

What is the lowest creatinine clearance (CrCl) for which valganciclovir has dosing recommendations?

A. CrCl 75 mL/min
B. CrCl 50 mL/min
C. CrCl 30 mL/min
D. CrCl 10 mL/min

Acknowledgements

Thank you to the following:

Chad Richardson, PharmD
Michael Postelnick, BS Pharm, BCPS AQ ID
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Milena McLaughlin, PharmD, MSc, BCPS, AAHIVP
Michael Ison, MD

Evaluation of the Safety and Efficacy of Valganciclovir Twice Weekly Dosing in Kidney Transplant Patients with Impaired Graft Function

Great Lakes Resident Research
Presented by: Rachel Ralph, PharmD

The speaker has no actual or potential conflict of interest in relation to this presentation

2015 Residency Project Pearls:
Accuracy and impact of a penicillin allergy label on hospitalized patient outcomes

Sara Vu, PharmD
September 12, 2015

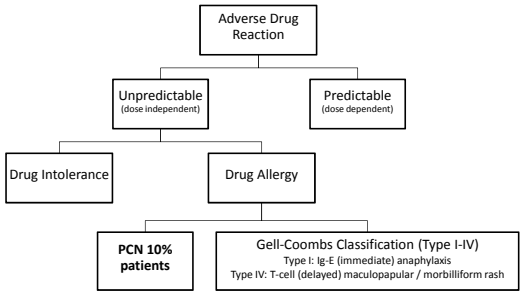
Conflict of Interest:

The speaker has no actual or potential conflict of interest in relation to this presentation.

Swedish Covenant Hospital
Chicago, IL
Community teaching hospital: 312 beds
Average daily census: 230

How often has a penicillin (PCN) allergy prevented you from using the drug of choice in a patient?

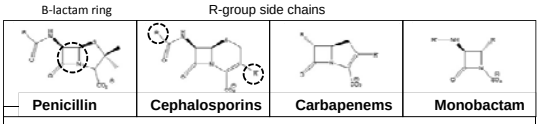
Most Common Allergy: Penicillin



Ann Allergy Asthma Immunol. 2010 Oct;105(4):259-273, e78.

Mechanism and Risk of Cross Reactivity

B-lactam ring R-group side chains



Penicillin	Cephalosporins	Carbapenems	Monobactam

Cross Reactivity between PCN and other B-lactams			
0.5% to 2.5% First & second generation cephalosporins	Less then 1% Third & fourth generation cephalosporins	0.3% to 4.3% carbapenems	0% monobactam

Amino-PCNs that Share Identical R_1-Group Side Chains with Cephalosporins	
Amoxicillin Cefadroxil Cefprozil	**Ampicillin** Cefaclor Cephalexin

Adapted from: J Allergy Clin Immunol 2010;125(Suppl):S126–S137.
Clin Infect Dis. 2014;59(8):1113.
J Emerg Med 2012; 42:612–20.
Ann Pharmacother. 2009 Feb;43(2):304-15.

Implications of PCN Allergy Label

- Electronic Health Record (EHR) Incentive Program
  - Stage 3 Meaningful Use Standards, 2016
    - Define drug allergy
    - Define intolerance
    - Define condition
- "PCN allergy" label associated with
  - Antibiotics
    - Broad spectrum: vancomycin, fluoroquinolones
    - *C. difficile* associated: clindamycin, fluoroquinolones
  - Increased rates of VRE, MRSA, *C. difficile*
  - Longer hospital days and greater admissions to the ICU

EHR Incentive Programs. Centers for Medicare and Medicaid Services.
J Allergy Clin Immunol 2014 Mar; 133(3):790-6.
J Allergy Clin Immunol Pract. 2013 May-Jun;1(3):252-7.
Pharmacotherapy. 2011 Aug;31(8):742-7.
Arch Intern Med. 2000 Oct 9;160(18):2819-22.

Research:

Accuracy and impact of a penicillin allergy label on hospitalized patient outcomes

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Objectives

The objectives of this study were to:

1) Assess the accuracy of penicillin allergy documentation
2) Assess the impact a PCN allergy label has on patient outcomes

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Study Design

- Retrospective, case-control study
  - Matched PCN allergic (case) to non-PCN (control)
    - ICD-9 discharge diagnosis
    - Age group
    - Sex
- EHR System
  - Query all patients who received antibiotic
    - Patient medical record number & visit number
    - Patient age
    - Drug allergies
    - Antibiotics prescribed

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Study Design

Inclusion Criteria

- Age ≥ 18
- Received IV or PO antibiotic
- Admitted January 1, 2013 – March 31, 2013

Exclusion Criteria

- Ophthalmic and topical antibiotics
- Only received one antibiotic dose in ED
- Admitted to same day surgery or obstetrics units

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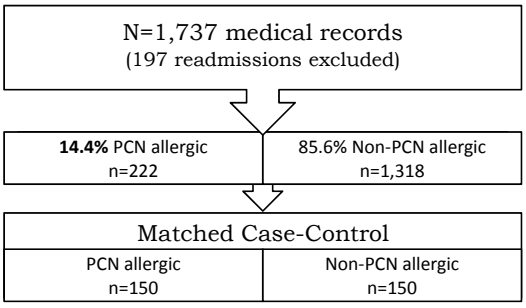
Study Design



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Study Design

Part one: 222 EHRs assessed for accuracy of PCN allergy documentation

Part two: PCN allergic vs. Non-PCN

Primary Endpoint: Hospital LOS

Secondary Endpoints: ICU LOS; MRSA; *C. difficile*

Statistical Analysis

- Dichotomous or binary variables were analyzed via chi-squared tests.
- Continuous variables were analyzed via two-tailed t-tests.
- A result was considered to be statistically significant if the p-value was < 0.05.

PCN Allergy Documentation

14.4% with Documented Penicillin Allergy (n=222)	
Allergic description – absent 60.3%	
Allergic description – present 39.2%	
"Anaphylaxis"	29 (13.0%)
"Skin rash" or "hives"	24 (10.8%)
"Itchiness" or "swelling"	15 (6.8%)
"Childhood allergy"	9 (4.1%)
"Nausea / vomiting" or "diarrhea"	6 (2.7%)
"Fast heart rate" or "I pass out"	4 (1.8%)
Adverse reaction – present 0.5%	
"Diarrhea"	1 (0.5%)
Severity of reaction – absent 48.6%	
Severity of reaction – present 51.4%	
Mild	41 (18.5%)
Intermediate	32 (14.4%)
Severe	41 (18.5%)

Patient Characteristics

	PCN Allergic n = 150	Non-PCN n = 150
Female, # (%)	136 (61.2%)	136 (61.2%)
Age, avg. (Range)	70.3 (21-103)	69.8 (20-103)

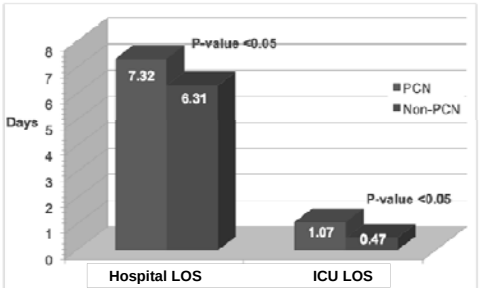
Matched Discharge Diagnosis

# Pts	ICD-9 Discharge Diagnosis	
30	590-595:	Pyelonephritis, Cystitis
24	480-486:	Pneumonia, NOS
21	038.9:	Septicemia, NOS
18	681-682:	Cellulitis/abscess
12	288.6:	Leukocytosis
12	490,493,496:	Bronchitis, Asthma, COPD
9	995.9:	SIRS, Sepsis
5	428.0:	Congestive heart failure
4	562,574:	Diverticulitis, cholelithiasis
15	Various:	Malignancy, OA, etc.

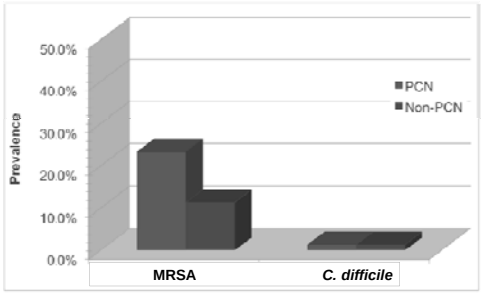
Antibiotic Exposure

	PCN Allergic n=150	Non-PCN n=150	P-value
Avg. # antibiotics (range)	1.99 (1-7)	2.15 (1-8)	0.48
Vancomycin, linezolid	**70**	**67**	**0.73**
Clindamycin	**15**	**4**	**<0.01**
Fluoroquinolone	**95**	**73**	**0.015**
Aztreonam	31	0	<0.0001
Penicillin	10	37	<0.0001
Cephalosporin	25	85	<0.0001
Carbapenem	10	14	0.39
Metronidazole	9	8	0.80
Azithromycin	11	16	0.31
Other (aminoglycosides, daptomycin, doxycycline, micafungin)	14	6	0.06

Primary & Secondary Endpoint



Secondary Endpoints



Primary & Secondary Endpoints

	PCN Allergic n=150	Non-PCN n=150	P-value
Hospital LOS, avg. (SD)	7.32 (5.67)	6.31 (4.26)	<0.05
ICU LOS, avg. (SD)	1.07 (3.23)	0.47 (1.69)	<0.05
# Patients admitted to ICU	26 (17.3%)	15 (10%)	0.06
MRSA prevalence	35 (23.3%)	17 (11.3%)	<0.01
C. difficile prevalence	2 (1.3%)	2 (1.3%)	No diff.

Limitations

- Small sample size, limited by match and time spent on data collection
- Confounding variables (comorbidities and severity of illness)

Study Conclusions

- Need for improving penicillin allergy documentation was identified.
- PCN allergy associated with longer hospital and ICU LOS
- PCN allergy associated with increase prevalence of MRSA but not *C. difficile*

Next Steps

- Guideline for the Use of Cephalosporins and Carbapenems in Patients with Reported Penicillin Allergy
  - PCN Allergy Questionnaire
  - Treatment Algorithm
- February 2015: Antimicrobial Stewardship Committee
- March 2015: P&T and the Medical Executive Committee
- March 2015: Nurse Counsel Meeting

Patient Case

March 10, 2015

A 72 yo **PCN allergic** male was admitted with infected **RLE calf wound**. The patient's wound began in November and since then he has been hospitalized two times in the past two months for surgical debridement & IV antibiotics. Pt was empirically started on:

Vancomycin
Aztreonam

Patient Case

March 13, 2015

Wound culture:

	PS AERUG		E COLI	
	M.I.C.	RX	M.I.C.	RX
AMIKACIN	<=16	S	<=16	S
AMP/SULBAC			>16/8	R
AZTREONAM	16	I		
CEFAZOLIN			<=8	S
CEFEPIME	8	S	<=4	S
CEFTAZIDIN	8	S	<=1	S
CEFTRIAXON			<=1	S
CEFUROXIME			<=4	S
GENTAMYCIN	<=4	S	>8	R
IMIPENEM	2	S	<=1	S
LEVOFLOXACIN	>4	R	>4	R
MEROPENEM	<=1	S	<=1	S
PIPERACILLIN/TAZ	>64	R	<=16	S
* TOBRAMYCIN	<=4	S		
TRIME/SULF			>2/38	R

Guideline for the Use of Cephalosporins and Carbapenems in Patients with PCN Allergy:
Questionnaire

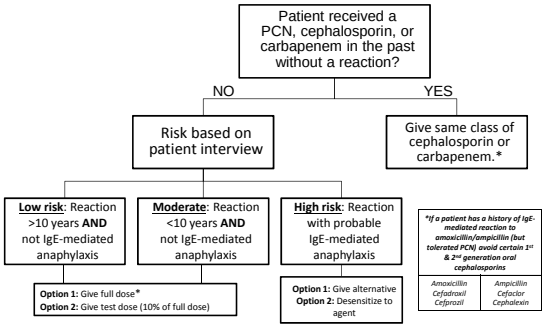
1. How long ago did you have the allergic reaction to PCN?
2. What allergic symptoms did you experience?
3. Has the patient received a PCN, cephalosporin, or carbapenem in the past without a reaction?
4. How was the PCN administered? (Oral vs. IV?)
5. How long after beginning PCN did your reaction occur? *(Immediate vs. delayed?)*
6. If a rash occurred, where was it located and what did it look like? *(Rash on face/mouth, blistering or exfoliative?)*
7. Did you take any other medications at the same time?
8. Did you receive treatment for the PCN allergic reaction?
9. What happened when the PCN was stopped?
10. Have you ever received a PCN skin test?

Patient Case

Patient interview:

- Occurred in college (> 40 years ago)
- Diffuse rash located on body
- Unsure of exposure to amoxicillin, cephalexin, or other B-lactam antibiotics
- Denies previous PCN skin test

Guideline for the Use of Cephalosporins and Carbapenems in Patients with PCN Allergy:
Treatment Algorithm



Self-Assessment Question #1

A 29 yo female patient with history of rash from amoxicillin returns to the ED with UTI after failing treatment with nitrofurantoin. The physician would like to discharge the patient and asks for your recommendation.

Urine cx - *E. coli*
- (R) Ciprofloxacin
- (I) TMP-SMX
- (S) Ampicillin
- (S) Cefazolin

Which antibiotic would be the best option for this patient?

a. Nitrofurantoin PO
b. Cefpodoxime PO
c. Levofloxacin IV
d. Imipenem/cilastatin IV

Self-Assessment Question #2

What is the risk of cross-reactivity between penicillin and third & fourth generation cephalosporins?

a. >10 %
b. 3 – 4 %
c. 1 – 2 %
d. < 1 %

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Questions?

Medication errors in hospitalized patients with HIV: Impact of prospective review by an on-call pharmacy resident

Katherine V. Zych, PharmD
PGY2 Drug Information Resident
University of Illinois- College of Pharmacy
Chicago, IL

Speaker has no conflicts of interest to dislose

Background

- Antiretroviral therapy (ART) has transformed HIV into a chronic, manageable condition
- 26 antiretroviral agents belonging to six different drug classes
- Maintaining a high level of adherence to ART is critical for virologic suppression and preservation of the immune system
  - A medication adherence rate of 95% is recommended

Ann Pharmacother.2014;48(8):998-1010
DHHS guidelines. 2014
J Antimicrob Chemother.2005;55:413-416

ART Error Rates

- Hospitalized patients with HIV: **5.8% to 86%**
  - Most errors occur **on admission**
- Incorrect inpatient ART therapy may be unintentionally continued at discharge
- Outpatient medication lists within the electronic medical record may not accurately reflect a patient's current ART regimen
  - **Accurate medication reconciliation on admission is critical in preventing medication errors** as patients move through care transitions

Ann Pharmacother.2014;48(8):998-1010

Review of Literature

Source No. pts	Description of study	Duration	No. pts with medication errors in the control group
Eginger et al, 2013 N= 86	Pharmacy resident reviewed admission orders of HIV-positive patients and intervened on ART and opportunistic infection (OI) prophylaxis prescribing errors	6 months	47/86 (55%)
Daniels et al, 2012 N = 68/78	Evaluation of rate of ART and OI prophylaxis errors, pre and post implementation of targeted intervention and daily review by clinical pharmacist trained in HIV care (admission to discharge)	4 months	49/68 (72%)
Corrigan et al, 2010 N= 21/20	A clinical ID pharmacist assessed medication errors 48 hours after admission, before and after a pharmacist-led medication reconciliation process	6 months	11/21 (52.4%)

Purpose

- To evaluate the impact of prospective medication reconciliation by an on-call pharmacy resident (ROC) on ART medication errors

Study Setting

- Rush University Medical Center (Chicago, IL)
- 677 beds
- An average of 40 HIV + patients admitted each month
- Most ART agents on formulary, with policies allowing patients to use their own supply if needed

RUMC Pharmacy ROC Program

Residents

- 8 PGY1s
- 6 PGY2s
  - 3 Critical Care
  - 1 Infectious Disease
  - 1 Heme/Onc
  - 1 Transplant

Responsibilities

- 24-hour code blue & rapid response coverage
- Overnight acute stroke/tPA evaluation pager coverage
- Overnight approval of restricted anti-infective agents
- Overnight kinetics follow-up and evaluation of all new orders for aminoglycosides and vancomycin for ICU and Heme/Onc patients
- Weekend INR follow-up for ortho patients

Current Practice

- Evaluation of ART orders is done by the pharmacist assigned to verify orders for that unit
- Medication histories are performed as time permits by both pharmacists and pharmacy students
- If discrepancies are identified, the pharmacist covering the unit will reach out to the primary medical team via phone/page or in person to discuss recommendations

Limitations and Consequences

- Limitations
  - Not all patients have a medication history obtained by a pharmacist/ pharmacy student
  - Hospitalized patients with HIV may not be seen by an infectious disease specialist
- Consequences
  - Incorrect ART regimen continued throughout the patients stay→ Incorrect discharge prescriptions
    - Increased viral load→ Increased risk of transmission
    - Decreased CD4 cell count→ Development of OIs
    - Development of resistance to drug(s)/drug class(s)
      - Limitation of future treatment options
    - Decreased overall health and survival

Self Assessment - Question 1

Which of the following events may occur if an incomplete ART regimen is administered to a patient during their hospital stay?

