



1-DAY REGIONAL MEETINGS

A Changing Paradigm in Cancer Care:

The Migration to Oral Oncolytic Agents



Presented in partnership with the ICHP Annual Meeting

Faculty

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Disclosures

Christopher A. Fausel, PharmD, MHA, BCOP has no financial relationships to disclose relating to the subject matter of this presentation.

Learning Objectives

- Describe the pharmacologic mechanisms and indications of newly available oral agents to treat various cancers
- Evaluate the reported toxicities for newer oral oncolytic drugs and discuss the therapeutic implications of these toxicities
- Review the factors that impact the potential success of treatment with oral oncolytic drugs such as adherence and drug procurement

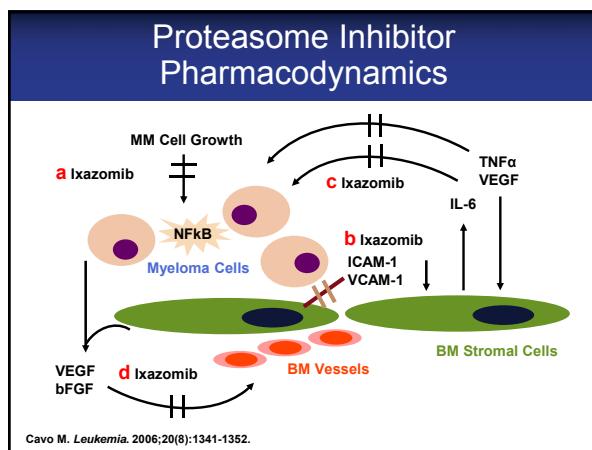
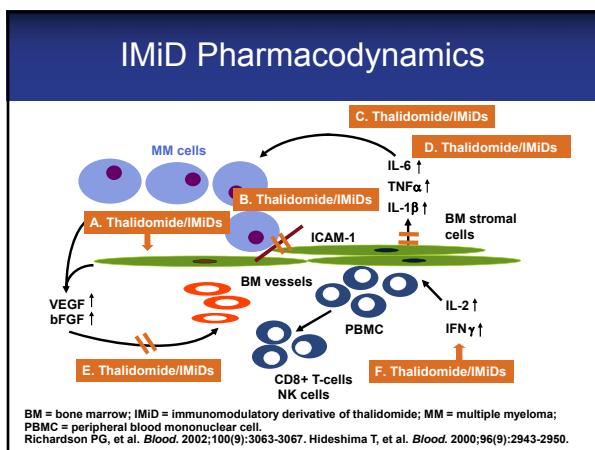
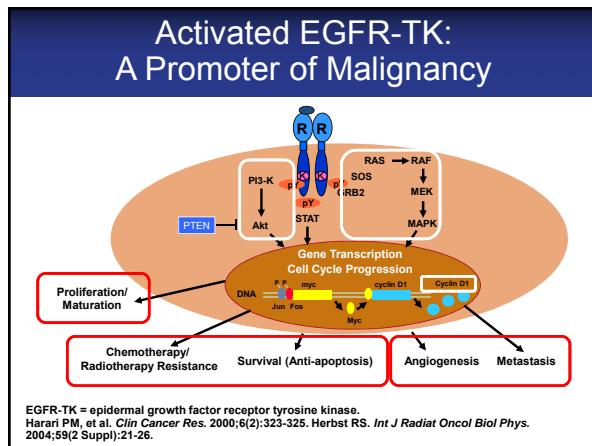
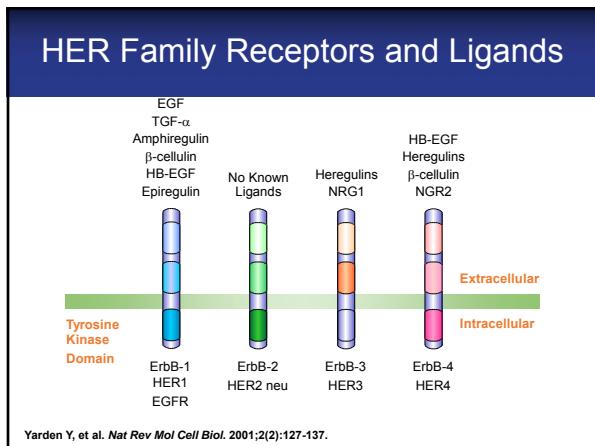
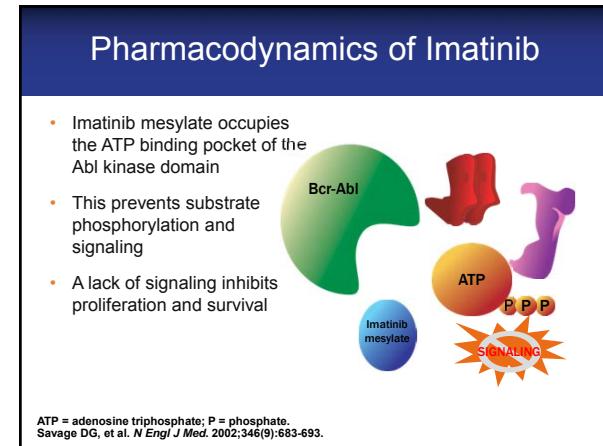
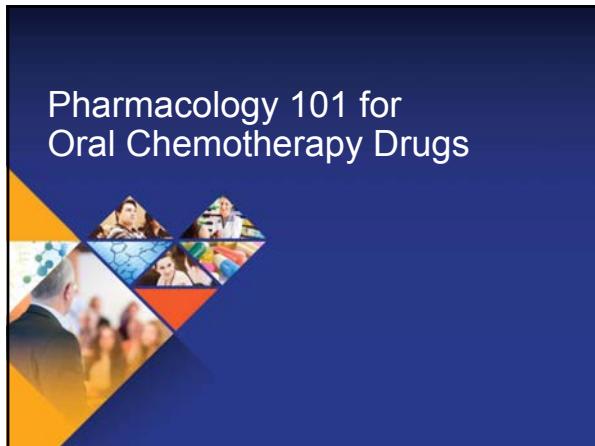
Technician Learning Objectives

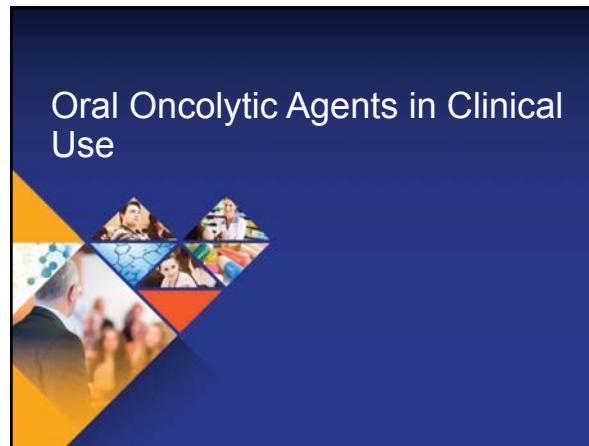
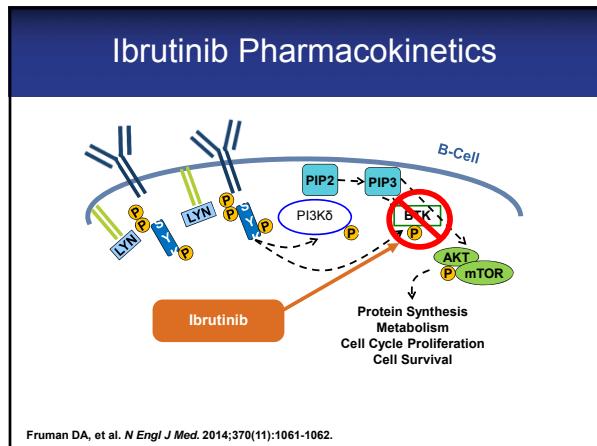
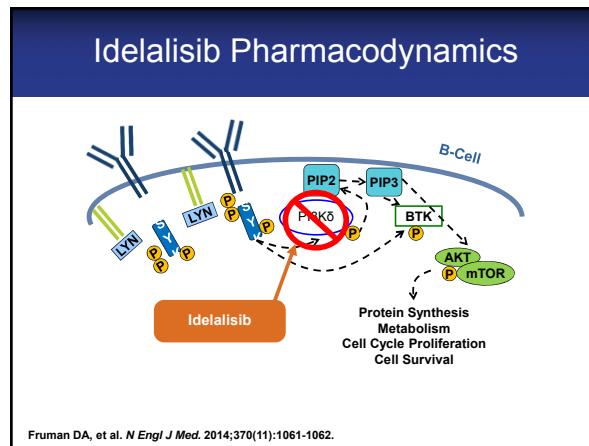
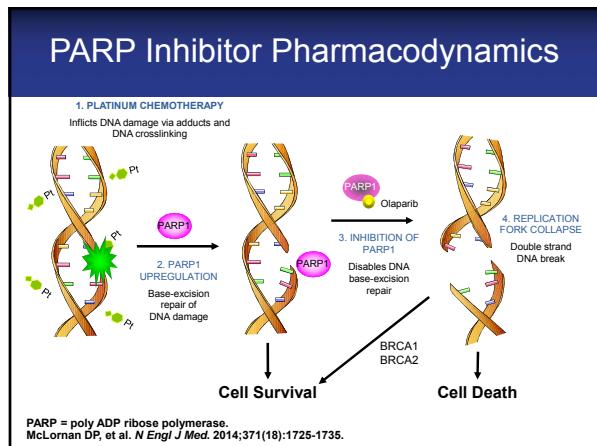
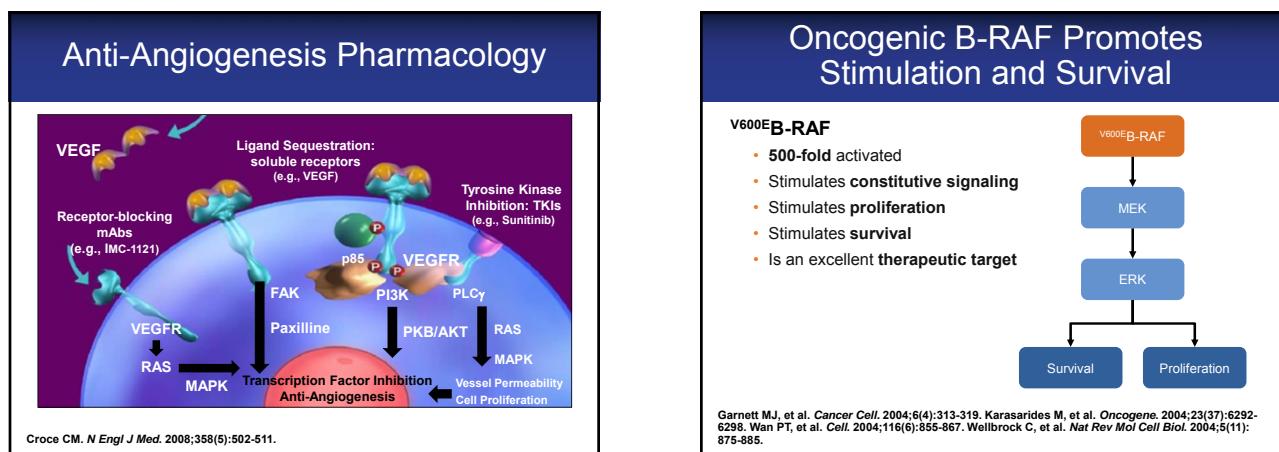
- Describe the indications for newly available oral agents to treat various cancers
- List the side effects for newer oral oncolytic drugs
- Review the potential success of treatment with oral oncolytic drugs related to drug procurement

Oral Chemotherapy Circa 2002

Drug	Class
Cyclophosphamide, Melphalan	Nitrogen mustard alkylating agent
Estramustine	Alkylating agent/estrogen
Lomustine	Nitrosourea alkylating agent
Methotrexate	Antifolate antimetabolite
Capecitabine	Pyrimidine antimetabolite
Mercaptopurine, Thioguanine	Purine antimetabolite
Etoposide	Epipodophyllotoxin
Hydroxyurea	Substituted ureas
Procarbazine	Methylhydrazine derivative
Temozolomide	Imidazotetrazine derivative
Tretinoin, Bexarotene	Retinoids
Tamoxifen/Letrozole/Flutamide/Nilutamide	Hormonal therapy
Imatinib	Tyrosine kinase inhibitor

Drug Facts and Comparisons. Facts and Comparisons; 2002:1957.





FDA Approvals Oral Oncolytics 2006-2008

Drug	Indication	Year
Imatinib	Dermatofibrosarcoma protuberans, HES, MDS/MPD, systemic mastocytosis	2006
Vorinostat	Cutaneous T-cell lymphoma – 3 rd line	2006
Lenalidomide	Myeloma – 2 nd line with dexamethasone	2006
Dasatinib	CML – 2 nd line	2006
Sorafenib	Advanced hepatocellular carcinoma	2007
Nilotinib	CML – 2 nd line	2007
Lapatinib (+capecitabine)	HER-2 +, metastatic breast; post trastuzumab/anthracycline/taxane	2007
Sunitinib	Advanced renal cell carcinoma	2007
Imatinib	Adjuvant gastrointestinal stromal tumor	2008

CML = chronic myeloid leukemia; HES = hypereosinophilic syndrome; MDS/MPD = myelodysplastic/myeloproliferative diseases.
US Food and Drug Administration. www.fda.gov/drugs/informationondrugs/approveddrugs/ucm279174.htm. Accessed on February 17, 2016.

FDA Approvals Oral Oncolytics 2009-2010

Drug	Indication	Year
Pazopanib	Advanced renal cell carcinoma	2009
Everolimus	Renal cell carcinoma; post sorafenib or sunitinib	2009
Everolimus	Giant cell astrocytoma	2010
Dasatinib	CML – Front line	2010
Nilotinib	CML – Front line	2010
Lapatinib	Hormone receptor +, metastatic breast cancer (with letrozole)	2010

US Food and Drug Administration. www.fda.gov/drugs/informationondrugs/approveddrugs/ucm279174.htm. Accessed on February 17, 2016.

FDA Approvals Oral Oncolytics 2011

Drug	Indication
Ruxolitinib	Primary myelofibrosis; PV or ET associated myelofibrosis
Crizotinib	ALK+ NSCLC
Vemurafenib	BRAF V600E metastatic melanoma
Abiraterone	Metastatic castration-resistant prostate cancer; post docetaxel
Vandetanib	Metastatic medullary thyroid cancer
Everolimus	Progressive neuroendocrine tumors of pancreatic origin

ALK = anaplastic lymphoma kinase; ET = essential thrombocythemia; NSCLC = non-small cell lung cancer; PV = polycythemia vera.
US Food and Drug Administration. www.fda.gov/drugs/informationondrugs/approveddrugs/ucm279174.htm. Accessed on February 17, 2016.

FDA Approvals Oral Oncolytics 2012

Drug	Indication
Ponatinib	Refractory CML; Ph+ ALL
Abiraterone	Metastatic castration-resistant prostate cancer
Cabozantinib	Progressive medullary thyroid cancer
Regorafenib	Metastatic colorectal cancer, previous irinotecan, VEGF inhibitor therapy
Bosutinib	CML
Enzalutamide	Metastatic castration-resistant prostate cancer (post docetaxel)
Everolimus	Hormone receptor + breast cancer post letrozole/anastrazole; HER-2 negative
Pazopanib	Soft tissue sarcoma; post chemotherapy
Vismodegib	Basal cell carcinoma
Axitinib	Renal cell carcinoma – 2 nd line

Ph+ ALL = Philadelphia chromosome positive acute lymphoblastic leukemia
US Food and Drug Administration. www.fda.gov/drugs/informationondrugs/approveddrugs/ucm279174.htm. Accessed on February 17, 2016.

FDA Approvals Oral Oncolytics 2013

Drug	Indication
Sorafenib	Metastatic differentiated thyroid carcinoma
Afatinib	1 st line NSCLC EGFR+ exon 19 or 21 deletions
Erlotinib	1 st line NSCLC EGFR+ exon 19 or 21 deletions
Lenalidomide	Third-line mantle cell lymphoma
Dabrafenib	BRAF V600E metastatic melanoma
Trametinib	BRAF V600E or V600K metastatic melanoma
Pomalidomide	Myeloma – 3 rd line

US Food and Drug Administration. www.fda.gov/drugs/informationondrugs/approveddrugs/ucm279174.htm. Accessed on February 17, 2016.

FDA Approvals Oral Oncolytics 2014

Drug	Indication
Idecalisib	CLL/follicular NHL
Ceritinib	ALK + NSCLC post crizotinib
Mercaptopurine suspension	Pediatric ALL
Ibrutinib	CLL, including 17p deletions
Trametinib/dabrafenib	Combination therapy for BRAF V600E or V600K metastatic melanoma
Olaparib	BRCA mutated advanced ovarian cancer

CLL = chronic lymphocytic leukemia; NHL = Non-Hodgkin lymphoma.
US Food and Drug Administration. www.fda.gov/drugs/informationondrugs/approveddrugs/ucm279174.htm. Accessed on February 17, 2016.

FDA Approvals Oral Oncolytics 2015

Drug	Indication
Palbociclib	ER+, HER-2-Neu negative metastatic breast cancer
Levatinib	Metastatic thyroid cancer
Panobinostat	Multiple myeloma
Sonidegib	Basal cell carcinoma
Trifluridine/tipiracil	Metastatic colon cancer
Cobimetinib	Metastatic melanoma
Osimertinib	Metastatic NSCLC - EGFR
Alectinib	Metastatic NSCLC – ALK +
Ixazomib	Multiple myeloma

US Food and Drug Administration. www.fda.gov/drugs/informationondrugs/approveddrugs/ucm279174.htm. Accessed on February 17, 2016.

Practical Matters in Managing Oral Oncolytics for Pharmacists



Drug-Drug Interactions

- How to navigate the complexity of drug interactions with oral oncolytics
 - Assume **all** targeted agents have numerous CYP450-mediated drug-drug interactions (because most of them do)
- Use proven resources to review a patient medication profile
 - IUSM Clinical Pharmacology interactions table
 - Online drug information database: Lexicomp, Micromedex
 - Call people like us

Indiana University Department of Medicine. <http://medicine.iupui.edu/clinpharm/ddis/clinical-table/>. Accessed on February 16, 2016.

CYP450-Mediated Drug Interactions

- Enzymes of relevance
 - 1A2, 2B6, 2C8, 2C9, 2D6, 3A4/5/7
- Remember the inducer drugs
 - Antiepileptics: carbamazepine, phenobarbital, phenytoin, primidone
 - Anti-tuberculin agents: rifampin, rifabutin
 - HIV drugs: efavirenz, nevirapine, ritonavir
 - Others: pioglitazone, troglitazone, St. John's Wort

Indiana University Department of Medicine. <http://medicine.iupui.edu/clinpharm/ddis/clinical-table/>. Accessed on February 16, 2016.

Select End-Organ Toxicities with Oral Chemotherapy Agents

Organ Toxicity	Drug
Cardiac	Afatinib, BCR-ABL TKIs, ceritinib, crizotinib, dabrafenib, ibrutinib, lapatinib, pazopanib, regorafenib, ruxolitinib, trametinib, vismodegib
Pulmonary	Afatinib, ceritinib, crizotinib, erlotinib, everolimus, idelalisib, lapatinib, trametinib
Hepatic	Abiraterone, afatinib, BCR-ABL TKIs, ceritinib, crizotinib, idelalisib, lapatinib, regorafenib
Renal	Everolimus, ibrutinib
Vascular	IMIDs, BCR-ABL TKIs, cabozantinib, everolimus, pazopanib
Endocrine	Ceritinib, crizotinib, pazopanib, sorafenib, sunitinib
Ocular	Afatinib, crizotinib, dabrafenib, trametinib
Secondary malignancies	IMIDs, dabrafenib, trametinib, vemurafenib, everolimus, vismodegib

Carcelero E, et al. *Expert Opin Drug Saf.* 2013;12(3):403-420.

Barriers to Adherence

Patient-specific Factors	Provider-related Factors	Treatment-related Factors
Health beliefs	Relationships	Complexity of regimen
Patient history	Satisfaction with care	Behavioral changes required for treatment
Social support	Insurance coverage	Cost
Socioeconomic status	Convenience of care	Duration of therapy
Age	Continuity of care	Adverse effects
Comorbid conditions and polypharmacy		Immediacy of evidence of benefit

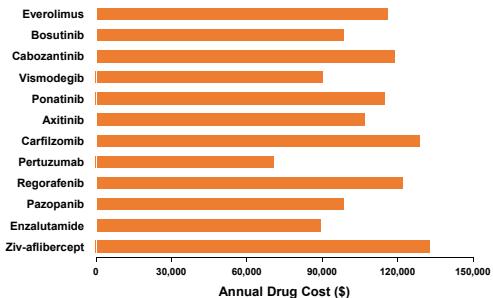
Hartigan K. *Clin J Oncol Nurs.* 2003;7(6 Suppl):21-24. Patridge AH, et al. *J Natl Cancer Inst.* 2002; 94(9):652-661. Winkeljohn DL. *Clin J Oncol Nurs.* 2007;11(6):793-796. Ruddy K, et al. *CA Cancer J Clin.* 2009;59(1):56-66.

Patient/Caregiver Safety

Dos for Oral Oncolytics	Don'ts for Oral Oncolytics
Review Rx and ensure understanding of directions	Leave medications in open area
Use gloves and wash hands when handling	Store med where food/drink are
Keep list of ADEs	Crush, break, or chew
Return unused, expired, damaged, discontinued med to pharm or hospital	Double up on doses
Minimize number of people administering	Assume oral is safer than IV
Wash pts clothes and linen separately	Skip doses
Double-flush toilet after use, during use and 4 to 7 days after d/c	Discard med down toilet or in garbage
Report all medications/OTC/herbals you are taking	

ADEs = adverse drug events; OTC = over-the-counter.
Goodin S, et al. *J Oncol Pract.* 2011;7(1):7-12.

Annual Cost for Selected Oncolytics



Hirsch BR, et al. *Health Aff.* 2014;33(10):1714-1720.

Financial Toxicity

Grade	Description
1	Lifestyle modification (deferral of large purchases or reduced spending on vacation and leisure activities) because of medical expenditures. Use of charity/grants/fundraising/copayment program mechanisms to meet costs of care.
2	Temporary loss of employment resulting from medical treatment. Need to sell stocks/investments for medical expenditures. Use of savings accounts, disability income, or retirement funds for medical expenditures.
3	Need to mortgage/refinance home to pay medical bills. Permanent loss of a job as a result of medical treatment. Current debts > household income. Inability to pay for necessities such as food or utilities.
4	Need to sell home to pay for medical bills. Declaration of bankruptcy because of medical treatment. Need to stop treatment because of financial burden. Consideration of suicide because of financial burden of care.

Khera N. *J Clin Oncol.* 2014;32(29):3337-3338.

Questions?





1-DAY REGIONAL MEETINGS

Ensuring Safe and Effective Treatment of Invasive Fungal Infections



Presented in partnership with the ICHP Annual Meeting

Presenter

James S. Lewis II, PharmD, FIDSA
ID Clinical Pharmacy Coordinator
Oregon Health and Science University
Departments of Pharmacy and Infectious Diseases

Disclosures

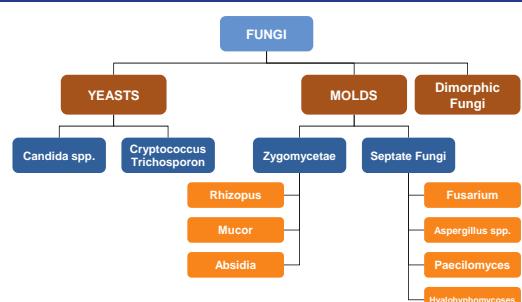
James S. Lewis II, PharmD, FIDSA: Consultant—Accelerate Diagnostics, Allergan, Astellas, The Medicines Company, Merck & Co., Inc.

Objectives

- Describe the mechanisms-of-action, efficacy/safety, and tolerability of available antifungal therapies for IFIs
- Evaluate recent clinical trial data on the benefits and limitations of conventional and newer antifungal agents, including adverse effect profiles and resistance patterns
- Outline best practices for IFI diagnostic testing and monitoring to ensure appropriate and timely treatment, including medication modifications, reconciliation, and prevention of toxicities and drug interactions
- Proactively lead the healthcare team in making informed prophylaxis, empiric, preemptive, and targeted antifungal treatment decisions to improve patient outcomes

IFIs = invasive fungal infections.

The Fungal World



Pathogens Associated with Healthcare Associated Infections (HCAs)

Pathogen	All HCAs (N=504) Number/ (%)		Surgical Site Infections (N=110)	GI Infections (N=6)	UTIs (N=65)	Bloodstream Infections
	Pneumonia (N=110)					
<i>C. difficile</i>	61 (12.1)	0	0	61 (70.9)	0	0
<i>S. aureus</i>	54 (10.7)	18 (16)	17 (16)	1 (1)	2 (3)	7 (14)
<i>K. pneumoniae</i> or <i>oxytoca</i>	50 (9.9)	13 (12)	15 (14)	1 (1)	15 (23)	4 (8)
<i>E. coli</i>	47 (9.3)	3 (3)	14 (13)	1 (1)	18 (28)	5 (10)
<i>Enterococcus</i>	44 (8.7)	2 (2)	16 (15)	5 (6)	11 (17)	6 (12)
<i>P. aeruginosa</i>	36 (7.1)	14 (13)	7 (6)	1 (1)	7 (11)	2 (4)
<i>Candida</i>	32 (6.3)	4 (4)	3 (3)	3 (4)	3 (5)	11 (22)

GI = gastrointestinal; UTIs = urinary tract infections.
Magill SS, et al. *N Engl J Med*. 2014;370:1198.

The Impact of Candidemia

- Fourth most common bloodstream isolate
- Leading fungal pathogen in US hospitals
- 14.5% attributable increase in mortality in adults
- 10.1-day increased length of stay
- \$39,331 increased hospital charges

Zaoutis TE, et al. *Clin Infect Dis.* 2005;41(9):1232-1239. Weinberger M, et al. *J Hosp Infection.* 2005; 61(2):146-154. Bilir SP, et al. *Future Microbiol.* 2015;10:1133-1144.

Big News!!

Clinical Infectious Diseases
IDSA GUIDELINE



Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America

Peter G. Pappas,¹ Carol A. Kauffman,² David R. Andes,³ Cornelius J. Clancy,⁴ Kieren A. Marr,⁵ Luis Ostrosky-Zeichner,⁶ Annette C. Reboli,⁷ Mindy G. Schuster,⁸ Jose A. Vazquez,⁹ Thomas J. Walsh,¹⁰ Theoklis E. Zerbeitis,¹¹ and Jack D. Sobel¹²

Pappas PG, et al. *Clin Infect Dis.* 2016;62(4):e1-e50.

Invasive Candidiasis: Who Is at Risk?

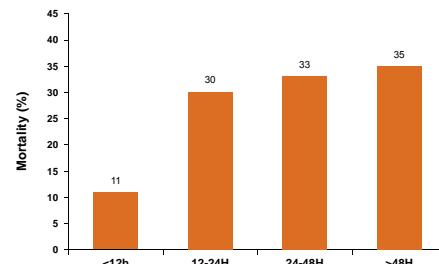
Risk Factors

- Central venous catheters
- Candida colonization
- Increasing severity of illness
- Exposure to broad spectrum antibiotics
- Recent major surgery – especially abdominal
- Necrotizing pancreatitis
- Dialysis
- Parenteral nutrition
- Corticosteroids

- A subset of postsurgical patients may be at uniquely high risk for candidiasis
 - Recurrent GI perforation
 - Anastomotic leaks
 - Acute necrotizing pancreatitis

Pappas PG, et al. *Clin Infect Dis.* 2016;62(4):e1-e50.

Candidemia – Time to Initiation of Therapy and Mortality



Morell M, et al. *Antimicrob Agents Chemother.* 2005;49:3640-3645.

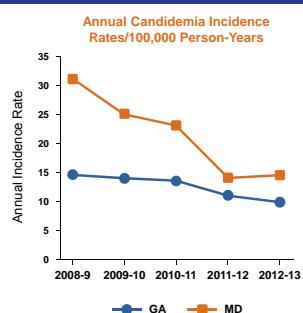
General Susceptibility Patterns of *Candida* spp

	Fluconazole	Itraconazole	Voriconazole	Posaconazole	Candins	AmB
<i>C. albicans</i>	S	S	S	S	S	S
<i>C. glabrata</i>	S-DD to R	S-DD to R	S-DD to R	S-DD to R	S	S to I
<i>C. tropicalis</i>	S	S	S	S	S	S
<i>C. parapsilosis</i>	S	S	S	S	S to R	S
<i>C. krusei</i>	R	S-DD to R	S	S	S	S to I

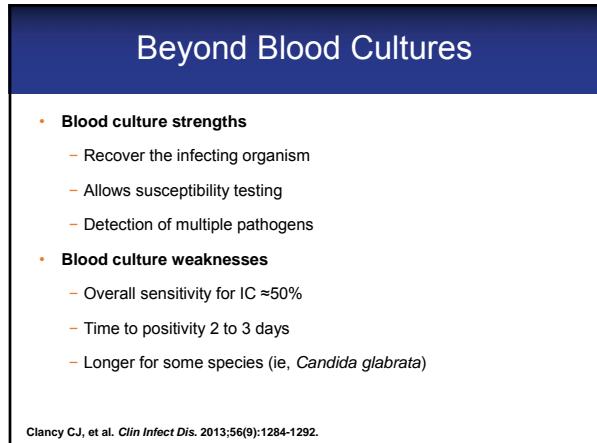
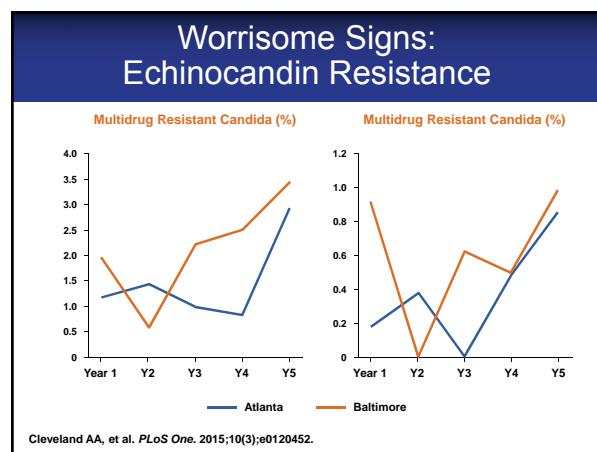
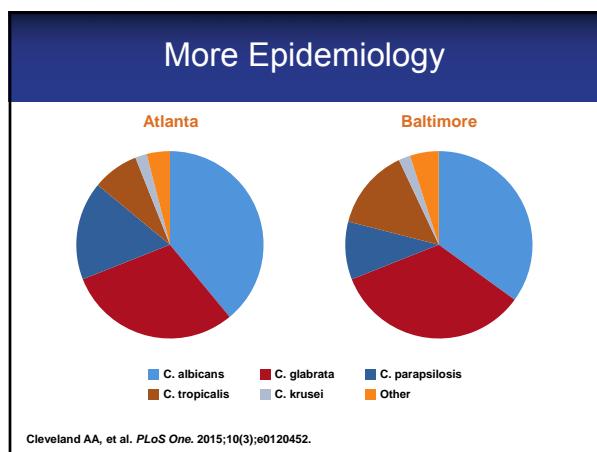
AmB = amphotericin B; S = susceptible; SDD = susceptibility-dose dependent; R = resistant;
I = intermediate.
Pappas PG, et al. *Clin Infect Dis.* 2009;48(5):503-535.

Current Epidemiology

- Most common groups
 - Adults > 65
 - Infants < 1
- Declines across all age groups except age 1-19 in MD
- Fluconazole resistance rates decreased in:
 - GA = -10%
 - MD = -25%
 - Overall rate = 7% resistant



Cleveland AA, et al. *PLoS One.* 2015;10(3):e0120452.

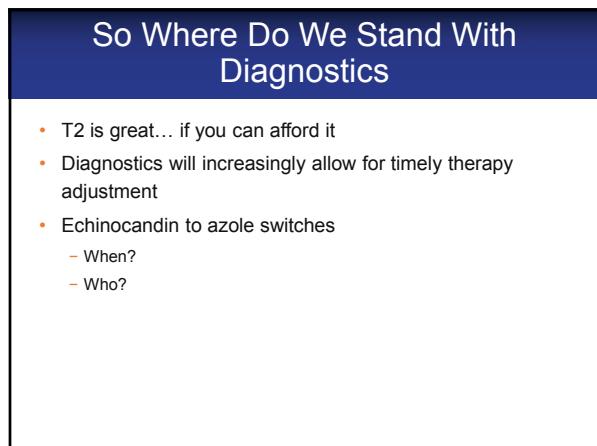


Overall Sensitivity and Specificity of the T2 Magnetic Resonance Method

Sensitivity	Number	%	95% CI
Overall per patient	233 / 256	91.0	86.8-94.2
Overall per assay	234 / 257	91.1	86.9-94.2

Specificity	Number	%	95% CI
Overall per patient	1516 / 1545	98.1	97.3-98.7
Overall per assay	5114 / 5146	99.4	99.1-99.6

CI = confidence interval.
Myelonakis E, et al. Clin Infect Dis. 2015;60:892-899.



The Continuing Challenge of Empiric Therapy

- "...considered in critically ill patients with risk factors for invasive candidiasis and no other known cause of fever"
- "Preference should be given to an echinocandin in:
 - hemodynamically unstable patients
 - previously exposed to an azole
 - colonized with azole-resistant *Candida* species"
- "Fluconazole may be considered in:
 - Hemodynamically stable patients
 - Colonized with azole-susceptible *Candida* species
 - No prior exposure to azoles"
- Duration = candidemia if patient responds
- Stop therapy if no clinical response & cultures + surrogate markers negative

Pappas PG, et al. Clin Infect Dis. 2016;62:e1-e50.

Prophylaxis – We Still Can't Get it Right

- Caspofungin vs placebo
- 222 patients
- Prediction rule used
- ICU patients at “high-risk”
- Primary endpoint – Proven/probable IC

ICU = intensive care unit.
Ostrosky-Zeichner L, et al. *Clin Infect Dis.* 2014;58(9):1219-1226.

Prophylaxis/MITT Population

Variable	Caspofungin (n=102)	Placebo (n=84)	P Value
Incidence of proven/ probable IC (%)	9.8	16.7	.14
Incidence of proven IC (%)	1.0	4.8	.11
Use of antifungals within 7 days of EOT	13.7	17.9	.35
All cause mortality within 7 days of EOT	16.7	14.3	.78

MITT = modified intent-to-treat; IC = invasive candidiasis; EOT = end of therapy.
Ostrosky-Zeichner L, et al. *Clin Infect Dis.* 2014;58(9):1219-1226.

AmB vs Fluconazole vs Echinocandin: Which One is Best for Candidemia?

- Patient-level review of recent randomized trials for candidemia
- Data for all 3 classes of drugs used
- Data from 1915 patients from 7 trials
- Overall mortality was 31.4%
- Rate of treatment success was 67.4%

AmB = amphotericin B.
Andes DR, et al. *Clin Infect Dis.* 2012;54(8):1110-1122.

Bad Prognostic Signs...

Predictors of Mortality Using Logistic Regression

Predictor	OR	(95%) CI
Increasing age	1.01	1.00-1.02
Increasing APACHE 2 score	1.11	1.08-1.14
Immunosuppressive therapy	1.69	1.18-2.44
Infection with <i>C tropicalis</i>	1.64	1.11-2.39

OR = odds ratio; APACHE = Acute Physiology and Chronic Health Evaluation.
Andes DR, et al. *Clin Infect Dis.* 2012;54(8):1110-1122.