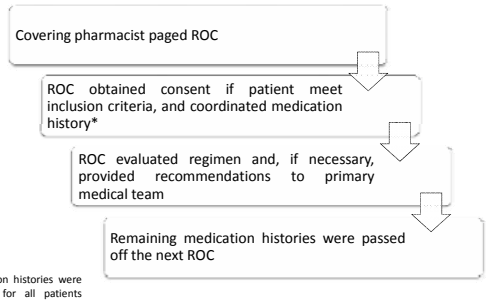
a) Increase in CD4 cell count
b) Increase in viral load
c) Prevention of opportunistic infections
d) Decreased development of resistance

Methods

- Study design
  - Two phase study

Phase 1: Pre-intervention phase (09/10/2014 – 11/30/2014)	Phase 2: Intervention phase (12/1/2014 – 02/28/2015)
• Retrospective cohort study in order to establish the incidence of ART and OI prophylaxis medication errors prior to implementation of ROC participation in ART-focused medication reconciliation	• The pharmacy ROC coordinates completion of a medication history with subsequent medication reconciliation for ART and OI prophylaxis agents ordered for hospitalized patients with HIV

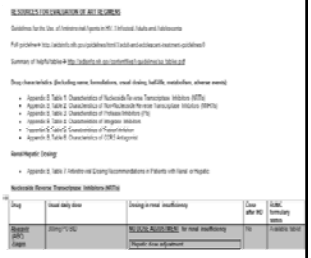
Intervention Phase



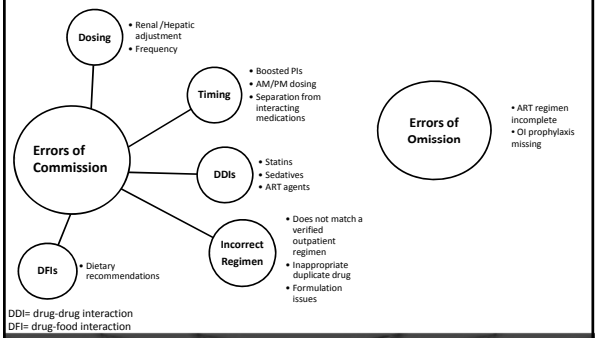
* Medication histories were preformed for all patients regardless of consent status

Training

- Live teaching session
- Orientation to DHHS guidelines and other resources
- Distribution of materials



Regimen Evaluation



DDI= drug-drug interaction
DFI= drug-food interaction

Study Population

- Hospitalized adult patients with HIV who have orders for ART with or without OI prophylaxis agents

Inclusion	• Adults ≥ 18 years of age • Patients administering ART for the treatment of HIV/AIDS prior to admission
Exclusion	• Patients seen in the emergency department but not admitted • Unable to take oral meds • Pregnant or breastfeeding • Admitted for a psychiatric related diagnosis • No consent provided (interventional phase)

Study Endpoints

- Primary: Proportion of resolved ART medication errors in hospitalized patients with HIV prior to and after implementation of prospective review by a pharmacy ROC
- Secondary: Specific types of ART and OI prophylaxis errors and time to error correction

Statistics

- Statistical analysis performed using SPSS statistical software (version 22)
- Continuous data
  - Normally distributed: Student's t-test
  - Non-normally distributed: Mann-Whitney U
- Nominal and ordinal data
  - Fisher's exact test
  - Chi-square

Baseline Characteristics

Demographics	Preintervention phase (n=40)	Intervention phase (n=40)
Age, years, mean(SD)	47.6 (13.5)	51.0 (10.0)
Sex, male, n(%)	25 (62.5)	32 (80.0)
Race, n(%)		
African American	33 (82.5)	27 (67.5)
Caucasian	4 (10.0)	11 (27.5)
Hispanic/Latino	3 (7.5)	2 (5.0)
Estimated CrCl ml/min, mean (SD)	76.4 (39.9)	74.7 (35.1)
Hemodialysis, n(%)	5 (12.5)	3 (7.5)
CD4+ cell counts ,cells/mm³, mean(SD)	347 (273)	438 (333)
CD4+ cell %, mean(SD)	23.9 (15.0)	27.7 (16.0)
Mean (SD) HIV-1 RNA conc, log10 copies/mL	2.44 (1.5)	2.67 (1.5)
No. (%) patients with undetectable HIV RNA conc.	26 (65.0)	23 (57.5)
Length of Stay, days, mean(SD)	5.9 (5.1)	5.6 (4.0)
Hospital location, n(%)		
General medicine floor	26 (65.0)	24 (60.0)
Surgery	5 (12.5)	3 (7.5)
Intensive Care Unit	8 (20.0)	9 (22.5)
Hematology/oncology	1 (2.5)	4 (10.0)
ID consult with in 48 hours of admission, n(%)	13 (32.5)	14 (35.0)

Results: Error Resolution

ART Error Evaluation				
	Pre-intervention (n=40)	Intervention (n=40)	Mean difference, % (95% CI)	p-value
Patients with ART error(s), n (%)	18 (45.0)	20 (50.0)	n/a	0.654
Total number of ART errors	30	40	n/a	0.348
ART proportion resolved errors, %	46.7	82.5	-53.4 (-79.77 to -26.96)	<0.001
OI Prophylaxis Error Evaluation				
Patients with OI error(s), n (%)	8 (20.0)	8 (20.0)	n/a	1.000
Total number of OI prophylaxis errors	11	10	n/a	0.506
OI ppx proportion resolved errors, %	54.5	70.0	12.5 (-51.75 to 26.75)	0.506

Results: ART Error Type

	Preintervention (n=40)	Intervention (n=40)	Total (n=80)	p-value
Type of ART error, n (%)				
Omitted drug	6 (15.0)	6 (15.0)	12 (16.3)	0.625
Regimen does not match outpatient therapy	10 (25.0)	8 (20.0)	18 (22.5)	0.592
Dosing error	3 (7.5)	6 (15.0)	9 (11.3)	0.481
Renal dosing error	0 (0.0)	4 (10.0)	4 (5.0)	0.116
Hepatic dosing error	1(2.5)	0 (0.0)	1(1.3)	1.000
Frequency error	6 (15.0)	4 (10.0)	10 (12.5)	0.499
Timing error	9 (22.5)	8 (20.0)	17 (21.3)	0.785
Duplication error	1 (2.5)	0 (0.0)	1 (1.3)	1.000
Drug-drug Interaction	4 (10.0)	8 (20.0)	12 (15.0)	0.210
Drug-food interaction	0 (0.0)	0 (0.0)	0 (0.0)	n/a
Formulation Error	0 (0.0)	1 (2.5)	1 (1.3)	1.000

Results: OI Prophylaxis Error Type

	Pre-intervention (n=40)	Intervention (n=40)	Total (n=80)	p-value
Type of OI prophylaxis error, n (%)				
Omitted drug	3 (7.5)	2 (5.0)	5 (6.3)	0.473
Dosing error	4 (10.0)	7 (17.5)	11 (13.8)	0.505
Renal dosing error	0 (0.0)	0 (0.0)	0 (0.0)	n/a
Hepatic dosing error	0 (0.0)	0 (0.0)	0 (0.0)	n/a
Frequency error	2 (5.0)	5 (12.5)	7 (8.8)	0.432
Duplication error	1 (2.5)	1 (2.5)	2 (2.5)	1.000
Drug-drug interaction	0 (0.0)	0 (0.0)	0 (0.0)	n/a
Drug-food interaction	0 (0.0)	0 (0.0)	0 (0.0)	n/a
Formulation Error	0 (0.0)	0 (0.0)	0 (0.0)	n/a

Results: Time to Resolution

ART regimen	Preintervention (n*=18)	Intervention (n*=20)	P-value
Time to resolution of errors, n (%)			
<24 hours	3 (16.7)	10 (50.0)	0.031
< 48	6 (33.3)	17 (85.0)	0.001
Never	10 (55.6)	2 (10.0)	0.003

OI regimen	Preintervention (n*=16)	Intervention (n*=9)	P-value
Time to resolution of errors, n (%)			
<24 hours	12 (75.0)	5 (55.6)	0.394
< 48	12 (75.0)	6 (66.7)	0.673
Never	1 (6.3)	2 (22.2)	0.530

*n= patients with ≥ 1 medication error

Study Limitations

- Single center
- Patients may have been missed due to pharmacist not notifying the ROC
- Errors of omission may have been underestimated
- Time to evaluate regimens was not captured
- Possible inconsistencies in the knowledge, skills and interventions of the residents
- Differences in errors based on regimen type were not evaluated
- Pre intervention group was a retrospective cohort study

Conclusion

- ART prescriber errors are common and a pharmacist focused on managing these errors can have a major impact on both decreasing error rates and time to resolution of errors
- ROC participation in ART focused prospective medication reconciliation significantly increased the proportion of resolved ART errors in the interventional group vs. the pre-intervention group [33/40 (82.5%) vs. 14/33 (46.7%), respectively]
- A significantly greater proportion of patients with ART errors had a resolution of errors within 48 hours in the interventional group vs. the pre-intervention group [17/20 (85.0%) vs. 6/18 (33.3%), respectively]
- Implementation into a pharmacy residency program provides benefit to patients, providers, and residents

Next Steps

- Continuation of medication histories targeted towards HIV patients admitted on ART therapy
  - Workflow and ROC involvement to be determined
- Changes to electronic physician order entry to minimize common preventable errors
  - Timing of PIs to coincide with ritonavir
  - Darunavir 600mg dosing to default to BID dosing
  - Drug interaction alert to fire when rilpivirine ordered with H2RAs or PPIs
- Incorporation of ART and OI prophylaxis dosing tables into an anti-infective stewardship handbook that is currently in progress

Self Assessment - Question 2

During which of the following time points of a patients hospital stay do most ART medication errors occur?

a) Admission
b) Unit transfer
c) Room change
d) Discharge

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Lana Wong, PharmD	

Medication errors in hospitalized patients with HIV: Impact of prospective review by an on-call pharmacy resident

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PGY2 Drug Information Resident
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Pearls for developing structured abstracts

How to get your abstracts accepted and published

Michelle L. Bryson, PharmD, BCPS
Clinical Assistant Professor
UIC Drug Information Group, Chicago, IL

The speaker has no conflicts of interest to disclose.

WHY ARE WE HERE?

Acceptance rates & errors

- ASHP Midyear Clinical Meeting
  - 16% rejected in 2015
- 33% of abstracts in major pharmacy journals contained inaccuracies or omissions
- Major international meetings
  - <30% chance of acceptance

Alexandrov AV et al. Cerebrovasc Dis. 2007;23:256-259
Blair DA et al. J Med Lib Assoc. 2014;102(2):110-114.

How does this happen?

- Writing a good abstract takes TIME, attention to detail, big-picture understanding, and multiple edits

Objectives

- Describe the process of developing abstracts for professional meetings and manuscript submissions.
- List the components of a structured abstract.
- Provide a list of Do's and Don'ts when writing abstracts.
- Compose feedback for a submitted abstract.

TERMINOLOGY

What is an abstract?

- Summarizes the main points of an article
- Condensed version of a full scientific paper
- Directs readers to articles that will be of clinical or research interest
- Intermediate reporting of unfinished project or manuscript

AMA Manual of Style: A Guide for Authors and Editors. 10th ed
Pierson DJ. Respir Care. 2004;49(10):1206-1212.

Purpose of an abstract

- Address, in an abbreviated format:
  - What was done and why
  - What was found
  - What the implications are

Pierson DJ. Respir Care. 2004;49(10):1206-1212.
Taboulet P. Eur J Emerg Med. 2000;7(1):67-72.

What is a *structured* abstract?

- An abstract that uses predefined headings
- Many journals have 250 to 300 word limit

AMA Manual of Style: A Guide for Authors and Editors. 10th ed

Example – structured abstract

Treatment of acute myocardial infarction at United States academic hospitals. Bradley G. Phillips, Pharm.D., Josephine M. Yim, Pharm.D., Edward J. Brown, Jr., M.D., Neville Bittar, M.D., Timothy J. Hoon, Pharm.D., Catherine Celestin, Pharm.D., Peter H. Vlasses, Pharm.D., FCCP, Jerry L. Bauman, Pharm.D., FCCP; University of Illinois at Chicago; University Hospital Consortium, Oak Brook, IL; Bronx-Lebanon Medical Center, Bronx, NY; University of Wisconsin; Bristol-Myers Squibb Company, Princeton, NJ.

Purpose: This study documented drug therapy received by patients surviving acute myocardial infarction (AMI) at U.S. academic hospitals in order to 1) compare prescribed drug therapy to established guidelines defined in the medical literature, and 2) evaluate evolving prescribing trends in pharmacologic management.

Methods: Medical records of 500 survivors of AMI admitted between April 1 and October 31, 1993 to 12 academic centers in the United States were reviewed. Patients' medical history, in-hospital course, and specific drug management prior to admission, during the first 72 hours post AMI, and at hospital discharge, were documented.

Results: Thrombolytic therapy was prescribed in 29% of 500 patients studied and included: intravenous streptokinase (49%), tissue-type plasminogen activator (43%), acylated plasminogen-streptokinase activator complex (5%), and intracoronary urokinase (3%). A greater proportion of eligible patients received ß-blocker therapy than calcium channel antagonist therapy within the initial 72 hours (61% vs 40%, p<0.005) and at discharge (51% vs 35%, p<0.005). Women were less likely to receive thrombolytic therapy (OR=0.61; CI 0.54, 0.69) or β-blocker therapy within the first 72 hours (OR=0.61; CI 0.55, 0.67) and at hospital discharge (OR=0.53; CI 0.48, 0.58).

Conclusions: Streptokinase was the predominant thrombolytic agent used at academic hospitals studied during the period of data collection. Use of acute and chronic ß-blocker therapy has now surpassed that of calcium channel antagonist therapy in this setting. These changes may be due to the impact of large clinical trials. With few exceptions, the majority of surviving patients received appropriate pharmacologic therapies during the initial 72 hours and at hospital discharge.

Meeting vs Manuscript

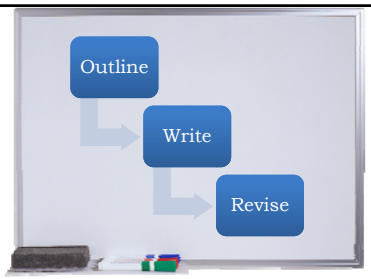
- Format may differ
- Meeting abstracts:
  - are NOT peer-reviewed at same caliber as scientific paper
  - are NOT publications
  - usually have more liberal requirements

Pierson DJ. Respir Care. 2004;49(10):1206-1212.

Advantages of writing a meeting abstract

- For the author or investigator, it can help clarify the project
- Subjects the work to peer review
- Speeds up the spread of knowledge and practice

Pierson DJ. Respir Care. 2004;49(10):1206-1212.
Taboulet P. Eur J Emerg Med. 2000;7(1):67-72.



Objective 1

DESCRIBE THE PROCESS OF DEVELOPING ABSTRACTS FOR PROFESSIONAL MEETINGS AND MANUSCRIPT SUBMISSIONS.

Step 1. Outline the project

- Why did you decide to do this project? What prompted this question?
- What did you do?
- What did you find/hope to find?
- What do you think about that/what does it mean?

Pierson DJ. Respir Care. 2004;49(10):1206-1212.
Taboulet P. Eur J Emerg Med. 2000;7(1):67-72.

Step 2. Pick a venue

- What society would be most interested in what I did and why?
- Does not have to be a pharmacy organization
  - Medical
  - Nursing
  - Dentistry
  - Informatics

Step 3. Read the requirements

- Automatic elimination from consideration if you do not follow the requirements!
- Must choose the correct category

Examples

- https://accp.confex.com/accp/2015am/cfp.cgi
- http://www.accp.com/meetings/abstractguide.aspx
- https://us.sagepub.com/en-us/nam/annals-of-pharmacotherapy/journal202238#submission-guidelines

Step 4. Read examples from that journal/society

- Further confirm that your project would fit in with this society's mission
- Look for trends to help you write your own abstract
- CAUTION: Do not plagiarize!

Step 5. Write the draft

- Use your outline!
- Follow a *structured abstract* format

Objective 2

LIST THE COMPONENTS OF A *STRUCTURED ABSTRACT*.

Don't underestimate the TITLE

- Convey as much as possible about the study
  - Scope
  - Design
  - Goal
- No jargon or acronyms
- 10 to 12 words
- No results, biased language

Pierson DJ. Respir Care. 2004;49(10):1206-1212.
Taboulet P. Eur J Emerg Med. 2000;7(1):67-72.

Set the stage with the INTRODUCTION/BACKGROUND

- 1 or 2 sentences
  - What is known
  - What is unknown
  - Why did you do this study?
- End with the hypothesis or objective
  - Helps to focus you and your audience as to what the essence of the abstract is

Pierson DJ. Respir Care. 2004;49(10):1206-1212.
Taboulet P. Eur J Emerg Med. 2000;7(1):67-72.

Introduction/Background

- Common mistakes
  - Absence of a question to be answered
  - Multiple questions to be answered
  - Pseudo-questions
    - "We evaluated the effect of IV acetaminophen in orthopedic surgery."
      - Effect on post-operative opioid use?
      - Effect on patient satisfaction?
      - Effect on ability to rehabilitate?

Pierson DJ. Respir Care. 2004;49(10):1206-1212.
Taboulet P. Eur J Emerg Med. 2000;7(1):67-72.

Tell the METHODS to your mother

- Answer this: "What did you do?"
  - Who, What, When, Where, How?
- Most common reason for rejection of submitted manuscripts
- Must be concise

Byrne DW. Publishing your medical research paper. What they don't teach in medical school. Baltimore: Lippincott Williams & Wilkins; 1998.

Make your RESULTS pop

- Results start with the baseline characteristics
- Data only; no commentary or discussion
- Avoid trying to make a nonsignificant difference that is "approaching significance" more important than it really is

Pierson DJ. Respir Care. 2004;49(10):1206-1212.
Taboulet P. Eur J Emerg Med. 2000;7(1):67-72.

Wrap it up with a thoughtful CONCLUSION

- State why the results are important
- Give your interpretation of the results
- Address applicability to other settings
- Do not overstate the conclusion

Pierson DJ. Respir Care. 2004;49(10):1206-1212.
Taboulet P. Eur J Emerg Med. 2000;7(1):67-72.

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Step 1. Outline the project

- Why did you decide to do this project? What prompted this question?
- What did you do?
- What did you find/hope to find?
- What do you think about that/what does it mean?

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Step 6. Revise the draft

- After a short break from looking at or thinking about the project, start the first revisions

Rereading reveals rubbish and redundance.
~ Duane Alan Hahn

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Step 6. Revise the draft

Copy-editing
- Focus on grammar, spelling, punctuation
- Line-by-line

Substantive editing
- Focus on content and organization
- Overall concept and intended use

http://www.jeanweber.com/newsite/?page_id=28

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Step 7. Ask a colleague to look

- Outside perspective can help catch inconsistencies, questionable methodology, additional questions to consider
- Someone familiar with subject matter
- Keep it professional

Pierson DJ. Respir Care. 2004;49(10):1206-1212.
Taboulet P. Eur J Emerg Med. 2000;7(1):67-72.

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Step 8. Revise and edit

The time to begin an article is when you have finished it to your satisfaction. By that time you begin to clearly and logically perceive what it is you really want to say.

~ Mark Twain

Step 9. [illegible]d the requ[illegible]nts

REMINDER:

Automatic eliminat[illegible] from consideration if you [illegible] not follow the requirements!

Make sure your abstract follows the requirements; make changes if needed

Step 10. Revise and edit

"So the writer who breeds **more words than he needs**, is making a **chore** for the reader who reads."

— Dr. Seuss

Step 10. Revise and edit

Copy-editing
- Focus on grammar, spelling, punctuation
- Line-by-line

Substantive editing
- Focus on content and organization
- Overall concept and intended use

http://www.jeanweber.com/newsite/?page_id=28

Objective 3

PROVIDE A LIST OF DO'S AND DON'TS WHEN WRITING ABSTRACTS.

Yes, do that!

- Seek a mentor if you have limited or no experience writing abstracts
- Edit and revise frequently
- Use simple language and concise sentence structure
- Give yourself ample time to complete several rounds of revisions
- Look at examples from the specific society or journal you are submitting to
- Ask someone to proofread (copy-edit)
- Respect the formatting requirements

No, don't do that!

- Try to answer multiple research questions
- Use biased language
- Use brand names, manufacturer names, healthcare system names, etc
- State that a result "approached significance"
- Make conclusions with results that were not presented
- Use too much passive voice
- Plagiarize

Objective 4

COMPOSE FEEDBACK FOR A SUBMITTED ABSTRACT.

Docendo discimus

The best way to learn is to teach

The best way to learn how to write/edit an abstract is to review one!

ASHP Midyear Clinical Meeting 2015

POSTER REVIEWER COMMENTS

http://www.ashp.org/menu/events/getinvolved

Title

- "Title leads one to think that the abstract will show improved patient encounters and data to support the model, but only data presented shows that pharmacists don't have prior empathy training."

Introduction

- "Not enough information was provided concerning the project. How is this project important? Why do other hospital administrators need to know this information?"

Methods

- "Methods did not mention that root cause analysis would be conducted. The statement "Root causes analysis identified causative factors which include the ward surface area, an increase in drug storage locations, patient turnover and amendments to outpatient clinic locations" is a result, not a conclusion. Also, the apparent design and analysis did not address a clear, discernible research question. Many details of the number of observations and statistical approach were absent."
- "Other interesting things to possibly include: Was the dose of either class related to fall risk? Were the disease states being managed related to the fall risk?"

Results

- "To strengthen the results section, consider using number and percent for all of the results."
- "The results do not reflect all of the 'tasks' to be implemented outlined in the methods section"
- "Results were presented in the conclusion section"

Conclusion

- "The conclusion does not reflect or support the information provided in this description report. Rather, it is citing other research and studies."
- "I don't think existing literature should be summarized in the conclusion or that this describes an innovative role or service in pharmacy practice."

Overall

- "This topic is relevant and timely; however, there isn't enough info in the abstract to evaluate. Has the study been completed? There is no data.
- The results and conclusions were not specific. The primary objective was to show an increase in patient safety and decrease in 30-day readmissions but the results of this were not discussed. No values were given for pre and post clinic set-up. The conclusion stated that the addition of the clinic has decreased readmissions and has promoted patient outcomes, but I don't know how this is concluded when no data was provided.
- Abstract was very confusing to me. Unsure of what patients they were looking at (specific disease state/age/number of meds). Didn't have a clear number of patients and how many patients benefited.
- Misleading title. Poorly defined objective and results."

Grammar

- "The abstract was extremely difficult to understand due to numerous grammar and syntax issues as well as unfamiliar terminology."
- "The abstract is free of spelling or grammar errors and flowed nicely."
- "Due to several spelling and grammar mistakes, I would suggest additional editing and review before re-submission."
- "Lastly, there are minor spelling and grammar errors that should be edited in review."

Don't be a meanie.

- "This is old data from 2013 on an old tired subject that has been around for many many years"
- "The beginning of this sentence ("Data are limited…") is a contradiction to the sentence below "…weight heparin have been studied…". Which is it? Has it been studied or not?"
- "Abstract was poorly written with significant content missing. There are some rules that the writer needs to follow when writing abstracts for ASHP. Capital letters need to be removed from the title. Abbreviations need to be spelled out then used (C.difficile & FDA)."

Don't be a meanie.

- "Although mildly interesting, this article does not seem to be referring to anything about pharmacotherapy."
- "The discussion of the Friedman et al. article as presented in this manuscript is disingenuous. This trial had two arms, but the trial design did not intend for the arms to be compared to each other. The authors need to re-write this paragraph to present this information accurately to the audience"
- "Go back and look at your sentences. Many of them are too long. Break them down."

Maintain a professional tone

- Avoid condescending or passive aggressive statements
- Resist the urge to let the author know how you feel about their project
- Resist the urge to make the author feel bad for mistakes or omissions
- Use appropriate grammar
- Remember that everyone is trying, and investigators have voluntarily subjected their work to scrutiny

Be the reviewer!

- Provide comments for the following abstract
  - ASHP Summer Meeting
  - Informatics/Automation category
  - 500 word count maximum

Resources

- Alexandrov AV, Hennerici MG. Writing good abstracts. *Cerebrovasc Dis.* 2007;23:256-259
- AMA Manual of Style: A Guide for Authors and Editors. 10th ed.
- Blair DA, Hughes PJ, Woolley TW. Pharmacy journal abstracts published in PubMed that abide by the CONsolidated Standards Of Reporting Trials (CONSORT) guidelines. *J Med Lib Assoc.* 2014;102(2):110-114.
- Guide to writing an abstract. American College of Clinical Pharmacy website. http://www.accp.com/meetings/abstractguide.aspx.
- Pierson DJ. How to write an abstract that will be accepted for presentation at a national meeting. *Respir Care.* 2004;49(10):1206-1212.
- Taboulet P. Advice on writing an abstract for a scientific meeting and on the evaluation of abstracts by selection committees. *Eur J Emerg Med.* 2000;7(1):67-72.

Title: Design and implementation of an algorithm that improves detection of LA/SA medication errors: a pilot study

Purpose: Look-alike/sound-alike (LA/SA) medications are associated with many medication errors and ADRs. The safe use of LA/SA medications is a standard required by the Joint Commission for accreditation. Despite the knowledge that LA/SA medications are problematic, interventions to eradicate these errors have not been identified. The design and implementation of an algorithm to identify likely LA/SA errors in a database of medication orders and billing claims at an academic medical center was conducted as a proof of concept pilot study.

Methods: A database of inpatient and ambulatory medication orders and clinician billing claims at UIHHSS over 1 year (1/1/2011 to 12/31/2011) was produced. This dataset was interrogated for likely LA/SA errors using an algorithm based on drug name similarity, the sequence of ordering and cancellation of medications, patient identifiers, and diagnostic info from clinician billing claims. The results of detection algorithm yielded a set of patient charts in which a LA/SA error was thought to be likely. A convenience sample of charts was reviewed by experienced clinicians (PharmD or attending physician) to determine if the drug identified from the detection algorithm was a true error.

Results: Of the 84 charts reviewed, 5 were true errors, 4 were questionable errors and 75 were not errors. This yielded a Positive Predictive Value (PPV) of 7%. The drug pairs (ordered drug/intended drug) associated with the 5 definite errors were aminophylline/amitriptyline, caffeine/codeine, levocarnitine/levothyroxine, penicillamine/penicillin, and pyridostigmine/pyridoxine. First-year medical residents were the most likely to be involved in the true and questionable errors identified in this study.

Conclusion: This pilot study showed that an algorithm based on drug name similarity, diagnosis, and drug order sequence was able to find LA/SA medication errors. The PPV was low in this initial analysis, but continued work should be able to raise the PPV. Because the purpose of the algorithm is to find errors, the PPV does not need to be very high to still have utility for patient safety. The long-term goal in this work is to develop a learning algorithm which could be used both in real-time with computerized order entry (CPOE) and retrospectively to identify and/or prevent LA/SA medication errors.

(Word count: 366)

Pearls for Developing Structured Abstracts
Michelle Bryson, PharmD

1. What section of an abstract, when written poorly, is the most common reason for rejection?
   a. Background
   b. Methods
   c. Results
   d. Conclusion

2. What section of an abstract should contain the following sentence?
Over the 20-month study period, 66 patients on extracorporeal membrane oxygenation were initiated on the pharmacy-managed heparin protocol for anticoagulation.
   a. Background
   b. Methods
   c. Results
   d. Conclusion

3. Which of the following phrases should be avoided in an abstract?
   a. The difference between intraocular pressure approached significance, with a decrease of 4 in group A vs 2 in group B.
   b. Palatability of fexofenadine as measured by a visual analog scale was significantly improved with ice cream compared to fexofenadine alone (1.8 vs 2.5; $p<0.001$)
   c. Title: Presence of a clinical pharmacist in the rehabilitation unit improves documented clinical activities
   d. Title: Comparison of length of stay after total knee replacement surgery in patients who received liposomal bupivacaine vs bupivacaine hydrochloride: a retrospective chart review

4. Select the MOST appropriate comment to provide to the author of a submitted abstract.
   a. This has already been done tens of times and I don't see why you are submitting it for this meeting.
   b. Is it not true that people who have had recurrent C. difficile often end up needing pulsed vancomycin? Or did I miss something?
   c. As written, it was unclear how many patients were evaluated for the main endpoint. Consider re-wording the paragraph to have this number as part of the first sentence.
   d. There were majr spelling and grammar issues whicn definitely needs to be addressed, before this cna be presented as poster

5. Which of the following is NOT an advantage of writing an abstract?
   a. Writing an abstract helps the author or investigator to clarify their project methods
   b. Submitting an abstract for consideration as a poster subjects the abstract to peer review
   c. Accepted abstracts for a meeting are considered publications under the authors' names.
   d. Abstracts can help readers identify if the article is relevant to their clinical interest or need

Translating the Evidence: From Publication to Practice

Lara K. Ellinger, PharmD, BCPS

September 12, 2015

I have no relevant financial disclosures.

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Objectives

1. Compare the benefits and risks of 12 months and 30 months of dual antiplatelet therapy after placement of drug-eluting stents.
2. Review the findings of the HEAT-PPCI trial on heparin versus bivalirudin in percutaneous coronary intervention
3. Describe what effect vitamin D has on fall prevention in elderly women
4. List limitations of the randomized controlled trials reviewed

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Duration of DAPT?

12 OR 30 MONTHS OF DUAL ANTIPLATELET THERAPY AFTER DRUG-ELUTING STENTS

N Engl J Med. 2014;371(23):2155-2166.

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Background

- IHD affects 13 million in the U.S.
- PCI most common revascularization procedure
  - Performed twice as often as CABG
- PCI indicated when
  - IHD unstable
  - Persistent symptoms
  - Severe ischemia or high-risk anatomy
  - Diabetes
  - Impaired LV function
- Efficacy: improves outcomes
  - In UA (>95%)
  - When used early in MI ± cardiogenic shock

Harrison's Principles of Internal Medicine

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Background

- Stents
  - BMS
    - Restenosis in 20% within 6 months
  - DES
    - Restenosis reduced to <10%
- Stent complication: thrombosis
  - Greatest risk within first 30 days
  - Similar between BMS and DES?
  - Everolimus may be safest (reduces MI and stent thrombosis compared to BMS)
  - Everolimus, sirolimus, and zotarolimus most efficacious

Circulation. 2012;125(23):2873-2891.
Harrison's Principles of Internal Medicine

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Background

- DAPT
  - Aspirin + P2Y12 receptor inhibitor
- DAPT benefits
  - Decreases stent thrombosis
  - More intensive antiplatelet therapy helps further reduce thrombosis during time when metal stent is not endothelialized
  - Decreases MI

JAMA. 2005;293(17):2126.

Guidelines

- ACCF/AHA/SCAI 2011 and CHEST 2012
  - For ACS and PCI with stents, 12 months of DAPT:
    - Low-dose aspirin (75 mg to 162 mg)
      and
    - Ticagrelor 90 mg bid
      or
    - Clopidogrel 75 mg daily
      or
    - Prasugrel 10 mg daily
  - Continue low dose aspirin plus P2Y12 inhibitor for 12 months for all stents
  - Continue single antiplatelet therapy indefinitely

Durations vary depending on
- Indication
- Stent type
- Emergent/elective

J Am Coll Cardiol. 2011;58(24):e44-122.
Chest. 2012;141(2 Suppl):e637S-668S.