Predictors of a Good Outcome...

- Removal of central venous catheter
 - OR = 0.50; 95% CI = .35-.72; P = .0001
- Treatment with an echinocandin
 - OR = 0.65, 95%CI=.45-.94; P = .02
- Similar findings using the clinical success endpoint

Andes DR, et al. *Clin Infect Dis.* 2012;54(8):1110-1122. Clancy CJ, et al. *Clin Infect Dis.* 2012;54(8):1123-1125.

Candidemia in Nonneutropenic Patients

- Echinocandin is recommended as initial therapy
 - (strong recommendation; high-quality evidence)
- Fluconazole, IV or PO, 800-mg (12 mg/kg) load, then 400 mg (6 mg/kg) daily is an acceptable alternative... in selected patients
 - A. Not critically ill
 - B. Not likely to have a fluconazole-resistant *Candida* species
 - (Strong recommendation; high-quality evidence)

IV = intravenous; PO = orally.
Pappas PG, et al. *Clin Infect Dis.* 2016;62:e1-e50.

Susceptibility Testing

- Testing for azole susceptibility is recommended for:
 - All bloodstream isolates
 - Other clinically relevant *Candida* isolates
- Testing for echinocandin susceptibility should be considered in:
 - Patients who have had prior treatment with an echinocandin
 - Among those who have infection with *C. glabrata* or *C. parapsilosis* (strong recommendation; low-quality evidence)

Pappas PG, et al. *Clin Infect Dis.* 2016;62:e1-e50.

Candida: Conclusions

- Echinocandins are first-line choice in 2016
- Pull the lines when possible
- Epidemiology appears stable
- Know your institutional epidemiology
- Emergence of multidrug-resistant *C. glabrata*?

Aspergillus and the Azoles



Clinical Infectious Diseases
IDSA GUIDELINE



Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America

- Primary treatment with voriconazole still recommended
- Initiate therapy early
- Alternatives to voriconazole for primary therapy
 - Liposomal AmB
 - Isavuconazole
 - Other lipid amphotericin products
- Echinocandins NOT recommended for primary therapy

Patterson TF, et al. *Clin Infect Dis.* 2016;63(4):e1-e60.

Voriconazole — Strengths

- The current gold standard for IA
- Broad spectrum
- IV and oral formulations
- Oral formulation now generic
- High oral bioavailability

IA = invasive aspergillosis.

Voriconazole — Weaknesses

- Increasing concern over skin cancer risk
- Is the bioavailability as good as we thought?
- P450 nightmares continue
- When to weigh base dose and when to not
- Toxic at high levels?
 - LFTs
 - Hallucinations

Zwail FO, et al. *Dermatol Surg.* 2012;38(8):1369-1374. Pascual A, et al. *Clin Infect Dis.* 2012;55(3):381-390.

Posaconazole

- Strengths
 - The broadest spectrum of the currently available azoles
 - Mortality benefit in select populations
 - Well-tolerated...or is it?
- New formulations available – gamechangers!
 - IV – highly wallet toxic!!
 - Enhanced bioavailability solid oral dosage form – daily!!

Krishna G, et al. *J Antimicrob Chemother.* 2012;67(11):2725-2730.

Posaconazole — Weaknesses

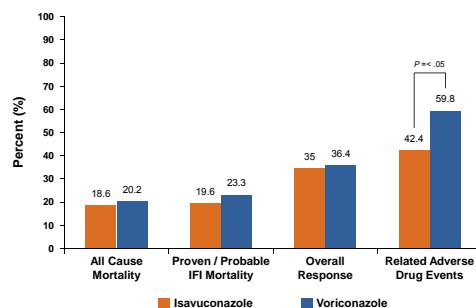
- Kill the oral suspension!!! Exceptions??
- New tablets are a marked improvement
- Once daily! – tablets and IV only!
- Saturable absorption – not an issue with tablets?
- Erratic absorption – tablets?
- Drug interactions – no help there!
- pH issues - appear much less with tablets

Isavuconazole

- Yes that really is the name!
- Spectrum between vori and posa?
- Once daily & prodrug issues
- IV and oral
- No cyclodextrin in the IV
- Better tolerated than voriconazole?
- Treatment indications – no prophylaxis data

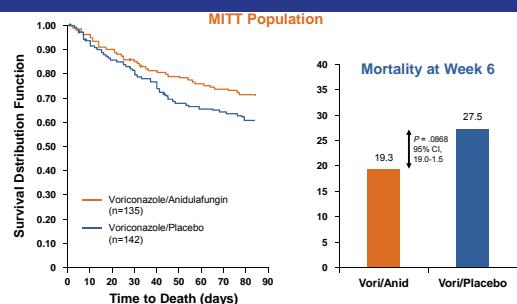
Cresemba [package insert]. Northbrook, IL: Astellas Pharma US, Inc.; 2015.

Voriconazole vs Isavuconazole: IA and Other Mold



Maertens JA, et al. *Lancet.* 2015 [epub ahead of print].

Voriconazole + Anidulafungin vs Voriconazole Monotherapy for IA: MITT Population Crashing



Marr KA, et al. Presented at: 22nd European Congress of Clinical Microbiology and Infectious Disease; April 2, 2012; London, United Kingdom. Abstract LB 8212. Marr KA, et al. *Ann Intern Med.* 2015;162(2):81-89.

The Anti-Aspergillus Azoles: Toxicity and Monitoring

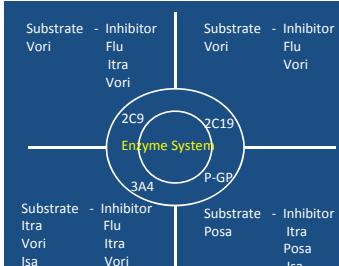
- Voriconazole is not benign
 - Unpredictable PK
 - Skin cancer
 - Hallucinations
 - Monitoring required – trough >1-6
- Posaconazole tablets – do they even need monitoring?
- Isavuconazole – we don't know what we don't know

Williams K, et al. *Clin Infect Dis.* 2014;58:997-1002. Moon WJ, et al. *Clin Infect Dis.* 2014;59:1237-1245. Pascual A, et al. *Clin Infect Dis.* 2012;55:381-390. Andes D, et al. *Antimicrob Agent Chemother.* 2009;53:24-34. Pham A, et al. *Mycoses.* 2016 [epub ahead of print].

Drug Interaction Challenges

"New information is emerging rapidly, and thus, this review is by its very nature incomplete."

Bruggemann RJM, et al.
Clin Infect Dis 2009;48:1441.
US Food and Drug Administration.
Advisory Committee Briefing Document.
<http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AntiinfectiveDrugsAdvisoryCommittee/UCM430748.pdf>. Accessed February 29, 2016.



So...Advanced Azoles 2016

- And then there were 3
- How different are they?
- Do the indications matter?
- How different are the spectrums and PK/PD?
- Are they interchangeable?

Questions?



PLN PHARMACY LEARNING NETWORK **1-DAY REGIONAL MEETINGS**

A Multidisciplinary Approach to Preventing Medication Errors Associated with Insulin Therapy



Presented in partnership with the ICHP Annual Meeting

ICHP

Faculty

Matthew Grissinger, RPh, FISMP, FASCP
 Director, Error Reporting Programs
 Institute for Safe Medication Practices
 Manager, Medication Safety Analysis
 PA Patient Safety Authority
 Horsham, Pennsylvania

Disclosures

Matthew Grissinger, RPh, FISMP, FASCP: Spouse's Employer—Johnson and Johnson

Learning Objectives

- Describe common preventable adverse events with insulin therapy and their causes
- Illustrate the importance of preventing errors through improved order communication, administration, monitoring, and patient education
- Develop a standardized approach to the use of insulin throughout the medication use process
- Describe strategies healthcare practitioners can use to prevent medication errors and improve insulin therapy for the effective management of diabetes

Technician Learning Objectives

- Describe common preventable adverse events with insulin therapy and their causes
- Illustrate the importance of preventing errors through improved order communication, administration, monitoring, and patient education
- Develop a standardized approach to the use of insulin throughout the medication use process
- Describe strategies healthcare practitioners can use to prevent medication errors and improve insulin therapy for the effective management of diabetes

Prescribing



Barriers to Effective Communication of Insulin Orders

- Handwritten orders
- Dangerous abbreviations
- Verbal orders
- Look-alike names
- Sliding-scale orders
- Ambiguous orders
- Hold orders

Sliding-Scale Insulin

7 tablets to 54 Units PLS
 Novolog 6 units 54 TID AC —
 add 1 unit: 60mg B6 > 150
 $60 - 150 = 141, \frac{141}{220} = 14+2, \text{etc}$
 $-12 -$

Novolog 6 tablets 50 TID AC
 Add 1 unit: 40mg B6 > 120 mg/dl
 $\frac{40}{120} = 6+1$
 $181 - 220 = 6+2, \text{etc}$

Standardize Order Communication

- Use standardized insulin protocols
 - ADA Guidelines 2014
- Use standardized order forms
 - List specific products
 - Include prompts to enter dose
 - Incorporate times and meals
 - Standardized correction scales
 - Monitoring parameters
 - Reversal agents

Blood Glucose (BG) Monitoring: <input type="checkbox"/> Before meals and at bedtime. <input type="checkbox"/> 1 hr after meals. <input type="checkbox"/> 2-3 am			
Goal Premeal BG: <input type="checkbox"/> 90-150 mg/dL for most patients			
Prandial Orders	Breakfast	Lunch	Dinner
	<input type="checkbox"/> Lirag (Humalog #)	<input type="checkbox"/> Lirag (Humalog #)	<input type="checkbox"/> Lirag (Humalog #)
<input type="checkbox"/> NPH	<input type="checkbox"/> NPH	<input type="checkbox"/> NPH	
<input type="checkbox"/> Lente	<input type="checkbox"/> Lente	<input type="checkbox"/> Lente	
<input type="checkbox"/> Ultralente	<input type="checkbox"/> Ultralente	<input type="checkbox"/> Ultralente	
<input type="checkbox"/> Regular	<input type="checkbox"/> Regular	<input type="checkbox"/> Regular	
Basal Insulin Orders	Give _____ units of:	Give _____ units of:	Give _____ units of:
	<input type="checkbox"/> NPH	<input type="checkbox"/> NPH	<input type="checkbox"/> NPH
<input type="checkbox"/> Lente	<input type="checkbox"/> Lente	<input type="checkbox"/> Lente	
<input type="checkbox"/> Ultralente	<input type="checkbox"/> Ultralente	<input type="checkbox"/> Ultralente	
<input type="checkbox"/> Regular	<input type="checkbox"/> Regular	<input type="checkbox"/> Regular	

Suggested Lag Times for Prandial Insulin:
 Aspart/Lispro: 0-15 minutes before eating
 30 minutes before eating

For BG<60 mg/dL

- If patient can take PO, give 15 grams of fast acting carbohydrate
- If patient cannot take PO, give 22oz of D50 as IV bolus
- If patient finger stick glucose <15 minutes and repeat above if BG<60

Premed "pre-meal" dose: If patient has hypoglycemia. To be administered in addition to scheduled insulin dose to correct premeal hypoglycemia.

Aspart

<input type="checkbox"/> Low Dose Algorithm (Per 100 mg/dL drop in glucose of basal insulin)	<input type="checkbox"/> Medium Dose Algorithm (Per 100 mg/dL drop in glucose of basal insulin)
100-199 Additional insulin	100-199 Additional insulin
200-249 2 units	200-249 3 units
250-299 3 units	250-299 4 units
300-349 4 units	300-349 5 units
>349 6 units	>349 6 units

High Dose Algorithm
(Per 100 mg/dL drop in glucose of basal insulin)

Prandial BG Additional insulin
100-199 2 units
200-249 3 units
250-299 4 units
300-349 5 units
>349 6 units

Individualized Algorithm

Prandial BG Additional insulin
100-199 2 units
200-249 3 units
250-299 4 units
>349 5 units

Trence DL, et al. J Clin Endocrinol Metab. 2003;88:2430-2437.

Prescribing U-500 Insulin

- An endocrinologist wrote an order for “25 units of U-500 insulin” to be given in the morning
- In reality, he wanted the patient to receive 125 units
- Since each mL of U-500 insulin contains 5-fold more insulin than U-100, he was actually citing the “25 units” marking on the U-100 insulin syringe scale

Patient Assessment, Administration, and Monitoring



Patient Assessment: Before Administration

- Prior to the administration of subcutaneous insulin, practitioners (ie, nurses, nursing assistants) perform an assessment of the following:
 - Bedside POC blood glucose value (finger stick)
 - Symptoms of HYPOglycemia
 - Symptoms of HYPERglycemia
 - Nutritional status (eg, NPO, receiving enteral or parenteral nutrition, last oral intake)
 - Changes in the patient's condition (eg, infection)
 - Changes in the patient's medication regimen (eg, addition or discontinuation of a medication that may impact blood glucose levels [eg, corticosteroid])

NPO Status

- A patient with diabetes on continuous enteral feedings was also receiving subcutaneous NPH insulin, 24 units BID, to control elevated glucose levels.
- The feedings were then held for a CT scan but no one discontinued the insulin
- By the time the BG was checked again, it measured only 26 mg/dL

Insulin orders on MARs

INSULIN ASPART (NOVOLOG) *HIGH* 100 UNIT/M (None)
 (NOVOLOG INSULIN)
 DOSE: SEE SLIDING SCALE SUBQ AS NEEDED/PRN
 COMMENTS: DOSE PER SLIDING SCALE BELOW AND DOCUMENT ON DIABETES RECORD FORM. *HIGH DOSE*
 BS < 60 OR SYMPTOMATIC REFER TO ROUTINE 1/2 A
 HYPOGLYCEMIA ORDERS. OBTAIN STAT LAB GLUCOSE AND NOTIFY MD. 151-200= 6 UNITS.
 201-250= 8 UNITS. 251-300= 10 UNITS. 
 301-350= 12 UNITS. 351-400= 14 UNITS.
 401-500= 16 UNITS. >500 GIVE PRESENT REGIMEN DOSE FOR BS 401-500. OBTAIN STAT LAB BLOOD SUGAR AND CALL MD WITH RESULTS.
 (SUBSTITUTE FOR HUMALOG)
 CAUTION: MAY LOOK/SOUND ALIKE OTHER DRUGS!

MAR = Medication Administration Record.



Monitoring



Wrong Dose Errors Due to Wrong Blood Glucose Values

- 12.9% of the wrong-dose events involved breakdowns with obtaining and/or communicating patients' blood glucose values
- Specific problems include:
 - Reporting an incorrect value
 - Confusing the patient's weight for his or her blood glucose level
 - Verbally communicating the wrong patient's value
 - Documenting the wrong result

Wrong Dose Errors Due to Breakdowns in Communicating Blood Glucose Results

- The nurse asked the nursing assistant for the patient's AccuCheck results. The nurse was told that the blood glucose was 377. The patient was covered with 10 units of Humalog per sliding scale guidelines. When the nursing assistant wrote the AccuChecks on the bulletin board, the blood glucose of 97 was written for that patient.
- A nurse extern came out of patient's room at the time AccuChecks are performed. The nurse extern stated "211," and RN repeated "211, right?" The nurse extern was referring to the patient's daily weight, which is supposed to be performed at 7:30 a.m. The nurse covered the patient with 4 units of regular insulin then five minutes later the nurse extern informed the RN that the patient's blood glucose level was 130.

Blood Sugar Levels or?

- The nurse picked up a piece of scrap paper that listed several patients with a number next to each name. All of the numbers were well above 200
- Assuming the numbers were blood sugar levels, she gave each patient insulin using a sliding-scale protocol
- Afterwards, she realized that the numbers were actually patient room numbers!

Bedside POC Blood Glucose

- Process for documenting bedside POC blood glucose values in a standard location that allows nurses to determine an appropriate dose of insulin and track the patient's overall response to therapy
- Prohibits verbal communication of bedside POC blood glucose values from staff who obtain bedside POC blood glucose values to nurses who are administering insulin

How many patients are harmed with insulin in your organization?



Triggers

- An easily identifiable, focused item representing an opportunity (or clue) that may lead to an adverse event
- Medications, laboratory tests, patient conditions
- "Something went wrong"
- Effective method for measuring the overall level of harm

Insulin "Triggers"

Triggers	Possible ADE
Dextrose 50%	Hypoglycemia
Glucagon	
Blood glucose more than 300 or less than 50	
Rapid response team call	

Outcome Measures: Insulin

Numerator: Number of episodes of blood glucose results (bedside and lab testing) less than or equal to 50 mg/dL

Denominator: Number of inpatients who are prescribed insulin

Numerator: Number of episodes of administering Dextrose 50% to treat hypoglycemia for patients prescribed insulin

Denominator: Number of inpatients who are prescribed insulin

Questions?



Improving Long Term Outcomes in Heart Failure:

Practical Implications for Pharmacists



Presented in partnership with the ICHP Annual Meeting

Faculty

Mark A. Munger, PharmD, FCCP, FACC, FHFSA

Professor, Pharmacotherapy
Adjunct Professor, Internal Medicine
University of Utah
Salt Lake City, Utah

Disclosure

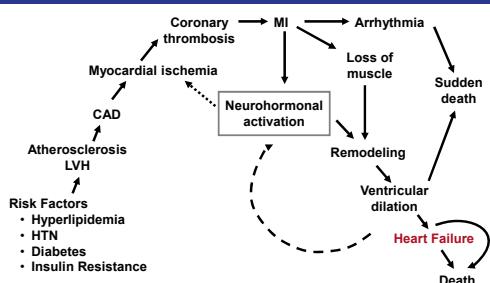
Mark A. Munger, PharmD, FCCP, FACC, FHFSA has no financial relationships to disclose relating to the subject matter of this presentation.

Objectives

- Recognize and classify HF patients according to disease stage and class
- Review current guidelines for the pharmacologic treatment and management of patients with chronic HF
- Assess clinical evidence on existing and emerging treatments in chronic HF to provide personalized therapy toward decreasing hospitalizations and mortality
- Develop strategies to maximize cost-effectiveness of new FDA-approved HF drugs

HF = heart failure; FDA = Food and Drug Administration.

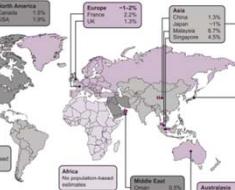
Risk Factors for HF in the Cardiovascular Continuum



Prevalence and Burden of HF

- HF affects ~5.1 million people in the United States, 26 million worldwide
- The estimated risk for developing HF for individuals ≥40 years of age is ~20%
- ~50% of people who develop HF die within 5 years
- Reported hospitalizations for HF exceed 1 million each year and are associated with a 30-day readmission rate of 25%
- IN 2013, >\$30 billion was spent on HF with the reported costs of hospitalizations alone being ≥\$23,077/patient

Ponikowski P, et al. Heart failure: preventing disease and death worldwide. https://www.escardio.org/static_file/Escardio/Subspecialty/HFAWHFA-whitepaper-15-May-14.pdf. Accessed January 29, 2016. Go AS, et al. *Circulation.* 2013;127(1):e6-e245.



Definition of Heart Failure

- Complex, progressive, clinical syndrome
- Results from structural or functional impairment of ventricular filling or contractility
- Major clinical manifestations
 - Dyspnea and fluid retention
 - Fatigue
- Patient presentation is variable
- HFrEF: Heart failure with reduced ejection fraction
- HFpEF: Heart failure with preserved ejection fraction

ACCF/AHA Guidelines. *J Am Coll Cardiol.* 2013;62:e147-e239. Rodriguez JL, et al. *Heart Lung.* 2008; 37:257-265.

Definition of Heart Failure

Patient Perspective

"When you have heart problems, you always worry [that] your next breath is your last one. That's something you never know."

Patient Perspective

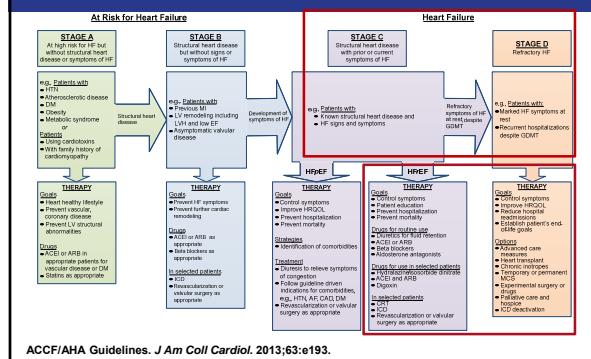
"I'm not depressed...not really depressed...It's just a low feeling and it's not a happy feeling, and you never feel your life's worth anything at times."

Patient Perspective

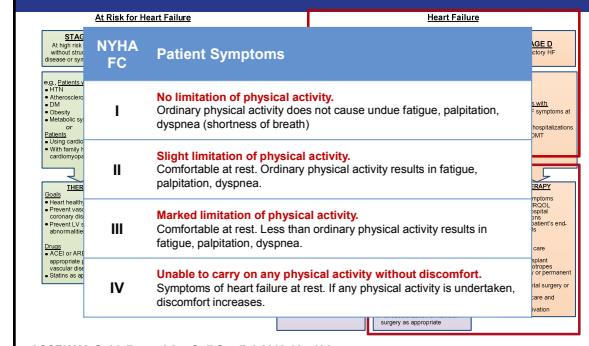
"I did at times start having queasy feelings and pains in my one side. And it all happened once or twice while driving. I pulled off the road, but I didn't do anything about it. All of a sudden, I was developing sleep apnea or wasn't breathing right but sloughed it off until I could hardly breathe at all the last few days. I did ignore the original symptoms. The last day I woke up and couldn't breathe well and told my kid to take me to the hospital. I was unconscious when I got to the hospital."

ACCF/AHA Guidelines. *J Am Coll Cardiol.* 2013;62:e147-e239. Rodriguez JL, et al. *Heart Lung.* 2008; 37:257-265.

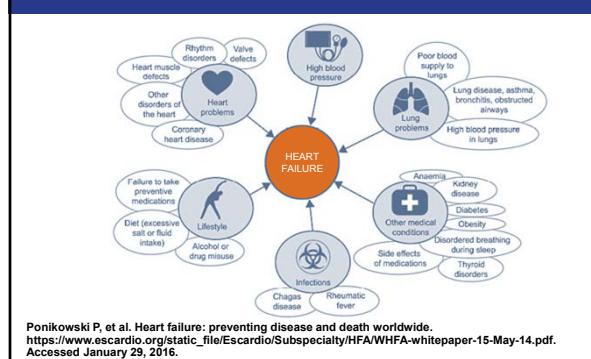
Stages, Phenotypes and Treatment of HF



Stages, Phenotypes and Treatment of HF



Common Causes of Heart Failure



Ponikowski P, et al. Heart failure: preventing disease and death worldwide. https://www.escardio.org/static_file/Escardio/Subspecialty/HFA/WHF-whitepaper-15-May-14.pdf. Accessed January 29, 2016.

Case Study: Background

- 64-year-old female
- Remote history of smoking
- Moderate alcohol consumption
- T2DM (controlled with metformin; HbA1c=6.9%)
- Mild COPD
- Reports increasing dyspnea on exertion over the previous month
- Orthopnea; bilateral pedal edema
- Moderate weight gain despite increased appetite
- Creatinine: 1.4 mg/dL (Creatinine Clearance: 66.3 mL/min)

T2DM = type 2 diabetes mellitus; COPD = chronic obstructive pulmonary disease.

Case Study: Physical Exam and Laboratory Tests

- BP: 130/86 mmHg; HR: 90 bpm; Respirations: 24/minute
- O2 Saturation: 97% on room air
- Lung Sounds: clear
- JVD: 15 cm + + Kussmaul's sign (JVP rise on inspiration-indicative of right-sided heart failure)
- BNP Level: 689 pg/mL
- TSH and Cardiac Enzymes: Normal
- CXR: Mild pulmonary vascular redistribution
- Echo: LVEF 31%; RV mild dysfunction

BP = blood pressure; HR = heart rate; bpm = beats per minute; JVD = jugular venous distention; JVP = jugular venous pressure; BNP = brain natriuretic peptide; TSH = thyroid stimulating hormone; CXR = chest x-ray; LVEF = left ventricular ejection fraction; RV = right ventricle.

Case Question

Based on the findings presented, how would you classify this patient with HF?

- HFrEF; Stage C, NYHA FC III
- HFrEF: Stage C, NYHA FC IV
- HFpEF; Stage C, NYHA FC I
- HFpEF; Stage C, NYHA FC IV

HF_rEF = heart failure with reduced ejection fraction; NYHA FC = New York Heart Association Functional Classification; HF_pEF = heart failure with preserved ejection fraction.

Case Question

What is your initial treatment(s)?

- Start β-adrenergic blocker when euvolemic
- Start ACEI or ARB unless contraindicated
- Start loop diuretic for congestive signs and symptoms
- Low-salt diet
- All are correct

ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker.

Guideline-Recommended Pharmacologic Treatments

Therapy for Stage C HFrEF	NYHA Functional Class			
	1	2	3	4
ACEI, ARB	Yes	Yes	Yes	Yes
β-adrenergic blockers	(Yes)	Yes	Yes	(Yes)
Aldosterone Antagonists		(Yes)	Yes	Yes
Diuretics		(Yes)	Yes	Yes
Digoxin			(Yes)	(Yes)
Hydralazine and Isosorbide dinitrate		(Yes)	(Yes)	(Yes)

ACCF/AHA Guidelines. *J Am Coll Cardiol.* 2013;62:e147-239.

Ten Commandants of HFrEF

- Maintain patient on 2- to 3-g sodium diet. Follow daily weight. Monitor standing blood pressures in the office, as these patients are prone to orthostasis.
- Determine target/ideal weight, which is not the dry weight. In order to prevent worsening azotemia, some patients will need to have some edema. Achieving target weight should mean no orthopnea or paroxysmal nocturnal dyspnea. Consider home health teaching.
- Avoid all nonsteroidal anti-inflammatory drugs because they block the effect of ACEIs and diuretics.
- Use ACEIs in all heart failure patients unless they have an absolute contraindication or intolerance. Use doses proven to improve survival and back off if they are orthostatic. In those patients who cannot take an ACEI, use an ARB.

ACCF/AHA Guidelines. *J Am Coll Cardiol.* 2013;62:e147-239.

Ten Commandants of HFrEF

- Use loop diuretics (like furosemide) in most NYHA class II through IV patients in dosages adequate to relieve pulmonary congestive symptoms. Double the dosage (instead of giving twice daily) if there is no response or if the serum creatinine level is >2.0 mg/dL.
- For patients who respond poorly to large dosages of loop diuretics, consider adding 5 to 10 mg of metolazone one hour before the dose of furosemide once or twice a week as tolerated.

ACCF/AHA Guidelines. *J Am Coll Cardiol.* 2013;62:e147-239.

Ten Commandments of HFrEF

7. Consider adding 25 mg spironolactone in most class III or IV patients. Do not start if the serum creatinine level is >2.5 mg/dL (220 µmol/L).
8. Use metoprolol, carvedilol, or bisoprolol in all class II and III heart failure patients unless there is a contraindication. Start with low doses and work up.
Do not start if the patient is decompensated (excessively dry or wet).
9. Use digoxin in some symptomatic heart failure patients.
10. Encourage a graded exercise program.

ACCF/AHA Guidelines. *J Am Coll Cardiol.* 2013;62:e147-239.

Objectives

- Assess clinical evidence on emerging treatments in chronic HF to provide personalized therapy toward decreasing hospitalizations and mortality
- Develop strategies to maximize cost-effectiveness of new FDA-approved HF drugs

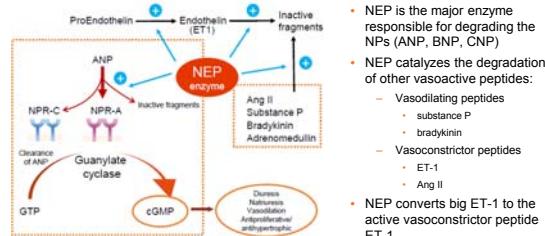
Emerging Therapies for the Treatment of HFrEF

- **Angiotensin Receptor-Nepriylin Inhibitor (ARNI) (Entresto®)**
 - Combines ARB with inhibition of nepriylin, inhibiting RAAS and augmenting natriuretic peptide activity
 - Approved in July 2015 for patients with chronic HF (NYHA FC II-IV) with reduced ejection fraction
- **Ivabradine (Corlanor®)**
 - Selectively inhibits the sinus node If (funny channel)-reduces SA node pacemaker activity thereby decreasing HR, no effect on contractility or blood pressure
 - Approved in April, 2015 for patients with stable, symptomatic HF, with LVEF ≤35% and in **sinus rhythm** with resting HR ≥70 bpm and on maximally tolerated dose of β-adrenergic blocker or with contraindications to β-adrenergic blocker

King JB, et al. *Pharmacotherapy.* 2015;35:823-837. DiFrancesco D. *Heart Rhythm.* 2012;9(2):299-301
Rosa GM, et al. *Expert Opin Drug Metab Toxicol.* 2014;10(2):279-291.

Nepriylin (neutral endopeptidase 24.11; NEP)

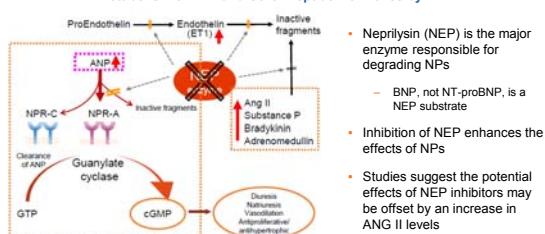
Role in Natriuretic Peptide Degradation Metabolism of ANP and Other Peptide Hormones by NEP



Erdos, Skidgel. *FASEB J.* 1989;3:145-51. Levin, et al. *N Engl J Med.* 1998;339:321-8. Stephenson, et al. *Biochem J.* 1994;303:17-27. Jiang, et al. *Am J Physiol.* 1992;262:H19-23. Kenny, et al. *Biochem J.* 1993;291:83-8. Skidgel, et al. *Peptides.* 1994;5:763-7. Abassi, et al. *Metabolism.* 1992;41:603-5. Murphy, et al. *Br J Pharmacol.* 1994;113:137-42. Jiang, et al. *Hypertens Res.* 2004;27:109-17.

Nepriylin Inhibition

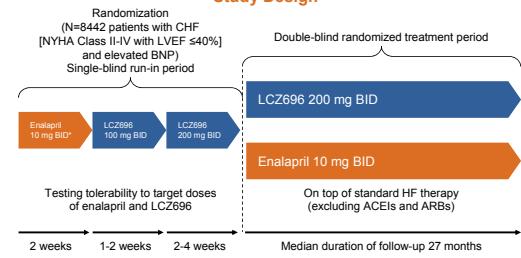
Effects on Natriuretic Peptides Metabolism of ANP and Other Peptide Hormones by NEP



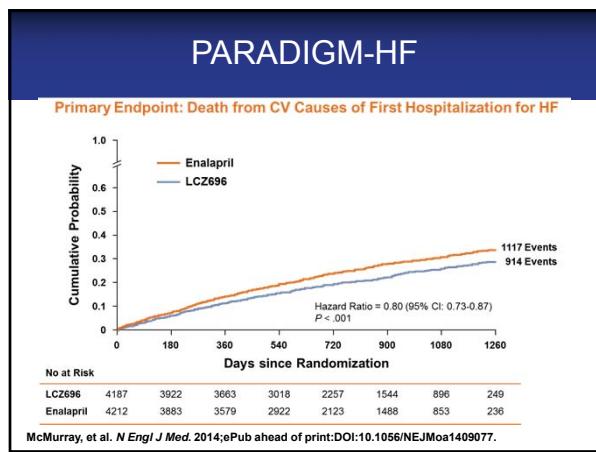
Erdos, Skidgel. *FASEB J.* 1989;3:145-51. Levin, et al. *N Engl J Med.* 1998;339:321-8. Murphy, et al. *Br J Pharmacol.* 1994;113:137-42. Jiang, et al. *Hypertens Res.* 2004;27:109-17. Ferro, et al. *Circulation.* 1998;97:2323-30. Martinez-Rumayor, et al. *Am J Cardiol.* 2008;101(suppl):3A-8A. Richards, et al. *Hypertens.* 1993;11:407-16.

PARADIGM-HF

Study Design



*Enalapril 5 mg BID for 1-2 weeks followed by enalapril 10 mg BID as an optional starting run-in dose for those patients who are treated with ARBs or with a low dose of ACEI.
McMurray, et al. *Eur J Heart Fail.* 2013;15:1062-73. McMurray, et al. *Eur J Heart Fail.* 2014;16:817-25. McMurray, et al. *N Engl J Med.* 2014;pub ahead of print;DOI:10.1056/NEJMoa1409077.



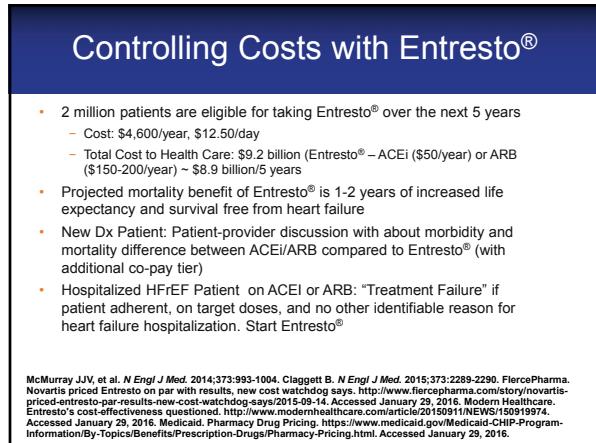
PARADIGM-HF

Prospectively Defined Safety Events

Event, n (%)	LCZ696 (n=4187)	Enalapril (n=4212)	P-Value
Hypotension			
Symptomatic	588 (14.0)	388 (9.2)	<.001
Symptomatic with SBP <90 mmHg	112 (2.7)	59 (1.4)	<.001
Elevated serum creatinine			
≥2.5 mg/dL	139 (3.3)	188 (4.5)	.007
≥3.0 mg/dL	63 (1.5)	83 (2.0)	.10
Elevated serum potassium			
>5.5 mmol/L	674 (16.1)	727 (17.3)	.15
>6.0 mmol/L	181 (4.3)	236 (5.6)	.007
Cough	474 (11.3)	601 (14.3)	<.001
Angioedema (adjudicated by a blinded expert committee)			
No treatment or use of antihistamines only	10 (0.2)	5 (0.1)	.19
Catecholamines or glucocorticoids without hospitalization	6 (0.1)	4 (0.1)	.52
Hospitalized without airway compromise	3 (0.1)	1 (<0.1)	.31
Airway compromise	0	0	—

Fewer patients in the LCZ696 group than in the enalapril group stopped their study medication because of an AE (10.7% vs 13.3%, P=.03).

McMurray, et al. *N Engl J Med.* 2014; ePub ahead of print: DOI:10.1056/NEJMoa1409077.

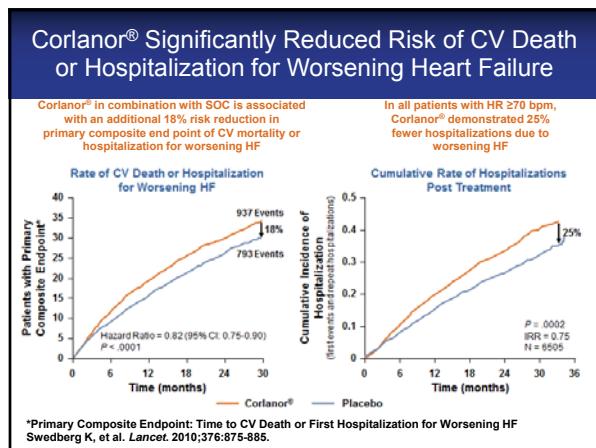


Ivabradine for Moderate-to-Severe HF and LV Systolic Dysfunction: SHIFT Study

- Randomized, double-blind, placebo-controlled (Ivabradine)
- 6505 NYHA FC II-IV Subjects
 - Male (77%), Caucasian (89%), LVEF <35%, HR >70 bpm
 - Admission for HF in previous 2 months
 - On optimal medical management (90% BB, 84% on ACEi/ARBs, 60% ARAs)
- Primary Endpoint: Composite of CV death or hospital admission for HF

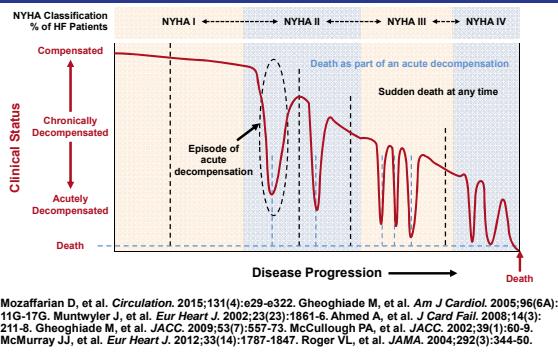
Heart Rate	# of Events (CV Death or Hospital Admission)	Hazard Ratio (95% CI) vs Lowest HR group	P-value
70 to <72	92	1.00	—
72 to <75	157	1.15 (0.88-1.48)	.308
75 to <80	197	1.33 (1.03-1.70)	.027
80 to <87	205	1.80 (1.40-2.31)	<.001
> 87	286	2.34 (1.84-2.98)	<.001

Borer JS, et al. *Eur Heart J.* 2012;33(22):2813-2820. Swedberg K et al. *Lancet.* 2010;376(9744):875-885.



- ## Considerations with Ivabradine
- Improvement in NYHA FC and outcomes
 - Limited Side Effect Profile (phosphenes-sudden change in brightness of light-2%) and lowers atrial fibrillation threshold (1%+) (208 treated/1 case Afib)
 - Effect largely contingent on basal HR
 - Is not a β-adrenergic blocker and is "add-on" therapy
 - "Personalized" medicine based on HR?
 - Estimated Population: 1.4 Million persons
 - Cost: \$375.00 (WAC)/month [5mg and 7.5mg] \$4500/year
 - Cost-Effectiveness: 9-18,000 Euros (\$9.8-\$19.5) [UK Cost: 42.1 Euros/month]

Heart Failure Progression, Morbidity, and Mortality



Case Study: Background

- 54-year-old male
- Four previous hospital admissions for worsening HF over 2 years
- Non-obstructive CAD on cardiac catheterization at time of initial diagnosis
- LVEF 26%, PAS 55 mmHg, EDD 6.7 cm
- Chronic bilateral edema of legs, has difficulty bathing and dressing, no PND, no orthopnea
- BP 106/78 mmHg; HR 82 bpm (sinus rhythm), +S4
- Creatinine: 2.0 mg/dL (CrCl ~ 32 mL/min)
- Meds: lisinopril 20mg qday, carvedilol 25mg qday (max tolerated dose), furosemide 40mg qday, Spironolactone 12.5mg qday, ICD

To Add or Not to Add?

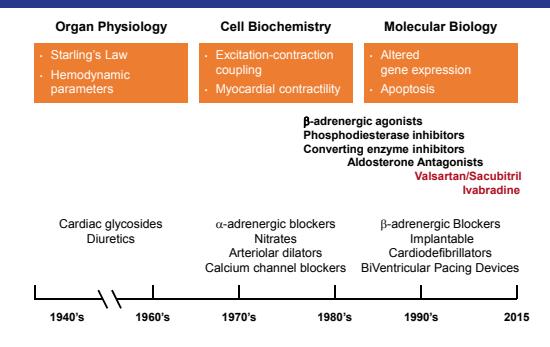
Which of the following treatment options is best after bolus dosing of loop diuretics with vasodilator therapy in-hospital over 24 hours?

1. Up-titrate furosemide to 80mg qday and follow weights on outpatient basis, no other changes to medications
2. Start ivabradine 5mg BID (with up-titration furosemide)
3. Start sacubitril/valsartan 24/26mg BID, D/C lisinopril
4. Discharge patient on outpatient therapy at admission, follow-up in 1 week with cardiologist

To Add or Not to Add?

- Up-titrate furosemide to 80mg qday and follow weights on outpatient basis, no other changes to medications
 - Patient admitted 4 times in past 2 years
- Start Ivabradine 5mg BID (with up-titration furosemide)
 - Patient eligible: YES, cost-effective, YES through reduction in hospitalizations, no all-cause mortality benefit
- Start sacubitril/valsartan 24/26mg BID, D/C lisinopril
 - Patient eligible: YES, cost-effective, YES through reduction in hospitalization and reduction in mortality (+ 2years)
- Discharge patient on outpatient therapy at admission, follow-up in 1 week with cardiologist
 - Patient admitted 4 times in past 2 years

Changing Treatment Strategies in Heart Failure



Questions?



PLN PHARMACY LEARNING NETWORK **1-DAY REGIONAL MEETINGS**

Preventing Errors: Look- and Sound-Alike Medications



Presented in partnership with the ICHP Annual Meeting

ICHP

Faculty

Matthew Grissinger, RPh, FISMP, FASCP

Director, Error Reporting Programs
Institute for Safe Medication Practices

Disclosure

Matthew Grissinger, RPh, FISMP, FASCP: Spouse's Employer—Johnson and Johnson

Learning Objectives

- Identify the types of medication errors that are the result of look-alike and sound-alike names
- Describe strategies for health-system pharmacists for reducing errors due to similarity in drug names

Technician Learning Objectives

- Identify the types of medication errors that are the result of look-alike and sound-alike names
- Describe strategies for health-system pharmacists for reducing errors due to similarity in drug names

FDA Name Differentiation Project

Established Name	Recommended Name	Established Name	Recommended Name
Acetohexamide	AcetylHEXAMIDE	Hydralazine	HydRALAZINE
Acetazolamide	AcetAZOLAMIDE	Hydromorphone	HYDROmorphone
Bisoprolol	BuPIROl	Hydroxyzine	HydROXYZINE
Chlorpromazine	ChloroPROMAZINE	Medroxyprogesterone	MedroPROGESTERone
Chlorpropamide	ChloroPRAmIDE	Methylprednisolone	MethyLPREDNIsolone
Clomiphene	ClomPHENE	Methyltestosterone	MethyLTEStOsterOne
Compramine	ComPRAMINE	Mitoxantrone	MitoXANTRONE
Cyclobenzaprine	CycloBENZAPRINE	Nicardipine	NICArdipine
Cyclosorine	CycloSERINE	Nifedipine	NFEEdipine
Danazol	DAUzol	Prednisone	PrediSOne
Doxorubicin	DOXOrubicin	Prednisolone	PrediSol ONE
Doxylamine	DOXYlamine	Risperidone	rispeRIDOne
Doxylamine	DoxYLamine	Ropivacaine	rOPINRicaine
Dobutamine	DOBUTamine	Sulfadiazine	SulfADIAZINE
Dopamine	DOPAmine	Sulfisoxazole	SulfSOXAZOLE
Glycopyrrolate	GlyPODE	Tolazamide	TOLUAzamide
Glyburide	GlyBURIDE	Tolbutamide	TOLBuTamide

US Food and Drug Administration. www.fda.gov/Drugs/DrugSafety/MedicationErrors/ucm164587.htm. Accessed on February 16, 2016.

ISMP's List of Confused Drug Names

Drug Name	Confused Drug Name	Drug Name	Confused Drug Name
Alosetron	aztreonam B	Anakinra	krovert
Acyclovir	Acycloc	enfamil	enf.001Pre
acutAZOLamide	acutHEXAMIDE	amoxiclav	amoxicline
acthar	acthar	amifamtrpin	amifamtrpin
acevateEXAMIDE	acevateZLAMIDE	amphoterin B	Albact
Aciphex	Aciprill	amphoterin B	Ambisome
Aspirin	Acetamin	Acicid	Azoxin-3
Atorvastatin	Catol	Acicid	Azoxin
Atosiban	TNKase	Acitac	Azoxin
Beta-	Act	Acitac	Azoxin
Advair (Symbicort)	Daptacel (HibP)	Antagonist Citrate Dexamethasone Fumarate A	Antagonist Sulfur Glucide Sulfonate Fumarate A
Advair	Defendil	Antagonist Citrate Sodium Fumarate A	Antagonist Sulfur Glucide Sulfonate Fumarate A
Aderal	Defendil XR	Acitretin	Acitretin
Aderal XR	Defendil	Acicmet	Acivendmet
ado-Biotinimeth esteramine	trebutamine	Aciglycemic	Acivitene
Admir	Advisor	Acipretin	Acipretin
Admocor	Admir	Acisop	Acisop
Admox	Admox	Acitacitin	Acitacitin
Altro (topicalized)	Altro (salve)	Acitacitin	Acitacitin
Altro (salve)	Altro (topicalized)	Acitacitin	Acitacitin
Alprazolam	Alprazolam	Acitacitin	Acitacitin
Alros	Alros	Acitacitin	Acitacitin
Aluron	Leukeran	Acicat	Acicat
Aluron	Mylorin	Acicat	Acicat
Alzys	Alzys	Acicat	Acicat
Alzys Anti-Cancer	Alzys Anti-Cancer	Acicat	Acicat
Alzys	Waix	Acicat	Acicat
Alzys Anti-Cancer	Alzys Anti-Cancer	Acicat	Acicat
Alzys	Waix	Acicat	Acicat
Alzys	Waix	Acicat	Acicat

Institute of Safe Medication Practices. www.ismp.org/Tools/confuseddrugnames.pdf. Accessed on February 16, 2016.

USP MedMarx Data Report

USP identified 1,470 drugs involved in look-alike and/or sound-alike (LASA) errors.

MEDMARX® Data Report

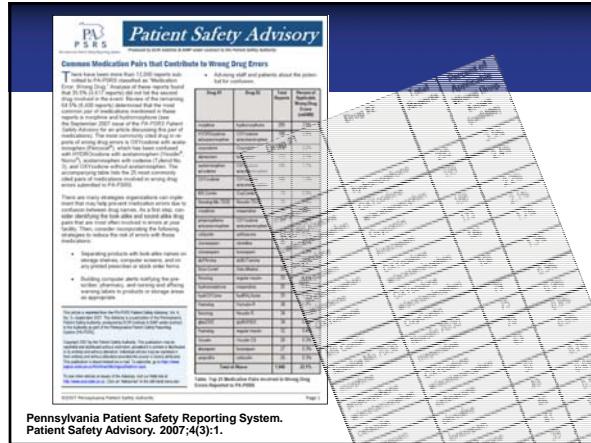
A Report on the Relationship of Drug Names and Medication Errors in Response to the Institute of Medicine's Call for Action

Rewards justify itself, and Results justify itself.

FEATURING:

- Look-alike and/or sound-alike drug names from her recent medication error reporting programs
- The drug naming process in the U.S.
- Summary of USP's LASA research findings
- Summary of other information on look-alike and sound-alike errors

U.S. Pharmacopeia. www.uspsteepharma.com/wp-content/uploads/2012/02/2008MEDMARX-DataReport.pdf. Accessed on February 16, 2016.



Wrong Drug Errors Involving Morphine or HYDROmorphine

- Of all wrong drug error reports that include morphine and/or HYDROmorphine, 36% involve a mix-up between those 2 drugs
- Of wrong drug reports that involve these 2 drugs
 - 62% show morphine as the prescribed medication and HYDROmorphine given in error
 - 71% of reports indicate that the errors occurred when these medications were obtained from unit stock

Pennsylvania Patient Safety Reporting System. *Patient Safety Advisory*. 2007;4(3):69-108.

Types of “Look-Alike” Names

- Handwritten orders
 - Some pairs are only confused when handwritten
- Beginning of drug name is same
 - metFORMIN – metroNIDAZOLE
 - traMADol – traZODone
- Look-alike drug names
 - hydRALAZINE & hydrOXYzine
 - DOPamine & DOBUTamine
 - morphine & HYDROmorphine
 - Drug names with and without suffixes
 - Immediate-release and extended-release products

Additional Factors

- What factors contribute to names that “look-alike”?
 - Strengths/concentrations
 - Frequency
 - Usage in organization (may affect how often it happens)
 - Indication
 - Serzone & Seroquel

Where Are Names Confused?

- Medication Orders
 - Handwritten Orders
 - Order forms, preprinted orders
 - CISplatin/CARBOplatin
 - vinCRISTine/vinBLASTine
 - DOPamine/DOBUTamine
- Order Entry Screens

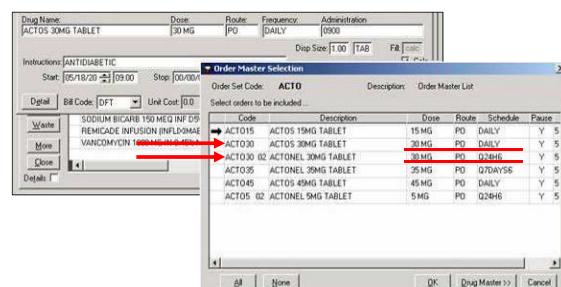
Handwritten Look-Alike Names

Carvedilol 4 mg po qd
Regitab 40 mg PO po.

Handwritten Look-Alike Names (continued)

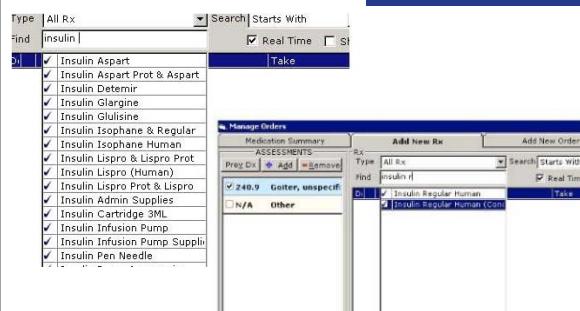
Axcel 150 mg bid
Tigase 200 mg qd
Nyzamt qd
Zyprexa 10, 150 mg

Electronic Order Entry



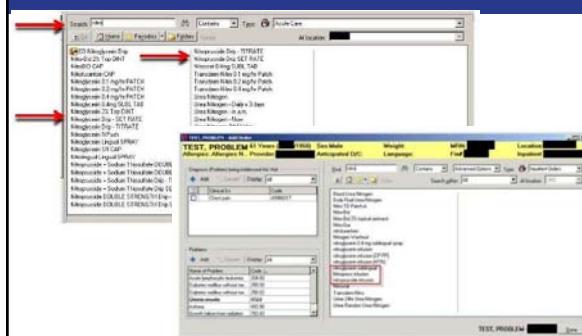
Used with permission from the Institute for Safe Medication Practices, Horsham, Pennsylvania.

Electronic Order Entry (continued)



Used with permission from the Institute for Safe Medication Practices, Horsham, Pennsylvania.

Electronic Order Entry (continued)



Used with permission from the Institute for Safe Medication Practices, Horsham, Pennsylvania.

Which Regular Insulin?

Ln	Drug#	Drug Name	Strength/Volume	Enter Line # -----	Pack Sz
1	13928	INSULIN-HUMANLIN L	100U-1ML	INJ	10.000
2	46002	INSULIN-NOVOLIN N	100U-1ML	INJ	10.000
3	61501	INSULIN-HUMANLIN U	100U-1ML	INJ	10.000
4	64042	PINK-INSULIN	0 .50U-1ML	SYRG	25.000
5	64043	BLUE-INSULIN	0 .50U-1ML	SYRG	50.000
6	64044	WHITE-INSULIN	100U-1ML	SYRG	50.000
7	64098	INSULIN-B DILUTED	0 .10U-1ML	VIAL	10.000
8	97012	INSULIN-BE HUMAN	10U-25ML	SYRG	25.000
9	98192	INSULIN-NOVOLIN N	100U-1ML	INJ	10.000
10	98192	INSULIN-BE HUMAN	100U	INJ	100.000
11	98192	INSULIN-NOVOLIN	100U	INJ	100.000
12	99669	INSULIN-HUMAN R (PS)	100U	INJ	100.000
13	99818	INSULIN-HUMAN REG	100U	INJ	100.000
14	31421	INSULIN NPH INNOLET	1U	INJ	300.000
15	31321	INSULIN REG INNOLET	1U	INJ	300.000
16	31721	INSULIN 70/30 INNOLET	100U	INJ	300.000
17	31721	INSULIN 70/30 INNOLET	100U	INJ	10.000
18	30631	INSULIN,NOVOLIN 70/30	100U	INJ	10.000

Enter Line# at top of screen, press ENTER.
F1=Help F2=Restart F3=Exit F4=Prompt
F7=Bkwd F8=Fwd F12=Previous F13=Disp Msg F14=Send Msg

Used with permission from the Institute for Safe Medication Practices, Horsham, Pennsylvania.

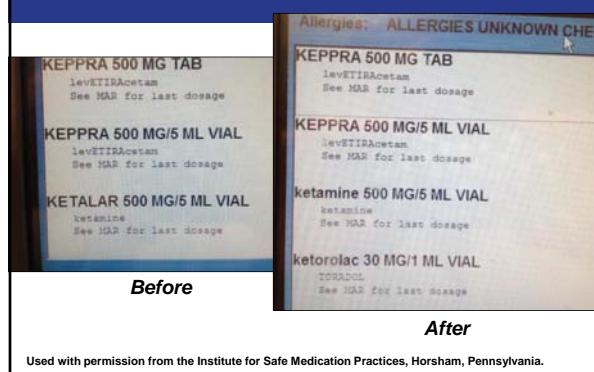
Drug Errors Involving Immediate- and Extended-Release Products

"OxyCONTIN" from CPOE system listed as.....

Medication: OXYCODONE HCL TBCR 10 MG OR
Qty: 60 **Ref:** 0 **Start:** 3/12/
Route: **DAW:**
Sig: 1 TABLET TWICE DAILY

Used with permission from the Institute for Safe Medication Practices, Horsham, Pennsylvania.

Medication Devices



Used with permission from the Institute for Safe Medication Practices, Horsham, Pennsylvania.

Medication Devices (continued)

Test Patient View of MAR

ALL	Scheduled	PON	Continuous	Pysas Override	Chems Mads	Adm Times	Phases of Care	MAR Hold	Read-only	Cabinet Override	Action
Sort by: Medication Name ▾											
Pre-admit from 2012 in PASS											
Discontinued Medications											
LEVETIRACETAM 500 MG IN LEVY 250 MG SYR 30ML											
Route: Intravenous Order Date: 8/5/2012 at 10:45 AM Admin Amount: 0.83757 mg/min Ordered Infusion Rate: 11.81 ml/hr Order Start Time: 13 1425 Order End Time: 13 1425 ▼ Future Administration Information											
HYDROXYPEROXIDE 50 MG IN USP 250 MG SYR 30ML											
Route: Intravenous Order Date: 8/5/2012 at 10:45 AM Admin Amount: 0.83757 mg/min Ordered Infusion Rate: 11.81 ml/hr Order Start Time: 13 1425 Order End Time: 13 1425 ▼ Future Administration Information											

Used with permission from the Institute for Safe Medication Practices, Horsham, Pennsylvania.

Where Are Names Confused?

- Drug Labeling and Packaging
 - Pharmacy
 - Manufacturer
- Drug Storage
 - Pharmacy
 - Care Areas
 - ADCs
 - Floor Stock

Pharmacy IV Labels



Manufacturer Bulk Packaging



Used with permission from the Institute for Safe Medication Practices, Horsham, Pennsylvania.

Wellbutrin, Zyban, Bupropion.....SR, XL.....



Used with permission from the Institute for Safe Medication Practices, Horsham, Pennsylvania.

Manufacturer Unit-Dose Packaging



Used with permission from the Institute for Safe Medication Practices, Horsham, Pennsylvania.

Manufacturer Unit-Dose Packaging



Used with permission from the Institute for Safe Medication Practices, Horsham, Pennsylvania.

Manufacturer Cartons



Used with permission from the Institute for Safe Medication Practices, Horsham, Pennsylvania.

Manufacturer IV Solutions



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Manufacturer Vials



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Pharmacy Labeling



Used with permission from the Institute for Safe Medication Practices, Horsham, Pennsylvania.

Look-alike names, Packaging & Storage



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Identifying the Problem

• Need to know

- Where in the medication use process the pairs of drugs are being confused before you implement risk reduction strategies

Identifying the Problem (continued)

- Identify problematic name pairs in your organization
 - Need to know what drug name pairs are being confused before you take action
- **Proactive**
 - Observation
- **Concurrent**
 - Pharmacy checks
 - Cart fills
 - New orders
 - Orders vs label
 - Labels vs drug

Identifying the Problem (continued)

- **Retrospective**
 - Error reports
 - Limited – who does the reporting?
 - Usually wrong meds given to patient or pharmacy dispensing errors caught by nursing
 - Other care areas – OR, ED, radiology
 - Doesn't usually include those that are caught in pharmacy
 - Triggers
 - Opiates – morphine & HYDROMORPHONE
 - Insulin products

Error Reduction Strategies

- **Failure Mode and Effects Analysis (FMEA)**
 - Med-ERRS (www.med-errs.com)
- **Constraints**
 - Do you really need it on formulary?
 - Limit concentrations/strengths
 - Morphine 2 mg/mL vs HYDROmorphine 1 mg/mL
- **Separation/segregation**

FMEA = Failure Mode and Effects Analysis.

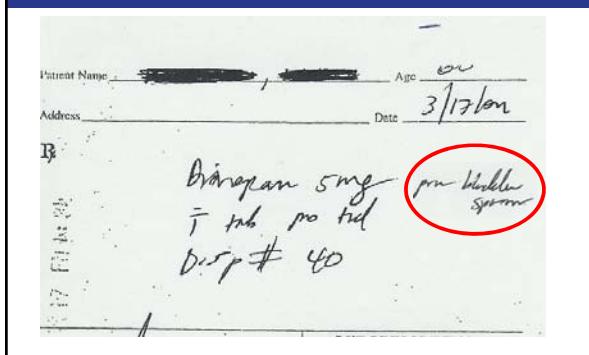
Error Reduction Strategies

- **Redundancies**
 - Independent double checks
- **Differentiation**
 - Tallman lettering
 - Studies with TML
 - www.ismp.org/tools/
 - Include indication for use with orders
 - Highlighting, color (red)
 - Stickers (LAN)



Institute of Safe Medication Practices. www.ismp.org/Tools/tallmantable.pdf. Accessed on February 16, 2016.

Look-Alike Name Error Due to Lack of Patient Information



Error Reduction Strategies

- **Education**
 - Staff need to know
 - What is being confused?
 - What are you doing about it?
 - What do those stickers mean?
- **Report errors and near-misses**
 - Internally
 - Externally
 - ISMP

pln PHARMACY LEARNING NETWORK 1-DAY REGIONAL MEETINGS

Questions?



1-DAY REGIONAL MEETINGS

Clinical Decision Making in Febrile Neutropenia:

The Critical Role of Health-System Pharmacists



Presented in partnership with the ICHP Annual Meeting

Faculty

Val R. Adams, PharmD, BCOP

Associate Professor
College of Pharmacy
University of Kentucky
Lexington, Kentucky

Disclosures

Val R. Adams, PharmD, BCOP: Advisory Board—Teva Pharmaceuticals

Learning Objectives

- Describe the impact of FN on patient outcomes including increased mortality, morbidity, delays in cancer treatment, and increased healthcare costs
- Outline guideline recommendations for FN risk assessment and primary and secondary prophylaxis
- Explain the role of G-CSF in FN prevention and treatment as well as differences and clinical and cost implications
- Proactively lead the healthcare team in making informed FN prevention and treatment decisions to improve patient outcomes

FN = febrile neutropenia; G-CSF = granulocyte-colony stimulating factor.

Febrile Neutropenia

Definition

- Fever: Temperature $\geq 38.5^{\circ}\text{C}$ ($\geq 101.3^{\circ}\text{F}$)
- One of the following:
 - ANC $<500 \text{ cells/mm}^3$
 - ANC $<1000 \text{ cells/mm}^3$ with predicted fall to $<500 \text{ cells/mm}^3$ over next 48 hours

ANC = absolute neutrophil count.
Aapro MS, et al. *Eur J Cancer*. 2011;47(1):8-32.

Febrile Neutropenia (Cont)

- >60,000 admissions annually in the United States
- Approximately 6% of adults receiving chemotherapy for solid tumors
- Risk higher in those with hematologic malignancies

Culakova E, et al. *Cancer Med*. 2014;3(2):434-444. Caggiano V, et al. *Cancer*. 2005;103(9):1916-1924.

Impact on Therapy

- 20% to 56% of patients receive <85% of planned-dose intensity
- 25% of patients have treatment delays ≥ 7 days
- 37% of patients have dose reductions $\geq 15\%$



Full dose on time – Approach for curable patients

Lyman GH, Kuderer NM. *Support Cancer Ther.* 2003;1(1):23-35. Lyman GH, et al. *JCO.* 2003;21(24):4524-4531.

Impact of Febrile Neutropenia

- In-hospital mortality rate: 6.8% to 10.6%
- Cost per hospitalization: \$13,372 to \$22,839
- 60,000 admissions \times \$22,839 per admission = \$1,370,340,000/year

Note: Based on data from 1995-2008.
Caggiano V, et al. *Cancer.* 2005;103(9):1916-1924. Kuderer NM, et al. *Cancer.* 2006;106(10):2258-2266. Schilling MB, et al. *Exp Ther Med.* 2011;2(5):859-866.

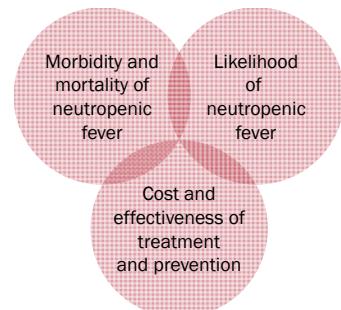
Guidelines HELP is Available

- National Comprehensive Cancer Network®
 - Updated 2015
- American Society of Clinical Oncology (ASCO®)
 - Updated 2015
- European Organisation for Research and Treatment of Cancer (EORTC)
 - Updated 2010

All agree to use CSFs when risk for FN is $\geq 20\%$

http://www.nccn.org/professionals/physician_gls/f_guidelines.asp. <http://www.asco.org/>. <http://www.eortc.org/investigators/guidelines/>. Accessed October 11, 2015.

Factors to Consider



Severity of Neutropenia and Fatalities

- Direct correlation
- Severity of neutropenia is directly related to infection
- This was the “game-changing” publication: *THE BEGINNING of EMPIRIC ANTIBIOTICS* for neutropenic fever

		Granulocyte Level (/mm ³)		Episodes	
Initial	Change	Total (no)	Fatal (%)		
<100	None	15	80		
<1000	None or fall	44	59		
<1000	Rise, but still <1000	15	40		
<1000	Rise to >1000	26	27		
>1000	Rise	44	32		

Bodey GP. *Ann Intern Med.* 1966;64(2):328-340.

Mortality in Modern Era

Drug	Predominant Risk (n)	DSN (days)	Mortality (%)
Ceftazidime	High risk >50% heme disease (n = 276)	5	6.2% (2.2% from initial infection, 4% from secondary infection)
Cefepime	High risk >50% heme disease (n = 281)	8	2.5%
Meropenem	High risk >50% acute leukemia (n = 958)	5	0.8%
Cefazidime/amikacin			
Cefoperazone/amikacin	High risk 48%-49% acute leukemia, 40%+ other heme disease (n = 867)	9	1.2%
Piperacillin/tazobactam/amikacin			
Moxifloxacin	Low risk (n = 338) MASCC 24-26 = 57%	NR	1 patient – 19 days after stopping treatment
Ciprofloxacin + amoxicillin/clavulanic acid			

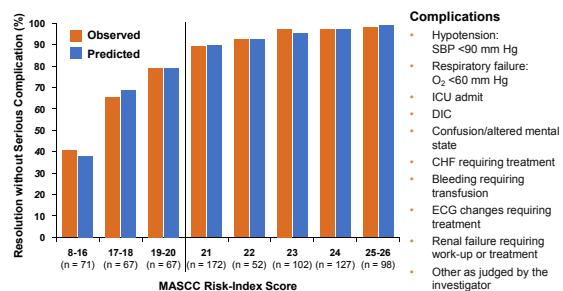
DSN = duration of severe neutropenia; MASCC = Multinational Association for Supportive Care in Cancer™;
NR = not rated.
JGIM. 2015. *Journal of Clinical Review of NDA 50-5797 SE1-002*. www.accessdata.fda.gov/drugsatfda_docs/nda/50-5797SE1-002_maxipime_medi_P2.pdf. Accessed October 25, 2015. *Journal of Clinical Statistical Review of NDA 50-5797 SE1-002*. www.accessdata.fda.gov/drugsatfda_docs/nda/50-5797SE1-002_maxipime_medi_P3.pdf. Accessed October 25, 2015. Comella A, et al. *Antimicrob Agents Chemother.* 1996;40(5):1108-1115. Sanz MA, et al. *J Antimicrob Chemother.* 2002;50(1):79-88. Kern WV, et al. *J Clin Oncol.* 2013;31:1149-1156.

Febrile Neutropenia and Individual Risk of Major Complications

- Frequent complication of chemotherapy, but risk of morbidity and mortality is not equal in all patients
- Talcott groups and MASCC criteria are useful tools to determine risk
- Main point: **low risk patients can be treated at home**

Talcott JA, et al. *Arch Intern Med.* 1988;148:2561-2568. MASCC™. <http://www.mascc.org/mascc-fn-risk-index-score>. Accessed November 11, 2015.

MASCC Risk Score



MASCC Scoring Criteria

Scoring System

Characteristic	Weight
Burden of illness	
No or mild symptoms	5
Moderate symptoms	3
No hypotension	5
No chronic obstructive pulmonary disease	4
Solid tumor or no previous fungal infection	4
No dehydration	3
Outpatient status	3
Age <60 years	2

The maximum theoretical score is therefore 26

Klastersky J, et al. *J Clin Oncol.* 2000;18(16):3038-3051. MASCC™. <http://www.mascc.org/mascc-fn-risk-index-score>. Accessed November 11, 2015.

Complications by Talcott Grouping

Medical Complications during Febrile Neutropenia

Risk Group	No. of Patients	% with Complications	Complications	No. of Patients	%
Inpatients (Group I)	101	34	Hypotension	25	9.6
Acute comorbidity (Group II)	22	55	Respiratory failure	14	5.4
Uncontrolled cancer (Group III)	26	31	Altered mental status	12	4.6
No risk factors (Group IV)	112	2	ECG changes	10	3.8
All patients	261	21	Focal neuro abnormalities	8	3.1
			Bleeding (≥3 U)	8	3.1
			Congestive heart failure	3	1.2
			Other	13	5.0
			Any complication	56	21.5

Talcott JA. *The Oncologist.* 1997;2(6):365-373.

Great Tools, But They Do Not Consider the Etiology of Infection

- A favorable history of exposure can be a “game changer” regardless of risk
- Gram-positive bacteria (commonly not fatal in first 72 hours)
 - Predominant cause of bacteremia
 - Slower infection rate
 - Indolent
- Gram-negative bacteria
 - Pose great threat
 - Associated with rapid death if not adequately treated (as quickly as 12 hours)
- Fungal
 - Superinfection (consider with recurrent temperature)

DE Is a 46-Year-Old Male with Pancreatic Cancer

- History of current illness**
 - DE is currently at hospital day 3 and day 7 of receiving FOLFIRINOX cycle 1. At 6:00 am, his temperature increased to 102°F (38.9°C). The patient was admitted for diarrhea, dehydration, and abdominal pain, and he has mild complaints of mouth sores
- Past medical history**
 - None prior to admission
- Social history**
 - Works as OR technician at local hospital
 - Has two healthy children (ages 14 and 17 years)
 - Denies smoking, illicit drug use, or alcohol use
- Home medications**
 - Multivitamin; 1 tablet “when he needs one”

FOLFIRINOX = folinic acid, fluorouracil, irinotecan, and oxaliplatin; OR = operating room.

DE Is a 46-Year-Old Male with Pancreatic Cancer (Cont)

- Vitals**
 - T (current/24-hour range): 99.6/99.6-102.0
 - BP (current/mean 24-hour range): 119/81 / 78-95
 - RR (current/24-hour range): 14/14-20
 - SAT (current/24-hour range): 95/90-96
- Laboratory results**



Ca = calcium; Mag = magnesium; Phos = phosphorus; Uric acid = uric acid; AST = aspartate transaminase; ALT = alanine transaminase; Alk Phos = alkaline phosphatase; Bili = bilirubin; Albumin = albumin; ANC = absolute neutrophil count.

DE Is a 46-Year-Old Male with Pancreatic Cancer (Cont)

CXR findings

- No definite airspace opacification is seen to suggest pneumonia. The tip of the left PICC line is in the area of the distal left brachiocephalic vein

Culture results

- Blood cultures** from port X1, indwelling (Foley) catheter X1, and peripheral X2 drawn 30 minutes apart: *Results pending*
- Urinalysis:** (-) WBC, (-) nitrites, (-) leukocyte esterase, (-) bacteria
- Urine culture:** No growth to date (day 1)
- Admission surveillance screen:** Negative for known MDROs

CXR = chest x-ray; PICC = peripherally inserted central catheter; WBC = white blood cell count; MDRO = multi-drug resistant organism.

DE Is a 46-Year-Old Male with Pancreatic Cancer (Cont)

Current Medications

Morphine sulfate ER 30 mg PO BID	D5W ½ NS w/20 mEq K at 125 mL/h
Loperamide 2 mg PO every 4 hours	Ondansetron 4 mg PO q6 PRN nausea/vomiting
Octreotide 100 mcg SQ TID	Oxycodone 5-10 mg PO q6 PRN pain
Paroxetine 20 mg PO daily	Promethazine 6.25-12.5 mg IV q6 PRN nausea/vomiting
Famotidine 20 mg PO BID	Senna 18.6 mg PO BID PRN constipation

When you arrive to the hospital at 7:00 am, the medical resident asks for your opinion on antimicrobial therapy for DE

ER = extended release; PO = orally; BID = twice daily; D5W = 5% dextrose; ½ NS = ½ normal saline; q6 = once every 6 hours; PRN = as needed; SQ = subcutaneously; TID = three times daily; IV = intravenously.

Selecting Empiric Therapy

High risk

- MASCC Risk Index score of <21
- Inpatient status at time of fever
- Significant medical comorbidity or clinically unstable
- Anticipated prolonged severe neutropenia:** ≤100 cells/mm³ and ≥7 days
- Hepatic insufficiency (5 X ULN - ALT/AST)
- Renal insufficiency (CrCl <30 mL/min)
- Uncontrolled/progressive cancer
- Pneumonia or other complex infections
- Alemtuzumab OR mucositis grades 3-4

Low risk

- Outpatient status at time of development of fever
- No associated acute comorbid illness, independently indicating inpatient treatment or close observation
- Anticipated short duration of severe neutropenia (≤100 cells/µL for <7 days)
- Good performance status (ECOG 0-1)
- No hepatic insufficiency
- No renal insufficiency
- MASCC risk index score ≥21**

ULN = upper limit of normal; CrCl = creatinine clearance; ECOG = Eastern Cooperative Oncology Group.
NCCN: Prevention and treatment of cancer-related infections v2.2015. Freifeld AG, et al. *Clin Infect Dis*. 2011;52(4):e56-e93.

What antibiotic therapy would you recommend?