DAPT Duration Controversy

- Longer duration (>12 months)
  - Benefit
    - Further decrease in risk for events
  - Increased risk for bleeding?
- Evidence
  - Multiple studies on DAPT duration that were not adequately powered
  - ISAR-SAFE
    - 6 months NI to 12 months of DAPT in drug eluting stents

Eur Heart J. 2015;36(20):1252-63.

12 or 30 Months of DAPT?

- Study objective
  - Determine the safety and efficacy of continuing DAPT beyond 1 year in patients with coronary stents
- Methods
  - Multicenter, randomized, placebo-controlled trial
  - Open-label from stent placement through month 12, then randomization to DAPT or aspirin + placebo

12 or 30 Months of DAPT?

Inclusion
- Adults undergoing PCI with stent placement
- Either BMS or DES
- "12 month clear"

Exclusion

At enrollment
- Concomitant anticoagulation
- Planned surgery

At randomization
- Death
- MI or repeat PCI at >6 weeks
- CABG
- Stroke
- Major bleed

Interventions				
Months	Aspirin Dose	Thienopyridine Dose		Placebo
		Clopidogrel	Prasugrel	
0 to 6	75 mg to 325 mg	Loading: 300 to 600 mg Maintenance: 75 mg daily	Loading: 60 mg Maintenance: 10 mg daily	NA
6 to 12	75 mg to 162 mg	75 mg daily	10 mg daily	NA
12 months: Randomization to T or P				
12 to 30	75 mg to 162 mg	75 mg daily	10 mg daily	✓

12 or 30 Months of DAPT?

- Follow-up
  - 33 months post-procedure
  - 6, 12, 15, 24, 30, and 33 months post-PCI
  - Months 30 to 33 were "off-treatment"
  - Events adjudicated by independent committee

Primary Endpoints

Efficacy

- MACCE
  - Death
  - MI
  - Stroke
- Stent thrombosis

Safety

- Severe/moderate bleeding (GUSTO)
- BARC bleeding (secondary)

Bleeding Classification

GUSTO

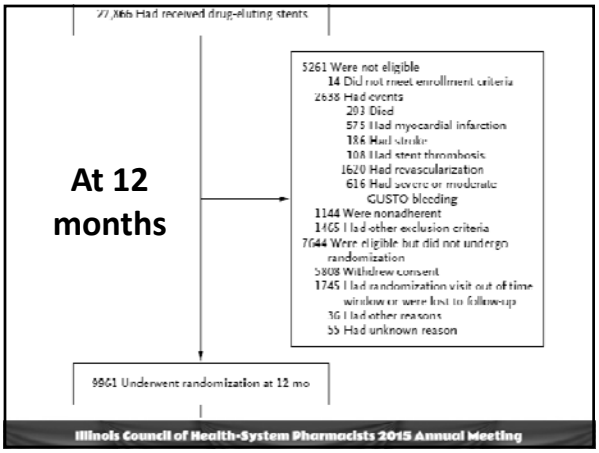
- Severe or life-threatening:
  - ICH or hemodynamic compromise
- Moderate:
  - Transfusion needed but no hemodynamic compromise
- Mild:
  - Bleeding that does not meet above criteria

BARC

- Type 0:
  - No bleeding
- Type 1:
  - Bleeding that is not actionable
- Type 2:
  - Overt bleeding requiring nonsurgical intervention
- Type 3:
  - Overt bleeding plus various Hgb drops defined by subtypes
- Type 4:
  - Related to CABG
- Type 5:
  - Fatal bleeding

12 or 30 Months of DAPT?

- Statistical considerations
  - Hochberg approach
    - Error rate controlled at 0.05
  - Efficacy (ITT)
    - 9,800 DES patients at 12 months = 85% power for superiority
  - Safety (PP)
    - 9960 DES patients if NI margin set at 0.8% = 80% power for noninferiority



Baseline Characteristics

- N=5020 continued thienopyridine
- N=4941 placebo
- Mean age 61 years
- 25% female
- Nonwhites: 8.8%
- Comorbidities
  - DM: 33%
  - HTN: 75%
  - Smokers: 25%
  - Previous stroke: 3%
  - CHF: 5%
  - PAD: 6%
  - Prior PCI: 30%
  - Prior CABG: 11%
  - Prior MI: 21%

12 or 30 Months of DAPT?

- Indication for PCI
  - STEMI: 10%
  - NSTEMI: 15%
  - Angina
    - Unstable: 17%
    - Stable: 38%
  - Other: 20%
- Stent type
  - Everolimus: 47%
  - Paclitaxel: 27%
  - Zotarolimus: 13%
  - Sirolimus: 11%
- Thienopyridine
  - Clopidogrel 65%
  - Prasugrel 35%

Efficacy Outcomes – 12 to 30 months

	T No. of patients (%)	P No. of patients (%)	Hazard ratio T vs. P (95% CI)	P-value	NNT
Stent thrombosis	19 (0.4)	65 (1.4)	0.29 (0.17 to 0.48)	<0.001	100
MACCE	211 (4.3)	285 (5.9)	0.71 (0.59 to 0.85)	<0.001	63
Death (overall)	98 (2.0)	74 (1.5)	1.36 (1.00 to 1.85)	0.05	NA
Death (cardiac)	45 (0.9)	47 (1.0)	1.00 (0.66 to 1.52)	0.98	NA
Death (vascular)	5 (0.1)	5 (0.1)	0.98 (0.28 to 3.39)	0.98	NA
Death (noncardiovascular)	48 (1.0)	22 (0.5)	2.23 (1.32 to 3.78)	0.002	NNH: 200
MI	99 (2.1)	198 (4.1)	0.47 (0.37 to 0.61)	<0.001	50
Stroke	37 (0.8)	43 (0.9)	0.80 (0.51 to 1.25)	0.32	NA

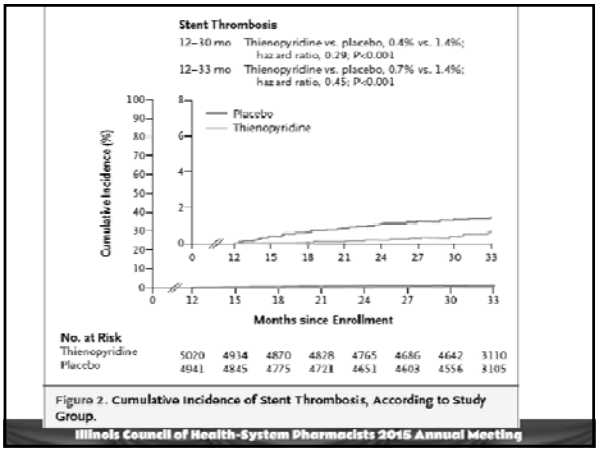


Figure 2. Cumulative Incidence of Stent Thrombosis, According to Study Group.

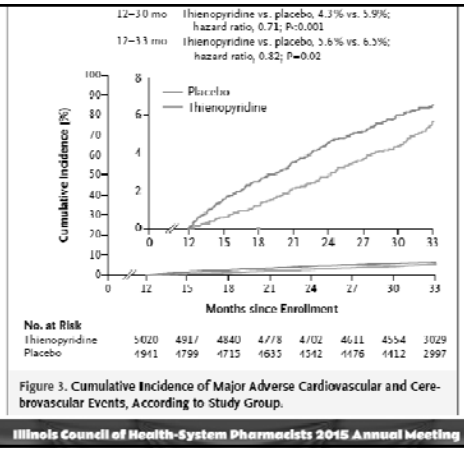


Figure 3. Cumulative Incidence of Major Adverse Cardiovascular and Cerebrovascular Events, According to Study Group.

Safety (Bleeding) Outcomes – 12 to 30 months

	T No. of patients (%)	P No. of patients (%)	Hazard ratio T vs. P (95% CI)	P-value	NNH
GUSTO (severe or moderate)	119 (2.5)	73 (1.6)	1.0 (0.4 to 1.5)	0.001	111
GUSTO (severe)	38 (0.8)	26 (0.6)	0.2 (-0.1 to 0.6)	0.15	NA
GUSTO (moderate)	81 (1.7)			0.004	142
BARC type 2, 3, or 5	263 (5.6)			<0.001	37
BARC Type 2	145 (3.1)			<0.001	62
BARC Type 3	122 (2.6)	68 (1.5)	1.1 (0.6 to 1.7)	<0.001	90
BARC Type 5	7 (0.1)	4 (0.1)	0.1 (-0.1 to 0.2)	0.38	NA

Noninferiority for bleeding not found (difference not <0.8)

Limitations

Strengths

- Strong design
  - 1st RCT to assess longer duration
- Used appropriate populations for data analysis
  - ITT – superiority
  - PP – noninferiority
- Major undertaking/coordination

Limitations

- Only those who did not have an event in 1st 12 months were randomized
- BMS data analyzed separately
- No data for ticagrelor
- Selection bias
- Pts not randomized to thienopyridine or stent type
- No net clinical benefit analysis done
- Limited external validity for race and gender

12 or 30 months of DAPT?

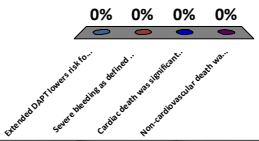
- Conclusion
  - Extension of DAPT beyond 1 year of DES placement
    - Provides additional benefit for reduction of ischemic events
      - Stent thrombosis
      - Myocardial infarction
    - Results in an increase in bleeding events
    - Increase in non-cardiovascular mortality?

12 or 30 months of DAPT?

- From publication to practice:
  - Consider extending DAPT after DES for 30 months total for those who
    - Have lower bleeding risks
    - Are able to adhere to the regimen
    - Are white males

Which of the following was NOT a finding of the DAPT trial?

A. Extended DAPT lowers risk for stent thrombosis
B. Severe bleeding as defined by both GUSTO and BARC criteria was significantly greater with extended DAPT treatment
C. Cardiac death was significantly greater with extended DAPT treatment
D. Non-cardiovascular death was significantly greater with extended DAPT treatment



HEAT-PPCI

UNFRACTIONATED HEPARIN VERSUS BIVALIRUDIN IN PRIMARY PERCUTANEOUS CORONARY INTERVENTION

Lancet. 2014;384(9957):1849-1858.

Background

- Antithrombin agents during PCI
  - Bivalirudin (class I; Level B)
    - Regardless if prior treatment with UFH
    - Possible reduced bleeding compared to UFH?
      - But not with concomitant GP IIb/IIIa inhibitor
    - Increase in ischemic events?
  - UFH (class I; Level C)

Levine, et al. *Circulation*. 2011;124(23):2574-2609

Background

HORIZONS-AMI 2008

- STEMI pts and PPCI
- Bivalirudin had lower "net adverse clinical events" than heparin + GP IIb/IIIa inhibitors
- RR, 0.76; 95% CI, 0.63 to 0.92; P=0.005
  - Lower bleeding with B
  - Higher stent thrombosis within 24 hours with B
  - Lower cardiac and overall death with B

N Engl J Med. 2013;369(23):2207-17

EUROMAX 2013

- STEMI pts and PPCI
- Bivalirudin reduced composite of death or major bleeding compared to UFH/LMWH
- RR, 0.60; 95% CI, 0.43 to 0.82; p=0.001
  - Lower bleeding with B
  - Higher stent thrombosis with B
  - No difference in death or MI

N Engl J Med 2008;358(21):2218–30.

Bivalirudin vs. Heparin

- Study objective
  - To assess the relative safety and efficacy of heparin and bivalirudin during PPCI
- Methods
  - Open-label, single-center, randomized controlled trial
    - Stratified by age and cardiogenic shock
  - Duration: 28 days

Bivalirudin vs. Heparin

Inclusion

- Adults scheduled for PPCI

Exclusion

- Intolerance or C/I to any study drug
- Active bleeding
- Artificial ventilation
- Impaired consciousness

Bivalirudin vs. Heparin

- Interventions
  - Heparin (n=907)
    - 70 U/kg body weight before PCI
    - Add'l doses if ACT <200 seconds
  - Bivalirudin (n=905)
    - 0.75 mg/kg bolus + infusion of 1.75 mg/kg/hour
    - Re-bolus of 0.3 mg/kg if ACT <225 seconds
  - GP IIb/IIIa inhibitor (abciximab) allowed if
    - Massive thrombus
    - Slow or no re-flow
    - Thrombotic complication

Primary Outcomes

Efficacy

- Proportion of patients with ≥1 MACE at 28 days
  - All-cause mortality
  - CVA
  - Reinfarction
  - Add'l revascularization

Safety

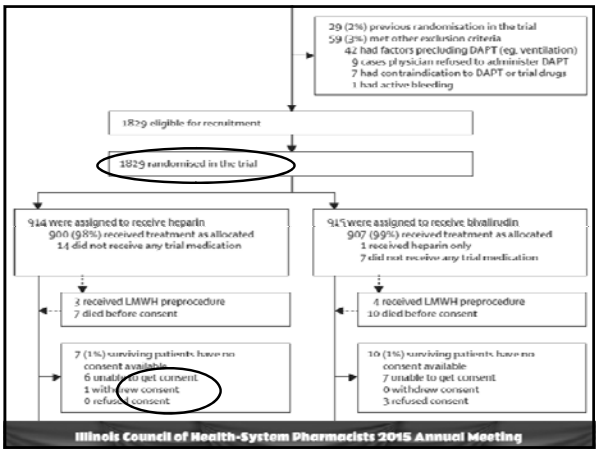
- Proportion of patients who had major bleeding by 28 days per BARC definition (types 3-5)

Bivalirudin vs. Heparin

- Secondary outcomes
  - Stent thrombosis rates
  - Cardiac enzymes
  - Minor bleeding (BARC type 2)
- Subgroup analyses
  - Arterial vascular access route
  - Left ventricular function
  - Age
  - Diabetes
  - Type of P2Y12 inhibitor
  - Whether or not PCI was attempted

Bivalirudin vs. Heparin

- MACE rate estimated to be 7.5% in both groups
- Chi-squared test for primary outcomes
- ITT
- α=0.05



Baseline Characteristics

- 77% STEMI
- Mean age 63 years
- 28% female
- 96% white
- 37% - 45%:
  - DM
  - HTN
  - HL
  - FH of CVD
  - Smoked
- Noteworthy differences
  - Previous MI
    - Bivalirudin: 14%
    - Heparin: 10%
  - Previous PCI
    - Bivalirudin: 8%
    - Heparin: 6%

Baseline Characteristics

- P2Y12 inhibitor
  - Ticagrelor (62%)
  - Prasugrel (27%)
  - Clopidogrel (11%)
- 82% managed with PCI
  - 90% of these had stent
    - 80% had DES
- GP IIb/IIIa inhibitor use
  - Bivalirudin: 13%
  - Heparin: 15%
- Aspirin use in all
- 80% had radial access site
- 45% had normal EF after event
- Approximately 80% - 90% had meds at d/c:
  - ACE or ARB
  - Aspirin
  - Beta blocker
  - P2Y12 inhibitor
  - Statin

Efficacy Outcomes

	Bivalirudin No. of patients (%)	Heparin No. of patients (%)	Relative risk (95% CI)	P-value	NNT
Primary efficacy outcome	79 (8.7)	52 (5.7)	1.52 (1.09 to 2.13)	0.01	34
Death	46 (5.1)	39 (4.3)	1.18 (0.78 to 1.79)	0.43	NA
CVA	15 (1.6)	11 (1.2)	1.37 (0.63 to 2.96)	0.43	NA
MI or re-infarct	24 (2.7)	8 (0.9)	3.01 (1.36 to 6.66)	0.004	56
Revascularization	24 (2.7)	6 (0.7)	4.01 (1.65 to 9.76)	0.001	50

Safety (Bleeding) Outcomes

	Bivalirudin No. of patients (%)	Heparin No. of patients (%)	Relative risk (95% CI)	P-value	NNH
Major bleed (primary safety)	32 (3.5)	28 (3.1)	1.15 (0.70 to 1.89)	0.59	NA
Minor bleed	83 (9.2)	98 (10.8)	0.85 (0.64 to 1.12)	0.25	NA
Any bleed	113 (12.5)	122 (13.5)	0.93 (0.73 to 1.18)	0.54	NA

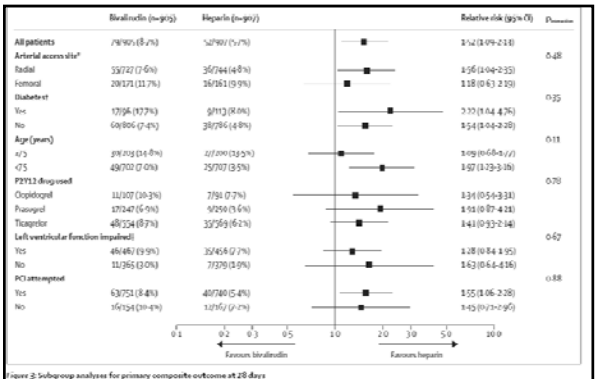


Figure 3: Subgroup analyses for primary composite outcome at 28 days
*Procedures completed exclusively via radial access (radial group) versus all other cases (femoral group). †Patients receiving oral hypoglycaemic or insulin therapy. ‡Left ventricular ejection fraction <55% in surviving patients after index event.