- Ceftriaxone
- Vancomycin and levofloxacin
- Piperacillin/tazobactam
- Ceftazidime
- Doxycycline

Empiric Antibiotics

Initial antibiotic therapy should be based on:

- Infection risk assessment
- Broad-spectrum coverage, including antipseudomonal activity
- Potential infecting organisms, including multi-drug resistant organisms (MDROs)
- Colonization with or prior infection with methicillin-resistant *Staphylococcus aureus* (MRSA)
- Site of infection
- Local antibiotic susceptibility patterns
- Organ dysfunction/drug allergy
- Previous antibiotic therapy
- Bactericidal

Uncomplicated

- IV antibiotic monotherapy (choose 1)
 - Cefepime (category 1)
 - Imipenem/cilastatin (category 1)
 - Meropenem (category 1)
 - Piperacillin/tazobactam (category 1)
 - Ceftazidime (category 2B)
- Oral antibiotic combination therapy for low-risk patients:
 - Ciprofloxacin + amoxicillin/clavulanate (category 1)
 - Moxifloxacin (category 1)
 - Oral antibiotic regimen recommended should not be used if quinolone prophylaxis was used

Complicated

- IV antibiotic monotherapy (preferred)
- IV combination therapy could be considered, especially in cases of resistance

NCCN: Prevention and treatment of cancer-related infections v2.2015.

Should we add adjunctive colony stimulating factor (CSF) use with antibiotics?

1. Yes
2. No

Adjunctive CSF with Antibiotics

- "CSFs should not be routinely used as adjunctive therapy with antibiotics" – ASCO Guidelines 2015
- They can be considered for patients at high risk of infection-associated complications or those who have prognostic factors predictive of poor clinical outcomes

Risk Factors for Poor Clinical Outcomes

Sepsis syndrome	Aged >65 years
Profound neutropenia (ANC <100/mm ³)	Neutropenia expected to be >10 days
Pneumonia	Invasive fungal infection or other clinically documented infection
Hospitalized at time of fever	Prior episode of FN

NCCN Practice Guidelines in Oncology – v.2.2015.

Recent Systematic Analysis from Cochrane Library

Outcome	Relative Risk (95% CI)
Overall mortality (n = 1335)	0.74 (0.47-1.16; P = .19)
Infection-related mortality (n = 897)	0.75 (0.47-1.20; P = .23)
Hospitalized for >10 days (n = 1087)	0.65 (0.44-0.95; P = .03)
Duration of grade IV neutropenia (n = 1135)	1.7 standard deviation below control
Time to recovery from fever	0.49 standard deviation below control
Time to withdrawal from antibiotics	1.5 standard deviation below control

Conclusions: No change in mortality, faster time to recovery, fewer patients in hospital for 5-10 days, fewer days of IV antibiotics, and shorter time to fever resolution

CI = confidence interval.
Mhaskar R, et al. Cochrane Database of Systematic Reviews. 2014;10. doi:10.1002/14651858.CD003039.pub2.

Summary

- Occurrence
 - 10% to 50% of patients with solid tumor
 - >80% of those with hematologic malignancy
- Infection
 - Half have documented infection
 - One-third microbiologic diagnosis
- Empiric antibiotics that cover *Pseudomonas* species (piperacillin/tazobactam at UK)
- Addition of CSF in this patient maybe? (not at UK)
- Length of stay
 - 11 days, mean
- Financial impact
 - >\$1700/day
 - \$12,000 to \$37,000/hospitalization
- As CSF prices decrease, use to shorten stay seems reasonable

Klastersky J. *Clin Infect Dis*. 2004;39(Suppl 1):S32-S37. Lyman GH, Kuderer NM. *Crit Rev Oncol/Hematol*. 2004;50(2):129-146.

What About Using a CSF to Prevent FN?



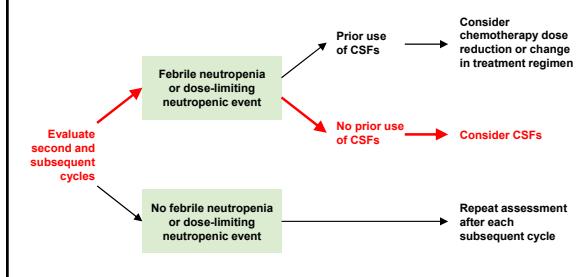
DE Is a 46-Year-Old Male with Pancreatic Cancer

- Return to clinic for cycle 2 of FOLFIRINOX
- History of current illness
 - Locally advanced pancreatic cancer diagnosed 1 month ago; first cycle of FOLFIRINOX given 3 weeks ago
- Past medical history
 - DE recovered from the diarrhea, abdominal pain, and FN after 7 days in the hospital. He completed 7 days of antibiotics yesterday
- Social history
 - Works as OR technician at local hospital
 - Has two healthy children (ages 14 and 17)
 - Denies smoking, illicit drug use, or alcohol use
- Plan
 - Reduce infusion fluorouracil dose (decrease from 2400 mg/m² to 1800 mg/m²)

Despite the dose reduction, we should add a CSF to his regimen.

1. True
2. False

Secondary Prophylaxis



NCCN Guidelines Myeloid Growth Factors v1.2015.

Should We Have Used a CSF with Cycle 1?



©Johnny Sajem. www.ClipartOf.com/1090876.

Colony Stimulating Factors

- Secondary prophylaxis (after documented neutropenia), subsequent cycles when maintaining dose intensity is beneficial (eg, lymphoma, breast)
- Primary (before cycle 1)
 - Recommended if likelihood of FN exceeds 20%
 - With dose-dense chemotherapy to prevent FN
- After high-dose chemotherapy with BMT
- Do not use concurrently with chemotherapy

BMT = bone marrow transplantation.
NCCN Guidelines Myeloid Growth Factors v1.2015.

Determining Primary Use (with Cycle 1)

Treatment Intent			
Risk of FN	Cure	Prolong Survival/QOL	Symptom Management/QOL
High risk >20%	CSF	CSF	CSF
Intermediate risk 10%-20%	Consider CSF	Consider CSF	Consider CSF
Low risk <10%	No CSF	No CSF	No CSF

- **Goal of treatment:** Locally advanced pancreatic – plan to shrink it and then surgically remove the tumor. Small chance of cure; more likely prolongation of life and to provide QOL
- **What is the risk?**

QOL = quality of life.
NCCN Guidelines Myeloid Growth Factors v1.2015.

Select Regimens Associated with High Risk of FN (>20%)

Disease	Regimen	Disease	Regimen
Acute lymphoblastic leukemia	All induction regimens	Non-Hodgkin lymphoma	ICE +/- rituximab ddCHOP – RituXimab HyperCVAD – RituXimab
Bladder cancer	MVAC	Small cell lung cancer	Topotecan
Breast cancer	Docetaxel/trastuzumab Dose-dense AC-T TAC	Ovarian cancer	Topotecan Paclitaxel Docetaxel
Esophageal and gastric cancers	DCF	Soft tissue sarcoma	MAID Ifosfamide/doxorubicin
Hodgkin lymphoma	BEACOPP	Testicular cancer	VelIP, VIP BEP TIP
Kidney cancer	Doxorubicin/gemcitabine		

NCCN Guidelines Myeloid Growth Factors v1.2015.

Patient Risk Factors That Increase Risk of FN

Risk Factor

- Age ≥65 years
- Advanced disease
- Previous chemotherapy or radiation therapy
- Preexisting neutropenia or bone marrow involvement with tumor infection
- Open wounds or recent surgery
- Poor performance status or poor nutritional status
- Poor renal function
- Liver dysfunction, most notably elevated bilirubin
- Cardiovascular disease
- Multiple comorbid conditions
- HIV infection

Determining Primary Use (with Cycle 1)

Risk of FN	Treatment Intent		
	Cure	Prolong Survival/QOL	Symptom Management/QOL
High risk >20%	CSF	CSF	CSF
Intermediate risk 10%-20%	Consider CSF	Consider CSF	Consider CSF
Low risk <10%	No CSF	No CSF	No CSF

- **Goal of treatment:** Locally advanced pancreatic – plan to shrink it and then surgically remove the tumor. Small chance of cure; more likely prolongation of life and to provide QOL
- **What is the risk?** Chemotherapy risk is intermediate
- **What about individual risk?** None

NCCN Guidelines Myeloid Growth Factors v1.2015.

Primary prophylaxis could be considered,



but we did not drop the ball!

It does not matter which CSF you choose because they are all interchangeable.

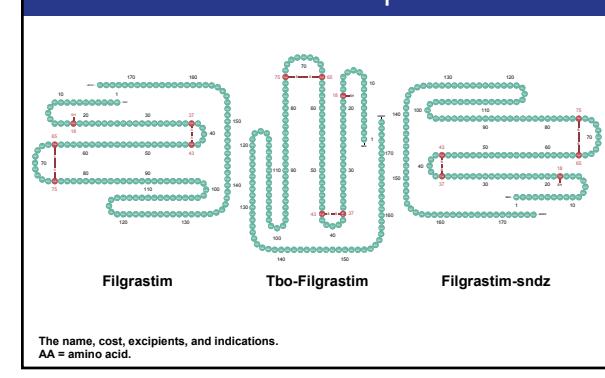
1. True
2. False

What Do the Guidelines Say?

Product	Indication(s)
Filgrastim	After myelotoxic chemotherapy, after autologous HSCT, and for peripheral blood progenitor cell mobilization
Filgrastim-sndz (biosimilar)	After myelotoxic chemotherapy, after autologous HSCT, and for peripheral blood progenitor cell mobilization
Tbo-filgrastim	After myelotoxic chemotherapy
Pegfilgrastim	After myelotoxic chemotherapy
Sargramostim	Peripheral blood progenitor cell mobilization; after autologous HSCT, after allogeneic BMT, for patients with AML

HSCT = hematopoietic stem cell transplantation; AML = acute myeloid leukemia.
NCCN Guidelines Myeloid Growth Factors v1.2015.

What Is the Difference between These 175 AA Sequences?

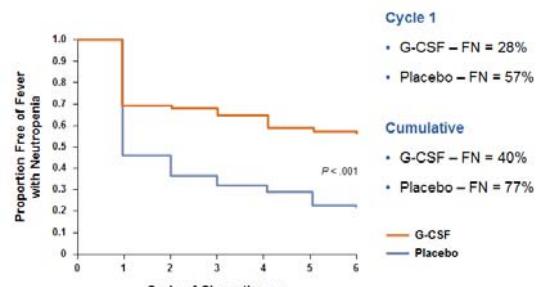


Comparison of the 300- μ g/0.5-mL Injectable Syringe Formulations

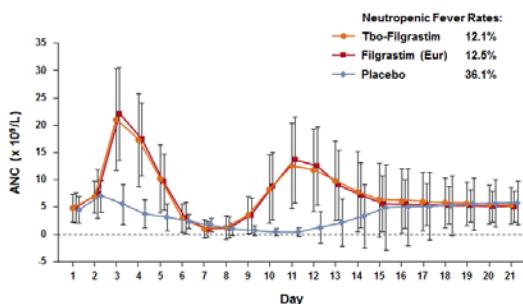
Constituent	Filgrastim	Tbo-Filgrastim	Filgrastim-Sndz
Methionyl human G-CSF	300 mcg	300 mcg	300 mcg
Sorbitol	25 mg	25 mg	25 mg
Polysorbate 80	0.02 mg	0.0275 mg	0.02 mg
Water for injection	QS to 0.5 mL	QS to 0.5 mL	ad to 0.5 mL
Glacial acetic acid		0.3 mg	
Glutamic acid		0.736 mg	
Acetate	0.295 mg		
Sodium	0.0175 mg		
Sodium hydroxide	QS to pH 4.2	QS	

QS = quantity sufficient.
US Food and Drug Administration. http://www.accessdata.fda.gov/drugsatfda_docs/label/2002/filgamg052902LB01.pdf; http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/125553lbl.pdf; http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/125294s035lbl.pdf. Accessed November 12, 2015.

G-CSF vs Placebo



Are Tbo-Filgrastim and Filgrastim Interchangeable?



Del Giglio A, et al. *BMC Cancer*. 2008;8:332.

Biosimilar Filgrastim-Sndz

- As a biosimilar, randomized comparative trials were not performed; however, results from a prospective trial compared with historical controls show equivalence

Cycle	Zarzio®	Neupogen®	Holmes et al
	Mean \pm SD	Mean \pm SD	Mean \pm SD
1	1.8 \pm 1.4	1.6 \pm 1.1	1.8 \pm 1.4
2	1.3 \pm 0.5	0.9 \pm 1.0	1.1 \pm 1.1
3	1.4 \pm 0.6	0.9 \pm 1.1	1.2 \pm 1.4
4	1.7 \pm 0.6	1.0 \pm 1.3	1.3 \pm 1.5

Gascon P, et al. *Ann Oncol*. 2010;21(7):1419-1429.

G-CSF vs GM-CSF

Not completely relevant for DE (our case) based on the indication and data

- Small studies show similar results, but large comparative trials in solid tumors are absent
 - Filgrastim, G-CSF
 - E. coli derived
 - Dose 5 μ g/kg/d
 - Target cells are late precursors to granulocytes
 - Sargramostim, GM-CSF
 - Yeast derived
 - Dose 250 μ g/m²
 - Target cells are early precursors to monocytes and granulocytes

GM-CSF = granulocyte-macrophage colony stimulating factor. <http://www.drugs.com/pro/neupogen.html>; <http://www.drugs.com/pro/leukine.html>. Accessed November 12, 2015.

G-CSF vs GM-CSF (Cont)

Filgrastim and derivative products, including pegfilgrastim

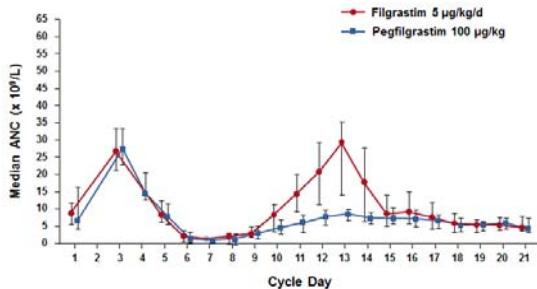
- Warnings**
 - Allergic reactions
 - Bleomycin-containing regimens: pulmonary toxicity
 - Splenic rupture
 - Acute respiratory distress syndrome
 - Alveolar hemorrhage and hemoptysis
 - Sickle cell crises (only in patients with sickle cell disease)
 - MDS and AML
- Precautions**
 - Cutaneous vasculitis
 - Immunogenicity
- Adverse reactions**
 - Bone pain

MDS = myelodysplastic syndrome; AML = acute myeloid leukemia; GI = gastrointestinal. NCCN Practice Guidelines in Oncology - v.2.2015.

Sargamostim

- Warnings**
 - Fluid retention
 - Respiratory symptoms
 - Cardiovascular symptoms: Occasional transient supraventricular arrhythmia
 - Renal and hepatic dysfunction
- Adverse events** occurring in >10% of patients receiving sargamostim in controlled clinical trials and reported in a higher frequency than placebo
 - Pain, fever, skin reactions, metabolic disturbances, nausea, vomiting, weight loss, edema, anorexia, asthenia, malaise, diarrhea, urinary tract disorder, chills, hematemesis, dysphagia, GI hemorrhage, bone pain, arthralgia, eye hemorrhage, hypertension, tachycardia, bilirubinemia, increased creatinine, pharyngitis, epistaxis, dyspnea, insomnia, anxiety

Filgrastim and Pegfilgrastim Provide Comparable Neutrophil Recovery



Holmes FA, et al. *J Clin Oncol*. 2002;20:727-731.

Comparison between Filgrastim and Pegfilgrastim According to Sources

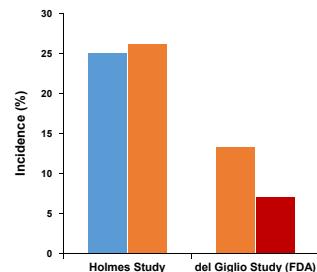
	Holmes et al		Green et al	
	Filgrastim 5 µg/kg/d (n = 147)	Pegfilgrastim 100 µg/kg (n = 149)	Filgrastim 5 µg/kg/d (n = 62)	Pegfilgrastim 6-mg fixed dose (n = 68)
Mean DSN (days)	1.8	1.7	1.6	1.8
95% CI (%)*	-0.36 to 0.30	-0.15 to 0.63		

*Confidence interval for difference of the means.
Holmes FA, et al. *J Clin Oncol*. 2002;20(3):727-731. Green M, et al. *Proc ASCO*. 2001;20:23a.

tbo-filgrastim, Filgrastim, and Pegfilgrastim Bone Pain

Most common Toxicity

- Treated with APAP or NSAID (evaluate Kidney and plt)
- Similar between agents



Holmes FA, O'Shaughnessy JA, et al. *J Clin Oncol*. 2002;20:727-731. <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/MedicalImagingDrugsAdvisoryCommittee/UCM351839.pdf> accessed 11/24/2015.

What Is Best for DE (Our Case)? Key Question: Do CSFs Differ in Efficacy?

ASCO Guidelines addressed this question
(clinical question 11)

Clinical Interpretation

Filgrastim, tbo-filgrastim, filgrastim-sndz, and pegfilgrastim are all effective in the reduction of the risk of febrile neutropenia. Choice of agent will depend on factors such as **convenience** and **cost** and may in some cases be dictated by the patient's **treatment plan** (eg, weekly chemotherapy).

Smith TJ, et al. *J Clin Oncol* [Epub ahead of print] July 13, 2015. doi:10.1200/JCO.2015.62.3488.

Convenience

- Outpatient chemotherapy given weekly
 - Pegfilgrastim is not an option because of the long half-life
 - Filgrastim is best option
 - Started 1-3 days after chemotherapy
 - Given daily until ANC ≥2000-3000/µL
- Outpatient chemotherapy every 14 or 21 days
 - Pegfilgrastim as a one-time injection is most convenient
 - 1 dose given 1-3 days after chemotherapy
- Inpatient chemotherapy
 - Equally convenient
 - When done for transplant patients, pegfilgrastim lacks data and indication (dosed as above)
- Inpatient neutropenic fever
 - Equally convenient
 - Pegfilgrastim lacks data and indication (dosed as above)

Smith TJ, et al. *J Clin Oncol* [Epub ahead of print] July 13, 2015. doi:10.1200/JCO.2015.62.3488.
Biganzoli L, et al. *Sem Oncol*. 2004;31(3 Suppl 8):27-34.

How Does the Cost Compare?

Significant differences based on patient size/dose and number of treatment days

Agent	Payment Limit (CMS)	Payment Limit per Dose (70 kg)	Payment Limit per Pt/10-day Tx (70 kg)	Payment Limit per Dose (85 kg)	Payment Limit per Pt/10-day Tx (85 kg)
Filgrastim	\$0.999/ 1 µg	\$299.70	\$2997	\$479.52	\$4795
Tbo-filgrastim	\$3.862/ 5 µg	\$231.72	\$2317	\$370.75	\$3708
Filgrastim-sndz	\$0.969/ 1 µg	\$290.70	\$2907	\$465.12	\$4651
Pegfilgrastim	\$3772.787/ 6 mg	\$3779.79	\$3780	\$3779.79	\$3780

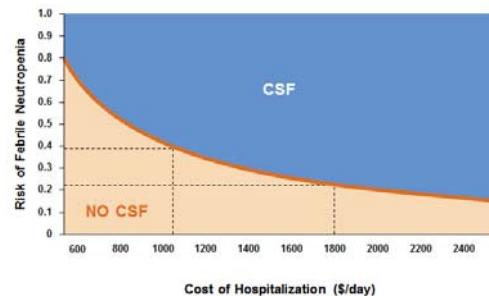
CMS = Centers for Medicare & Medicaid Services; Pt = patient; Tx = treatment.
<https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice/2015ASPFiles.html>. October 2015. Accessed October 27, 2015.

Primary Prevention of CSF Based on Cost

Model Baseline Assumptions		Threshold Risk of Hospitalization for Febrile Neutropenia*				
Variable	Value	Cost per Day (\$US)	7.5	10	12.5	15
Probabilities	Risk of hospitalization for febrile neutropenia	0.55				
	Risk reduction of CSF	0.50				
Durations (days)	Hospitalization	10				
	CSF administration	8				
Costs (\$US/day)	Febrile neutropenia					
	Direct medical	1000				
	Indirect medical	500-1000				
	Direct non-medical*	0-500				
	Indirect/intangible*	0-1000				
	CSF	250				
		5000	0.11	0.08	0.06	0.05

*G-CSF use is associated with a lower cost whenever the risk of hospitalization is greater than the calculated threshold.
Lyman GH, Kuderer N, et al. Eur J Cancer. 1998;34:1857-64.

CSF-Calculated Cost Model



Lyman GH, Kuderer N, et al. Eur J Cancer. 1998;34:1857-64.

Summary: Management of Febrile Neutropenia

- Rapid evaluation and empiric initiation of antibiotics
 - Low-risk patients can be treated as outpatients (ciprofloxacin and amoxicillin/clavulanic acid)
 - High-risk patients should preferably be treated with monotherapy (must cover *Pseudomonas species*)
- Consider adding G-CSF for patients with a high risk of unfavorable outcomes
 - No change in mortality
 - Decreased time to neutrophil recovery
 - Decreased time of IV antibiotics
 - Decreased hospital length of stay

Summary: Prevention of Febrile Neutropenia

- For myelotoxicity filgrastim, pegfilgrastim, filgrastim-sndz, and tbo-filgrastim, all decrease risk of FN, duration of severe neutropenia, and hospitalization
- Choosing an agent is based on convenience, cost, and treatment plan
- Guidelines suggest primary prophylaxis if risk is >20% and considered if risk is 10% to 20%
 - Based on costs that can be individualized to an institution
 - Calculation includes cost of CSF, hospital day, and hospitalization duration
- Assuming competition will decrease the cost of CSF and hospital costs will increase, we could start using prophylaxis in more patients

Questions?





1-DAY REGIONAL MEETINGS

DOACs and Reversal Agents: Considerations for Health-System Pharmacists



Presented in partnership with the ICHP Annual Meeting

Faculty

Mark A. Munger, PharmD, FCCP, FACC, FHFS

Professor of Pharmacotherapy
Adjunct Professor, Internal Medicine
University of Utah
Salt Lake City, Utah

Disclosures

Mark A. Munger, PharmD, FCCP, FACC, FHFS has no financial relationships to disclose relating to the subject matter of this presentation.

Learning Objectives

- Outline the pharmacologic profiles, clinical characteristics, patient-centric considerations, and cost-effectiveness of DOACs
- Evaluate the role of DOACs in the management of VTE and AF-related stroke risk reduction and bleeding risk
- Describe new and emerging DOAC reversal agents and their clinical utility in patients who may require interruption of anticoagulant therapy
- Develop or augment protocols for patients requiring the prompt reversal of DOACs due to risk of bleeding, severe bleeding, or urgent/emergent invasive procedures

DOAC = direct oral anticoagulant

The “Ideal” Anticoagulant

- Oral, fixed dosage (preferably once daily)
- Rapid onset
- Rapid offset of action
 - Perhaps not in valves?
- No need for renal or hepatic adjustment
- Predictable pharmacokinetics/dynamics
- No need to ever “switch” therapies
- Wide therapeutic window
- No need for routine anticoagulation effect monitoring
- Low propensity for food/drug interactions
- Available antidote
- Reasonable cost

New Oral Anticoagulants Pharmacodynamics & Pharmacokinetics

Property	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
MOA	Direct IIa Inhibitor	Direct Xa Inhibitor	Direct Xa Inhibitor	Direct Xa Inhibitor
Bioavailability	6 – 7%	80%	50%	62%
T _{max}	1.5 hours	2 – 4 hours	2 – 3 hours	1 – 2 hours
T _½	12 – 14 hours	9 – 13 hours	8 – 15 hours	8 – 11 hours
Hepatic Metabolism	No	Yes	Yes	Yes
Drug Interactions	P-gp	CYP3A4	CYP3A4	P-gp
Protein Binding	35%	90%	87%	55%
Dialyzable	Yes	No	No	No
Measurement	ECT, TT, aPTT	Anti-Xa, PT	Anti-Xa, dPT	Anti-Xa, PT
Renal Elimination	80%	35%	25%	40%
Renal Dosing	Yes	Yes	No?	Yes
Antidote	No	No	No	No

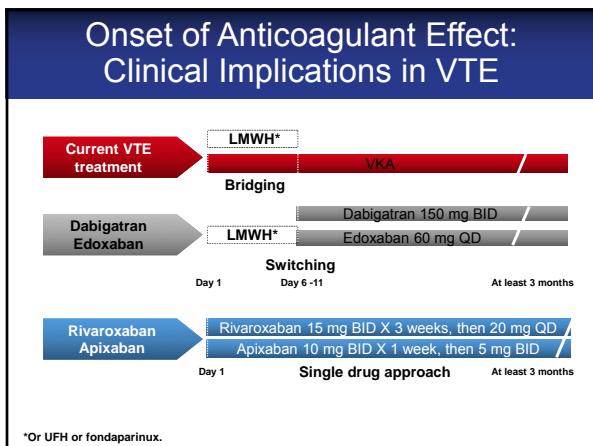
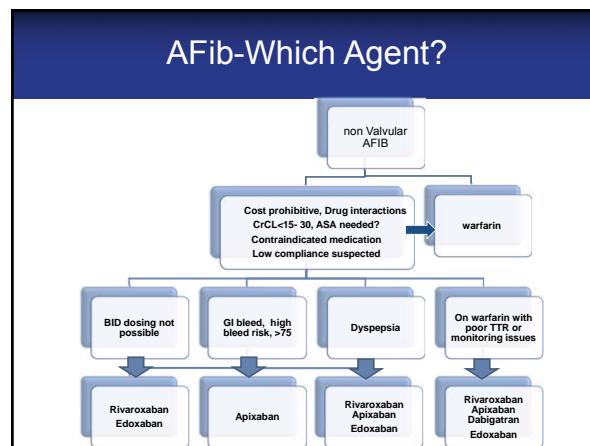
New Oral Anticoagulants				
Pharmacodynamics & Pharmacokinetics				
Property	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
MOA	Direct IIa Inhibitor	Direct Xa Inhibitor	Direct Xa Inhibitor	Direct Xa Inhibitor
Bioavailability	6 – 7%	80%	50%	62%
Tmax	1.5 hours	2 – 4 hours	2 – 3 hours	1 – 2 hours
T½	12 – 14 hours	9 – 13 hours	8 – 15 hours	8 – 11 hours
Hepatic Metabolism	No	Yes	Yes	Yes
Drug Interactions	P-gp	CYP3A4	CYP3A4	P-gp
Protein Binding	35%	90%	87%	55%
Dialyzable	Yes	No	No	No
Measurement	ECT, TT, aPTT	Anti-Xa, PT	Anti-Xa, dPT	Anti-Xa, PT
Renal Elimination	80%	35%	25%	40%
Renal Dosing	Yes	Yes	No?	Yes
Antidote	No	No	No	No

	Warfarin	Dabigatran	Rivaroxaban	Apixaban
Special Instructions	None	Do not chew, break open capsules -↑ bioavailability by 75% Keep in original bottle and tightly capped. Must use within 4 months of opening	None	None
Pre-Procedure Dosing	Stop 5-6 days prior procedure May need bridging	Skip 2-8 doses depending on procedure and renal function. No need for bridging	Stop > 24 hours before OR and other interventions	Stop 24-48 hours before elective OR and other interventions
Diet Considerations	Consistent intake of Vitamin K containing foods	None	None	None
Cost	\$4/month + \$20/INR (Annual cost = \$1000)	\$200-400/month Patient Assistance Program (Annual Cost ≈ \$2400-4800)	\$300/month (AWP) CarePath™ Patient Support and Assistance Program (Annual Cost ≈ \$3500)	\$250/month (AWP) Eliquis® 360 Support Patient Support and Assistance Program (Annual Cost ≈ \$3000)

DOACs: Clinical Trials

	Stroke Prophylaxis/AF	VTE Prevention	DVT/PE Treatment
Dabigatran	RE-LY	RE-NOVATE RE-MODEL RE-MOBILIZE	RE-COVER I RE-COVER II
Rivaroxaban	ROCKET-AF	RECORD 1-4	EINSTEIN DVT EINSTEIN PE
Apixaban	ARISTOTLE AVEROES	ADVANCE 1-3	AMPLIFY
Edoxaban	ENGAGE AF – TIMI 48	STARS E-3 STARS J-5 STARS J-4	HOKUSAI-VTE

AF = atrial fibrillation; VTE = venous thromboembolism; DVT = deep vein thrombosis; PE = pulmonary embolism.



Choosing an Anticoagulant

A 75-year-old man requires anticoagulation therapy for non-valvular AF. He is also taking carbamazepine and his creatinine clearance is 31 mL/min.

Which of the following is the best choice for this patient?

1. Dabigatran
2. Edoxaban
3. Warfarin
4. Rivaroxaban

New Oral Anticoagulants Pharmacokinetics & Pharmacodynamics				
Property	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
MOA	Direct IIa Inhibitor	Direct Xa Inhibitor	Direct Xa Inhibitor	Direct Xa Inhibitor
Bioavailability	6-7%	80%	50%	62%
T_{max}	1.5 hours	2-4 hours	2-3 hours	1-2 hours
T_{1/2}	12-14 hours	9-13 hours	8-15 hours	8-11 hours
Hepatic Metabolism	No	Yes	Yes	Yes
Drug Interactions	P-gp	CYP3A4	CYP3A4	P-gp
Protein Binding	35%	90%	87%	55%
Dialyzable	Yes	No	No	No
Measurement	ECT, TT, aPTT	Anti-Xa, PT	Anti-Xa, dPT	Anti-Xa, PT
Renal Elimination	80%	35%	25%	40%
Renal Dosing	Yes	Yes	No?	Yes
Antidote	Yes	No	No	No

aPTT = activated partial thromboplastin time; dPT = dilute prothrombin time; ECT = Ecarin clotting time; MOA = mechanism of action; PT = prothrombin time; TT = thrombin time.
US Food and Drug Administration. www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. Accessed February 25, 2016.

Role of Clotting Assays for DOACs Measuring vs. Monitoring

- **Dabigatran** (direct thrombin inhibitor)
 - ECT or TT best (diluted TT very good)
 - There is an effect on the aPTT
 - PT/INR lacks sensitivity to be useful
- **Rivaroxaban, apixaban, edoxaban** (direct Xa inhibitors)
 - Anti-Xa is probably the best test
 - There is an effect on the PT (rivaroxaban > apixaban)
 - Less variability in PT compared to INR
 - aPTT lacks sensitivity to be useful

INR = international normalized ratio; PT = prothrombin time; aPTT = activated prothrombin time
Pradaxa [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; 2015. Xarelto [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; 2011. Eliquis [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2015. Savaysa [package insert]. Parsippany, NJ: Daiichi Sankyo, Inc.; 2015.

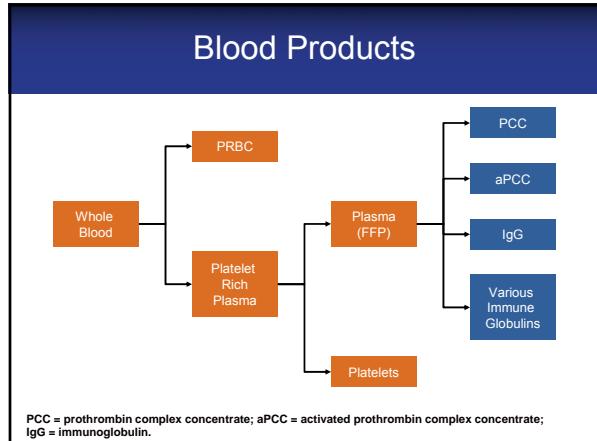
Supportive Care				
<ul style="list-style-type: none"> • Mechanical compression • Surgical hemostasis <ul style="list-style-type: none"> - Electrical tissue cauterization - Vessel ligation - Application of hemostatic agents (gelatins, collagens, oxidized celluloses, thrombin and fibrin sealants, synthetic glues) • Fluid resuscitation (0.9% normal saline or lactated ringers, dextran, or albumin) • Maintain renal function (maintain blood pressure and fluid status) • Blood product transfusion 				

Kaatz S, et al. *Am J Hematol*. 2012;87(Suppl 1):S141-S145.

Massive Transfusion Considerations

- **Definition**
 - 30% to 40% blood volume loss with hypotension
 - 10 units PRBC in 24 hours
 - Transfuse entire blood volume in 24 hours
 - 50% replacement in 3 hours
 - 4 units PRBC in 4 hours (ongoing need is foreseeable)
- **Concerns**
 - Dilutional thrombocytopenia
 - Citrate induced hypocalcemia
 - Hyperkalemia
 - Acidosis

PRBC = packed red blood cells; FFP = fresh frozen plasma; HCT = hematocrit.
Shander A, et al. *Pharmacotherapy*. 2007;27(9 Pt 2):575-685.



FFP				
<ul style="list-style-type: none"> • Prepared from fresh whole blood or from plasma collected from apheresis <ul style="list-style-type: none"> - 80% to 92% plasma from multiple donors - 8% to 20% citrate anticoagulant - Variability between units - Frozen within 8 hours • Shelf-life 12 months • Similar risk to other blood product infusions 				

Patanwala AE, et al. *Annals of Pharmacother*. 2011;45.

PCC

- Developed for hemophilia B
 - Dose based on amount of factor IX
 - Now mainly treated with recombinant human factor IX
- Types (many different products)
 - 3-factor: II, IX, and X
 - 4-factor: II, IX, X, and VII^a
 - Activated PCC (FEIBA): II, IX, X and VIIa
 - Contain varying concentrations of protein C and S, and may have heparin
- Concentration of clotting factors about 25 x higher than in human plasma

^aFEIBA = factor eight inhibitor bypassing activity.
Patanwala AE, et al. *Ann Pharmacother*. 2011;45(7-8):990-999. Shander A, et al. *Pharmacotherapy*. 2007;27(9 Pt 2):57S-68S.

PCC (continued)

PCC Product	Factor II	Factor VII	Factor IX	Factor X
4-Factor PCC				
Beriplex® (Europe)	133	69	100	161
Octaplex® (Europe)	98	66	100	96
Kaskadil® (Europe)	160	100	100	160
Cofact® (Europe)	75	25	100	75
3-Factor PCC				
Profilnine® (USA)	≤150	35	100	100
Bebulin® (USA)	?	?	100	?

- Factor content ratios are based on the content of factor IX
- All PCC products contain about 20 to 30 U/mL of factor IX

Brand names are included in this table for participant clarification purposes only. No product promotion should be inferred.
Levy JH, et al. *Anesthesiology*. 2008;109(5):918-926.

FFP vs PCC

- FFP (\$250) requires larger volumes to provide the same quantity of clotting factors compared to PCC (\$4500)
 - FFP usual dose 15 to 20 mL/kg (1.2-1.6 L)
 - FFP dose in critically ill 30 mL/kg (2.4 L)
 - PCC dose typically 1 to 2 mL/kg (200 mL)
- Risk of allergic reactions and bacterial infection
 - FFP has same risk as PRBC
 - PCC undergoes viral inactivation
- FFP requires thawing (30-45 min)
- PCC recommended over FFP for reversal of warfarin activity

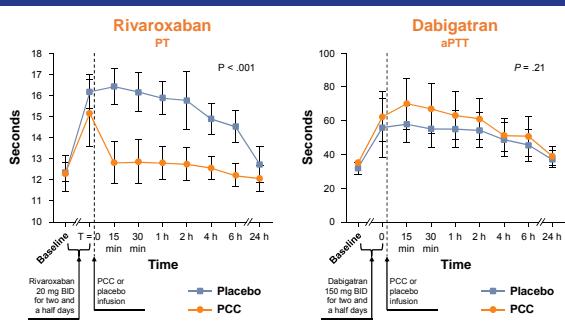
Shander A, et al. *Pharmacotherapy*. 2007;27(9 Pt 2):57S-68S. Patanwala AE, et al. *Ann Pharmacother*. 2011;45(7-8):990-999. Holbrook A, et al. *Chest*. 2012;141(2 Suppl):e152S-e184S.

Reversal of Rivaroxaban/Dabigatran by PCC (Netherlands)

- Randomized, double-blind, placebo controlled, crossover study
- Healthy male participants (N=12)
- Anticoagulants
 - Rivaroxaban 20 mg bid x 2.5 days
 - Dabigatran 150 mg bid x 2.5 days
- PCC
 - Cofact® (4-factor PCC)
 - 50 IU/kg single bolus

Eerenberg ES, et al. *Circulation*. 2011;124(14):1573-1579.

Reversal of Rivaroxaban and Dabigatran by PCC



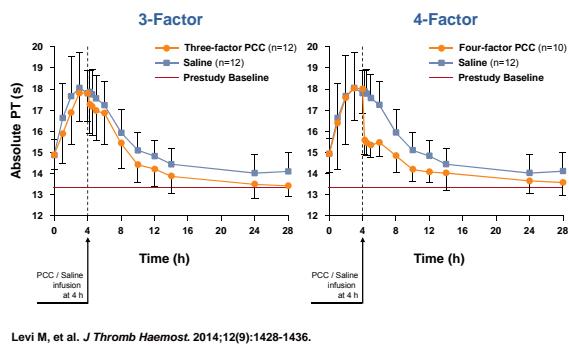
Eerenberg ES, et al. *Circulation*. 2011;124(14):1573-1579.

3-Factor vs 4-Factor PCC for Rivaroxaban Reversal

- Randomized, single-center, open-label trial
 - 35 healthy participants
 - Rivaroxaban 20 mg bid with meals x 9 doses
- PCC given 4 hours after last dose
 - 3-Factor PCC (Profilnine®) 50 U/kg
 - 4-Factor PCC (Beriplex®) 50 U/kg

Levi M, et al. *J Thromb Haemost*. 2014;12(9):1428-1436.

3-Factor vs 4-Factor PCC for Rivaroxaban Reversal (continued)



Kcentra®

- First available 4-factor PCC in the United States
- Provided as a lyophilized powder
- Reconstituted with provided 20 mL diluent
- Cost: 80 Kg = \$4000 to \$5080

Pre-Treatment INR	2<4	4-6	>6
Dose in units/kg	25	35	50
Maximum dose	2500	3500	5000

Kcentra [package insert]. Kankakee, IL: CSL Behring LLC; 2014.

Kcentra®

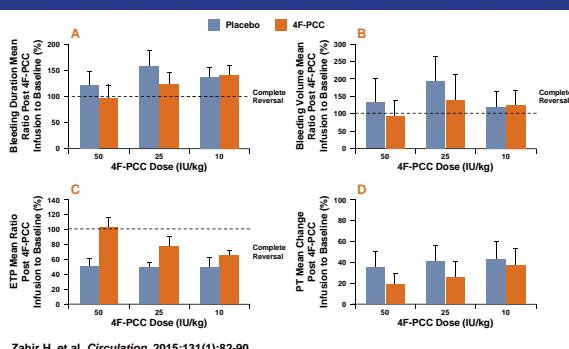
Study	Treatment	Baseline	30 Min	1 Hr	2-3 Hr	6-8 Hr	12 Hr	24 Hr
Acute Major Bleeding Study	Kcentra (N=98)	3.90 (1.8-20.0)	1.20 (0.9-6.7)	1.30 (0.9-5.4)	1.30 (0.9-2.5)	1.30 (0.9-2.1)	1.20 (0.9-2.2)	1.20 (0.9-3.8)
	Plasma (N=104)	3.60 (1.9-39.9)	2.4 (1.4-11.4)	2.1 (1.0-11.4)	1.7 (1.1-4.1)	1.5 (1.0-3.0)	1.4 (1.0-3.0)	1.3 (1.0-2.9)
Subgroup								
Major Bleeding Study								
Kcentra Plasma								
N Fluid Overload N (%) N Fluid Overload N (%)								
All Subjects	103	6 (5.8)	109	14 (12.8)				
With history of CHF	46	4 (8.7)	44	11 (25.0)				
Without history of CHF	57	2 (3.5)	65	3 (4.6)				
Subgroup								
Acute Major Bleeding Study								
Kcentra Plasma								
N TE Events N (%) N TE Events N (%)								
All Subjects	103	9 (8.7)	109	6 (5.5)				
With history of TE event	69	8 (11.6)	79	3 (3.8)				
Without history of TE event	34	1 (2.9)	30	3 (10.0)				

4-Factor PCC for Edoxaban Reversal

- Double-blind, placebo-controlled, randomized, crossover trial
 - 93 healthy participants
 - 60 mg single dose of edoxaban
 - 3 doses of 4-factor PCC (Beriplex®)
 - 10, 25, and 50 IU/kg
 - 5 mm diameter/5 mm depth punch biopsy
- Endpoints
 - Bleeding duration and bleeding volume
 - ETP and PT time

Zahir H, et al. *Circulation*. 2015;131(1):82-90.

4-Factor PCC for Edoxaban Reversal (continued)



Reversal Suggestions

Method	Dabigatran	Rivaroxaban	Apixaban
Oral activated charcoal	Yes	Yes	Yes
Hemodialysis	Yes	No	No
FFP	No	No	No
rFVIIa	Unclear	Unclear	Unclear
3-factor PCC	Unclear	50 U/kg	50 U/kg
4-factor PCC	50 U/kg	25-50 U/kg	25-50 U/kg
Activated PCC	50 U/kg	50 U/kg	50 U/kg

*Some protocols call for 1 unit of 3-factor PCC with 2 to 4 units of FFP

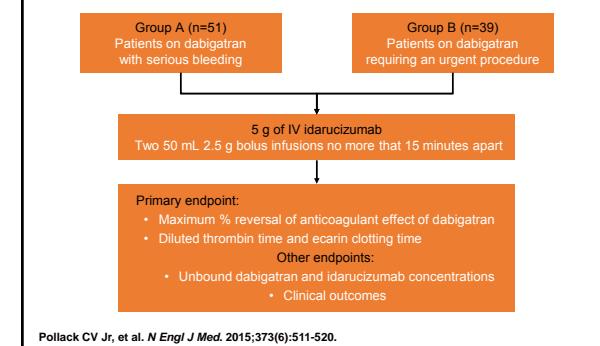
Kaatz S, et al. *Am J Hematol*. 2012;87 Suppl 1:S141-S145.

Idarucizumab

- Development
 - Injected mice with dabigatran derived haptens coupled with carrier proteins
 - Creation of murine antibody to dabigatran
 - FC portion removed
 - Fab portion fully humanized
- Affinity 350-fold compared to thrombin
- Does not bind other thrombin substrates
 - FV, FVIII, FXIII, fibrinogen, protein C
 - PAR-1, vWF, on impact on platelet aggregation

Schiele F, et al. *Blood*. 2013;121(18):3554-3562. Pollack CV Jr, et al. *Thromb Haemost*. 2015;114(1):198-205.

RE-VERSE AD Trial Design



Pollack CV Jr, et al. *N Engl J Med*. 2015;373(6):511-520.

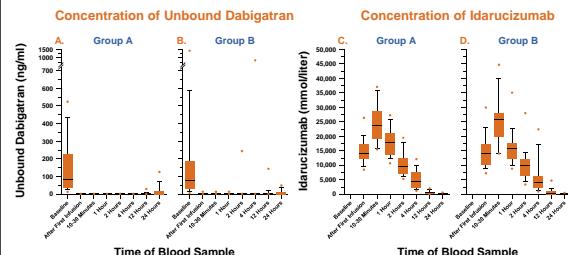
RE-VERSE AD Patient Characteristics

Group A	Group B
- Median age = 77 years	- Median age = 76 years
- CrCl = 59 mL/min	- CrCl = 65 mL/min
<ul style="list-style-type: none"> <30 mL/min: 10% 30 to <50 mL/min: 27% 	<ul style="list-style-type: none"> <30 mL/min: 18% 30 to <50 mL/min: 15%
- Dabigatran Dose	- Dabigatran Dose
<ul style="list-style-type: none"> 150 BID: 27% 110 BID: 67% 	<ul style="list-style-type: none"> 150 BID: 38% 110 BID: 62%
- Atrial fibrillation: 92%	- Atrial fibrillation: 100%
- Time since last dose	- Time since last dose
<ul style="list-style-type: none"> <12 hrs: 33% 12 to <24 hrs: 41% ≥24 hrs: 26% 	<ul style="list-style-type: none"> <12 hrs: 38% 12 to <24 hrs: 26% ≥24 hrs: 36 %

Pollack CV Jr, et al. *N Engl J Med*. 2015;373(6):511-520.

RE-VERSE AD Results and Conclusion

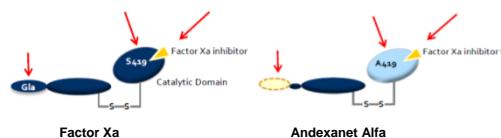
- Idarucizumab completely reversed the anticoagulant effect of dabigatran within minutes



Pollack CV Jr, et al. *N Engl J Med*. 2015;373(6):511-520.

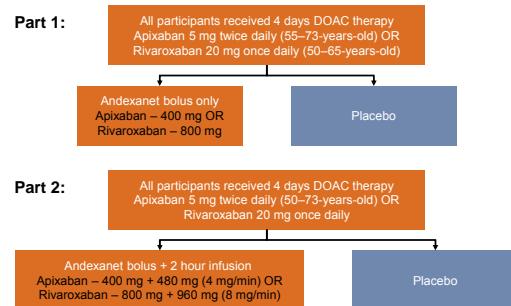
Andexanet Alfa (PRT06445)*

- Acts as a factor Xa decoy and retains high affinity for all direct factor Xa inhibitors
- Change in serine to alanine to eliminate catalytic activity and prevent prothrombin cleavage to thrombin
- γ-carboxylglutamic acid domain removed to prevent anticoagulant effect
- Retains high affinity for AT – inhibitor complex and can reverse anticoagulant effects of enoxaparin and fondaparinux



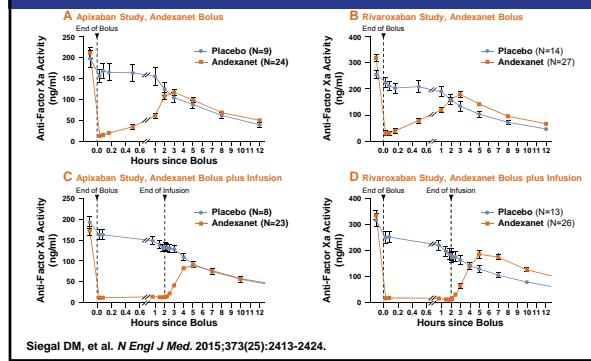
*Andexanet alfa has only completed Phase 2 trials (proof-of-concept). Lu G, et al. *Nat Med*. 2013;19(4):446-451. Portola Pharmaceuticals. www.portola.com/clinical-development/andexanet-alfa-prt06445-fxa-inhibitor-antidote/. Accessed on February 11, 2016.

ANNEXA-A and ANNEXA-R (Phase 3)



Siegal DM, et al. *N Engl J Med*. 2015;373(25):2413-2424.

Time Courses of Anti-Factor Xa Activity before and after Administration of Andexanet



Case Study: Background

- 76-year-old male
- Presentation: fell in home with trauma to right occipital plate
 - Sx: headache (9/10), R vision blurred
 - A&O: 1
 - BP 82/58 mmHg; HR 92 bpm (Afib)
 - Creatinine: 1.4 mg/dL (CrCl: 52 mL/min)
- Atrial fibrillation × 5 years (CHA2DS2-VASc: 6 [high risk for stroke])
- Hx: Type 2 DM, HTN, osteoarthritis
- Meds: Dabigatran 150 mg BID (last dose 12 hours ago), HCTZ 25 mg qday, lisinopril 10 mg qday, ibuprofen 200 mg PRN osteo pain, metformin/glipizide 2.5/500 mg BID

What to Do?

- Patient is sent for cranial CT scan:
 - Results: small acute subarachnoid hemorrhage in the L occipital lobar region
- Which of the following should be instituted in this patient?
 1. Supportive measures to maintain circulatory support and renal function
 2. Supportive measures with administration of activated charcoal now
 3. Supportive measures with administration of 4-factor PCC (Beriplex®) 50 U/kg now
 4. Supportive measures with administration of idarucizumab 5 g now



PLN PHARMACY LEARNING NETWORK **1-DAY REGIONAL MEETINGS**

Antibiotic Stewardship:



2016 IDSA/SHEA Guideline Preview and the Impact of New Regulatory Requirements on the Hospital Pharmacist

ICHP

Presented in partnership with the ICHP Annual Meeting

Faculty

James S. Lewis II, PharmD, FIDSA
ID Clinical Pharmacy Coordinator
Oregon Health & Science University
Departments of Pharmacy & Infectious Diseases

Disclosures

Dr. Lewis: Consultant—Accelerate Diagnostics, Astellas, Allergan, Merck & Co, Inc., The Medicines Company

Objectives

- List the key components of an antibiotic stewardship program
- Describe the key roles of the health system pharmacist in antibiotic stewardship
- Explain the highlights of recent antibiotic stewardship literature and government requirements

NATIONAL ACTION PLAN FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

MARCH 2015



www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf. Accessed on February 18, 2016.

Appropriate Use of Medical Resources

Antimicrobial Stewardship Toolkit

www.ahaphysicianforum.org/resources/appropriate-use/antimicrobial/ASP-Toolkit-v3.pdf. Accessed on February 18, 2016.

Clinical Infectious Diseases
IDSA GUIDELINE

Implementing an Antibiotic Stewardship Program:
Guidelines by the Infectious Diseases Society of America
and the Society for Healthcare Epidemiology of America

- Strong recommendation with moderate or better evidence
 - Preauthorization/prospective audit and feedback
 - Target antibiotics associated with *C. difficile*
 - PK monitoring services – aminoglycosides
 - IV to oral conversion
 - Develop guidelines and strategies to minimize treatment durations

Barlam TF, et al. *Clin Infect Dis.* 2016;62(10):e51-e77.

Clinical Infectious Diseases
IDSA GUIDELINE

Implementing an Antibiotic Stewardship Program:
Guidelines by the Infectious Diseases Society of America
and the Society for Healthcare Epidemiology of America

- Weak recommendations any level of evidence
 - Develop institutional guidelines
 - Target antibiotic use in specific indications
 - Strategies to encourage provider led antibiotic review
 - Computerized decision support
 - PK monitoring services – vancomycin
 - Alternative dosing strategies for beta-lactams
 - Promote penicillin skin testing

Barlam TF, et al. *Clin Infect Dis.* 2016;62(10):e51-e77.

Clinical Infectious Diseases
IDSA GUIDELINE

Implementing an Antibiotic Stewardship Program:
Guidelines by the Infectious Diseases Society of America
and the Society for Healthcare Epidemiology of America

- More - Weak recommendations any level of evidence
 - Develop stratified antibiograms
 - Selective and cascade reporting of susceptibility
 - Use of rapid viral tests for respiratory pathogens
 - Rapid diagnostics for blood cultures
 - Procalcitonin in the ICU
 - Monitor antibiotic use in days of therapy
 - Antifungal stewardship & febrile neutropenia guidelines

Barlam TF, et al. *Clin Infect Dis.* 2016;62(10):e51-e77.

The Joint Commission Proposed Standard for Antimicrobial Stewardship

- Applies to all of the following
 - Ambulatory Health Care (AHC), Critical Access Hospital (CAH), Hospital (HAP), Nursing Care Center (NCC), Office-Based Surgery (OBS)
- Leaders establish ASP as an organizational priority
- Educate staff and licensed independent practitioners involved in antimicrobial ordering... and monitoring... about antimicrobial resistance and ASP practices
- Education occurs upon hire and annually thereafter

ASP = Antimicrobial Stewardship Program.
https://jointcommission.az1.qualtrics.com/CP/File.php?F=F_5tDHGzIVDMHenDn. Accessed on February 18, 2016.

Patient and Family Education

- Educate patients and their families as needed regarding the appropriate use of antibiotics
- Example of educational tools
 - CDC – “Viruses or Bacteria – What’s got you sick?” www.cdc.gov/getsmart/community/downloads/getsmart-chart.pdf
 - CDC – Get Smart about Antibiotics Web site www.cdc.gov/getsmart/
 - Notice tools for health care, community, food/farms, the world
- Required across all health care settings

https://jointcommission.az1.qualtrics.com/CP/File.php?F=F_5tDHGzIVDMHenDn. Accessed on February 18, 2016.

Required Members of the ASP Multidisciplinary Team

- Pharmacist(s)**
- Infectious disease physician
- Infection preventionist(s)
- Note: part-time or consultant staff are acceptable as members
- Key people missing from the required group
 - Microbiology
 - Hospitalist(s)
 - Surgeon(s)
 - Intensivist(s)
 - Nursing?

https://jointcommission.az1.qualtrics.com/CP/File.php?F=F_5tDHGzIVDMHenDn. Accessed on February 18, 2016. Oians RN, et al. *Clin Infect Dis.* 2016;62(1):84-89.

Core Elements of the ASP Team

- Accountability
- Drug expertise
- Action
- Tracking
- Reporting
- Education
- Core elements taken from CDC core elements of an ASP
 - www.cdc.gov/getsmart/healthcare/pdfs/core-elements.pdf

https://jointcommission.az1.qualtrics.com/CP/File.php?F=F_5tDHGzIVDMHenDn. Accessed on February 18, 2016.

Develop and Use Organization-Approved Multidisciplinary Protocols

- IV to PO conversion
- Guidelines for antibiotic use in adults – scope?
- Formulary restriction
- Preauthorization requirements for specific antimicrobials
- Assessment of appropriateness for community acquired pneumonia – only disease state specifically called out
- Think low hanging fruit – urinary tract, skin and soft tissue, etc
- Guidelines for antimicrobial use in pediatrics

https://jointcommission.az1.qualtrics.com/CP/File.php?F=F_5tDHGzIVDMHenDn. Accessed on February 18, 2016.

One of the More Challenging Pieces...

- The organization collects and analyzes data on its ASP
- Including
 - Antimicrobial prescribing
 - Resistance patterns
- Resistance patterns – again, get to know micro!
- Challenges in collecting prescribing and utilization data
- Epic, Theradoc, etc.

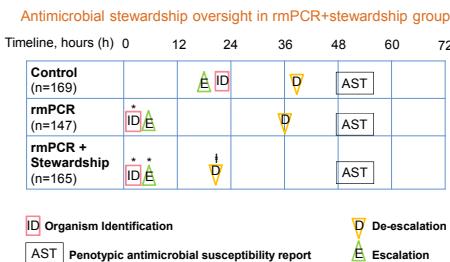
https://jointcommission.az1.qualtrics.com/CP/File.php?F=F_5tDHGzIVDMHenDn. Accessed on February 18, 2016.

And then... You Have to Act on Your Data!

- Once you get the data...
- “The hospital takes action on improvement opportunities identified in its [ASP].”
- This is where the people involved in your team become critical

https://jointcommission.az1.qualtrics.com/CP/File.php?F=F_5tDHGzIVDMHenDn. Accessed on February 18, 2016.

The Impact of Rapid Diagnostics



*P<.05 vs control. IP<.05 vs control and rmPCR groups.
PCR = polymerase chain reaction; rm = rapid multiplex.
Banerjee R, et al. *Clin Infect Dis*. 2015;61(7):1071-1080.

Duration of Antibiotic Use Comparisons between Groups

- Vancomycin use for non-vancomycin requiring BSIs - median
 - rmPCR & rmPCR/AS = 0 h
 - Standard = 8.2 h ($P=.03$)
- Duration of cefazolin/nafcillin/oxacillin - median
 - rmPCR & rmPCR/AS = 71 h & 85 h
 - Standard = 42 h ($P=.04$)
- Duration of piperacillin-tazobactam
 - rmPCR & rmPCR/AS = 44 h & 45 h
 - Standard = 56 h ($P=.012$)

BSI = bloodstream infection.
Banerjee R, et al. *Clin Infect Dis*. 2015;61(7):1071-1080.

Clinical, Microbiologic, and Cost Outcomes

Outcome	Control (n=207)	rmPCR (n=198)	rmPCR + Stewardship (n=212)	P Value Comparing 3 Groups
LOS after enroll – median (IQR)	7 d (4-12)	6 d (4-12)	7 d (4-12)	.61
LOS ICU after enrollment – median (IQR)	3 d (2-4)	2 d (1-5)	3 d (2-4)	.90
30-day Mortality	22 (10.6%)	20 (10.1%)	18 (8.5%)	.74
Overall hospital \$ – mean (median)	\$65,450 (\$27192)	\$66,887 (\$23935)	\$68,729 (\$29064)	.78
Test \$ – mean (median)	\$5377 (\$2082)	\$5680 (\$2585)	\$5743 (\$2774)	<.001

ICU = intensive care unit; IQR = interquartile range; LOS = length of stay.
Banerjee R, et al. *Clin Infect Dis.* 2015;61(7):1071-1080.

Continuous Infusion β-Lactams: Does It Matter?

- Multicenter, randomized trial
- Continuous vs intermittent β-lactam infusion in severe sepsis
- 25 ICUs
- Piperacillin-tazobactam, ticarcillin-clavulanate, or meropenem randomized to either continuous or 30-minute intermittent infusion for the remainder of the treatment course or until ICU discharge
- Primary outcome was the number of alive ICU-free days at day 28
- 432 participants, median age = 64 years
- Median Apache II score of 20

Dulhunty JM, et al. *Am J Resp Crit Care Med.* 2015;192(11):1298-1305.

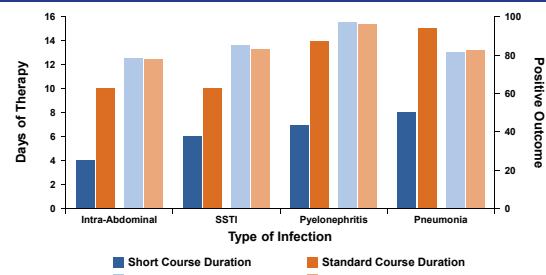
Continuous Infusion β-Lactams: Does It Matter? (continued)

	Continuous (n=212)	Intermittent (n=220)	P Value
Alive ICU-Free Days	18 (2-24)	20 (3-24)	0.38
ICU Survival	180 (84.9%)	182 (82.7%)	0.54
Clinical Cure	111 (52.4%)	109 (49.5%)	0.56
ICU Length of Stay	7 (3-13)	6 (3-11)	0.042
Hospital Length of Stay	16 (8-32)	14 (8-27)	0.25

- So what happened?
 - Antibiotic regimens – mostly piperacillin-tazobactam & meropenem, almost no ticarcillin-clavulanate
 - The microbiology
 - The Kaplan Meier

*Data presented as n (%) or n (IQR)
Dulhunty JM, et al. *Am J Resp Crit Care Med.* 2015;192(11):1298-1305.

Shorter Courses Do Not Affect Outcome



SSTI = skin and soft tissue infection.
Sawyer RG, et al. *N Engl J Med.* 2015;372(21):1996-2005. Chastre J, et al. *JAMA.* 2003;290(19):2588-2598. Sandberg T, et al. *Lancet.* 2012;380(9840):484-490. Moran GJ, et al. *Lancet Infect Dis.* 2014;14(8):696-705.

Compromise of the Last Line

Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study



- Gene easily mobilized to an *E. coli*, *K. pneumoniae*, and *P. aeruginosa*
- Adds a phosphoethanolamine to lipid A = no binding of colistin
- 78 (15%) of 523 samples of raw meat
- 166 (21%) of 804 animals during 2011-2014
- 16 (1%) of 1322 samples from inpatients with infection

Liu YY, et al. *Lancet Infect Dis.* 2016;16(2):161-168.

Conclusions

- The light in the tunnel is a train... coming right at you!
- Pharmacist involvement is key in EVERY model of stewardship
- Standardization and expectations for accreditation
- Target “low hanging fruit” initially
- Use developed tools and don’t recreate the wheel



PHARMACY LEARNING NETWORK

1-DAY REGIONAL MEETINGS

Questions?





1-DAY REGIONAL MEETINGS

Protecting Yourself from Hazardous Drugs:

Is Your Institution following USP<800>?



Presented in partnership with the ICHP Annual Meeting

Faculty

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Clinical Manager, Oncology Pharmacy

Indiana University Health

Chair, Hoosier Cancer Research Network

Disclosure

Christopher A. Fausel, PharmD, MHA, BCOP has no financial relationships to disclose relating to the subject matter of this presentation.

Learning Objectives

- List criteria utilized for defining a hazardous drug
- Describe the criteria and methodology used by NIOSH to identify drugs as hazardous
- Describe potential health risks associated with exposure to hazardous drugs
- Explain strategies to employ proper use of PPE and engineering controls to protect healthcare workers from hazardous drugs
- Describe components of a surveillance program

NIOSH = National Institute for Occupational Safety and Health; PPE = personnel protective equipment.

Technician Learning Objectives

- List criteria utilized for defining a hazardous drug
- Describe the criteria and methodology used by NIOSH to identify drugs as hazardous
- Describe potential health risks associated with exposure to hazardous drugs
- Explain strategies to employ proper use of PPE and engineering controls to protect healthcare workers from hazardous drugs
- Describe components of a surveillance program

Evolution of Recommendations

- 1990, 2006 ASHP Guidelines on Handling Hazardous Drugs
- 2004 NIOSH Safety Alert
- NIOSH LIST of Antineoplastic and Other Hazardous Drugs in Healthcare Settings – most recent update 2014 (updated every 2 years)
- USP <797>
- USP <800> Final chapter published 2/1/16 – enforceable July 1, 2018

Definition of a Hazardous Drug (HD)

NIOSH	ASHP
Carcinogenicity	Carcinogenicity in animal models, in the patient population, or both as reported by the International Agency for Research on Cancer
Teratogenicity	Teratogenicity in animal studies or in treated patients
Reproductive toxicity	Fertility impairment in animal studies or in treated patients
Organ toxicity at low doses	Evidence of serious organ or other toxicity at low doses in animal models or treated patients
Genotoxicity	Genotoxicity (ie, mutagenicity and clastogenicity in short-term test systems)
Structure and toxicity profile of new drugs that mimic existing drugs determined hazardous by the above criteria	
ASHP. ASHP guidelines on handling hazardous drugs. <i>Am J Health-Syst Pharm.</i> 2006; 63:1172-1193.	

NIOSH List of HDs (2014)

- Group 1: Antineoplastic Drugs
- Group 2: Non-antineoplastic Drugs deemed hazardous by meeting one or more NIOSH criteria for a hazardous drug
- Group 3: Reproductive Risks
 - Drugs that primarily pose a reproductive risk to men and women who are actively trying to conceive and women who are pregnant or breast feeding, because of excretion in breast milk

NIOSH 2014. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2014.
By Connor TH, MacKenzie BA, DeBord DG, Trout DB, O'Callaghan JP. Cincinnati, OH US DHHS, CDC.

Listings in NIOSH Update 2014

Table	Content
1	Antineoplastic drugs including those with MSHG
2	Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a HD including those with MSHG
3	Non-antineoplastic drugs that primarily have adverse reproductive effects
4	Deleted drugs from the 2004 NIOSH listing
5	PPE and engineering controls for HDs

MSHG = manufacturer's safe handling guidelines
NIOSH 2014. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2014.
By Connor TH, MacKenzie BA, DeBord DG, Trout DB, O'Callaghan JP. Cincinnati, OH US DHHS, CDC.

HD Risk Categorization

- Assessment of risk to consider:
 - Type of HD (eg, antineoplastic, non-antineoplastic, reproductive risk only)
 - Risk of exposure
 - Packaging
 - Manipulation
- Entity must document containment strategies employed for specific dosage forms

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>). In: The United States Pharmacopeia 39th rev, and the National Formulary 34th ed. Rockville, MD: The United States Pharmacopeia Convention; 2016:285.

Maintenance of HD List

- Assessment of new drugs as they enter the marketplace
- Re-categorization as new toxicologic data becomes available
- Consider investigational agents hazardous if the mechanism of action suggests HD
- Consider dosage form and whether dosage form will be altered/crushed/compounded
- All hazardous drugs should be labeled

NIOSH 2014. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2014.
By Connor TH, MacKenzie BA, DeBord DG, Trout DB, O'Callaghan JP. Cincinnati, OH US DHHS, CDC.

Generating A List of Hazardous Drugs for Your Facility

- OSHA hazard communication requires employers to develop a hazard communication program appropriate for their unique workplace
- Identify all hazardous drugs that could be encountered by workers in the facility
- OSHA defines compliance as:
 - 1. Evaluation whether drugs meet criteria as a hazardous drug
 - 2. Posting a list of hazardous drugs to ensure worker safety

OSHA = Occupational Safety and Health Administration
NIOSH 2014. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2014.
By Connor TH, MacKenzie BA, DeBord DG, Trout DB, O'Callaghan JP. Cincinnati, OH US DHHS, CDC

Consequences of Exposure to HDs

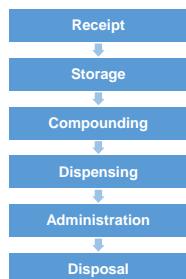
- Short-term:
 - Skin irritation/burning
 - GI toxicity
 - Flu-like symptoms
 - Ocular irritation
- Long-term:
 - Fertility impairment
 - Birth defects
 - Secondary cancers

ASHP. ASHP guidelines on handling hazardous drugs. *Am J Health-Syst Pharm.* 2006;63:1172-1193.

Containment Strategies

- Assessment of risk to consider:
 - Type of HD (eg, antineoplastic, non-antineoplastic, reproductive risk only)
 - Risk of exposure
 - Packaging
 - Manipulation
- Entity must document containment strategies employed for specific dosage forms

Chain of Custody: Hazardous Drugs



Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>). In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD: The United States Pharmacopeia Convention; 2016:285.

HD Exposure Risk Points

Job Function	Risk Points
Receipt	Drug residue is present on outer packaging of HDs
Dispensing	Counting or splitting tablets or opening capsules
Patient-care activities	Handling body fluids or contaminated linens
Spills	Spill management and disposal
Transport	Moving HDs within a healthcare setting
Waste	Collection and disposal of hazardous waste

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>). In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD: The United States Pharmacopeia Convention; 2016:285.

Pharmacy Staff Risk Points

Activity	Risk Points
Compounding and other manipulations	Crushing/splitting tablets or opening capsules Transferring oral or topical liquids between containers Weighing or mixing components Reconstituting powdered or lyophilized HDs and/or withdrawing or diluting injectable HDs from stock containers Expelling air or HDs from syringes Contacting HD residue present on PPE or other garments Cleaning activities on surfaces containing HD residue Maintenance activity on potentially contaminated equipment

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>). In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD: The United States Pharmacopeia Convention; 2016:285.

Potential HD Exposure Risk Points

Activity	Potential Opportunity for Exposure
Administration	Generating aerosols during administration by various routes (eg, injection, irrigation, oral, inhalation, topical) Performing certain specialized procedures (eg, intraoperative or intraperitoneal injection or bladder instillation) Priming an IV set
Patient Care Activities	Handling body fluids (eg, urine, feces, sweat, or vomit) or body-fluid contaminated clothing, dressing, linens, or other materials

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (chapter 800). In: The United States Pharmacopeia 39th rev., and the National Formulary 34 ed. Rockville, MD: The United States Pharmacopeia Convention; 2016:285.

Scope of USP Chapter <800>

- Standards apply to:
 - Areas where hazardous drugs (HDs) are compounded, stored, transported, and administered
- Health care personnel include, but are not limited to:
 - Pharmacists and pharmacy techs
 - Physicians and physician assistants
 - Nurses and home health care workers
 - Veterinarians and veterinary techs

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
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Facilities Impacted

- Pharmacies
- Hospitals and other health care institutions
- Patient treatment clinics
- Physician practice facilities
- Veterinarian's offices

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
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Definitions in <800>

- **Must** = Compliance is mandatory effective July 1, 2018
- **Should** = Recommendations only – not requirements

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
The United States Pharmacopeia Convention; 2016:285.

Who Is Responsible for Compliance?

- Each institution must have a designated person who is qualified and trained to be responsible for:
 - Developing and implementing appropriate procedures
 - Overseeing entity compliance with all applicable laws, regulations and standards
 - Environmental control of compounding and storage areas

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
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Facilities Layout

- HD handling areas must be designated with signage and restricted to authorized personnel
- Locate HD handling areas away from breakrooms/refreshment areas for staff/patients/visitors
- Designated areas must be available for:
 - Receipt and unpacking
 - Storage of HDs
 - Non-sterile HD compounding
 - Sterile HD compounding

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
The United States Pharmacopeia Convention; 2016:285.

Receipt of HDs

- Antineoplastic HDs and all HD active pharmaceutical ingredients (API) must be unpacked (removed from external shipping containers) in areas that are **neutral** or **negative** pressure relative to surrounding areas
- HD must **not** be unpacked from their external shipping containers in sterile compounding areas or in positive pressure areas

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In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
The United States Pharmacopeia Convention; 2016:285.

Storage of HDs

- HDs must be stored to prevent spillage/breakage if the container falls; no storage on the floor
 - **Storage of antineoplastic HDs** not in a final dosage form must be segregated from non-hazardous inventory in an **externally ventilated negative pressure environment** with ≥ 12 air exchanges per hour (ACPH)
 - Sterile and non-sterile HDs may be stored together
 - **Refrigerated HDs** must be stored in a dedicated unit in a **negative pressure room** with ≥ 12 ACPH
 - Reproductive risk only HD and final dosage forms of antineoplastic HDs may be stored with other inventory

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
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The United States Pharmacopeia Convention; 2016:285.

Personnel Protective Equipment (PPE)

- PPE provides worker protection to reduce exposure to HDs aerosols and drug residue
- Gowns, gloves, head, hair, and shoe covers are required for compounding sterile and nonsterile HDs
- Gloves and gowns are required when administering injectable HDs
- Institutions must develop SOPs for PPE based on risk of exposure and activities performed

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
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Use of Gloves with HD Handling

- Two pairs of gloves required for compounding and administering HDs
 - Use **sterile** gloves for **outer** pair for **sterile compounding**
- Gloves must meet standards set by American Society for Testing and Materials (ASTM)
- Chemotherapy gloves must be powder-free
- Inspect gloves for defects before using and do not use defective gloves
- Change gloves every 30 minutes or when torn, punctured or contaminated

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
The United States Pharmacopeia Convention; 2016:285.

Use of Gowns with HD Handling

- Gowns must be tested to resist permeability by HDs; polyethylene-coated polypropylene or other laminate materials preferred
- Gowns must close in the back and have no seams/closures to allow HDs to pass through
- Gowns changed per manufacturer's recommendations or every 2 to 3 hours and after any spills/splashes
- Clothing, lab coats, scrubs can retain HDs

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
The United States Pharmacopeia Convention; 2016:285.

Other Recommended PPE

- Head/hair covers (including beard/moustaches) required
- Second pair of shoe covers must be donned when compounding sterile HDs; remove when exiting buffer room
- Eye and face protection must use when risk for spills/splashes
- Use NIOSH certified N95 masks for respiratory protection—for spills, cleaning activities or potential airborne exposure

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
The United States Pharmacopeia Convention; 2016:285.

Disposal of PPE

- Consider all PPE worn when handling HDs as being contaminated with trace quantities of HDs
- PPE must be placed in an appropriate waste container and disposed per regulations
- PPE used during compounding should be disposed in the proper container in the C-SEC
- Chemotherapy gloves must be discarded in an approved HD waste container inside the C-PEC or contained in a sealable bag outside the C-PEC

C-SEC = containment secondary engineering control; C-PEC = Containment Primary Engineering Control.
Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
The United States Pharmacopeia Convention; 2016:285.