Limitations

Strengths

- Delayed consent
  - Allowed for sicker patients
- First RCT to compare bivalirudin and heparin with GP IIb/IIIA use in both groups
- Free from manufacturer bias

Limitations

- Delayed consent?
  - Ethical?
- Single-center study
- Homogeneous population in terms of race
- Lower heparin doses than in clinical practice?
- Higher rates of previous PCI and MI in bivalirudin

Bivalirudin vs. Heparin

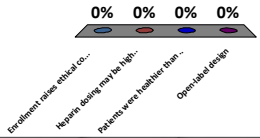
- Conclusions
  - Heparin provides a benefit over bivalirudin during PPCI for
    - Acute stent thrombosis
    - Reinfarction
  - Heparin does not increase the risk for bleeding as compared to bivalirudin

Bivalirudin vs. Heparin

- From publication to practice
  - Heparin may be preferred to bivalirudin during PPCI without increased safety concerns
    - When used in combination with newer P2Y12 inhibitors
  - Can't be as confident about this in females, non-whites
  - Both bivalirudin and heparin may be used per guidelines – evidence may increase strength of recommendation for heparin

Which is NOT a criticism of the HEAT-PPCI trial?

A. Enrollment raises ethical concerns
B. Heparin dosing may be higher than usual clinical practice
C. Patients were healthier than in other similar trials
D. Open-label design



Taking care of our elderly:

EXERCISE AND VITAMIN D IN FALL PREVENTION AMONG OLDER WOMEN

JAMA Intern Med. 2015;175(5):703-711.

Background

- Falls in the elderly
  - Leading cause of injury and injury-related death
  - 20% of falls require medical attention
  - <1/10 results in fracture

N Engl J Med. 2003;348(1):42-49.

Background

- Exercise
  - Individualized training and group exercise effective in preventing falls
  - Strength and balance training my reduce noninjurious and injurious falls by 15% to 50%

BMC Geriatrics. 2012;12;12.

Background

- Vitamin D deficiency
  - <25 nmol/L
  - Decreased muscle function, performance
  - Increased disability
  - Associated with frail phenotypes
  - Inversely associated with falls
- Evidence conflicting for benefits of supplementation

Ann Intern Med. 2013;158:691-696.
Biomed Res Int. 2015;2015:953241.

Background

- USPSTF Recommendations for home-dwelling postmenopausal women and primary prevention of fractures
  - **Inconclusive:** whether or not vitamin D >400 IU/day + calcium >1000 mg/day
  - **Recommends against** vitamin D ≤400 IU/day + calcium ≤1000 mg/day

Ann Intern Med. 2013;158:691-696.

Exercise and Vitamin D

- Study objective
  - Assess exercise training and vitamin D supplementation in reducing falls and improving bone density in older women at risk of falls
- Methods
  - Double-blind, placebo-controlled (vitamin D), and open exercise intervention trial with 4 arms; 2 year duration

Exercise and Vitamin D

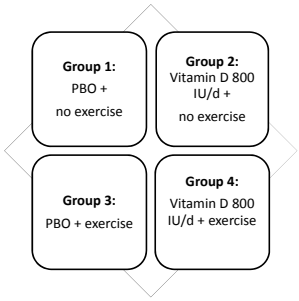
Inclusion

- Women 70 to 80 yrs in Finland
- Living at home independently
- History of ≥1 fall in past year
- No regular vitamin D supplements intake

Exclusion

- Exercise >2 hrs/wk
- Fx in previous 12 mo.
- Inability to exercise
- Marked decline in ADL
- Cognitive impairment
- Primary hyperthyroidism
- Degenerative dz

Interventions



Exercise Description

- Supervised, progressive group training
- 2x/wk for 12 months
- 1x/wk for remaining 12 months
- Balance challenging
- Weight bearing
- Strengthening
- Agility
- Weight machines
- Pulleys
- Free weights
- Home training

Endpoints

- Primary
  - Monthly reported falls
- Secondary
  - Injurious falls
    - Bruises, abrasions, contusions, sprains, fractures, head injuries
  - Number of fallers and injured fallers
  - Bone density
  - Physical functioning

Statistics

- Power calculation
- 260 pts provided 80% power to detect 30% between-group difference at 2 years (α=0.05)
  - Wanted to enroll more in order to eliminate type I error for interaction between vitamin D and exercise
- ITT

Exercise and Vitamin D

Baseline Characteristics

- Well-balanced groups
- Serum 25-hydroxyvitamin D level approx. 26-27 ng/mL
- Mean age 74 years
- Average # of meds: 2.5
- Sufficient calcium intake at baseline and 24 months
- Low alcohol consumption
- Relatively healthy

Results

- Exercise well-tolerated
- 98% pill compliance
- Vitamin D levels increased in Vitamin D groups compared to placebo
  - 25.1 ng/mL → 37.0 ng/mL
- Total of
  - 928 falls
  - 281 fallers
  - 190 multiple fallers
  - 117 multiple injured fallers

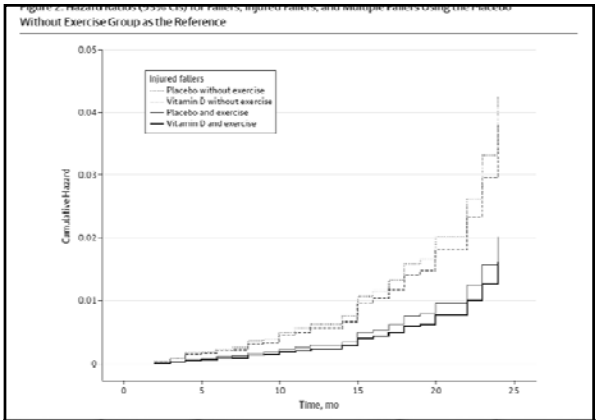
Rate of falls per 100 person-years

	Placebo without Exercise	Vitamin D without Exercise	Placebo and Exercise	Vitamin D and Exercise
All falls	118.2	132.1	120.7	113.1
Injurious falls	13.2	12.9	6.5	5.0
All falls IRR (95% CI)	Reference	1.08 (0.78 to 1.52)	1.07 (0.77 to 1.45)	0.99 (0.72 to 1.39)
Injurious falls IRR (95% CI)	Reference	0.84 (0.45 to 1.57)	0.46 (0.22 to 0.95)	0.38 (0.17 to 0.81)

Hazard ratios for falls

	Vitamin D Without Exercise	Placebo and Exercise	Vitamin D and Exercise
Fallers	0.77 (0.54-1.11)	0.93 (0.66-1.31)	0.91 (0.64-1.28)
Injured fallers	0.89 (0.47-1.69)	0.47 (0.23-0.99)[a]	0.38 (0.17-0.83)[a]
Multiple fallers	1.07 (0.71-1.62)	1.14 (0.76-1.71)	1.14 (0.77-1.71)

Exercise ± vitamin D reduces only injurious falls



Results - secondary

	Change at 24 mo	*P* Value[a]
Femoral neck BMD, g/cm^2		
Placebo without exercise	−1.22 (−4.75 to 2.45)	NA
Vitamin D without exercise	−0.87 (−4.47 to 2.86)	.02
Placebo and exercise	−0.98 (−4.55 to 2.73)	.01
Vitamin D and exercise	−1.24 (−4.72 to 2.38)	.04
Distal tibia trabecular density, mg/cm^3		
Placebo without exercise	−0.49 (−3.77 to 2.80)	NA
Vitamin D without exercise	0.03 (−3.36 to 3.42)	.12
Placebo and exercise	−0.16 (−3.43 to 3.11)	.41
Vitamin D and exercise	0.19 (−3.04 to 3.42)	.02

Results - secondary

Outcome	Change at 24 mo	*P* Value[a]
Backward walking, proportion of those able to do 6.1 min, %		
Placebo without exercise	7.76 (−2.87 to 18.47)	NA
Vitamin D without exercise	9.48 (−0.66 to 20.08)	.68
Placebo and exercise	26.27 (15.71 to 35.13)	.001
Vitamin D and exercise	25.47 (15.30 to 33.39)	.03
Muscle strength, N/kg		
Placebo without exercise	1.8 (−4.8 to 8.4)	NA
Vitamin D without exercise	1.5 (−5.0 to 8.1)	.10
Placebo and exercise	14.0 (7.8 to 20.2)	<.001
Vitamin D and exercise	15.6 (9.1 to 22.2)	<.001

Exercise and Vitamin D

Strengths

- Strong design, long duration
- High adherence
- Low withdrawal
- Recruited patients at risk for falls

Limitations

- No reporting of fractures
- Baseline levels of vitamin D high
- Relatively good health/physical condition
- Limited external validity

Conclusion

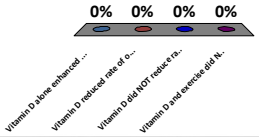
- Exercise ± vitamin D reduces the risk for injurious falls among elderly women
- Interventions alone and in combo do not decrease overall falls

Exercise and Vitamin D

- From publication to practice
  - Exercise ± vitamin D did not reduce risk for all fall types
  - Important to consider fall prevention strategies with osteoporosis prevention strategies, but this trial does not support
  - Justifies USPSTF recommendations
  - Don't prescribe vitamin D + exercise for purposes of preventing falls in elderly women

Based on this trial, which of the following statements is TRUE?

A. Vitamin D alone enhanced muscle strength and balance
B. Vitamin D reduced rate of overall falls
C. Vitamin D did NOT reduce rate of injurious falls
D. Vitamin D and exercise did NOT reduce the rate of multiple falls



Which of the following is a limitation common to ALL the trials discussed?

A. Selection bias
B. Single-center study
C. Manufacturer bias
D. Limited external validity

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- Uusi-Rasi K, Patil R, Karinkanta S, et al. Exercise and vitamin d in fall prevention among older women: a randomized clinical trial. *JAMA Intern Med.* 2015;175(5):703-711.

ASHP Midyear Meeting: Steps to a Successful Residency Showcase Experience

Carol Heunisch, Pharm.D, BCPS

OBJECTIVES

- Develop a timeline for Midyear planning & preparation
- Tips for successfully navigating the residency showcase

ASHP MIDYEAR CLINICAL MEETING

- **Residency Showcase**
  - Informal meetings with residents, program directors, and preceptors
  - Opportunity to ask questions and get program information
  - Programs listed by training site, not specific program type
    - Listings available early November
  - Dates for 2015
    - Monday December 7: 1-4PM
    - Tuesday December 8: 8-11AM & 1-4PM

ASHP MIDYEAR CLINICAL MEETING

- **ASHP Personnel Placement Service (PPS)**
  - Optional, additional fee for participation
  - Opportunity to schedule one on one interviews
  - Good to narrow potential programs for on-site interviews
  - Recruit for PGY1, PGY2 residents as well as fellowships
  - Search for "residency program postings" www.careerpharm.com
  - Registration opens September 16
  - Available at Midyear December 6-9, 730AM-5PM

TIMELINE FOR MIDYEAR PREPARATION

- **September**
  - Draft CV
  - Begin drafting cover letters
  - Letters of recommendation
    - Never too early to ask
    - Be respectful of time

TIMELINE FOR MIDYEAR PREPARATION

- **October**
  - Review ASHP Online Residency Directory
  - Contact programs of interest for additional information
  - Register to attend the ASHP Midyear Clinical Meeting (don't forget to book hotel & travel)
    - Personnel Placement Service (PPS)?
  - Register for PhORCAS
    - http://www.ashp.org/phorcas
  - Register for The Match
    - http://www.natmatch.com/ashprmp
  - Review your clothing

TIMELINE FOR MIDYEAR PREPARATION

- **November**
  - Finalize CV
  - Continue working on cover letters
  - Make selections for programs to visit at the residency showcase
    - Find out dates & times that the programs will be at the showcase
    - Look at the diagram to figure out where the program booth is located
    - Develop a list of questions
    - Do your homework—get to know the programs
  - Request transcripts to be sent to PhORCAS

RESIDENCY SHOWCASE

- **Residency Showcase**
  - **Professional appearance**
    - Wear clothes that fit well, comfortable yet professional shoes
    - Carry a folder or portfolio for papers, notes
  - **Be respectful & make good use of everyone's time**
    - Articulate your interests up front
    - Be prepared with questions
    - Programs may or may not accept CVs
    - Take notes, collect names/business cards

RESIDENCY SHOWCASE TALKING TIPS

- **Be prepared to ask:**
  - Opportunities (teaching, research, rotations)
  - How does the program assess potential candidates?
  - Unique features of a program/what sets it apart
- **Be prepared to answer:**
  - Why you are interested in the program
  - Unique qualities YOU bring to the program
  - How the residency program will help YOU meet your career goals
- **DON'T ask:**
  - "So, tell me about your program…"
  - Pay, location, vacation

RESIDENCY RESOURCES

- http://www.ashp.org
- http://www.natmatch.com/ashprmp
- http://www.careerpharm.com
- http://www.ichpnet.org
- http://www.ashp.org/phorcas

PGY-1 Residency Training Programs: What are my options in Community and Ambulatory Care?

Susan R. Winkler, PharmD, BCPS, FCCP
Midwestern University
Chicago College of Pharmacy

PGY-1 Programs

- Separate accreditation standards for:
  - Pharmacy
    - Most common
  - Community
  - Managed Care
- Even programs following the same accreditation standard can have a different look, feel

PGY-1 Programs

- Different Settings
  - Academic Medical Center/Community
  - Acute Care v. Ambulatory Care
  - College-based
- Different Patient Populations
  - Ambulatory Care
  - Pediatric Hospital
  - Veterans Affairs Medical Center

PGY-1 Pharmacy: Two Different Programs

Academic Health-Center Based

- Orientation
- Cardiology
- Internal Medicine
- Administration
- Drug Information
- Transplant
- Infectious Diseases
- Research/Project Month
- Internal Medicine II
- Ambulatory Care
- Pediatrics
- Longitudinal: Service/Staffing

College-based: Teaching & Ambulatory Care

- Amb Care I: Anticoagulation
  - Underserved Population
- Internal Medicine Inpatient
- Amb Care II: Diabetes
- Amb Care III: Medical Home
- Amb Care IV: Pulmonary
  - VA Setting
  - Community
- Community Practice
  - Service/Staffing/Management
- Longitudinal: Teaching/Precepting, Academia, Project

PGY-1 Program: Day in the Life

Patient Care

- Morning Rounds
  - Work rounds
  - Teaching rounds
- Patient appointments
- Medication Reconciliation
- Antibiotic Stewardship

Other

- Med Safety Meeting
- Topic Discussion with Students
- Project Meeting with Mentor
  - Data collection
- Staffing

PGY-1 Community

- Accredited by ASHP in partnership with APhA
- Various models exist for operation of residencies:
  - College of pharmacy and community pharmacy partnerships
  - Independent programs through colleges of pharmacy with their own pharmacies
  - Independent programs through community pharmacies or chain corporations

PGY-1 Community: Day in the Life

- Corporate experiences in leadership, practice management
- Development of business plan and implementation of pharmacy service
- Community Pharmacy Operations
- Community Pharmacy Clinical Services
- Ambulatory Clinic experiences
- Work within collaborative practice models
- Academic experiences
  - Didactic teaching
  - Practice-based research project
  - Grand Rounds

PGY-1 Managed Care

- Accredited by ASHP in partnership with AMCP
- Residencies often operated through large managed care systems and pharmacy benefit management companies
- Presidency focused on project management, leadership development, population-based care and MTM

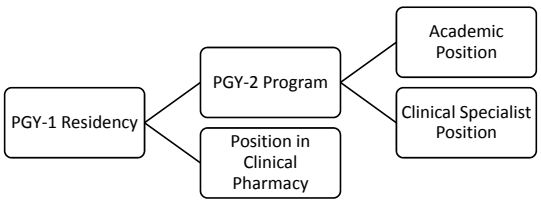
PGY-1 Managed Care: Day in the Life

- Pharmacy benefit design/benefit manager experience
- Drug information/formulary management
- Ambulatory care experiences
- Medication safety
- Prior authorization
- MTM/Medication Use Management
- Research project
- Academic experiences

All PGY-1 Programs

- Service Commitment
  - Staffing
    - Responsibilities
    - Time: How much? When? (weekend, evenings, on-call)
- Teaching Commitment
  - Is this something you want?
  - Is there teaching-related training?
- Program Size

What next?