HD Compounding and Engineering Controls

- Engineering controls are required to prevent cross- and microbial contamination using three controls:
 - Containment **primary** engineering control (C-PEC) - a ventilated device for direct handling of HDs
 - Containment **secondary** engineering control (C-SEC) – **the room** in which the C-PEC is placed
 - Supplemental engineering controls – closed-system transfer devices (CSTD)

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
The United States Pharmacopeia Convention; 2016:285.

HD Compounding and Engineering Controls

- HDs must be compounded in a C-PEC (hood) in a C-SEC (buffer room)
- C-PEC shall operate continuously
- Segregate non-sterile and sterile compounding C-PECs
- Laminar airflow workbench (LAFW) or compounding aseptic isolator (CAI) must not be used for compounding HDs

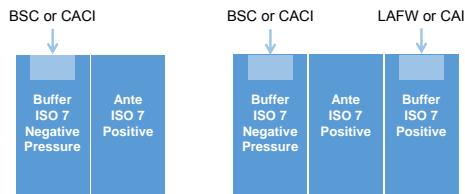
Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
The United States Pharmacopeia Convention; 2016:285.

Engineering Controls for Sterile HD Compounding

Configuration	C-PEC	C-SEC
ISO Class 7 buffer room with an ISO Class 7 ante-room	Externally vented Examples: Class II BSC or CACI	Externally vented 30 ACPH Negative pressure between 0.01 and 0.03 inches of water column relative to the adjacent areas
Unclassifiable C-SCA	Externally vented Examples: Class II BSC or CACI	Externally vented 12 ACPH Negative pressure between 0.01 and 0.03 inches of water column relative to adjacent areas

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
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The United States Pharmacopeia Convention; 2016:285.

Recommended Configurations for Sterile HD Compounding



Anterom:

Minimum positive pressure of 0.02 inches of water column to adjacent spaces;
at least 0.01 inches of water column to HD buffer room; 30 ACPH; hand washing sink.

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
The United States Pharmacopeia Convention; 2016:285.

Supplemental Engineering Controls

- Some** CSTDs shown to limit potential for generating hazardous aerosols during sterile compounding
- No** universal performance standard exists by which CSTDs are evaluated for containment
- CSTD **must** not be used as a substitute for C-PEC when compounding
- CSTDs **should** be used when compounding HDs when the dosage form allows
- CSTDs **must** be used when administering HDs when the dosage form allows

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
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Environmental Quality Control – Wipe Studies

- Environmental wipe studies for HDs **should** be performed routinely at least every 6 months
- Surface wipe sampling **should** include:
 - Interior of C-PEC and equipment contained in it
 - Staging or work areas near C-PEC/pass-through
 - Areas adjacent to CPECs (e.g., nearby flooring)
 - Areas outside of buffer room and patient administration areas
- Currently **no** studies exist demonstrating the effectiveness of a specific number of wipe samples in determining levels of HD contamination

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
The United States Pharmacopeia Convention; 2016:285.

Labeling/Packaging/Transport

- **Labeling:** HDs must be labeled as such at all times during their transport
- **Packaging:** Compounding personnel must select and use packaging containers to maintain physical integrity, stability and sterility during transport.
 - Packaging must protect from damage, leakage, contamination and degradation
- **Transport:** HDs must be transported in containers that minimize the risk of breakage/leakage.
 - Pneumatic tubes must **never** be used to transport liquid or antineoplastic HDs.

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
The United States Pharmacopeia Convention; 2016:285.

Dispensing Final Dosage Forms

- HDs not requiring further manipulation other than counting/repackaging of the final dosage form may be prepared for dispensing without further requirements for contamination except when:
 - Manufacturers recommendation state otherwise
 - Visual indicators of HD exposure exist (e.g., dust or leakage)
 - Segregate equipment used for dispensing activities for HD drugs

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
The United States Pharmacopeia Convention; 2016:285.

Compounding

- Institutions compounding HDs must be compliant with USP <795> (nonsterile) and USP <797> (sterile)
 - Use plastic-backed preparation mat on the work surface of the C-PEC; change regularly during use and following spills
 - Disposable or clean equipment dedicated only to HD compounding
 - Bulk containers of liquid and API HDs must be handled in C-PEC to prevent worker exposure

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
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Administration

- HDs must be administered safely by using protective medical devices and techniques (eg, priming IV tubing with non-HD solution in a C-PEC)
- Appropriate PPE to be worn when administering HDs and disposed properly thereafter
- CSTDs must be used for administration of antineoplastic HDs when the dosage form allows
- Avoid manipulating HD dosage forms (eg, crushing tablets, opening capsules) when possible; if necessary – use appropriate PPE

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
The United States Pharmacopeia Convention; 2016:285.

Cleaning Procedures

Cleaning Step	Purpose	Agents
Deactivation	Render compound inert or inactive	EPA-registered oxidizers (e.g., peroxide formulations, sodium hypochlorite, etc.)
Decontamination	Remove HD residue	Alcohol, water, peroxide or sodium hypochlorite or other materials validated to be effective for HD decontamination
Cleaning	Remove organic or inorganic material	Germicidal detergent
Disinfection	Destroy microorganisms	Sterile alcohol or EPA-registered disinfectant

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD:
The United States Pharmacopeia Convention; 2016:285.

Spill Control

- Train personnel about proper spill kit use
- SOPs are required for spill prevention and clean-up procedures including use of PPE and respirators
- Document circumstances of spill
- Provide immediate medical evaluation to potentially exposed personnel
 - Non-employees exposed to HD should report to designated emergency service for evaluation

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).
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The United States Pharmacopeia Convention; 2016:285.

Medical Surveillance

- Institutions **should** develop a surveillance program for workers handling HDs
- Purpose: minimize adverse health effects in personnel potentially exposed to HDs
- Secondary prevention tool for early detection
- Program involves:
 - Assessment and documentation of symptom complaints, physical and/or laboratory findings
 - Comparison of health variables over time in populations of workers

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>). In: The United States Pharmacopeia 39th rev., and the National Formulary 34th ed. Rockville, MD: The United States Pharmacopeia Convention; 2016:285.

Medical Surveillance

- Baseline assessment of worker's health and medical history
- Estimate of workers HD exposure over time
- Monitoring of organ function at risk for toxicity from HD exposure
- Follow-up plan for acute and long-term exposure to HDs

Pharmaceutical compounding – hazardous drugs – handling in healthcare settings (General Chapter <800>). In: The United States Pharmacopeia 39th rev., and the National Formulary 34 ed. Rockville, MD: The United States Pharmacopeia Convention; 2016:285.

What This Means for Pharmacy Practice

- **Compliance:**
 - A single published standard exists for defining requirements for HD handling
- **Work Procedures:**
 - Chain of custody of HDs
 - PPE
 - Cleaning methodology for HD handling areas

What This Means for Pharmacy Practice

- **Facilities:**
 - Updating existing buffer rooms - All HD compounding to be done in negative pressure C-SEC in externally vented C-PEC
 - Proper “de-boxing” areas for receiving HDs
- **Personnel:**
 - Designated person for overseeing compliance with HD handling is best suited for a trained oncology pharmacist

Conclusions

- Multiple guidelines/alert published over the course of several decades are now present in a single regulatory document
- A single standard of care will not exist for handling hazardous drugs
- Pharmacy department, infusion clinics and physician offices will be challenged to meet the physical structure requirements for engineering controls outlined in <800>



1-DAY REGIONAL MEETINGS

Questions?



PHARMACY LEARNING NETWORK

1-DAY REGIONAL MEETINGS

Examining the Necessity of Newer Insulins for In-Hospital Diabetes Management



Presented in partnership with the ICHP Annual Meeting

Faculty

Susan Cornell, PharmD, CDE, FAPhA, FAADE

Associate Professor of Pharmacy Practice

Associate Director of Experiential Education

Midwestern University Chicago College of Pharmacy

Medication Therapy Management/Diabetes Care Provider

Bolingbrook Christian Health Clinic & Assess Community

Health Clinic

Downers Grove, Illinois

Disclosures

- Susan Cornell, PharmD, CDE, FAPhA, FAADE:
Speakers' Bureau—Sanofi

Learning Objectives

- Describe the reasons for use of concentrated insulin formulations in the treatment of diabetes
- Discuss the clinical, pharmacokinetic, and pharmacodynamic profiles for current and emerging basal insulins
- Describe the pharmacist's role in counseling patients from inpatient to outpatient settings to minimize the risk of insulin administration errors and hospital readmissions

Technician Learning Objectives

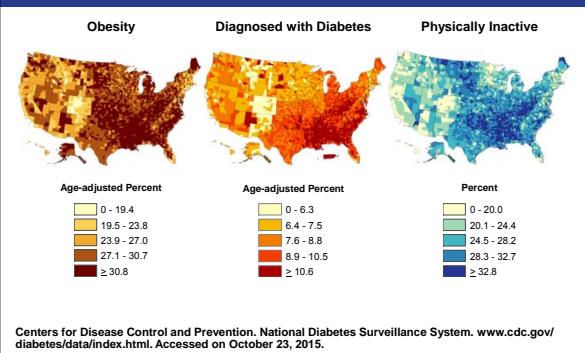
- Describe the reasons for use of concentrated insulin formulations in the treatment of diabetes
- List the available formulations of newer insulins
- Explain how to use an insulin pen

Concentrated Insulin:



The Diabesity
Epidemic

Type 2 Diabetes with Severe Insulin Resistance Due to Obesity and Physical Inactivity



Insulin Resistance

- Major defect in individuals with type 2 diabetes
- 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(2):310-314. Beck-Nielsen H, et al. *J Clin Invest*. 1994;94(5):1714-1721. Bloomgarden ZT. *Clin Ther*. 1998;20(2):216-231. Boden G. *Diabetes*. 1997;46(1):3-10.

Glucose-Lowering Comparison

Monotherapy	Route of Administration	Targets Insulin Resistance	Target Glucose: FPG or PPG	A1C Reduction (%)
Sulfonylurea	Oral	No	Both	1.5-2.0
Metformin	Oral	Yes	FPG	1.5
Glitazones	Oral	Yes	Both	1.0-1.5
Meglitinides	Oral	No	PPG	0.5-2.0
AGIs	Oral	No	PPG	0.5-1.0
DPP-4 inhibitors	Oral	No	PPG	0.5-0.7
Bile acid sequestrant	Oral	No	PPG	0.4
Dopamine agonists	Oral	No	PPG	0.4
SGLT-2 inhibitors	Oral	Maybe	FPG	0.7-1.1
GLP-1 agonists	Injectable	No	Short-acting – PPG Long-acting – Both	0.8-1.5
Amylin analogs	Injectable	No	PPG	0.6
Insulin	Injectable	Yes (to a degree)	Basal – FPG Bolus – PPG	↓ as much as needed

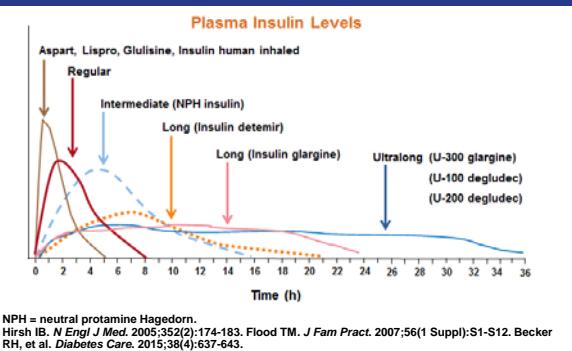
AGIs = alpha-glucosidase inhibitors; DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1; FPG = fasting plasma glucose; PPG = postprandial glucose; SGLT-2 = sodium-glucose cotransporter 2.
Unger J, et al. *Postgrad Med*. 2010;122(3):145-157. Cornell S, et al. *Postgrad Med*. 2012;124(4):84-94.

Insulin Therapy for Insulin Resistance

- Insulin, insulin, and yet more insulin!
 - Causes weight gain and fluid retention
 - Increased risk of hypoglycemia
 - Expensive at high volumes (especially the pens)
 - Multiple injections per day often needed
- Pumps not practical with high-volume insulin usage

American Diabetes Association. *Diabetes Care*. 2016;39(Suppl 1):S6-S12.

Pharmacokinetic Profile of Currently Available Insulins



The Basal-Bolus Concept

- Basal insulin: 50% of daily needs
 - Controls nighttime and between-meal glucose at a nearly constant level
- Bolus insulin: 50% of daily needs
 - Controls mealtime glucose
 - 10% to 20% of total daily insulin requirement at each meal
- Correction dose (sensitivity factor)
 - Correct hyperglycemia reactively

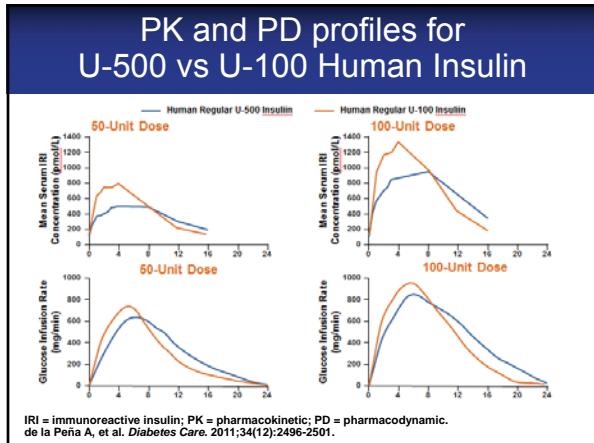
Concentrated Insulin:

The Pharmacokinetic, Pharmacodynamic, and Clinical Properties of Concentrated Insulin Products

U-100 Insulin vs U-500 Insulin

- Human Regular U-500 is highly concentrated and contains 5× as much insulin in 1 mL as standard U-100 insulin
 - Truly used for patients on high doses of insulin (usually >200 units daily)
- Both have onset of action at 30 minutes
 - U-500 insulin exhibits a delayed and lower peak effect relative to U-100
 - U-500 insulin typically has a longer duration of action compared with U-100 (up to 24 hours following a single dose)
- Clinical experience has shown that U-500 insulin frequently has time-action characteristics reflecting both prandial and basal activity

de la Peña A, et al. *Diabetes Care.* 2011;34(12):2496-2501.



Human Regular U-500 Pen

- Can deliver up to 300 units in a single injection
 - No dose conversion for pen
 - Vials/syringes will need dose conversion
 - Dials in 5-unit increments
 - Holds 1500 units of insulin in every pen
 - For severely insulin-resistant patients
 - When daily insulin requirements are in excess of 200 units/day



US Food and Drug Administration. www.accessdata.fda.gov/scripts/cder/drugsatfda/.

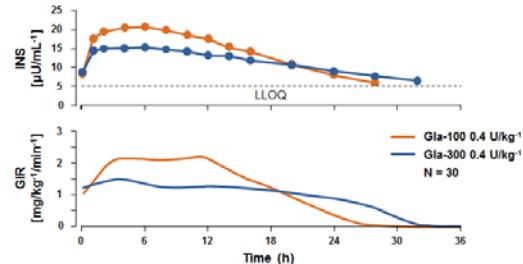
High-Concentration Glargine (U-300)

- Available only in a pen
 - U-300: 450 units/pen, max 80 units/injection
 - Can be used for patients on small and large volumes of insulin
- Offers a smaller depot surface area, leading to a reduced rate of absorption
- Provides flatter and prolonged PK and PD profiles and more consistency
 - Half-life is ~23 hours
 - Steady state in 4 days
 - Duration of action ≤36 hours

Garber AJ. *Diabetes Obes Metab.* 2014;16(6):483-491. Owens DR, et al. *Diabetes Metab Res Rev.* 2014;30(2):104-119. Steinaeisser A, et al. *Diabetes Obes Metab.* 2014;16(9):873-876. US Food and Drug Administration. www.accessdata.fda.gov/scripts/cder/drugsatfda/.

PK and PD of U-300 Insulin Glargine vs U-100 Insulin Glargine

U-300 glargine displays a more even and prolonged PK/PD profile compared with U-100 glargine, offering blood glucose control beyond 24 hours



LLOQ = lower limit of quantification; GIR = glucose infusion rate.
Becker RH, et al. *Diabetes Care.* 2015;38(4):637-643.

U-100 and U-200 Insulin Degludec

- Available only in a pen
 - U-200: 600 units/pen, max 160 units/injection
 - U-100: 300 units/pen, max 80 units/injection
- Can be used for patients on small and larger volumes of insulin
- Provides flatter and prolonged PK and PD profiles and more consistency
 - Duration of action >42 hours
 - Half-life ~25 hours
 - Detectable for at least 5 days
 - Steady state in 3 to 4 days

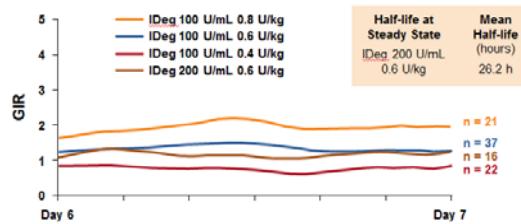


Garber AJ. *Diabetes Obes Metab.* 2014;16(6):483-491. Owens DR, et al. *Diabetes Metab Res Rev.* 2014; 30(2):104-119. US Food and Drug Administration. www.accessdata.fda.gov/scripts/cder/drugsatfda/.

Basal Insulin Degludec

Flat, stable profile of both 100 unit/mL and 200 unit/mL formulations

Mean 24-Hour GIR Profile of the Two Insulin Degludec Formulations at Steady State



GIR = glucose infusion rate.
Heise T, et al. *Diabetes.* 2012;61(suppl 1):A91 [abstract 349-OR]. Heise T, et al. *Diabetes Obes Metab.* 2012;14(10):944-950.

Importance of Patient Education



Overcoming Barriers to Insulin Therapy

- Avoid using insulin as a “threat,” but as a solution; discuss it as an option early
- Use insulin pens and regimens that offer maximum flexibility
- Give a “limited” trial of insulin
- Tell patient that injection is less painful than a finger stick; give an injection in the office/hospital/pharmacy
- Teach patient to recognize and treat hypoglycemia
 - Use basal analog insulin to minimize hypoglycemia

Kruger DF, et al. *Diabetes Educ.* 2010;36 Suppl 3:44S-72S. Funnell MM. *Clinical Diabetes.* 2007;25(1):36-38. Derr RL, et al. *Diabetes Spectrum.* 2007;20(3):177-185.

Patient Education: From Inpatient to Outpatient Setting

- Equipment and supplies needed to effectively manage insulin therapy at home
 - Insulin
 - Compare at home vs hospital (formulary) insulin
 - Syringes or pen needles
 - Blood glucose meter and strips
 - Lancets and lancing device
 - Glucagon emergency kit
 - Contact information of diabetes care provider(s)

What Patients Need to Know about Insulin AND Delivery Devices

- Storage and expiration
 - When it should be refrigerated
 - When it can be at room temperature
 - Time medication expires after first use
- How to prepare product for first use
- How to properly use the device
- How to dispose of the device

Product Expiration

Products/Device	Refrigerated	Unrefrigerated	Once used (opened)
Vials			
Insulin lispro U-100 Insulin aspart Insulin glulisine Insulin glargin	Expiration Date	28 days	28 days
Pens			
Insulin lispro U-100, U-200 Insulin aspart Insulin glulisine Insulin glargin U-100 Insulin glargin U-300	Expiration Date	28 days Glargine U-300: 42 days	Do not refrigerate Lispro, glargin, glulisine: 28 days Aspart: 14 days
Vials & pens: Insulin detemir	Expiration Date	42 days	42 days (pens should not be refrigerated)
Pens: Insulin degludec U-100, U-200	Expiration Date	56 days	56 days (pens should not be refrigerated)
Inhaled: Insulin human	—	Expiration Date	15 days for device

Physicians Desk Reference. www.pdr.net/browse-by-drug-name. Accessed on February 12, 2016.

Basal Insulin Delivery Options

Insulin	Concentration	Vial	Pen
NPH	U-100	X	X
Glargine	U-100	X	X
Glargine	U-300		X
Detemir	U-100	X	X
Degludec	U-100 U-200		X
Regular Human	U-500	X	X

US Food and Drug Administration. www.accessdata.fda.gov/scripts/cder/drugsatfda/.

First-Time Preparation

- Check the pen**
 - Make sure liquid is clear, colorless, and particle-free (N insulin and mixed insulin will be cloudy)
 - Wipe the rubber stopper with alcohol
- Attach the needle**
- Prime the needle**
 - Dial 2 to 3 units; hold up, depress the button
 - Repeat process until a drop of insulin appears at tip of the needle
- Dial up the dose**
- Inject straight into the skin**
 - Depress button to release insulin into subcutaneous tissue
- Hold for 5 to 10 seconds before removing needle from skin**
- Remove needle and dispose** into sharps container



Concentrated Basal Insulin Dosing Conversion Comparison

Glargine U-300		Degludec U-200		Human R-500	
True basal insulin	Pseudo-basal insulin	True basal insulin	Pseudo-basal insulin	Multiple daily injections of basal-bolus	Total daily dose divided into 2 or 3
1 daily injection	1 to 1	1 daily injection	1 to 1	Multiple daily injections of basal-bolus	Total daily dose divided into 2 or 3
2 daily injections	80% of total daily basal dose	2 daily injections	80% of total daily basal dose		
Maximum single-dose injection	80 units	Maximum single-dose injection	160 units	Maximum single-dose injection	300 units
Dialed in 1-unit increments		Dialed in 2-unit increments		Dialed in 5-unit increments	
450 units of insulin per pen		600 units of insulin per pen		1500 units of insulin per pen	
Expect higher daily dose of Glargin U-300 to maintain glycemic control				Monitor for hypoglycemia	

Clinical Pearls

- Watch for over basalization
 - High basal dose with no or little bolus insulin
- Continually increasing insulin doses does not reduce insulin resistance
- Humulin R U-500 is useful for patients on very high total daily insulin doses (eg, >200 TDD/day)
- Ultra long-acting basal insulins (Glargine U-300 and Degludec U-200) provide longer duration of action for better basal coverage with low nocturnal hypoglycemia

Take Aways

- Insulin resistance is a MAJOR problem**
 - Some concentrated insulin may help people on large doses of insulin
 - However, need to use combination drug therapy to improve insulin sensitivity
- Novel, long-acting basal insulin analogs in development may provide benefit compared with current agents**
 - Flatter time-action profiles with less variability
 - Less hypoglycemia, particularly nocturnal hypoglycemia
- Patients need to know how to properly use insulin devices**
 - Hospital pharmacists should review technique at discharge
 - Community pharmacists should review technique at initial fill and periodically thereafter



PHARMACY LEARNING NETWORK

1-DAY REGIONAL MEETINGS

Questions?



pln PHARMACY LEARNING NETWORK **1-DAY REGIONAL MEETINGS**

Meet the Experts



Panel Discussion with PLN Faculty

 Presented in partnership with the ICHP Annual Meeting

Objectives

- Discuss current evidence-based recommendations of the discussed disease states towards improving patient outcomes
- Utilize contemporary medical guidelines and strategies in the wide variety of medical disorders presented
- Explore new roles for health-system pharmacists in our ever expanding profession, as it relates to direct patient care

pln PHARMACY LEARNING NETWORK **1-DAY REGIONAL MEETINGS**

Questions?





**Opioid Misuse:
The Evolution of an Epidemic**

Carrie Vogler, Pharm.D. BCPS
Clinical Associate Professor
SIUE School of Pharmacy

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

Learning Objectives

- Explain the scope and impact of the U.S. opioid epidemic.
- Outline state and federal efforts to support safe and effective treatment of pain while reducing opioid use disorders.
- Describe how pharmacists and pharmacy technicians can be involved in curbing the opioid epidemic.
- List resources for pharmacists, technicians, and patients for pain management and opioid abuse.

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Meet Cassy



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Definitions

- Aberrant drug taking behavior
- Misuse
- Abuse
- Diversion
- Opioid use disorder
- Dependence
- Addiction

1. Webster LR, Fine PG. Approaches to improve pain relief while minimizing abuse liability. J Pain 2010; 11(7):602-611.
2. Centers for Disease Control and Prevention. Injury Prevention & Control: Opioid Overdose. <http://www.cdc.gov/drugoverdose/opioids/index.html>

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Definitions

- Aberrant drug taking behavior
 - Any drug-related behaviors other than taking the medication exactly as prescribed
- Misuse
 - The use of a medication for therapeutic intent, other than exactly as directed by the prescriber
- Abuse
 - The use of a substance for a non-medical purpose to alter one's state of consciousness

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Definitions

- Diversion
 - Knowingly transferring a controlled substance to a recipient other than for whom the substance is prescribed
- Opioid use disorder
 - A problematic pattern of opioid use that causes clinically significant impairment or distress. A diagnosis is based on specific criteria such as unsuccessful efforts to cut down or control use, as well as use resulting in social problems and a failure to fulfill obligations at work, school, or home.

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Definitions

- Dependence
 - A physiologic receptor response to an exogenous substance and the result from removing that substance
- Addiction (substance abuse disorder)
 - Impaired control over drug use, compulsive use, continued use despite harm, cravings

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A 50 year old male patient is currently taking oxycodone ER 20mg PO Q 8 hours and oxycodone IR 5mg q 4 hour prn back pain. He fills his prescriptions a few days early each month. His physician has tried to decrease his dose but the pain is uncontrolled at lower doses. His wife states that he doesn't seem like himself at home and is constantly talking about when his next dose of pain medication is due. He keeps missing work due to fatigue.

How would you best describe this patient's condition?

- a. opioid use disorder
- b. diversion
- c. abuse
- d. withdrawal



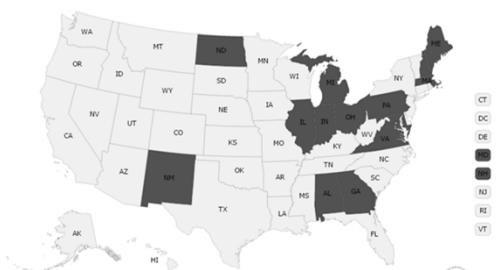
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The scope and impact of the U.S. opioid epidemic



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Statistically Significant Drug Overdose Death Rates Increase from 2013 to 2014, US



Centers for Disease Control and Prevention. Injury Prevention & Control: Opioid Overdose. "State Data." www.cdc.gov/drugoverdose/data/statedeaths.html

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Too close to home...

- Chicago ranked first in the nation for the number of ER mentions of heroin
- In 3 years, Illinois had 900 heroin overdose deaths
- In 2012, 400 Illinois residents died of prescription drug overdoses, 81% involving opioid pain killers like oxycontin and hydrocodone

Davis C., Carr D. The Network for Public Health Law. Drug Overdose Prevention Fact Sheet. Illinois Overdose Prevention Legislation. 1-5.

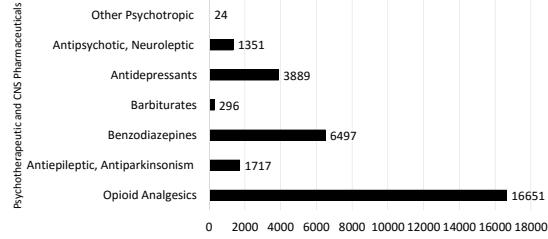
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Which of the following medications most commonly causes drug overdose?

- A. alprazolam
- B. morphine IR
- C. methadone
- D. sertraline

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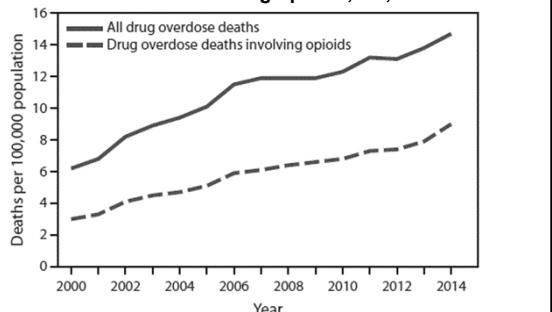
Overdose Deaths Involving Only a Single Drug Class, 2010



Jones, C. M., Mack, K. A., & Paulozzi, L. J. (2013). Pharmaceutical Overdose Deaths, United States, 2010. *JAMA : The Journal of the American Medical Association*, 309(7), 657-659.

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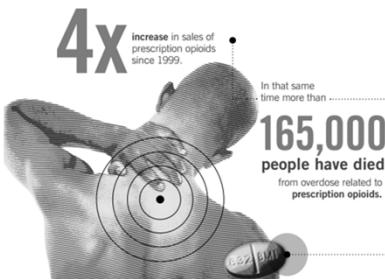
Age-adjusted rate of drug overdose deaths and drug overdose deaths involving opioids, US, 2000-2014



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REDUCE OVERDOSE. PRESCRIBE RESPONSIBLY.

OVERPREScribing LEADS TO MORE ABUSE AND MORE OVERDOSE DEATHS.



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- 249 million prescriptions for opioids were written by healthcare providers in 2013



Centers for Disease Control and Prevention, Injury Prevention & Control: Opioid Overdose: Drug Overdose Fact Sheet

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Heroin use is part of a larger substance abuse problem.

Nearly all people who used heroin also used at least 1 other drug.

Most used at least 3 other drugs.

Heroin is a highly addictive opioid drug with a high risk of overdose and death for users.

People who are addicted to...

	ALCOHOL		MARIJUANA		COCAINE		Rx OPIOID PAINKILLERS
are	2x	are	3x	are	15x	are	40x

...more likely to be addicted to heroin.

SOURCE: National Survey on Drug Use and Health (NSDUH), 2011-2013.

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Why Can't We Stop this Epidemic?



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Why Can't We Stop this Epidemic?

- Lack of coordination of approaches and resources
- Lack of effective implementation of promising practices
- Failure to engage with local communities and across multiple stakeholders
- Failure to spread promising practices
- Direct and indirect counter-forces by the pharmaceutical industry
- Lack of awareness among patients and consumers of the danger of prescription opioids

Martin L. Laderman M, Hyatt J, Krueger J. Addressing the Opioid Crisis in the United States. IHI Innovation Report. Cambridge, Massachusetts: Institute for Healthcare Improvement; April 2016.

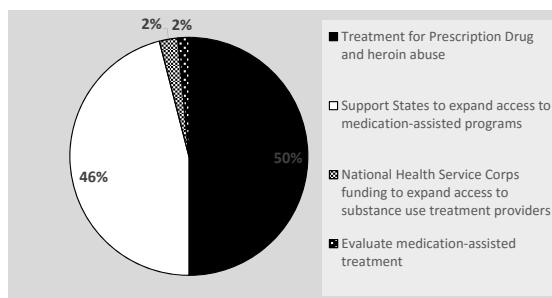
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State and federal efforts to support safe and effective treatment of pain while reducing opioid use



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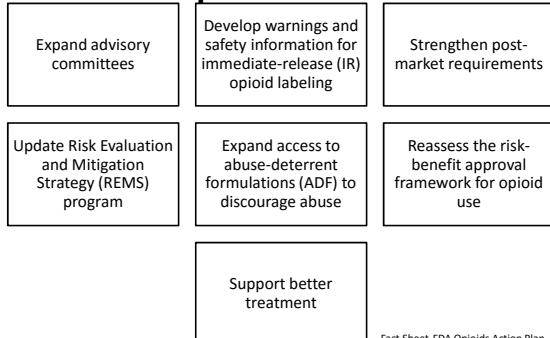
Federal Funding \$1.1 Billion for Prescription Opioid Abuse and Heroin Use Epidemic



Botticelli, Michael. Addressing the Epidemic of Prescription Opioid Abuse and Heroin Use. 2/21/2016. <https://www.whitehouse.gov/blog/2016/02/01>

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FDA Opioids Action Plan



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Guideline for Prescribing Opioids for Chronic Pain in the US, 2016

- Primary care clinicians
- Team-based care
- Treatment for patients ≥ 18 with chronic non-cancer pain
- Lack of long term studies using opioids ≥ 1 year or longer

Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep 2016;65(No. RR-1):1–49.

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CDC Guideline for Prescribing Opioids for Chronic Pain Methods

- GRADE methodology
 - Type 1-4:
 - Does not imply the strength of the recommendation
 - Category A or B

The diagram is a pyramid divided into four horizontal sections. Level 1 at the base is labeled '1 = RCT or overwhelming evidence from OS'. Level 2 is labeled '2: RCT with important limitations, or strong evidence from OS'. Level 3 is labeled '3: OS or RCT with notable limitations'. Level 4 at the top is labeled '4: Experience OS,RCT several limitations'.

RCT=randomized clinical trials
OS=observational studies

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CDC Guideline for Prescribing Opioids for Chronic Pain in the US, 2016

- 1-3 Determining when to initiate or continue opioids for chronic pain
- 4-7 Opioid selection, dosage, duration, follow-up, and discontinuation
- 8-12 Assessing risks and addressing harms of opioid use

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CDC Determining when to initiate or continue opioids for chronic pain

1. Use nonpharmacologic and nonopioid therapy first
2. Before starting opioids, discuss treatment goals with patients
 - functional status
 - pain control
3. Discuss risks and benefits with patients at start and periodically

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CDC Opioid selection, dosage, duration, follow-up, and discontinuation

4. Use immediate release opioids instead of ER/LA opioids
5. Prescribe lowest effective dosage.
 - Caution when increasing dose to ≥ 50 morphine milligram equivalents (MME)/day
 - Avoid increasing dosage to 90 MME/day

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CDC Opioid selection, dosage, duration, follow-up, and discontinuation

6. Prescribe 3 days of opioid therapy for acute pain, more than 7 days is rarely needed
7. Monitor benefits and harms within 1-4 weeks and then every 3 months

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CDC Assessing risks and addressing harms of opioid use

8. Mitigate risk and consider offering naloxone:
 - history of overdose
 - history of substance use disorder
 - higher opioid dosages (≥ 50 MME/day)
 - Concurrent benzodiazepine use
9. Review Prescription Drug Monitoring Program (PDMP)

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Assessing risks and addressing harms of opioid use

10. Urine drug testing prior to starting opioid therapy and at least annually*
11. Avoid concurrent benzodiazepines with chronic opioid therapy.
12. Offer and arrange medication-assisted treatment for opioid use disorder

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Based on the CDC Guidelines for Prescribing Opioids for Chronic Pain, which of the following statements is true?

- a. There are several long term studies that prove opioids can provide benefit for patients
- b. Benzodiazepines are safe to use with high dose opioids
- c. Reviewing the Prescription Monitoring Program is required before filling prescriptions
- d. Patients taking morphine ER 50mg PO BID should be offered a prescription and training for naloxone

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How can pharmacists and technicians help?

- 1-3
Determining when to initiate or continue opioids for chronic pain
- 4-7
Opioid selection, dosage, duration, follow-up, and discontinuation
- 8-12
Assessing risks and addressing harms of opioid use

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U.S. Department of Health and Human Services National Pain Strategy (NPS)

Purpose: Build off Institute of Medicine 2011 Report to “increase recognition of pain as a significant health problem in the U.S.”

Develop a Federal Pain Research Strategy to complement the NPS

NINDS. (2015). National Pain Strategy: A Comprehensive Population Health-Level Strategy for Pain, 1–72.