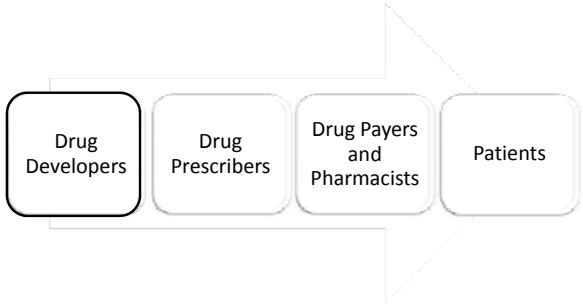


Questions?

Fellowships and Opportunities for PharmDs in the Pharmaceutical Industry

Mike Stamatis, Pharm.D.
Rutgers Post-Doctoral Fellow,
Genentech Inc.

Healthcare Simplified



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Opportunities for PharmDs in the Industry

Research & Development	Medical Affairs	Commercial	Regulatory Affairs
• Clinical pharmacology • Pre-clinical • Early Phase Development •Late Phase Development • Clinical operations	• Medical Strategy •Medical Information • MSL • Publications • Medical Education • HEOR	• Marketing • Market Research • Advocacy & Policy • Market Access • Business Development	• Advertising & Promotions • Regulatory Strategy • Drug Safety • Risk Management

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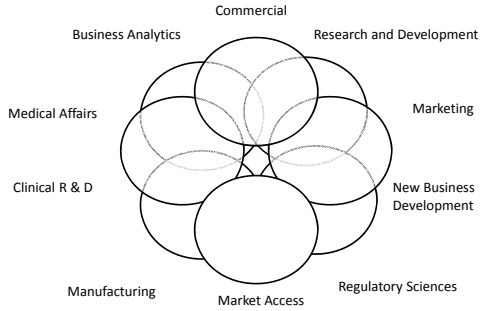
Cross Functional Interactions



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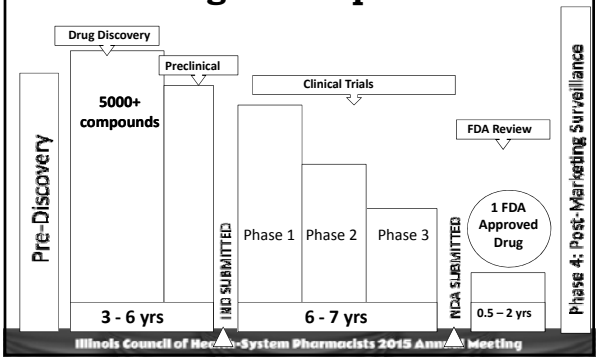
Drug Development



Illinois Council of Health-System Pharmacists 2015 Annual Meeting

What is an Industry Fellowship?

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Fellowship vs. Residency

Attribute	Fellowship	Residency
Impact on patient care	Global scale	Individual cases
Use of clinical knowledge	Varies depending on functional area	Direct patient care
General structure	1-2 year experience in core function ± rotations	1 year general practice ± 1 year specialty
Practice setting	Corporate	Inpatient/Outpatient
Scholarly activities	Teaching Research Publications	Teaching Research Publications
Salary	Competitive Stipend	Competitive stipend

Fellowship Components

Industry Component	Academic Component
• Hands on experience in specialty function and/or disease area • Guidance from preceptors, mentors, and alumni • Professional development through conferences, workshops, and more • Internal and External rotation opportunities	• Professional Development Series • Teaching opportunities • Research collaboration with faculty for publications/posters • Leadership opportunities as committee chairs and leads

Fellowship Candidate Eligibility

- Obtain a Doctor of Pharmacy (Pharm.D) and/or Doctorate of Philosophy (Ph.D.) degree by July 1, 2016 from an ACPE accredited pharmacy program
- Attend formal interview process at the ASHP Midyear Clinical Meeting in New Orleans

Leading Partner Companies for 2015-2016

ACORDA THERAPEUTICS, Genentech A Member of the Roche Group, janssen, NOVARTIS, Pfizer, MERCK, SUNOVION, Roche, AstraZeneca, Pfizer Consumer Healthcare, Catalent, Bayer HealthCare, TEVA PHARMACEUTICALS, Celgene, Bristol-Myers Squibb, Daiichi-Sankyo, Johnson & Johnson, SANOFI

Please find us at the showcase!

General PGY1 Information—What Are Your Options for Hospital & Informatics?

Noelle RM Chapman, PharmD, BCPS, FASHP
Northwestern Memorial Hospital

PGY1 Hospital Info

- WE are all individuals like YOU
  - This is why "fit" is most important
- What is your **goal**?

PGY1 Hospital Info

- Common themes to consider in hospital programs:
  - Service component
  - Ambulatory care/transitions of care requirements
  - Required learning experiences
  - Research

Different Strokes for Different Folks

- Large AMC
- Single site
- Well established
- Large class
- On-call
- Traditional PGY1 structure
- Small Community
- Health System
- Newer program
- Small class
- Service component
- Non-traditional experience

Informatics

- Growing field in pharmacy
- Typically focused as a PGY2 program

General PGY1 Information—What Are Your Options for Hospital & Informatics?

Noelle RM Chapman, PharmD, BCPS, FASHP
Northwestern Memorial Hospital

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

CV: The key to a top curriculum vitae

Karen M. Kelly, Pharm.D.
Clinical Pharmacy Manager
Evanston Hospital
NorthShore University HealthSystem

Curriculum vitae (CV)

- Latin = course or outline of your life
- Organized list of your professional qualifications, education, achievements & experiences
- Varies in length, more detailed than a resume
- Living document

What should be included in a CV

- Your contact information @ top of page
  - Name, address, current phone & professional email address
- Licensure Status
  - State & type of license
- Education
  - Most recent educational experience first
  - School & your degree

What should be included in a CV

- Professional experience
  - Most recent experience first
  - Position, name & location of employer, time frame of employment, name of supervisor including title
  - Description of position
  - Notable improvements & contributions to pharmacy practice
- Residency & Clerkship rotations
  - Spell out rotation & preceptor, including title
  - No abbreviations
  - Good to list if right out of school

What should be included in a CV

- Presentations, posters & publications
  - Include title & year
  - Name of group presented to & location
  - Use official citation method
- Honors & Awards
  - List title & year
  - Deans list – include quarter & year
- Professional & Community Service
  - Name of group, office held, describe the scope of responsibility & impact

What should be included in a CV

- Specialized Training & Certifications
  - CPR, ACLS, BCPS, immunization training
  - Include the full certification name and the year earned Membership in organizations
- Other special experiences or skills
  - Any unique quality, language, training
- References – list out

Tips for a Top Notch CV

- Update regularly to reflect work experience, presentations
- Focus on professional, pharmacy-related information
- Include positive information about your achievements
- Be honest in your content

Tips for a Top Notch CV

- Use headings to identify each section
- Use simple fonts
- High quality, conservative paper
- No abbreviations
- No colors
- Watch for spelling errors
- **Have someone proofread it for you**

What do employers look for?

- Professionalism
- Signs of achievement
- Hard worker, continue to have the willingness to work hard
- Patterns of stability & career direction

What NOT to Include in your CV

- Personal information
- Reason for changing jobs or no job
- Photo, unless requested
- High-school
- Interests and hobbies

Conclusion

- Be honest in your content
- Highlight your strengths & achievements
- Create a good first impression
- Your CV as an advertisement for YOU!

References

- American Society of Health-System Pharmacists. Curriculum Vitae Resource Center. Available at: http://www.ashp.org/menu/MemberCenter/SectionsForums/PSF/CareerCenter/Career-Planning/Curriculum-Vitae-Resource-Center.aspx. Accessed July 1,2015.
- CV-Resume.org. CV Resume and Cover Letter. Available at http://cv-resume.org. Accessed July 1, 2015.
- University of Kent, Careers and Employability Service. How to write a successful CV. Available at: http://www.kent.ac.uk/careers/cv.htm. Accessed July 1, 2015.

The Letter of Intent

Jen Phillips, PharmD, BCPS
Associate Professor, Midwestern University
September 12, 2015

Objectives

1. Identify the purpose of a letter of intent.
2. List things to include and not include in a letter of intent.

The Match Process

- Residencies are looking for the "best fit"
  - Clinical interests
  - Character
  - Learning style
  - Strength/type of clinical rotations
  - Professional involvement
  - Clinical aptitude
  - Personality

Why do I need one?

- Important way for you to DISTINGUISH yourself from other candidates
- Highlights things not included in a CV such as: skills, experience, goals, and communication skills

Overcoming Barriers

Issue	Recommendation
"I do not feel comfortable selling myself."	• Use comments/feedback from rotations to help you identify your strengths • Don't go overboard (i.e., "I am the best student ever.")
"I am not a good writer."	• Put down all of your ideas first • Enlist help (i.e., mentor, preceptor, etc.) when "smoothing it out" but make the changes YOURSELF
"I do not know what to put in the letter."	• Seek examples from current residents, websites, etc. • Refer to outside sources for suggestions (residency books, articles, this presentation, e.g.)

What to include

- Why you want to do a residency
- Why you want to do a residency THERE
- Current area(s) of interest
- Preferred environment
- Short and long-term goals
- Other information requested by the program (check recruiting materials!)

What NOT to include

- List or summary of rotations
  - This is already included in your CV
- Negative experiences
  - Pharmacy is a small world!
- Hobbies/outside interests

Format

- Standard business letter
  - Address to the appropriate person
  - Spell name correctly!
  - Separate letter for ***each*** site
  - Style
    - 1 page
    - 11-12 point font
    - No "frilly" font styles
    - Appropriate margins

Format

- 3-5 paragraphs
  - Intro
    - Why interested in the position/place
  - Body
    - Highlight skill set, successes, experiences
    - Use specific examples
    - Sell the match!
  - Conclusion
    - Summarize / reinforce interest
    - "Thank you for your time/consideration"

Additional "hints"

- Proofread, proofread, PROOFREAD!
- Spend a LOT of time thinking
  - Goals, preferences, etc.
- Customize your letter by site
  - People, experiences, examples that support your skill assessment
- Send a different letter to each place

Additional Reading

- Bauman JL, Sims KA. The ACCP Field Guide to Becoming a Standout Pharmacy Residency Candidate. American College of Clinical Pharmacy. 2012. p. 181-183.

Questions?

PhORCAs – The new on-line residency application system

Frank Paloucek, PharmD, DABAT, FASHP

No handouts available

Residency Interview Pearls

Abby A. Kahaleh, BPharm, MS, PhD, MPH
AACP Academic Leadership Fellow
Associate Professor of Clinical and Administrative Sciences

Roosevelt University College of Pharmacy

Main Goal of the Interview

- Residency program perspective:
  - Evaluate which candidate if the most qualified
  - Assess which candidate fits the best
- Residency applicant perspective:
  - Evaluate clinical management, opportunities available at the program
  - Find the program that fits the best with your interest

Prior to the Interview (1)

- Research the program
- Familiarize yourself with the location of the interview
- Gather information from current and/or previous residents
- Make sure all your documents have been received
- Ask about formal presentations, number of interviewers, and expectations

Prior to the Interview (2)

- ►Have electronic and hard copies of your CV, letter of intent
- ►Select your references carefully
- ►Share with your references the residency programs that you are interviewing with
- ►Dress professionally and have positive attitude
- ►Practice mock interviews with friends and/or family members

Types and Format Interviews

- Individual, group, combination
- Meeting with residents, preceptors, pharmacy directors, residency directors, staff
- Presentation, clinical case
- Tour of the facility
- Breaks/meals between interviews

Interview Questions

- Personal
- Behavioral
- Clinical
- Experiential
- Reflective

Personal Questions

- ►What are your short and long-term *career goals*?
- ►Why do you want to do a *residency*?
- ►What are your *strengths* and *weaknesses*?
- ►What is your greatest *professional accomplishment*?
- ►What makes you the *best candidate*?

Behavioral Questions

- Tell me about a time when you took the *lead* in a situation
- Share an example when you had a *conflict* with a colleague, preceptor, supervisor
- Describe your approach to *conflict resolution* and *stress management*
- Based on your personal experience explain the best strategy for handling *mistakes*

Clinical Questions

- Provide an example of a specific patient case during your rotations when you went *above* and *beyond* the call of duty
- Questions on *clinical trials*, *patient cases*, *guidelines* related to your presentation
- Share a specific example of a recommendation/suggestion that you made during *rounds* or at a *clinical site*

Experiential Questions

- ►Describe your best *clinical rotation*
- ►Share the most significant *contribution* that you made during your rotations?
- ►Describe your most favorite and memorable *patient*?
- ►What would your first and last *preceptor* say about you?
- ►Who was your *favorite* preceptor?

Reflective Questions

- ►What are your *best* and *worst* qualities?
- ►Why did you attend *pharmacy school*?
- ►Where do you see yourself *after residency*?
- ►What areas of *pharmacy practice* interest you?
- ►How would you define *pharmaceutical care*?

Tips for Answering Questions

- *Listen* carefully to the question
- Ask for a *clarification*, if you didn't understand the question
- Be *honest*, *confident*, and *straightforward*
- *Repeat* the question if you need time to gather your thoughts
- Provide *specific examples* and link them to the question
- Know your *strengths*, *weaknesses*, and your *plan of action*

The Match / Ranking Process and Post-match scramble

Nora Flint, PharmD, FASHP, BCPS

No handouts available

Get the inside scoop from a residency preceptor

Christopher W. Crank, PharmD, MS, BCPS AQ-ID

No handouts available

The Vibrant Shuffle on the Path to a Residency

Get the Inside Scoop from a Past Resident

Lana Wong, PharmD
PGY2 Solid Organ Transplant Pharmacy Resident
Northwestern Memorial Hospital

Objectives

- Reasons to do a residency
- Find your personal fit
- What to expect
- How to be successful
- Resources

Reasons to Do a Residency

- Personal development
  - Feedback
- Professional development
  - Leadership skills
  - Career opportunities
- Interests development
  - PGY2, fellowship, etc.

Personal Fit

- Class size
- Location
- Mentorship
- Specialty interests
- Experiences
  - Research, academia, patient populations

What to Expect in Residency

How to Be Successful in Residency

- Be open-minded
  - Adaptability
- Be organized
  - Time Management
- Be professional
- Be intentional
  - Plan ahead for your next step
- Be proactive
  - Ask for help and feedback

Resources

- Preceptors
- Faculty
- Current & past residents
- Informational meetings
  - Round tables & showcases
- Literature
  - *Get the Residency: ASHP's Guide to Residency Interviews and Preparation*

The Vibrant Shuffle on the Path to a Residency

Get the Inside Scoop from a Past Resident

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PGY2 Solid Organ Transplant Pharmacy Resident
Northwestern Memorial Hospital

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Danger, Will Robinson! Overview of USP Chapter <800>

Patricia C. Kienle, RPh, MPA, FASHP
Director, Accreditation and Medication Safety
Cardinal Health Innovative Delivery Solutions

Disclosure

- Patricia Kienle is an employee and stockholder of Cardinal Health
- She is an elected member of the USP Compounding Expert Committee, but is not speaking as a USP representative
- All conflicts resolved through peer review

Objectives for Pharmacists and Pharmacy Technicians

- Cite the document that defines hazardous drugs (HDs)
- List the three categories of HDs
- Explain the containment strategies related to HDs.
- Identify elements that could be used for an Assessment of Risk
- List the types of PPE that need to be used with HDs

Patti's Wish

- Identify three things that you can improve the next day you are at work

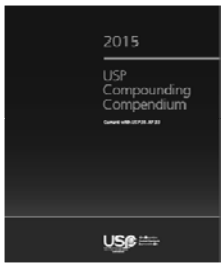
What's All the Fuss?

Why <800>?

- To promote patient safety, worker safety, and environmental protection when handling hazardous drugs (HDs)
- Addresses, but is not limited to
  - Receipt
  - Storage
  - Compounding
  - Dispensing
  - Administration
  - Disposal
- Applies to all healthcare personnel who handle HDs
- Applies to all healthcare entities that store, prepare, transport, or administer HDs

What Regulations Exist?

- USP <795> Pharmaceutical Compounding – Nonsterile Preparations
- USP <797> Pharmaceutical Compounding – Sterile Preparations
- OSHA regulations
- State regulations



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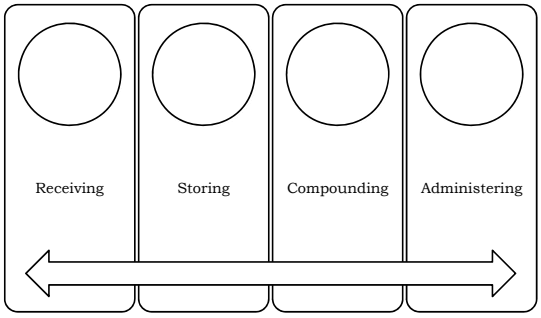
Is your site compliant with the hazardous drug part of <797>?

- Yes
- Partially
- No

What are the Upcoming Regulations?

- Proposed USP <800>
  - Federally-enforceable regulation
- Applies to both sterile and nonsterile compounding
- State regulations
  - Enforcement

HDs in Your Facility



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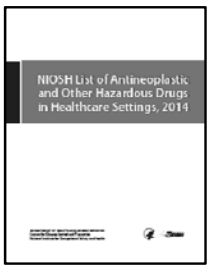
Hazardous Drug Definition

- Carcinogens
- Genotoxins
- Teratogens
- Reproductive toxins
- Organ toxicity at low doses
- Structure or toxicity similar to drugs classified as hazardous

12

NIOSH 2014 List of Hazardous Drugs



www.cdc.gov/niosh/docs/2014-138/pdfs/2014-138.pdf

13

NIOSH 2014 List of Hazardous Drugs

- Antineoplastic
- Non-antineoplastic
- Reproductive hazard only

- Drugs that are hazardous to personnel
  - Different from EPA-hazardous, which are hazardous to the environment

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Show Me the Science

www.cdc.gov/niosh/topics/hazdrug/

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Your HD List

- Review the NIOSH list
- Identify the meds you stock
- Determine the containment strategies

Your Handling Options

Treat all HDs the same

- Use all the containment strategies in <800>

Assess risk and stratify

- Identify and use alternative containment strategies and/or work practices for specific dosage forms of HDs that are not antineoplastic agents or are not API

Assessment of Risk

- Drug
- Dosage form
- Risk of exposure
- Packaging
- Manipulation
- Documentation of alternative containment strategies and /or work practices
- Review annually and document

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Can you identify HD packages when they are delivered?

- Yes
- No

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HD Receipt

- Your supplier should mark containers
- Your receiving personnel need to be inserviced to assess the integrity of the container
- You must provide
  - Chemo gloves
  - Chemo spill kit

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HD Storage

- Shall be stored separately from other inventory
- Shall be in
  - Negative pressure room
  - Vented to the outside
  - At least 12 air changes per hour
- Take the plastic-wrapped package into the negative pressure storage area to unwrap it

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Where are your HDs mixed?

- BSC or CACI in negative pressure cleanroom
- BSC or CACI in positive pressure cleanroom
- BSC or CACI in normal pressure room
- Outside of BSC or CACI

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HD Preparation

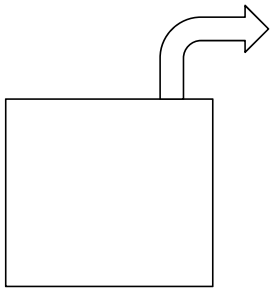
- Shall be in physically separate space
  - Negative pressure room
  - Vented to the outside
  - Appropriate number of air changes per hour

Engineering Controls

- Primary
  - Biological Safety Cabinet (BSC)
  - Compounding Aseptic Containment Isolator (CACI)
- Secondary
  - The room in which the PEC is placed
- Supplemental
  - Closed system drug-transfer devices

Two Tenets of Safety

- Containment
- Dilution



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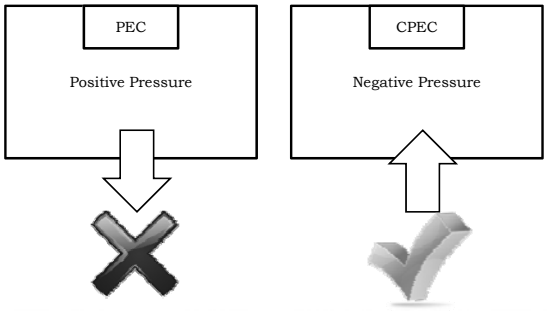
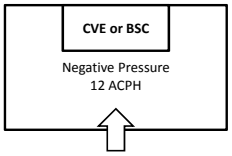
Why Negative Pressure?



Nonsterile Compounding

C-PEC	C-SEC Requirements
• Externally vented (preferred) OR redundant HEPA-filtered in series • **Examples:** CVE, Class I or II BSC, CACI	• 12 ACPH • Externally vented • Negative pressure between 0.01 and 0.03" w.c.



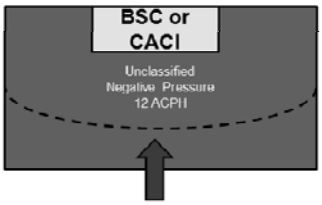
Sterile Compounding

Elimination of "low use" exemption in <797>

Configuration	C-PEC	C-SEC	Maximum BUD
ISO Class 7 Buffer Room	• Externally Vented • Examples: Class II BSC or CACI	• 30 ACPH • Externally vented • Negative pressure between 0.01 and 0.03" w.c.	As described in <797>
C-SCA	• Externally Vented • Examples: Class II BSC or CACI	• 12 ACPH • Externally vented • Negative pressure between 0.01 and 0.03" w.c.	12 hours

Containment Segregated Compounding Area

- Not currently allowed in <797>
- Not acceptable for high-risk



CSTDs

- Closed system drug-transfer devices
- Mechanically prohibits the transfer of environmental contaminants into the system and the escape of HD or vapor concentrations outside the system

Photo courtesy of BD

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Administering HDs

- Requires Supplemental Engineering Controls
- Why?

CSTD Resources

PPN, June 2013

PPPMag Supplement, February 2015

USP <797> and <800> Requirements

- Didactic
- Overseen by experts
- Monitored
- Media fill test
  - Initial
  - Requalifying
- Gloved fingertip test
  - Initial
  - Requalifying
- Surface sampling

Training Materials Available

- Policies and procedures
- Device manufacturers
- NIOSH
- ASHP
- Critical Point

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What gloves are worn to prepare hazardous drugs?

- Same as for non-hazardous compounding
- One pair of chemo gloves
- Two pairs of chemo gloves
- Compounder can decide which to wear

PPE Requirements in <800>

- Gloves
- Gowns
- Hair covers
- Shoe covers
- Face protection
- Respirators

Gloves for Handling HDs

- Chemo gloves tested to ASTM D6978
- Non-powdered
- Two pairs
- Outer gloves must be sterile when compounding sterile preparations

Gowns for Handling HDs

- Tested and shown to resist permeability by HDs
- Disposable
- Polyethylene-coated polypropylene or other laminate
- Close in back (no open front)
- Long-sleeved
- Elastic or knit closed cuffs
- No seams or closures that could allow HDs to pass through

PPPMag – January 2015

PPE

By Thomas H. Connor, PhD; Lori A. Power, MS, RPh; Firouzan Mastrobattista, Pharm.D., FASHP; and Martha Polovich, PhD, RN, AOCN

Are Gloves and Gowns Safe for Handling Chemotherapy?

Other Garb Issues

- Eye protection
  - BSC/CACI provide eye protection
  - Use goggles when working outside a PEC
- Respirators
  - Use when outside a PEC
- All garb is required when using a CACI

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Chemo hoods are cleaned with …

- Sterile alcohol
- Germicidal detergent
- Bleach
- Commercial product for hazardous drugs

Cleaning Process

- Deactivation and decontamination
- Use of detergent
- Disinfecting surfaces

PPPMag Articles

September 2013

October 2014

Environmental Monitoring

- USP <797> requirements
- Wipe samples

Screenshot courtesy of ChemoGLO

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How close to <800> compliant is your site?

- Less than half-way there
- Between 50-90%
- Close to compliant

Your Action Plan

-
-
-
-
-


Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Playing Your Role:
Handling Hazardous Drugs: Protecting Patients and Practitioners
Illinois Council of Health-System Pharmacists
September 12, 2015
Patricia C. Kienle

OBJECTIVES

- Cite the document that defines hazardous drugs (HDs)
- List the three categories of HDs
- Explain the containment strategies related to HDs
- Identify elements that could be used for an Assessment of Risk
- List the types of PPE that need to be used with HDs

SELF-ASSESSMENT QUESTIONS

1. Pharmacy mixes IV chemo for the health-system's inpatients and attached oncology clinic. Vials of antineoplastic HDs may be stored:
    a. Intermingled with regular stock since the vial is a final dosage form
    b. Intermingled with regular stock since the health-system does not identify it as a HD
    c. In the positive pressure anteroom
    d. In the negative pressure buffer room
2. HDs are sorted into which three groups?
    a. Oral antineoplastic, parenteral antineoplastic, reproductive hazards only
    b. Antineoplastic, non-antineoplastic, reproductive hazards only
    c. Antineoplastic, injectable reproductive hazards, other
    d. Antineoplastics, other oral HDs, other injectable HDs
3. Which of the following documents is the basis for the HDs identified in USP <800>?
    a. ASHP Drug Information
    b. EPA list of hazardous materials
    c. NIOSH list of hazardous drugs
    d. The Joint Commission Medication Management standards
4. A supplier follows the shipping recommendations in <800>. A tote with a HD indicator is received from the supplier. Can the tote be opened in the general pharmacy area?
    a. Yes, because it will have a sealed impervious wrapper around the HDs in the tote
    b. Yes, because all HDs may be unwrapped as long as the outside packaging of the vial or box is not opened
    c. No, because the tote must be taken into the positive pressure anteroom to open it
    d. No, because the tote must be taken into the negative pressure chemo hood to open it

5. What does <800> say about the use of Closed System Drug-Transfer Devices (CSTDs)?
    a. Must be used when compounding and should be used when administering
    b. Should be used when compounding and must be used when administering
    c. Should be used for both compounding and administering
    d. Must be used for both compounding and administering

The End of Life
Controversial Conversations

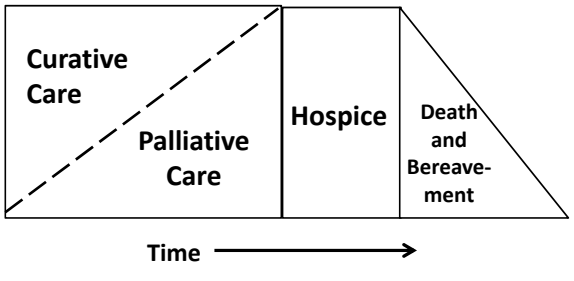
Lisa Anderson-Shaw, DrPH, MA, MSN
September 12, 2015

Speaker has no conflicts of interest to disclose

Objectives

1. **Define end-of-life care options for terminally ill patients.**
2. Describe common myths about palliative sedation.
3. Discuss the clinical and ethical controversies surrounding palliative sedation and other difficult medical decisions at the end-of-life.

End-of-Life Care Options



Adapted from *Hastings Cent Rep* 2005; Spec No: S14-18

Palliative Care Definition

- **Palliative Care** is:

  "patient and family-centered care that optimizes quality of life by anticipating, preventing, and treating suffering. Palliative care throughout the continuum of illness involves addressing physical, intellectual, emotional, social, and spiritual needs and to facilitate patient autonomy, access to information and choice"

  -National Hospice and Palliative Care Organization (NHPCO)

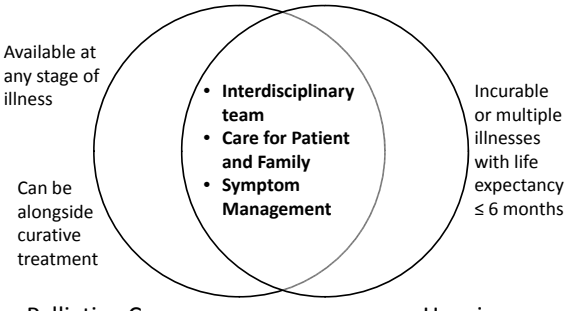
http://www.nhpco.org/palliative-care-4

Key Features of Palliative Care Philosophy

Team	• Care is provided by an interdisciplinary team • Patients, families, and non-palliative care providers collaborate
Care	• Palliative care services may be provided alongside curative care
Support	• Patient and family are supported through illness, the dying process, and after death

http://www.nhpco.org/palliative-care-4

Palliative Care and Hospice



Transition from Hospital to Home

- Clinical Ethics
- Ethics Consultation Service
- Hospital Ethics Committee (HEC)
- Palliative Care Service

Care Near the End of Life

- Goals of care conversations: with patient, family, care team members
  - (MD, APN, nurses, home care, pharmacist, others)
  - When cure is no longer possible, comfort and quality of life remain the goal
  - Family goals may be different than care team goals

Case Example

Ethical Obligation

- Principles of Ethics:
  - Respect for autonomy
  - Beneficence
  - Nonmaleficence
  - Justice (social, distributive, stewardship)
    - Veracity
    - Fidelity
      - Standard of Care

Tools

- Do – Not-Attempt-Resuscitation
- Power of Attorney for Health Care
- Living Will
- POLST (Practitioner orders for Life Sustaining Treatment) (www.POLST.ORG)
- Practitioner conversation and guidance (Key to all of the above)_

Barriers to Quality End of Life Care:

- Practitioner training
- Fear of taking away hope
- Patient fear of talking with family about end of life topics in general
- General lack of awareness related to Advance Directives by public and practitioners

Take-Home Thoughts

- Patients and family need informed guidance when a life limiting diagnosis has been made
- All care team members are in a position to begin education on end of life care
- Resources such as palliative care, Ethics Consultation and Pastoral Care are often available to patient, team and family

The End of Life Controversial Conversations: Options of Last Resort

Laura Meyer-Junco, PharmD, BCPS, CPE
September 12, 2015

Speaker has no conflicts of interest to disclose

Objectives

1. Define end-of-life care options for terminally ill patients.
2. **Describe common myths about palliative sedation.**
3. **Discuss the clinical and ethical controversies surrounding palliative sedation and other difficult medical decisions at the end-of-life**.

The "Right to Die" Movement

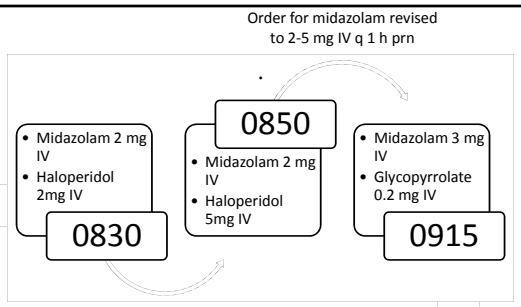
- Campaigns for physician-assisted death are gaining momentum across the United States
- In a recent poll, three-fifths of Americans support legalizing physician-assisted death
- What are potential interventions of last resort for terminally ill patients?

http://www.economist.com/node/21656253

Patient #1: Walter

- 79 year old male with large subdural hematoma after falling off of a ladder and hitting his head
  - Admitted to the hospital; neurosurgery consulted
- Walter was deemed unlikely to recover and continued to decline
  - Increasing restlessness
- Palliative Care was consulted
  - Goals of care discussed with family
  - Comfort care was agreed upon

Walter's Final Hours…



Am J Hosp Palliat Care 2012; 29(7) 522-524

0930 Restlessness improved

- Walter was no longer trying to pull out IV or get out of bed
- Morphine 4 mg IV given

1030 Restlessness returned

- Walter was waving his arms up and down around his head
- Daughter pleaded for "something for the restlessness" before the grandchildren saw him
- Midazolam 5 mg IV bolus; midazolam 0.5 mg/hr infusion

2200 Walter rests

- Family at bedside
- Death was pronounced

https://www.fraserhealth.ca/media/07EHSymptomGuidelinesDelirium.pdf

Patient #2: Carl

- 65 year old male with metastatic colon cancer refractory to treatment.
- Multiple admissions to the inpatient palliative care unit with severe debilitating pain.
- On his last admission, Carl was weak, jaundiced, and in severe distress from painful metastases to his spine, pelvis, and liver.
- Attempts to control his pain this time were unsuccessful, and Carl was becoming increasingly confused and agitated.
- Decision was to pursue sedation after team meeting and discussion with family.