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Key Areas Addressed in the National Pain Strategy

- Population research
- Prevention and care
- Disparities
- Service delivery and payment
- Professional education and training
- Public education and communication

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Key Areas in the National Pain Strategy where Pharmacists can Help

- Research
- Develop nationwide team-based pain self-management programs
- Pharmacists can help educate:
 - Patients
 - More clinician time with patients and less prescription opioid use
 - Health care providers
 - Training on safe opioid prescribing practices
 - Risks associated with prescription analgesics
 - Tapering opioid therapy
 - Alternative options for pain control
 - Students

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Working Groups

- Problem
- Objective
- Short term, medium term, and long-term strategies and deliverables
- Federal stakeholders
- Collaborators

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HCAHPS Pain Management Score

- Proposed removal of pain from scoring formula used by Hospital Value-Based Purchasing Program for FY 2018

12. During this hospital stay, did you need medicine for pain?
- Yes
 No ➔ If No, Go to Question 15

13. During this hospital stay, how often was your pain well controlled?
- Never
 Sometimes
 Usually
 Always

14. During this hospital stay, how often did the hospital staff do everything they could to help you with your pain?
- Never
 Sometimes
 Usually
 Always

Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS)

CAHPS 2.0 Adult Core Questionnaire- HCAHPS.
www.hcahpsonline.org

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Resources for pharmacists, technicians, and patients for management and opioid abuse

- Stop Overdose IL
www.stopoverdoseil.org
- ASHP Foundation Principles of Pain and Pain Management
<http://www.ashpfoundation.org/painmanagement>
- Prescribe to Prevent: Prescribe Naloxone, Save a life
www.prescribetoprevent.org
- Medicare Part D Opioid Drug Mapping Tool
<https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Medicare-Provider-Charge-Data/OpioidMap.html>

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Lali's Law: PA99-0480 Heroin and Opioid Overdose Prevention

- Dispensing of naloxone by pharmacists to first responders and other non-health care providers
- Approved training programs must be established and conducted prior to naloxone being dispensed or acquired
- You and overdose victim are covered by the Good Samaritan Law

Illinois Department of Public Health Public Act 099-0480.
<http://www.ilga.gov/legislation/publicacts/99/099-0480.htm>

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Signs of an Opioid Overdose

Slow or shallow breathing

Gasping for air

Pale or bluish skin

Person is unresponsive

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Dispensing Naloxone

Illinois State Opioid Antagonist Training Program



Presented by: Kelly Gable, PharmD, BCPP, Chris Herndon, PharmD, BCPS, Jessica Kerr, PharmD, CDE, & Garth Reynolds, BSPharm, RPh

Illinois Pharmacists Association. Illinois State Opioid Antagonist Training.
<http://www.ipha.org/isoatp-registration>

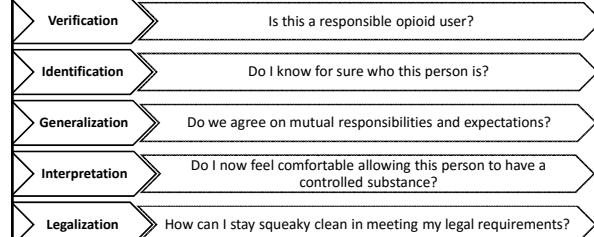
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A pharmacist completes an approved training program for dispensing naloxone. A patient that you dispensed naloxone for dies from a drug overdose. What happens to the pharmacist?

- a. Criminal prosecution for dispensing naloxone to a layperson
- b. License Termination
- c. No prosecution due to the Good Samaritan Law and Pharmacy Practice Act

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Screening Controlled Substances for Legitimacy: The VIGIL System



Brushwood, D. B. Screening Controlled Substance Prescriptions For Legitimacy : The VIGIL System.

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Where can pharmacists review comprehensive controlled substance prescription information for a specific patient?

- a. Primary care physicians' office
- b. Center for Medicare and Medicaid Services (CMS)
- c. Illinois Prescription Monitoring Program (ILPMP)
- d. Community Pharmacy

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Illinois Prescription Monitoring Program



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Date Filled	Label Name	Strength	Metric Qty/Days Supply	Payment Type ?	Pharmacy Name/ City	Prescriber Name
5/24/2013	HYDROCODONE BIT/ACETAMIN	325-10 MG	30/5	Medicare	WALGREENS/ MATTOON	MD
4/12/2013	HYDROCODONE BIT/ACETAMIN	325-10 MG	30/5	Medicare	WALGREENS/ MATTOON	MD
4/12/2013	MORPHINE SULFATE	15MG	60/30	Medicare	WALGREENS/ MATTOON	MD
2/22/2013	MORPHINE SULFATE	15MG	28/14	Medicare	WALGREENS/ MATTOON	
1/11/2013	MORPHINE SULFATE	15MG	60/30	Insurance	WALGREENS/ MATTOON	MD
12/27/2012	HYDROCODONE-ACETAMINOPHEN	5MG-500MG	240/60	Insurance	WALGREENS/ MATTOON	MD
12/21/2012	HYDROCODONE-ACETAMINOPHEN	10MG-325MG	84/14	Insurance	WALGREENS/ MATTOON	
12/21/2012	MORPHINE SULFATE	15MG	28/14	Insurance	WALGREENS/ MATTOON	
10/6/2012	HYDROCODONE-ACETAMINOPHEN	5MG-500MG	240/60	Insurance	WALGREENS/ MATTOON	MD
7/8/2012	TRAMADOL	50MG	60/15	Insurance	WALGREENS/ MATTOON	
7/6/2012	HYDROCODONE-ACETAMINOPHEN	5MG-500MG	240/60	Insurance	WALGREENS/ MATTOON	MD

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What can we do?

- Retrain providers
- Consider all providers
- Identify alternative treatment options for pain management
- Create a role for pharmacists and retail pharmacy “corresponding responsibility”
- Engage in public messaging
- “Flood the zone”
- Recognize geography is important
- Include law enforcement

Martin L, Laderman M, Hyatt J, Krueger J. Addressing the Opioid Crisis in the United States. IHI Innovation Report. Cambridge, Massachusetts: Institute for Healthcare Improvement; April 2016.

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Describe how pharmacists and pharmacy technicians can be involved with curbing the opioid epidemic.

- Write down one thing that you can do to help prevent another opioid overdose.



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What questions can I answer for you?



Opioid Misuse: The Evolution of an Epidemic

Carrie Vogler, Pharm.D. BCPS

Clinical Associate Professor

SIUE School of Pharmacy

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I Love You, I Love You Not Reflections on the Past, Present and Future Relationship Between Pharmacy and the Pharmaceutical Industry

Presented by
 Henri R. Manasse, Jr., Ph.D., Sc.D. (Hon.), FFIP
 Professor and Dean Emeritus
 University of Illinois at Chicago, College of Pharmacy

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Objectives of this Presentation

1. Describe the evolution of the pharmaceutical industry and its relationship with health care professionals (emphasis on pharmacists and pharmacy technicians) and patients
2. Explain the pharmaceutical industry's paradigm shift from patient-centered to profit-centered and the reasons for it
3. Identify current issues related to the industry-pharmacy-patient triad, including drug pricing, direct to consumer advertising, drug shortages, etc.
4. Discuss the differences in the relationship between pharmacists and the pharmaceutical industry in the 1970s and the present

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Acknowledgement

- This presentation was prepared with the assistance of Professor Larry Danziger
 University of Illinois at Chicago, College of Pharmacy

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No Conflicts of Interest

Perspectives based on 45 years
 of engagement and observation

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History of Pharmacy/Pharmaceutical Companies

- Beginning of time thru 1600s to 1700s
 - First Pharmacy thought to be found in Baghdad in about 792
- Empiric Era – 1600 / 1700 to 1940s
- Modern Pharmaceutical Era - 1870's to the 1930s
- Golden Era of Pharmaceutical Companies – 1930s to 1960s
- Patient Care and Clinical Pharmacy Era – 1960s to 1990s
- Industry Consolidation – 1990s to the present

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Evolution of Big Pharma:

Many of the first Pharmaceutical Companies started as Apothecary Shops

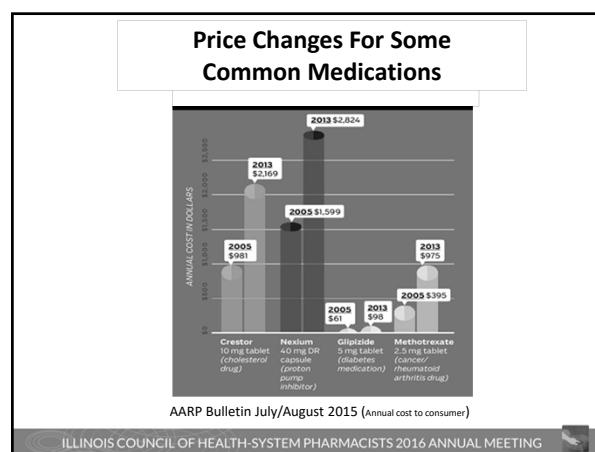
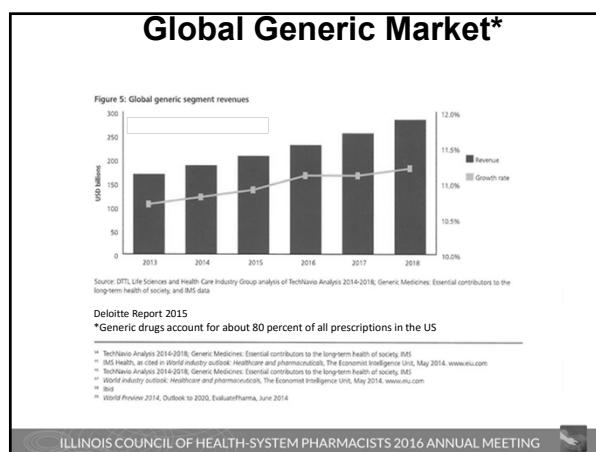
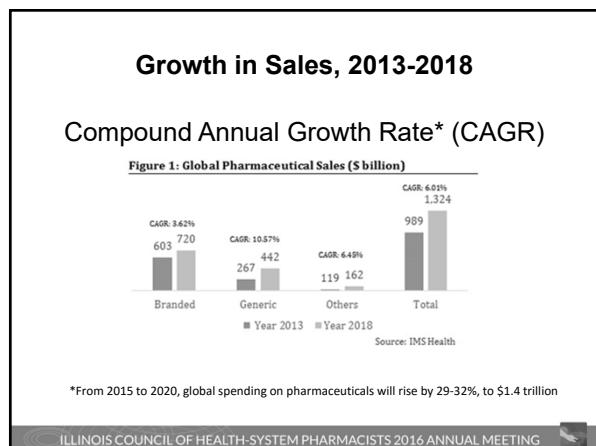
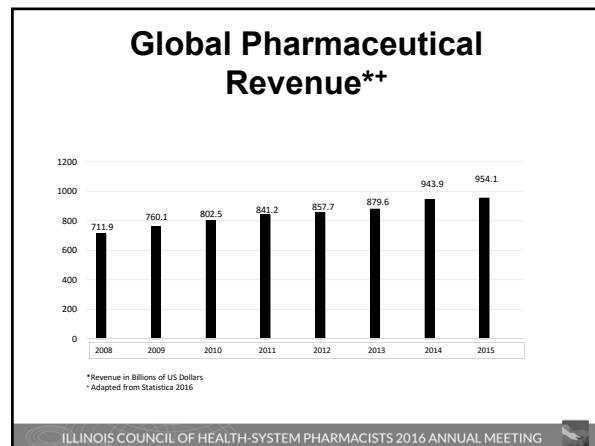
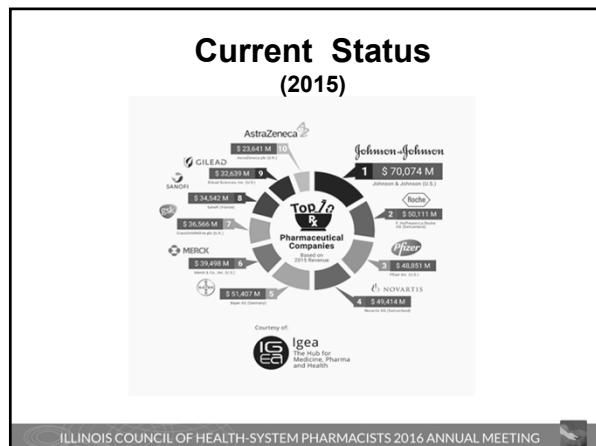
Europe

- Merck
- Schering
- Hoffmann-La Roche
- Burroughs Wellcome
- Etienne Poulenc

United States

- Abbott
- SmithKline
- Parke-Davis
- Eli Lilly
- Squibb
- Upjohn

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Generic Price Increases*

- Recent data reveal 222 drug categories increased in price by 100% or more (between 2013 and 2014)
- Some extreme cases (17 drug categories) price increases of more than 1000% were seen
- One product tetracycline, between 2013 and 2014 it's per tablet price increased from \$0.0345 to \$2.36
 - A 67-fold increase in one year

*Reported by Elsevier

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High Cost of Drugs

- Eli Lilly charges roughly \$13,000 a month for Cyramza
 - The newest drug to treat stomach cancer
- Novartis's Zykadia, costs almost \$14,000 a month
 - The latest medicine for lung cancer
- Amgen's Blincyto, will cost \$64,000 a month
 - For leukemia

New York Times, Jan 14, 2015

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High Cost of Drugs

- In Europe prescription drugs cost 50 percent less than what we pay in the US
 - Gleevec costs \$4,500 per month in Germany
 - Gleevec costs \$3,300 per month in France
 - This price is less than what Americans paid in 2001
 - Gleevec costs \$8,488 per month in the US

McKinsey study from 2008

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Drug Pricing “the Ideal”

- Sellers sell for as much as they can
- Buyers buy for as little as they can
- Ideally, through the process of competition, prices are determined based on benefits to buyers and sellers
- This process of competition is protected by law to prevent anticompetitive conduct

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Drug Pricing “the Reality”

- The law provides monopoly protection for sellers
- Public and private third party payment is the norm, and the physicians (the product selectors) are generally price insensitive
- For decades, public and private third party payers (buyers) have had their bargaining power systematically undermined

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Drug Pricing “the Reality”

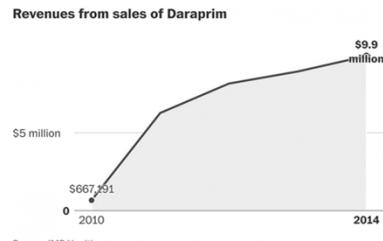
- Prices are increasing at an unsustainable rate
- Pharmaceutical market competitiveness has been systematically undermined for decades
- Americans pay the most for drugs and face significant obstacles to access

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Increased Pricing (Profiteering?? Gouging??)

- **Turing Pharmaceuticals** increased the price of Daraprim, overnight, in September 2015, from \$13.50 to \$750 a tablet, after acquiring Daraprim
- **Valeant Pharmaceuticals** increased prices of Isuprel, Nitropress, Cuprimine, and Syprine
 - Cuprimine's price for 100 capsules ↑ to \$26,189 from \$800
- **Rodelis Therapeutics** increased the price for Cycloserine 2,600 percent, from \$500 for 30 capsules to \$10,800
- **Ovation Pharmaceuticals** purchased Indomethacin from Merck, and raised the price from \$10 to \$36 per vial, but after buying the competing drug (NeoProfen) in 2006, it raised the price of both to nearly \$500 per vial

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Image Issues and Pharmaceutical Companies

- Pharmaceutical companies depend on illness to succeed
- Pharmaceutical companies have been accused of withholding potentially valuable information from patients
- Companies have been accused of “profiteering” at the expense of patients
- Patients have become far less trusting of the industry
- Industry seen as market traders with sole focus on stockholders not patient wellbeing

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Loss of Confidence in Big Pharma

Recent Lawsuits

- Glaxo paid out \$3 billion in fines for issues related to Paxil
 - illegally persuading doctors to prescribe the drug to children and teenagers despite internal evidence that it's ineffective and can trigger suicidal thoughts in adolescents
- Takeda paid out \$2.34 billion in settlements for Actos
 - failed to inform consumers and medical professionals about the risk of bladder cancer associated with use
- Johnson & Johnson and Bayer Corp. being sued for \$10 Million based on allegations that they deliberately concealed Xarelto's potential fatal side effect of internal bleeding

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Drug Shortages: Fact and Fiction

- Quality/manufacturing issues
- Companies have experienced delays receiving raw materials and components from suppliers
 - limitations with raw material
- Discontinuations of older products in favor of newer (more expensive products)
- Fewer companies making drug products (mergers/acquisitions)
- Increased demand from a growing world market

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Big Pharma: How Did we Get Here

- Historically, pharmaceutical companies led the way in medical research
- Knowledge generated by internal basic research programs or licensed from academic institutions to develop products
- This position was supported by the substantial capital and infrastructure investments, this drug development process created significant barriers to entry for companies
- Academic institutions and smaller companies lack the expertise, infrastructure, and financial resources to engage in drug discovery and development

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Big Pharma: The New Model

- Recently big Pharma has been disappointed by the performance of their in-house labs
- To address slowing productivity companies initially sought a quicker path to accessing new technologies and novel drug candidates
- As a result they have increasingly looked for small firms with promising ideas leading to a wave of industry mergers
- Interestingly some companies got more than 70% of their revenues from products that were not developed in-house
- Valeant, a Canadian drugs company, has grown fast by buying other companies and cutting R&D spending

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Big Pharma: The New Model

- These mergers failed to ignite productivity, even as sales and R&D spending dollars have increased
- Moreover, the number of new molecular entities (NMEs) being approved has been declining
- Only 19 new drugs or vaccines were approved in 2007, the lowest numbers since 1983.
- 2012: 39 NMEs approved
- 2014: 41 NMEs approved

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Big Pharma: Future

- A confluence of internal and external factors is now transforming the landscape for discovering, developing, commercializing, and marketing pharmaceuticals
- Industry Issues:
 - pressure to increase sales
 - pressure to decrease development time and cost
 - competition from smaller companies
 - looming patent expirations
 - increased regulatory scrutiny

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Big Pharma: Future

- Recent trends indicate a handful of companies controls 2/3 of NMEs
 - growth in the number of NMEs controlled by marketing organizations that have little or no internal drug discovery or development activities
- Instead of developing new drugs easier to take existing therapies and make them more effective
- Companies also working on different delivery methods, or combining different drugs in new ways

Kinch, Haynesworth, Kinch and Hoyer, 2014

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Pharmaceutical Industry Growth Drivers

- Demographic changes
 - Number of Americans over 65yo expected to double over next 50 years
 - health care expenditures 4 times higher for those over 65yo than those under 65yo
- Innovative medicines targeting life-style diseases
 - Cardiovascular agents, CNS products
Gastrointestinal/metabolism products
- New Drug Approval Outlook
 - Biotech drugs of increasing importance
 - Major Biotech companies raised more than \$32 billion in financing last year*

*EY Life Sciences 2016

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Pharmaceutical Industry Growth Drivers

Pharmacogenomics

- Predicts whether a patient will have a severe, negative reaction to a prescribed medication
- May aid in selection of better medications for patient
- Still in development
- Major Role for Pharmacy??

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Pharmaceutical Industry Growth Drivers

- Emerging Markets seen as growth engine for healthcare demand worldwide (India, China, Brazil)
- The growth of the Chinese pharmaceutical market in 2012 was 22 percent. In 2013, the increase was 14%
- Medicare Drug Benefit Plan should boost profits
- Increased access to medicines through the Affordable Care Act provisions and expansion of Medicaid

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Pharmacy – Pharmaceutical Representative Collaboration

- 1930s to 1970s: Collaborative Relationship
 - Open access to Pharmacist
- 1970s to 2000s: Competitive/Adversarial/legal
 - Restricted access Pharmacist
- 2000s – future: ???

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Direct To Consumer Advertising

- Up thru 1980's, the consumer garnered information through a friend or healthcare provider
- Prohibited by FDA until industry won a 'free speech' lawsuit against prohibition
- The first DTC advertisement
 - 1983-1985: FDA voluntary moratorium
 - 1985: new regulations provide "provides protections for consumers"
- 1990's: print advertisements begin to proliferate
- By mid 1990's, broadcast advertisements enters mix

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Specialty Pharmacy & Drugs

- Pharmaceuticals called "specialty drugs" – *including biologics*
- These drugs can change the course of a disease instead of just treating the symptoms
- Specialty drugs have increased between 15 – 20% over the past several years
- Created new models of distribution with limited number of distribution points
- These agents are only used by a small percentage of the population (1 to 5%)
- These agents expected to account for over 40 – 50% of U.S. drug spending in the future
- Annual drug cost ranges from \$20,000 - \$250,000+ per patient

Source: PRDMA.org 2013 Report

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Pharmacy-Pharma Collaboration

- Can we move to shared values and collaboration between the industry and the profession of pharmacy?
- Focus on the patient
- Accessibility to medicines: fiscal, physical and sustainability
- Rational pricing
- Clear scientific and clinical evidence of outcomes, safety and utility
- Quality products and packaging that meet regulatory requirements

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Thank You!

Questions/Discussion

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Leadership Through The Ranks



LEADERSHIP: IT'S NOT JUST FOR LEADERS

September 15 - 17, 2016 | Oakbrook Terrace, IL
ICHP 2016 Annual Meeting

Management & Leadership are Not the Same . . .

- Leadership is a function of relationships and influencing people
- Management is a function of titles and positions
- Leaders ignite a fire within people (including themselves); Managers ignite a fire under people

Personal Leadership Comes from Within Each of Us . . .

- Starts long before a paycheck
- Effects every aspect of our lives
 - o Personal & professional success
 - o Happiness & job satisfaction
 - o Relationships
 - o Customer service
- It's not just for "them"

It's Not All That Complicated . . .

- Start with a vision
- Accept responsibility for what you do; be accountable for the results & own your mistakes
- Know the way; show the way and go the way
- Be more concerned about being "respected" than being "liked"

What Gets in the Way . . .

- Pride, ego & emotions
- Over exposure to the "routine" & hearing the "same old stories"
- Seeing the world only though our "eyes"
- Thinking, "*It's not my job*"
- Acting as if "differences" are the same thing as "right & wrong"
- Day-to-day pressures, frustration, anger and disappointment
- Burnout (the hidden cost of dedication, passion and commitment)

Final Thoughts . . .

- Be the kind of leader you expect others to be (at work, home & play)
- Even the best information cannot and will not produce meaningful results unless you consistently apply it to everyday, real-life situations.
- What are you willing to begin doing immediately to achieve the results you want?



Informatics Pearls

Joshua Hartman, PharmD, MS
 Deanna Horner, PharmD, BCPS
 Vern Johnson, BS Pharm
 Brian Le, PharmD

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Learning Objectives

- Define the benefits of direct integration with the Illinois Prescription Monitoring Program with an Electronic Health Record.
- List steps to consider when standardizing the formulary across departments, hospitals and/or health systems.
- Recognize diversion opportunities and identify tools for prevention and detection.
- Explain the challenges involved with automated device standardization.
- Describe potential solutions that minimize complications and maximize chances for success with automated device standardization.

Integration of the Illinois Prescription Monitoring Program into Health Systems

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

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What is the IL Prescription Monitoring Program (PMP)?

- State program that aggregates controlled substance prescription information from pharmacies and makes that information available to authorized healthcare providers.
- Potential Uses:
 - Clinical Care
 - Law Enforcement
 - Research



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Are you currently registered with the IL PMP as an authorized user?

- Yes
- No

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Do you currently receive pharmacy claim (fill) data from your e-prescribing vendor directly into your EMR?

- Yes
- No
- I don't know

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IL PMP: Type of information Collected

- Patient ID (name, address, DOB)
- Prescriber
- Dispensing pharmacy information (retail & long-term care)
- Authorized Users include:
 - Prescribers, dispensers, requesting states (if reciprocity is allowed)

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What Benefits Does the Automated Connection Offer?

- Faster access → Improved efficiency
- Ability to access your facilities EMR functions as user authentication
- IT consulting service is available at no additional cost
- IL PMP more comprehensive if payer mix is heavily weighted toward Medicare/Medicaid.

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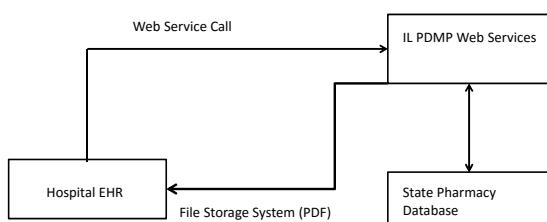
IL PMP Manual Process

- Register with DHS
- Verify employment with DHS
- User logs onto website and spends 2-3 minutes searching for results
- Results viewed on the PMP website



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IL PMP Automated Connection



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Successful Testing at Anderson Hospital in Maryville

- PMP searches increased from ~200 per month to more than 5,000 per month in their ED
- Minimal involvement from IT after initial interface setup



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All eligible users must be registered with the IL DHS in order to utilize the Illinois Prescription Monitoring Program (PMP) Automated Connection.

- True
- False

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References

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- "Illinois Prescription Monitoring Program - DHS 4183." Illinois Department of Human Services, n.d. Web. 22 Aug. 2016. <http://www.dhs.state.il.us/page.aspx?item=60121>.

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Formulary Standardization

Deanna Horner, PharmD, BCPS

7/16/16

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Conflict of Interest

- I have no actual or potential conflict of interest in relation to this presentation.

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Formulary Defined

- Continually updated list of medications
 - Incorporates clinical judgment of multidisciplinary experts
 - Encompasses agents used in diagnosis, prophylaxis or treatment of disease
 - Guides organizational med-use policies, protocols, processes, guidelines, decision support tools

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Step #1: Start with a tool that defines best practice

- Resources:
 - The Joint Commission
 - Centers for Medicare & Medicaid Services
 - American Society of Health-Systems Pharmacists
 - Institute for Safe Medication Practices
- Tool should align with vision

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Step #2: Take time to understand current state

- Perform a gap analysis

Standardization project scope	Means of gap analysis completion
Large	<ul style="list-style-type: none"> Survey platform (REDCap, SurveyMonkey) Benchmarking data Cross-comparisons of data
Medium-Small	<ul style="list-style-type: none"> Cross-comparisons of data <ul style="list-style-type: none"> Database set-up Purchase history Dispense history Administration Drug utilization evaluation Spot audits Observation without interference Group discussions

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Step #3: Hardwire as much as possible but educate on the “why”

Date	Examples within last 12 months	Reasons for formulary deletion
7/22/16	Docusate sodium liquid	FDA/CDC/IDPH alert re:multi-state <i>B. cepacia</i> outbreaks
2/25/16	Moxifloxacin (Vigamox) ophthalmic	Cost savings initiative; therapeutic interchange to generic gatifloxacin 0.5% ophthalmic
1/22/16	Insulin detemir (Levemir)	Contract changes; conversion to insulin glargine (Lantus)
12/11/15	Antipyrine/benzocaine products (Auralgan) otic	FDA removal of unapproved drugs
12/11/15	Donnatal oral liquid	Safety concerns, lack of evidence and significant price increase
4/24/15	Nitroprusside (Nitropress)	Significant price increase with available alternatives (ie nitroglycerin, labetalol or nicardipine)
2/27/15	Phentolamine	Manufacturer discontinuation of product

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The Joint Commission MM.02.01.01: The hospital selects and procures medications. Elements of Performance (EOP)
1 Members of the medical staff, licensed independent practitioners, pharmacists, and staff involved in ordering, dispensing, administering, and/or monitoring the effects of medications develop written criteria for determining which medications are available for dispensing or administering to patients.
2 The hospital develops and approves criteria for selecting medications, which, at a minimum, include the following: Indications for use; Effectiveness; Drug Interactions; Potential for errors and abuse; Adverse drug events; Sentinel event advisories; Population (s) served (for example, pediatrics, geriatrics); Other Risks; Costs
3 Before using a medication new to the hospital, the hospital determines a method to monitor the response of the patient.
4 The hospital maintains a formulary, including medication strength and dosage.
5 The hospital makes its formulary readily available to those involved in medication management.
6 The hospital standardizes and limits the number of drug concentrations available to meet patient care needs.
9 Medications designated as available for dispensing or administration are reviewed at least annually based on emerging safety and efficacy information.
13 The hospital implements its approved medication substitution protocols.

The Joint Commission E-dition, effective date: 1/1/16

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Step #4: Define/follow a process

Drug class reviews
TJC MM.02.01.01 EOP 6,9,13

New drug approval
TJC MM.02.01.01 EOP 1-4

Standardized formulary across hospitals and health systems

The Joint Commission E-dition, effective date: 1/1/16

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Formulary Road Map

- Longitudinal project to review products currently available on formulary
- Timeline based on American Hospital Formulary System (AHFS) classification



Formulary Road Map Timeline

Date	Market P&T Committee meeting - Review and recommendations due for the following:
1/22/16	16:00 Blood Derivatives – Albumin contract changes 68:00 Hormones and Synthetic Substitutes – Insulin contract changes 80:00 Serums, Toxoids, and Vaccines – Immune globulin contract changes
2/26/16	8:00 Anti-infective Agents – 2015 top 5 drug spend per site and action plan 20:00 Blood Formation and Coagulation – Anticoagulation order set revisions
3/25/16	8:00 Respiratory Tract Agents – Roflumilast (Daliresp) Formulary review 52:00 Eye, Ear, Nose, and Throat Preparations (EENT) – Ophthalmic fluoroquinolone update
4/22/16	Break
5/19/16	68:00 Hormones and Synthetic Substitutes – Insulin contract compliance 80:00 Serums, Toxoids, and Vaccines – Vaccine cross-walk, HIV smart pump settings
6/24/16	12:00 Autonomic Drugs – Phentolamine update 15:00 Best Practice – Antidiabetics, rescue and reversal agents
7/22/16	36:00 Endocrine Agents 44:00 Empagliflozin 56:00 Gastrointestinal Drugs
8/26/16	28:00 Central Nervous System Agents 40:00 Electrolytic, Caloric, and Water Balance
9/23/16	84:00 Skin and Mucous Membrane Agents (Topical) 88:00 Vitamins 92:00 Miscellaneous Therapeutic Agents
10/28/16	24:00 Cardiovascular Drugs
12/9/16	4:00 Antihistamine Drugs 72:00 Local Anesthetics 84:00 Smooth Muscle Relaxants
1/27/17	6:00 Cold Compounds 64:00 Heavy Metal Antagonists 76:00 Oxytocics

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Step #4: Define/follow a process

Drug class reviews
TJC MM.02.01.01 EOP 6,9,13

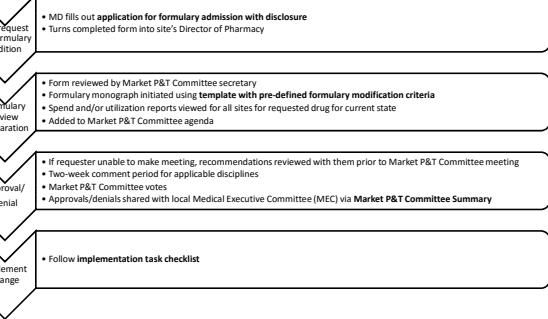
New drug approval
TJC MM.02.01.01 EOP 1-4

Standardized formulary across hospitals and health systems

The Joint Commission E-dition, effective date: 1/1/16

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Formulary addition process



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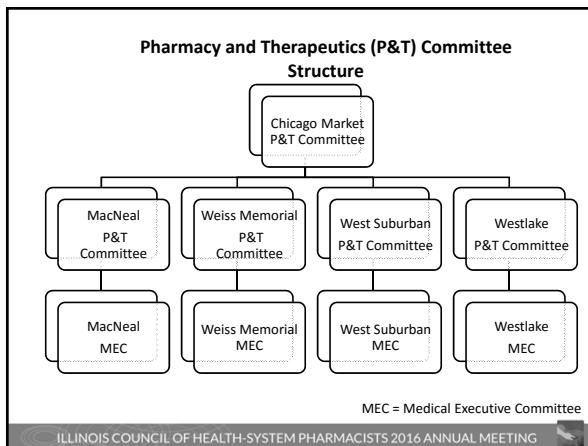
Market Pharmacy and Therapeutics Committee Application for Formulary Admission The physician making this request must complete all sections of this application. The completed application should be forwarded to the Director of Pharmacy.		Application for formulary admission with disclosure	
Generic name(s) of drug: Proprietary name(s) and manufacturer(s): Dosage form(s) and strength(s): Estimated annual usage:		Conflict of Interest Disclosure I, the undersigned, or an immediate family member has a financial interest/arrangement or affiliation with the following commercial companies whose product is requested for formulary consideration, and you have disclosed my conflict of interest.	
Please state briefly what advantage(s) this preparation has over any currently available formulary option: Will this drug: 1. Replace a drug or drugs on our formulary? <input type="checkbox"/> YES <input type="checkbox"/> NO 2. be in addition to the existing formulary? <input type="checkbox"/> YES <input type="checkbox"/> NO 3. be restricted to a certain department? <input type="checkbox"/> YES* <input type="checkbox"/> NO *If yes, please specify the department: 4. Require prescribing privileges? <input type="checkbox"/> YES* <input type="checkbox"/> NO *If yes, please specify: 5. Require restricted indications? <input type="checkbox"/> YES* <input type="checkbox"/> NO *If yes, please specify: If the addition of this drug to our formulary requires educational sessions and/or order forms developed by the manufacturer, please check the appropriate boxes below, fill in the requested information, and sign. Will this drug: 1. Replace a drug or drugs on our formulary? <input type="checkbox"/> YES <input type="checkbox"/> NO 2. be in addition to the existing formulary? <input type="checkbox"/> YES <input type="checkbox"/> NO 3. be restricted to a certain department? <input type="checkbox"/> YES* <input type="checkbox"/> NO *If yes, please specify the department: 4. Require prescribing privileges? <input type="checkbox"/> YES* <input type="checkbox"/> NO *If yes, please specify: 5. Require restricted indications? <input type="checkbox"/> YES* <input type="checkbox"/> NO *If yes, please specify: Disclosures: Please complete review section below. All disclosure information must be completed and accompanied by at least two witness signatures supporting the request to be considered for review by the committee. The requestor should be present at the meeting. Signature of Requestor _____ Date _____ Signature of Chair of Service _____ Date _____ Signature of Pharmacy Director _____ Date _____		Conflict of Interest Disclosure I, the undersigned, declare neither I nor members of my immediate family have any financial arrangements or affiliations with companies that may be perceived as a conflict of interest. I understand that my signature on this request for formulary addition will work diligently to ensure that an equitable and fair balance of information is presented.	
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TJC MM.02.01.01 EOP 2

Formulary modification criteria

<ul style="list-style-type: none"> • Generic/Trade Name and Manufacturer • FDA Approval rating • Pharmacology and Mechanism of Action • FDA approved indications • Potential Non-FDA-Approved (Off Label) Use • Dosage Forms and Storage • Dosing/Administration • Pharmacokinetics: <ul style="list-style-type: none"> - Absorption and Distribution - Metabolism and Excretion • Dosing/Use in Special Populations • Pregnancy Category and Lactation • Clinical Efficacy • Clinical Trial Critique and Analysis 	<ul style="list-style-type: none"> • Medication Safety review <ul style="list-style-type: none"> - Sentinel Event Advisories - Contraindications - Warning/Precautions (Black Box Warnings, etc) - Adverse Reactions - Drug-Drug / Drug-Food Interactions - Monitoring parameters - Special Administration, Storage or Stability Issues - Extravasation potential - Other Risks (Sound-alike, Look-alike; High-alert candidate) • Abuse potential • Cost and Product Availability • Formulary Recommendation • References
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Market Pharmacy and Therapeutics Committee: MacNeal Hospital • Weiss Memorial Hospital Westlake Hospital • West Suburban Medical Center	Summary of the June 24, 2016 meeting
<p>The committee approved:</p> <ul style="list-style-type: none"> • Phentolamine addition (back on U.S. market as of 5/16) to Market Non-cytotoxic Vesicant Extravasation and Administration Guidelines for vasopressor extravasation • Market Renal Dosing Policy updates pending ID MD sign-off from all 4 sites: <ul style="list-style-type: none"> o Revised cefepime and colistimethate (Colistin) dosing o HIV antiretroviral (ARV) additions • Market Safe Insulin Management Initiative (SIMI) <ul style="list-style-type: none"> o Subcutaneous insulin iForm - requesting 4 revisions noted on attachment o IV to subcutaneous insulin transition guidance - requesting to incorporate section into subcutaneous insulin iForm o DKA iForm revisions - requesting bolus removal/initial rate update and to copy West Sub algorithm content/point-of-care orders to MacNeal, Weiss and Westlake <p>The committee reviewed:</p> <ul style="list-style-type: none"> • 2016 Leapfrog CPOE Med Alert Test results • Proposed TJC Med Management Standard and organizational assessment on Antimicrobial Stewardship • ISMP Quarterly Action Agenda 	
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Market Pharmacy and Therapeutics Committee:		MacNeal Hospital • Weiss Memorial Hospital
Westlake Hospital • West Suburban Medical Center		
Summary of the June 24, 2016 meeting		
<p>*** The Chicago Market Pharmacy website and Market Pharmacy and Therapeutics (P&T) Committee document links are located in the Search/Reference Tabs under each facility bookmark section in Horizon Physician Portal. ***</p>		
<p>ILLINOIS COUNCIL OF HEALTH-SYSTEM PHARMACISTS 2016 ANNUAL MEETING</p>		