Quill TE, Miller FG. (2014). *Palliative Care and Ethics.*

Carl's Final Days

- Midazolam was added to his analgesic medications:
  - Midazolam 5 mg bolus x1
  - Midazolam 1 mg/hr infusion
- Within 5 minutes he was sedated, but after 30 minutes he was arousable and still in distress
- A second bolus of midazolam was administered and the infusion increased to 2 mg/hr.
- The infusion was titrated over the next several hours to midazolam 5 mg/hr
- He died 2 days later, sedated, comfortable, and with his family.

J Support Oncol 2004;2:181–186

Walter received which of the following?

A. Management of Terminal Restlessness
B. Palliative Sedation
C. Euthanasia
D. Physician Assisted Suicide or Physician Aid-in-Dying

Carl received which of the following?

A. Ordinary Sedation
B. Palliative Sedation
C. Euthanasia
D. Physician Assisted Suicide or Physician Aid-in-Dying

Myth #1:

PALLIATIVE SEDATION IS EUTHANASIA

What is Palliative Sedation (PS)?

- Several Definitions by Professional Societies (partial list)
  - American Academy of Hospice and Palliative Medicine (AAHPM)
  - Hospice and Palliative Nurses Association (HPNA)
  - American Medical Association (AMA)
  - European Association for Palliative Care (EAPC)
  - National Hospice and Palliative Care Organization (NHPCO)

Am J Hosp Palliat Care 2015; 32: 660-671

The Clearest Distinction is INTENT

Palliative Sedation (PS):
"The monitored use of medications intended to induce a state of decreased or absent awareness (unconsciousness) in order to relieve the burden of otherwise intractable suffering in a manner that is ethically acceptable to the patient, family, and healthcare providers."

-European Association for Palliative Care, 2009

Physician-assisted suicide and euthanasia:
deliberately intend to shorten life and cause death, and thus "categorically distinct" from palliative sedation.

-National Hospice and Palliative Care Organization, 2010

Palliat Med 2009; 23 (7): 581-593 *J Pain Symptom Manage* 2010; 39(5): 914-923

More Definitions..

Euthanasia

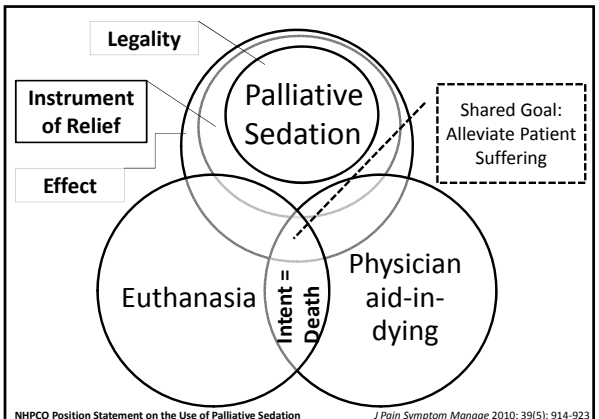
- Also known as: voluntary active euthanasia (VAE)
- "Administration of a **lethal agent** by another person to a patient for the purpose of relieving the patient's intolerable and incurable suffering"
  - AMA Code of Medical Ethics
- Competent patient requested
- **Intent: death**

Physician Aid-in-Dying (PAD)

- Also called: physician-assisted suicide (PAS)
- A physician prescribes a **lethal dose** of medication that is self-administered by the patient
- Competent patient requested
- **Intent: death**

Palliative Medicine 2003; **17:** 97 -101

http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion221.page



NHPCO Position Statement on the Use of Palliative Sedation *J Pain Symptom Manage* 2010; 39(5): 914-923

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~~Lethal~~ Agents for Palliative Sedation

Medication	Starting Dose	Usual Maintenance Dose
Midazolam (Palliative Sedation)	0.5-5 mg IV or SC bolus, then 0.5-1 mg/hr	0.5-10 mg/hr
Midazolam (Endoscopy)	0.5-2 mg IV PRN	Usual Total Dose: 2.5 -5 mg *Gastrointest Endosc* 2003; 58: 317-322
Midazolam (mechanical ventilation)	0.01 to 0.05mg/kg (0.5 to 4 mg) IV PRN	0.02-0.1 mg/kg/hr (1-7 mg/hr) *Crit Care Med* 2013; 41: 263-306

Am J Hosp Palliat Care 2002 19(5):295-297 *J Pain Palliat Care Pharmacother* 2012; 26:30-39

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Medication	Starting Dose	Usual Maintenance Dose
Propofol	20-50 mg IV bolus (may repeat), then 5-10 mg/hr	10-200 mg/hr
Pentobarbital*	1-3 mg/kg IV slow bolus (≥ 50 mg/min)	1-2 mg/kg/hr and titrate to desired level of sedation
Phenobarbital*	200 mg bolus SC or IV (may repeat q 10-15 min)	0.5 -1 mg/kg/hr (25-50 mg/hr) and titrate to effect

*Barbiturates may be used for refractory symptoms not relieved by other agents or in patients with extreme tolerance to other agents.

* Last resort option due to rapid onset of unconsciousness and long duration of action.

J Pain Palliat Care Pharmacother 2012; 26:30-39
Palliat Med 2009; 23 (7): 581-593 www.capc.org/fast-facts/107-controlled-sedation-refractory-suffering-part-ii

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Intermittent Dosing

- Location of care (non-ICU) may preclude use of continuous infusions of PS agents per hospital policy
- Transfer to ICU may not be feasible or desirable for patient/family

Mayo Clin Proc 2010; 85: 949-954

Intermittent Medication	Starting Dose	Usual Maintenance Dose
Lorazepam	0.5-2 mg every 1–2 hr (IV/SC, PO, or SL) *Am J Hosp Palliat Care* 2002 19(5):295-297	0.5-10 mg every 1-4 hours *J Pain Palliat Care Pharmacother* 2012; 26:30-39

"Instrument of Relief" aka Principles and Procedures

Double Effect

- A **double effect** refers to one action that has both a good and bad effect
- High doses for sedation (or opioids for analgesia) are permissible if:
  - the primary intention is to relieve suffering
  - the bad effect (death or respiratory depression) is not the means of achieving relief

Proportionality

- Sedation should be titrated to the **minimum** level needed to render symptoms tolerable
- For some, this may be total unconsciousness
- For most, relief is achieved when patients are sleepy but arousable

J Pain Symptom Manage 2010; 39(5): 914-923
J Pain Palliat Care Pharmacother 2012; 26:30-39

Types of Palliative Sedation

Ann Intern Med. 2009;151:421-424.

- Proportionate Palliative Sedation (PPS)
  - Uses the minimum amount of sedation necessary to relieve suffering at the end-of-life
  - Titration based on symptom relief
  - Unconsciousness is not the goal, but may be required if lower levels of sedation are ineffective

- Palliative Sedation to Unconsciousness (PSU)
  - Unconsciousness is the goal
  - For severe physical, refractory symptoms where continuing consciousness would be intolerable
  - Sedation rapidly escalated over minutes to a few hours until the patient is unresponsive
    - Level of sedation held there until the patient passes

Legal Basis for "Terminal Sedation"

- Supported by the United States Supreme Court in 1997
  - "terminal sedation" not clearly defined

Vacco v. Quill, 1997
Washington v. Glucksberg, 1997

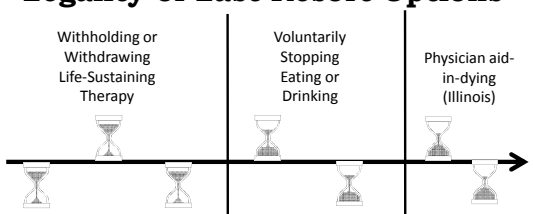
"…A patient who is suffering from a terminal illness and who is experiencing great pain has no legal barriers to obtaining medication from qualified physicians, even to the point of causing unconsciousness and hastening death"

-Justice O'Connor, Washington v. Glucksberg, 1997

Ann Intern Med. 2009;151:421-424. *J Pain Palliat Care Pharmacother* 2012; 26:30-39

Adapted from: Quill TE, Miller FG. (2014). *Palliative Care and Ethics.*

Legality of Last Resort Options



Legal and Widely Accepted	Legal, Mostly Accepted	Illegal

Myth #2:

PALLIATIVE SEDATION HASTENS DEATH

Impact on Survival

Annals of Oncology 2009; 20:1163-1169

Sedation Features	
Duration	4 days (mean)
Mild	62.2%
Deep	37.8%
BZDs	54.3%
Neuroleptics	84.2%
Opioids	25.5%
>2 Drugs	50.6%

+PS: 267 patients — Survival: 12 days (median)

-PS: 251 patients — Survival: 9 days (median)

P=0.330

"…Patients with poorly controlled pain, shortness of breath, and agitation actually die sooner because of the stress caused by this suffering. Studies clearly demonstrate that palliative sedation does not hasten death."
–Center to Advance Palliative Care, 2010

https://www.capc.org/about/press-media/press-releases/2010-1-6/palliative-sedation-myth-vs-fact/

Myth #3:

PALLIATIVE SEDATION (AND PHYSICIAN AID-IN-DYING) ARE COMMON PRACTICES

Frequency of Use

- "Palliative sedation is a treatment of last resort when symptom distress cannot be relieved using standard methods. It is used extremely rarely because the vast majority of patients get acceptable relief without sedation."
  - Center to Advance Palliative Care (CAPC), 2010
- Prevalence of palliative sedation
  - 1% to 50% of terminally ill patients
  - Great variability in the literature
  - Universial definition of palliative sedation lacking

J Pain Symptom Manage 2010; 39(5): 914-923 *J Pain Symptom Manage* 2008; 36:310-333
https://www.capc.org/about/press-media/press-releases/2010-1-6/palliative-sedation-myth-vs-fact/ *Curr Opin Oncol* 2014; 26: 389-394

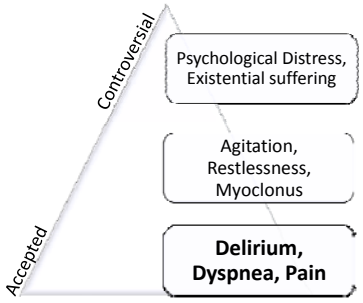
When is Palliative Sedation Appropriate?

Refractory Symptoms	• Aggressive efforts fail to alleviate the symptom • Label as "refractory" only after interdisciplinary evaluation and treatment by experts in palliative and pain management • Psychological and spiritual assessment performed by skilled clinician and chaplain (non-physical symptoms)
Informed Consent	The aims, benefits, and risks of palliative sedation have been discussed with the patient and/or family.
Imminent Death*	The patient is close to death. Prognosis of death within 14 days per NHPCO

*EAPC states that transient or "respite" sedation may be appropriate earlier

J Pain Symptom Manage 2010; 39(5): 914-923 *Palliat Med* 2009; 23 (7): 581-593 *J Palliat Med* 2003; 6 (3):345-50.

Indications for Palliative Sedation:



J Pain Symptom Manage 2008;36: 310-333 *Curr Opin Oncol* 2014; 26: 398-394

Legalized Physician Aid-in-Dying (PAD)

http://www.deathwithdignity.org/advocates/national

Oregon Death with Dignity Act 1997-2014

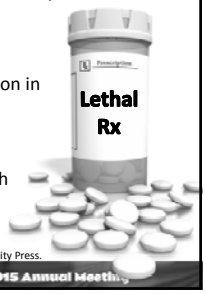
http://public.health.oregon.gov

1,327

Since becoming legal, 1327 Oregonians have had a lethal prescription written. 859 have died.

3 in 1000

Three in 1000 deaths in Oregon in 2014 were due to PAD.



1%

Only 1% of Oregonians who die each year request PAD. Fewer than that actually die by lethal ingestion.

Quill TE, Miller FG. (2014). *Palliative Care and Ethics.* New York, NY: Oxford University Press.

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

Physician Aid-in-Dying (PAD)

Requirements	Barriers to Patient	Concerns
Competent at time of request		Competent when ingested?
Terminal illness (≤6 months left)		Expertise in terminal illness not required.
Patient must make two oral requests (15 days apart) and one written request, then wait 48 hours for prescription	Many obstacles to obtaining PAD. Death may occur before completing requirements.	Intolerable suffering is not required; Patients often request PAD before symptoms develop.
Two physicians must certify that patient is eligible	Many physicians decline to participate.	
Must be able to self-administer and ingest Rx	May become unable to swallow	

Quill TE, Miller FG. (2014). *Palliative Care and Ethics.*

http://www.deathwithdignity.org/access-acts

In 2014, 105 Oregon residents died from PAD. What is the most common reason these patients requested PAD?

A. Pain
B. Dyspnea
C. Depression
D. Loss of Autonomy

http://public.health.oregon.gov/ProviderPartnerResources/EvaluationResearch/DeathwithDignityAct/Documents/year17.pdf

Journal of Pain and Symptom Management 2015; 49: 555-560

J Gen Intern Med 2007; 23: 154-7

Illinois Council of Health-System Pharmacists 2015 Annual Meeting

SUMMARY	Palliative Sedation	Euthanasia (VAE)	Physician Aid-in-Dying
Intent to hasten death?	No	Yes	Yes
Legal in United States?	Yes	No (only in Netherlands and Belgium)	Oregon Washington Vermont (Montana) (New Mexico)
Option if decisional capacity is lost?	Yes (consent from family)	No	No
Death must be imminent?	Yes	No	No (terminal)
Reason for Use	Physical	N/A	Existential
Most Common Agent	Midazolam	Barbiturate + Paralytic	Secobarbital Pentobarbital

Palliative Medicine 2003; 17: 97 -101 http://public.health.oregon.gov

Take-Home Thoughts

- Palliative interventions (including hospice referrals) result in some patients rescinding their requests for physician aid-in-dying/euthanasia.
  - *Journal of Clinical Ethics* 2004; 15:119-122
- Increasing the availability of end-of-life care (palliative/hospice) may just be the most "powerful alternative to calls for legalization of euthanasia and physician-assisted suicide."
  - EAPC Ethics Task Force, *Palliative Medicine* 2003; 17: 97-101
- "Pharmacists should ensure the rights of competent patients to know about all legally available treatment options while communicating to patients…the overall duty of health care professionals to preserve life."
  - ASHP Statement on Pharmacist's Decision-Making on Assisted Suicide* *Am J Health-Syst Pharm* 1999; 56:1661–4.

*"It is hoped that this framework…will virtually eliminate a patient's request for assisted suicide."

Resources for Patients

- Compassion and Choices
  - https://www.compassionandchoices.org
- Death with Dignity National Center
  - http://www.deathwithdignity.org/

Resources for Pharmacist

- Compassion and Choices
  - https://www.compassionandchoices.org/what-you-can-do/in-your-state/oregon/resource-for-healthcare-providers/resources-for-oregon-pharmacists/
- Compassion and Choices of Washington
  - http://compassionwa.org/wp-content/uploads/2012/09/Pharmacists-Guide-2.2015.pdf

Questions?

“The End of Life Controversial Conversations”

Post-test Questions:

1. Palliative can be distinguished from hospice by which of the following:

   A. Care provided by an interdisciplinary team
   B. Care provided alongside curative care
   C. Patients and families are supported
   D. Symptom management

2. Which of the following is a barrier to quality end-of-life care?

   A. Increased public awareness of palliative care
   B. Medicare coverage for hospice services
   C. Lack of practitioner training
   D. Utilizing interdisciplinary teams for delivery of care

3. Which of the following statements is correct?
   A. Palliative sedation is euthanasia
   B. Proportionate palliative sedation hastens death
   C. Palliative sedation is illegal in the United States
   D. The intention of palliative sedation is to relieve intractable suffering

4. The most commonly used agent in palliative sedation is: _____
   A. Midazolam
   B. Phenobarbital
   C. Secobarbital
   D. Propofol

5. Which of the following is a requirement for patients requesting Physician Aid-in-Dying (PAD)?
   A. The patient must be imminently dying (prognosis of death within 14 days)
   B. The patient must make one oral and one written request, 30 days apart
   C. Two physicians must certify that the patient is eligible and competent
   D. The patient must live in Illinois, Indiana, or Ohio.