Implementation Task Checklist Staff Education for Formulary Changes	Process for Formulary Additions or Modifications Implementation
<p>1. Horizon Meds Manager (HMM)</p> <ul style="list-style-type: none"> ✓ Get item numbers (Charge Description Master, CDM) for each facility. This requires: <ul style="list-style-type: none"> ✓ Acquire codes ✓ Facility-specific mark-ups ✓ J-code (if outpatient billing item) ✓ Billing units (if outpatient billing item) ✓ Item number for Horizon Meds Manager (HMM) ✓ Add to HMM if already available at another site ✓ Batch grouping ✓ Service and therapy type ✓ Appropriate order entry mode (e.g. 5, 8, 80 med, IV, IT or TPN) ✓ Therapeutic equivalents ✓ Standard and alternate (when applicable) concentrations ✓ Identify mnemonic to be used <p>2. Facility Inventory</p> <ul style="list-style-type: none"> ✓ Order physical inventory ✓ Allocate shelf space and label bins for stock location <p>3. Automated Dispensing Cabinets (ADC)</p> <ul style="list-style-type: none"> ✓ Provide ADC inventory-related customizations ✓ If product should be an ADC item, add to ADC site-specific master inventory list (need CDM) ✓ If product should be an ADC item, select applicable locations ✓ Add to controlled substance stock as appropriate <p>4. Smart Pump Library</p> <ul style="list-style-type: none"> ✓ Add (if applicable) using guidance from formulary addition checklist <p>5. Horizon Expert Orders (HEO)</p> <ul style="list-style-type: none"> ✓ Orderable additions/modifications <ul style="list-style-type: none"> ✓ Build if they do not exist in HMM during the process ✓ Add to HMM if already in HMM (item must be in HMM first) ✓ If affects Form, submit via Clinical Informatics Change Control Process ✓ Test in EMR TRAIN ✓ Release for CPOE selection based on operational timeline 	
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Step #5: Measure and report progress on a planned basis

Measure	Report
• Purchase reports	• Corporate
• Order set usage	• Regional meetings
• Contract compliance	• Medical Executive Committee
	• P&T Committee
	• Utilization Committee
	• Direct provider feedback
	• Staff feedback

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Example monthly savings report

Initiative	Data Source	Go-Live Date	Projected 2016 Cost Savings	2015 Total Spend	2015 Monthly Spend	June 2016 Spend	June Cost Savings	Savings YTD
sopoterenol	ABC Product Invoice Detail Report	5/1/2015	\$12,375.45	\$12,375.45	\$1,031.29	\$0.00	\$1,031.29	\$6,187.73
Nitroprouside	ABC Product Invoice Detail Report	5/1/2015	\$7,734.06	\$7,734.06	\$644.51	\$0.00	\$644.51	\$3,867.03
CSFs	ABC Product Invoice Detail Report	5/1/2015	\$4,959.69	\$22,959.69	\$1,913.31	\$269.03	\$1,644.28	\$3,600.26
Antimicrobial stewardship	ABC AHFS 8 Class Summary Report	1/1/2016	\$23,530.64	\$419,530.64	\$34,960.89	\$29,230.89	\$5,730.00	\$52,762.34
Basal insulin	ABC Product Invoice Detail Report	2/1/2016	\$7,458.81	\$29,835.23	\$2,486.27	\$1,642.28	\$843.99	\$5,369.28
Donnatal elixir	ABC Product Invoice Detail Report	2/1/2016	\$8,139.20	\$7,330.80	\$610.90	\$0.00	\$610.90	\$4,473.80
4th generation ophthalmic FQ	ABC Product Invoice Detail Report	4/1/2016	\$35,727.00	\$83,657.39	\$6,971.45	\$4,165.83	\$2,805.62	\$10,757.37
IVIG conversion	FFF Product Invoice Report	5/1/2016	\$55,837.07	\$279,185.35	\$23,265.45	\$22,684.80	\$580.65	\$55,445.28
Bicillin L-A Initiative	ABC Product Invoice Detail Report	5/1/2016	\$2,500.00	\$36,335.92	\$3,027.99	\$5,812.20	-\$2,784.21	\$14,736.35
Vaccine crosswalk	ABC AHFS 80 Class Summary Report	5/1/2016	\$23,463.21	\$234,632.13	\$19,552.68	\$35,015.64	\$15,462.96	\$11,713.08

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Step #6 Provide constant reinforcement/reminders

- Message repetition is key
- Communication tools: verbal, email, tip sheets, weekly update, monthly summaries, SBAR, formulary list, WEBSITE

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As discussed in the presentation, when standardizing the formulary across departments, hospitals and/or health systems, what are key steps to incorporate?

- a) Ensure all sites are using the same systems.
- b) Perform a gap analysis to understand current state.
- c) Define a process to be applied from drug selection to implementation.
- d) a, b, c

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Summary

- Step #1: Emulate best practice
- Step #2: Perform a gap analysis
- Step #3: Communicate reason
- Step #4: Standardize the process
- Step #5: Use metrics to report
- Step #6: Provide reinforcement

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Conclusion

- Formulary standardization is becoming a common target in order to optimize buying power, reduce system redundancies and consolidate efforts as a means to improve patient care.
- Six steps discussed outline an approach to formulary standardization across departments, hospitals and/or health systems.

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Drug Diversion

Vern L. Johnson R.Ph.

The speaker has no conflicts of interest to declare

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What is Drug Diversion?

- In the terminology of the United States Drug Enforcement Administration, **diversion** is the use of prescription drugs for recreational purposes. The term comes from the "diverting" of the drugs from their original purposes.
- Drug diversion is the redirecting of legitimate drugs into illicit channels.

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Diversion Opportunities

- Purchasing
- Storage
- Restock
- Administration
- Waste

- An opportunity exists whenever a Controlled Substance is touched or moved.

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Detection, Investigation, Prevention

- Adopt a Zero-tolerance attitude
- Develop policies for accountability and enforce them.
- Use reports to routinely validate that your policies are being followed.
- Use technology reports for Investigation when a possible Diversion is identified.
- Use Overt and Covert Cameras, Drug Testing, Interviews

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Detection, Investigation, Prevention

- Develop a Diversion Monitoring Team.
 - Pharmacy administration (PIC)
 - Nursing administration
 - Nursing operations
 - Human Resources
 - Occupational Health
 - Security
 - Education Specialists

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Detection, Investigation, Prevention

- Report it!
 - DEA
 - IDFPR
 - Pharmacy Board
 - Nursing Board (if a nurse)
 - CEO or President of the Organization

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A Diversion opportunity exists during:

- A. Restock, Administration, Drug Testing, Waste
- B. Purchasing, Waste, Storage, Drug Testing,
- C. Purchasing, Storage, Restock, Administration
- D. Administration, Waste, Storage, Investigation

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Tools for the Detection and Prevention of Diversion include:

- A. Anomalous Reports, ADMs, Policies, Cameras
- B. Cameras, Policies, Anomalous Reports
- C. Diversion Monitoring Team, ADMs, Anomalous Reports
- D. Waste Witness, Policies, Drug Testing, Anomalous Reports

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Automated Device Standardization

Brian Le, Pharm.D.
PGY-2 Pharmacy Informatics Resident
HSHS St. Elizabeth's Hospital
Belleville, IL

Speaker has no conflicts of interest to disclose

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Hospital Sisters HEALTH SYSTEM

- Multi-institutional health care system comprised of 14 hospitals and an integrated physician network across Illinois and Wisconsin
- Predominantly utilizing MEDITECH electronic medical record (EMR) across health system
- Transitioning to Epic over the next few years



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Background

- Automated dispensing cabinet standardization is challenging with many facets to consider
- Two years ago implemented Pyxis ES
 - Most of our hospitals on Pyxis 3500
 - Problem: maintained at local level
 - Had project management and consultants from Pyxis
- During new version implementation, many unexpected issues since implementing standards across health system

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Multi-facility Conversion

- Multiple Pyxis 3500 servers migrating to single Pyxis ES server
 - Pyxis ES (web-based) vs. 3500 (local environment)
 - 13 environments converting to 2 environments
- Multiple pharmacy information systems
 - Epic and MEDITECH interfaces required

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Pyxis 3500 / ES



Pyxis ES



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To Standardize or Not To Standardize

- Some things can be standardized
 - Drugs are same although facility formulary settings differed
 - Want to avoid building multiple copies of a drug for each site
 - Build main formulary, copy down to other hospitals, and then customize
 - Controlled medications handled the same way
- Some things cannot be standardized
 - Override list - different hospitals have different needs

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Frequency Mapping

- 9800+ mappings with MEDITECH in Pyxis ES
- 210 mappings with Epic
- Factors to consider with mapping decisions
 - Had to evaluate times setup in pharmacy information systems
 - Validate fields that crossed over interface

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User Role Standardization

- Operate in Wisconsin and Illinois
 - Need state specific roles since techs are different
- Wanted practice consistency since operating under same state laws
- Pro
 - Users could easily work at two different hospital (training simplification)
- Con
 - Pushback: when users lose functionality they previously had

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Sample User Role

CareFusion		User Roles Pyxis™ ES System v1.0															User Roles for HHS MedS Implementation																																	
Role User Role		User Roles for HHS MedS Implementation															User Roles Pyxis™ ES System v1.0																																	
Function	Permissions	Description	HOME ALONE			FACIAL WASH			PHARM ACIST			PHARMACY ASSTN			PHARM TECH			RN MANAGER			SUPERVISOR/CLINIC COORD			RN PREP/STOCK ROOM			AS PREP/STOCK ROOM			CPS			RN			DEPTER/ANESTHESIST			ANESTHESIST			SUPPLY & MEDS REC'D			EMR			STUDENT NURSE		
Standard User Role		User role to represent individual working alone in the facility.	<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>																																
Manage Facility	Manage Facility	Manage facility and determine the settings common between all sites. Set up facility specific variables (e.g., facility name, address, management of users).	<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>																																
Manage Facility		Manage facility and determine the settings common between all sites. Set up facility specific variables (e.g., facility name, address, management of users).	<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>																																
Manage Facility	Manage Facility	Manage facility and determine the settings common between all sites. Set up facility specific variables (e.g., facility name, address, management of users).	<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>																																
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Minimizing Complications

- Reach out to other institutions that are similar in structure as your organization to gain perspective of challenges
- If something doesn't make sense, question it
- No one best answer and it will depend on what best suits your institution
- Test, test, test the work that was done

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Maximizing Success

- Project management
 - Make sure you take the right amount of time to do things
 - Don't let them rush you
- Test to make sure it works
 - This goes out to multiple institutions and affects everyone
 - Bad quality in means bad quality out, so get it done right the first time

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Which of the following is true?

- A. Automated dispensing cabinet conversion is a straight-forward process
- B. When converting to a new automated device cabinet, standardizing the configuration among all hospitals is the best option
- C. It is important to always test your work in order to minimize complications
- D. It is not possible to customize during a standardization process

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QUESTIONS FOR PANEL?

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Using Technology to Address Sepsis

Elise Wozniak, PharmD
Heather Harper, PharmD,
BCPS
Brian Le, PharmD

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Learning Objectives

- Review the use of technology in the management of sepsis.
- Describe the screening for the sepsis patient population in order to provide early identification.
- Explain the steps for antimicrobial surveillance.
- Discuss how the technology is operationalized to activate a multidisciplinary team including pharmacy.

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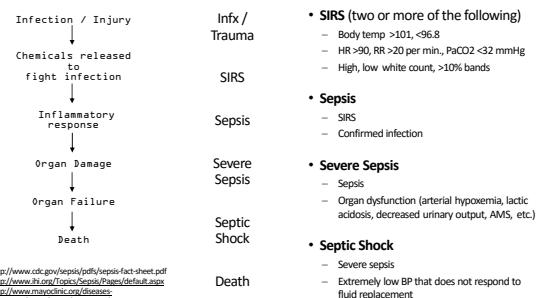
Overview and Northwestern System

Elise Wozniak, PharmD
Northwestern Memorial Hospital
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No conflicts of interest to disclose

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What is Sepsis?



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Sepsis Treatment: Early Goal-Directed Therapy (EGDT)

- Rivers et al. developed a protocol called early goal-directed therapy (EGDT), 2001
 - Control group: 46.5% mortality
 - Intervention group: 30.5% mortality
- Guidelines were adopted by the Surviving Sepsis Campaign (SSC), 2004
 - Incorporated into recommended care bundles

Surviving Sepsis Campaign

Gastr et al. Critical Care (2015) 19:286.
Rivers et al. NEJM (2001) 345:394-409.
www.survivingsepsis.org/About-SSC/Pages/History.aspx

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Sepsis Treatment: Early Goal-Directed Therapy (EGDT)

- Agreement that early diagnosis and antibiotics improve patient survival; however, methods of initial resuscitation and hemodynamic monitoring are still debated.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1822

MAY 1, 2014

VOL. 370 NO. 18

A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*

• ProCESS Investigators, 2014

- Unable to replicate Rivers' conclusions
- No significant differences in 90-day, 1-year mortality, or need for mechanical support.

Rivers et al. NEJM (2001) 345:394-409.
ProCESS Investigators. NEJM (2014) 370:370.

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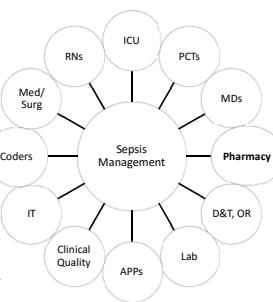
CMS Severe Sepsis and Septic Shock: Management Bundle Measure

- Beginning Oct. 1, 2015 CMS requires that hospitals who participate in Inpatient Quality Reporting (IQR) Program collect data for Severe Sepsis and Septic Shock: Management Bundle Measure
- Developed from recent clinical studies, Surviving Sepsis Campaign and NQF endorsed sepsis bundle measure
- Evaluates care provided to patients with Severe Sepsis and Septic Shock
- Consists of measuring lactate level, blood cultures, broad spectrum antibiotics, fluid bolus if lactate elevated or hypotensive
<http://www.hcup-us.ahrq.org/2015/severe-sepsis-and-septic-shock-management-bundle-measure-nqf-0500.htm>
- Begins with 'time of presentation' with 3 hour and 6 hour clocks

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NMH Strategies to Improve Sepsis Management

- Utilize the EHR for Measure Documentation
 - PowerChart notifications/tools
 - Order sets
 - Physician documentation
- Defining Time Zero (presentation)
- Appropriate Antibiotic Selection
- Educate all members of interdisciplinary team
- Provide clinician support for bundle elements



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Cerner Predictive Model

At least 2 SIRS Criteria

- Temperature > 101°F or < 96°F
- Heart Rate > 95
- Respirations > 22
- Glucose >160 or <200 mg/dL
- WBC >12,000 or <4,000

WITH

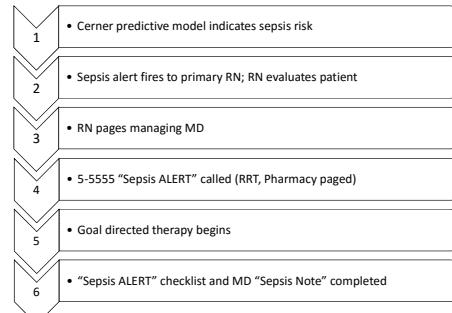
Any 1 criteria of organ dysfunction

- Systolic BP < 90 or MAP </= 65
- Lactate >2.4
- Bilirubin between 2 - 10
- Creatinine increase of >/= 0.5 over last 72 hours
- "Shock Index" as indicated in Sepsis alert

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NMH "SEPSIS ALERT"

Always Launch Early Rapid Treatment



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CLINICAL PROTOCOL

Subject: SEPSIS CARE	Page 1 of 6	Protocol # NMH CCP 07.0045
Title: SEPSIS 3 & 6 HOUR BUNDLE AND NURSING DRIVEN LACTATE	Revision of: NEW	Version: 1.0 Effective Date: 02/22/2016 Removal Date:

I. PURPOSE:

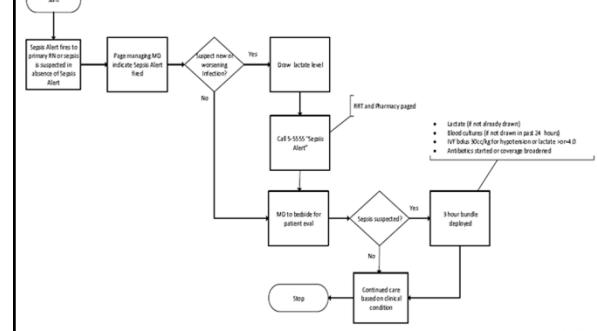
To ensure appropriate early goal directed therapy for patients with clinical indication of sepsis, severe sepsis and septic shock.

II. PERSONS AFFECTED/SCOPE:

All inpatients units and clinicians caring for patients 18 years and older, suspected or diagnosed with sepsis/severe sepsis/septic shock.

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Sepsis 3 Hour Bundle/ Nursing Driven Lactate Guideline



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Cerner: Sepsis Note

- Image removed due to proprietary content

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Cerner: Sepsis Care Order Set

- Image removed due to proprietary content

ILLINOIS COUNCIL OF HEALTH-SYSTEM PHARMACISTS 2016 ANNUAL MEETING

Cerner: Checklist

- Image removed due to proprietary content

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Sepsis Alert: Pharmacist Role

- Sepsis Alert pager covered by a pharmacist 24/7
- Pharmacist to go to bedside (except overnight)
- Expedite antibiotic selection and administration
 - GOAL: Antibiotic administration within 1 hour from time zero
- Common Pharmacist Interventions
 - Antibiotic selection
 - Compatibilities
 - Loading dose/infusion time adjustment
 - Prioritizing empiric gram-negative coverage with limited intravenous access

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At NMH, how does the pharmacist become aware of a sepsis alert?

- A. Pop up within Cerner
- B. Automated phone call to the pharmacy
- C. An automatic page to the sepsis alert pager
- D. Automated communication order within PharmNet

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Acknowledgements

- Kevin Bajer, PharmD
- Matthew Groth, RN, MSN, CCRN
- Barb Buckley, RN, MS
- Northwestern Sepsis DMAIC Team

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OSF System

Heather Harper, PharmD,
BCPS

OSF Healthcare

Peoria, IL

No conflicts of interest to disclose

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Sepsis Best Practice Advisory (BPA)

- Clinical alert based on patient data
- Rules calculate a Sepsis Score

• Image removed due to proprietary content

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Sepsis BPA

- Trigger
 - ED Sepsis score greater than 2
 - Fires when ED patient chart opened
- Suppressed if patient on abx
 - Looks for active inpatient anti-infective order
 - Will not be satisfied by abx on the prior prescription

Linked Criteria Record
 Name: OSF B SEPSIS SCORE > 2 (ED NUR)
 Linked Criteria
 1 OSF C SEPSIS SCORE > 2 [159]
 2 OSF C IN PATIENT ON AN ANTI-INFECTION MEDICATION [1567]
 3 OSF C IN AGE 18YO AND OLDER [760]
 Logic: 1 AND 3 AND NOT 2

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Sepsis BPA

- Piloted November 2013
- System wide rollout 2015
- Fires for ED patients only
 - Adults (18yrs or above)
 - Pediatric alert in development
- 3 Versions based on role
 - PCT
 - RN
 - Provider

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Sepsis BPA - RN

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Sepsis BPA - Provider

- Image removed due to proprietary content

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OSF ConstantCare - eICU

- Critical care RNs and MDs remotely monitor patients in 14 ICUs
- Equipped with remote camera technology and monitor feeds
- Patient identification
 - Sepsis BPA
 - Sepsis surveillance in Philips eCare Manager
- Virtual rounds on septic patients with



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OSF ConstantCare - eICU

- Study underway in rural EDs
- Goals
 - Assess impact of simulation training
 - Adoption of technology
 - Enhance safety and impact outcomes for sepsis
- Mobile carts equipped with camera

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Sepsis Explorer - Metrics

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Which of the following criteria is used to screen patients to provide early identification of sepsis?

- A. WBC less than 4,000, above 12,000 or bands >10%
- B. Positive blood culture
- C. Scr above 2
- D. Lactic acid less than 2

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Pharmacist Role in Addressing Sepsis

- Epic Antimicrobial Stewardship (AMS) tool
- Scoring System
 - Pushes data to pharmacists in patient lists
 - Prioritizes patients
- Documentation
 - Records recommendations
 - Tracks time since last review

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AMS Navigator

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AMS Navigator - Triggers

Bug-Drug Mismatch	De-escalation	Duplicate Therapy	IV to PO	Targeted Agents
Candida in sputum on fluconazole	Broad Spectrum agent(s) ≥ 48 hours	Metronidazole AND Piperacillin/Tazobactam, Ampicillin/Sulbactam, OR Meropenem	Levofloxacin	Ampicillin B Micafungin Voriconazole Fosfomycin
Cefepime MIC > 4 to enterobacteriaceae	Asymptomatic bacteruria	Levofloxacin AND Azithromycin Levofloxacin AND Doxycycline	Metronidazole	Ertapenem Meropenem Daptomycin Linezolid Tigecycline
Levaquin MIC > 1 to <i>Pseudomonas</i> or <i>Strep.</i> , <i>Pneumoniae</i>			Fluconazole	Non-formulary: Ceftazidime Ceftazidime/vibacastam Ceftolozane/tazobactam
Vancomycin MIC ≥ 2 to MRSA		Two Beta-Lactams ordered on same patient	Azithromycin	
Organism grown does not match antibiotic ordered			Doxycycline	Dalbavancin Diflucan Isavuconazonium Oritavancin
VRE on Vancomycin			Linezolid	Posaconazole
Resistant to drug patient is on			Rifampin	Quinupristin/dalfopristin

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AMS Navigator - Documentation

- Report displays trigger
- Document recommendations and interventions

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The OSF AMS system identifies patients with the following antimicrobial issue...

- A. Bug-drug mismatches
- B. Supratherapeutic trough levels
- C. Patients on broad spectrum therapy over 48 hours
- D. A and C

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Acknowledgments

- Ronald Luce - Physician, Informatics
- Toni Bortell - RN, Manager OSF ConstantCare
- Michelle Geurink- Pharmacist, Informatics

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HSHS System

Brian Le, Pharm.D.
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HSHS St. Elizabeth's Hospital
Belleville, IL

Speaker has no conflicts of interest to disclose

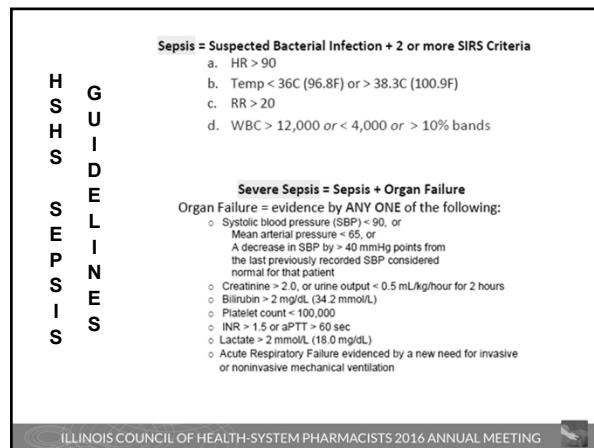
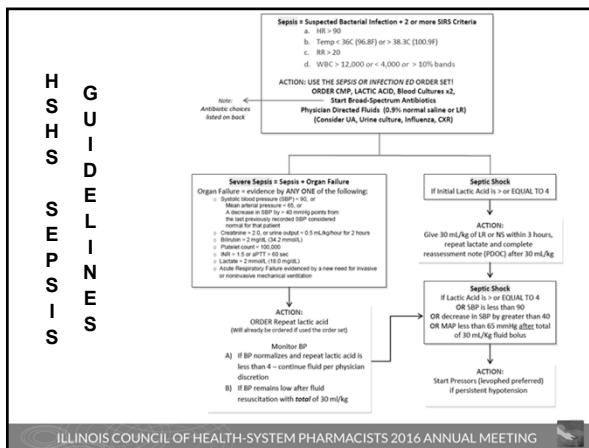
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- Multi-institutional health care system comprised of 14 hospitals and an integrated physician network across Illinois and Wisconsin
- Predominantly utilizing MEDITECH electronic medical record (EMR) across health system
- Transitioning to Epic over the next few years



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Our Goals for Sepsis

- Utilize EMR data to immediately identify septic patients for further evaluation
- Sends various team members alerts when septic patients are identified

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Identifying Septic Patients

- Used paper-based tick sheet to identify septic patients
 - Problem: lacks prospective monitoring
- MEDITECH was not able to perform background alerts for patient identification
- How can we quickly identify septic patients?

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Real-Time Alerts with CDSS

- TheraDoc
 - Clinical Decision Support Software (CDSS)
 - Pulls data from EMR
 - Allows rules to be created on discrete data points
 - Great except lacked discrete vital signs data

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Never Accept No for an Answer

- When there is a will, there is a way
- Always ask your vendors if their product is capable
- Creative approaches - we had failures with fake meds - sometime lean on your vendor and you may be surprised
 - No cost to us
 - Before asking the vendor, ask yourself "What can I gain?"
 - Once they developed, it can be turned into functionality for them (development vs. enhancement)
 - Worked with development pharmacist at TheraDoc
 - Pros: can combine with other things we already use
 - Why would vendor want to know about something that is very important?
 - Good marketing for them
 - Cons: maintenance by vendor and us

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Customization with TheraDoc

- **Problem**
 - TheraDoc does not have a way to store vital signs in their system discretely
- **Solution**
 - Auto-create a diagnosis that identified vital signs discretely

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Building Out the Rules

SIRS Patient Identification

- Sepsis Patient Identification
- Sepsis Patient Identifier APTT
- Sepsis Patient Identifier Bilirubin
- Sepsis Patient Identifier INR
- Sepsis Patient Identifier Lactate
- Sepsis Patient Identifier MAP
- Sepsis Patient Identifier Platelets
- Sepsis Patient Identifier SBP
- Sepsis Patient Identifier SCR

Sepsis = Suspected Bacterial Infection + 2 or more SIRS Criteria

- HR > 90
- Temp < 36C (96.8F) or > 38.3C (100.9F)
- RR > 20
- WBC > 12,000 or < 4,000 or > 10% bands

Severe Sepsis = Sepsis + Organ Failure

Organ Failure = evidence by ANY ONE of the following:

- o Systolic blood pressure (SBP) < 90, or mean arterial pressure (MAP) < 65 mmHg
- o A decrease in SBP by > 40 mmHg points from the last previously recorded SBP considered nonbaseline measurement
- o Creatinine > 2.0, or urine output < 0.5 mL/kg/hour for 2 hours
- o Bilirubin > 2 mg/dL (34.2 mmol/L)
- o Platelet count < 100,000
- o GGT > 1.5 times upper limit of normal
- o Lactate > 2 mmol/L (18.0 mg/dL)
- o Acute Respiratory Failure evidenced by a need for invasive or noninvasive mechanical ventilation

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SIRS Patient Identification

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Severe Sepsis Identification

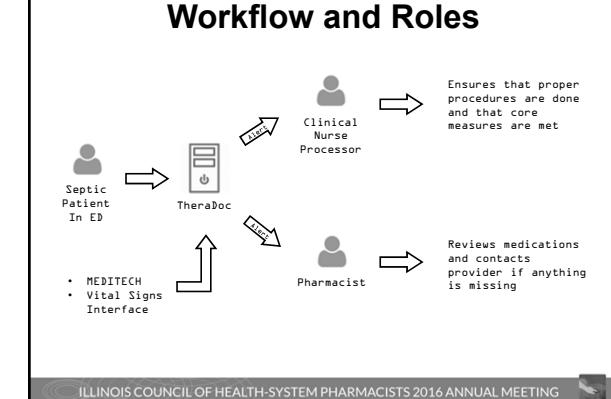
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Emergency Department Pilot

- When patients met criteria for SIRS/sepsis, message is sent by TheraDoc via email to members of sepsis team
 - Currently, only pharmacists and clinical process nurses
 - These team members have iPads that are set up for push notification of emails
 - Notifications pop up on home screen and allow for users to be alerted

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Sample Email to Providers

EZ Alert: SIRS Patient Identification

Demographics & renal function Admit Diagnosis Private

Age: Private
SCr: 0.37 (02/12/2014)
GCr: N/A

Sex: Private
Height: Private
Weight: Private

This alert uses interfaced vital sign data to identify patients that meet 2 of the SIRS criteria

Current Admit Diagnosis:
There were 7 diagnoses found for the current admission. The diagnosis 'respiration rate greater than 20' dated 08/15/2016 14:10:44 matches the alert criteria.

Current Admit Diagnosis:
There were 7 diagnoses found for the current admission. The diagnosis 'heart rate greater than 99' dated 08/15/2016 14:10:44 matches the alert criteria.

[Launch TheraDoc web application](#)

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Future Directions

- Evaluate alert success and timing success
- Expand into other areas of sepsis monitoring
 - Ex. IV fluid bolus administration

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Which of the following is true?

- A. It is not possible to receive sepsis alerts if the EHR does not have the built-in functionality for it.
- B. CDSS can be utilized to build sepsis alerts if the EHR is not capable of it.
- C. New development by the vendor will always cost your organization a lot of money.

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Questions for Panel

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Standardization Across the Enterprise

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Speaker has no conflicts of interest to disclose

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Learning Objectives

- Define processes to achieve and maintain standardization across enterprise for medication use in the EHR and other technologies.
- Identify considerations when implementing and maintaining standardized enterprise formulary.
- Recognize areas where standardized enterprise formulary cross with information technology

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Agenda

- Where We Started
- Where We Wanted to Go
- How We Got There
- How We Stay There

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Where We Started

- Formularies & Order Sets
- Therapeutic Interchanges
- Smart Pump Library

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Where We Started

- Federated model for hospital formulary processes
- Each facility had a local P&T committee structure
- Each hospital had different medical staff by-laws governing formulary process
- Uncoordinated effort by hospitals to review medications for formulary addition
- Some hospitals had different suppliers for medications
- There were unique medication needs at some hospitals
 - Neonatology
 - Transplantation
 - Oncology

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Where We Started By the Numbers

- 6 Different Formularies (1 per hospital)
- 5273 Items in legacy EMR (17 % Duplication)
- Physician Specific Order Sets (not all)
- 2059-3228 Items in individual facility formularies

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Where We Wanted to Go

- Common system formulary for all hospitals
- System Wide Therapeutic Interchanges (auto-subs)
- Evidence Based System Wide Order Sets (effort began prior to EMR)

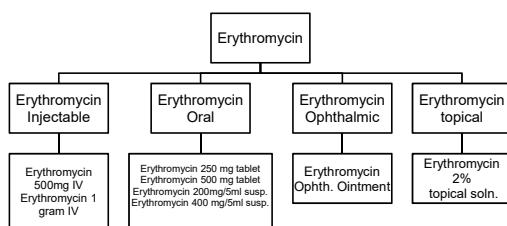
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Data Analysis

- Information from legacy (by hospital)
 - Usage (medication orders)
- “Formulary” counts determined by routed drug
 - Not all routes of all drugs are formulary (e.g. ketorolac oral not available at SFMC, but ketorolac injectable is available)
- The formulary recommendation were based on the counts (routed medications)

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Example



One medication generated 4 routed drug items (formulary items) and 8 line items in the medication lists

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Analysis-'Ordered' Criteria

- Medications counted as ‘ordered’ in past year (May 2007-May 2008) if:
 - Facility Formulary: Any number of orders
 - Facility non-formulary:
 - SFMC and SAMC: 10 orders or more
 - SJMC, SMMC, SFH, SJWAMC: 5 orders or more

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Analysis-Ordered at all facilities

- Every facility has ordered (based on criteria) OR
- SAMC and SFMC have ordered AND formulary everywhere else
- Results
 - Routed Drugs : 726
 - Medication list items: 2581

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Final Formulary and Compendium Recommendations

• Routed Drugs		
– All	726	
– SFMC & SAMC	165	
– SFMC	304	
– SAMC	161	
		}
		Total
		1356
• Medication List items		
– All	2581	
– SFMC & SAMC	289	
– SFMC	452	
– SAMC	229	
		}
		Total
		3551

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Final Formulary and Compendium Recommendations

- Formulary (routed medications) item total = 1356
- Medication list item total = 3551
 - Current compendium = 5273
- Reduction in med list items = **33.7%**

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Final Formulary and Compendium Review and Recommendations

- Use recommended list for system formulary
- Due diligence on the part of the system P&T sub-committee to resolve any issues
 - A review of the list of medications and meds to be removed
 - Example—no orders for snake anti-venom but need to keep
- Further design and ratification of a system-wide process for common formulary (routed medication) list
- Commitment from hospital leadership to support this effort
- Central and standardized process for safety and quality review
- Each hospital will create a medication list based on the system formulary (routed medication) list (not everyone has everything)

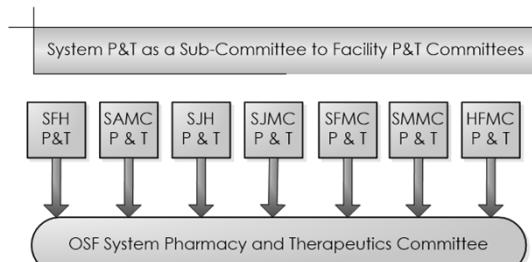
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Timeline

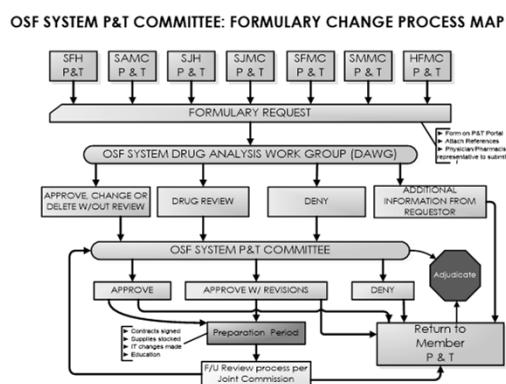
- February 2008-P&T subcommittee formed
- March 2008-1st P&T subcommittee meeting
- April & May 2008-Legal discussions
- June 2008-Formulary presentation to subcommittee, Review of list to remove by pharmacy directors (400 routed drugs)
- August 2008-System P&T charter work
- October 2008-Work begins on auto-subs

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Original Structure



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How We Got There Just the Beginning

- Therapeutic Interchanges (auto-subs)
- Work Group by Drug Class
 - Clinical Subject Matter Experts
 - Pharmacy Contract Administrator
 - Informatics Pharmacist
- Approved by System P&T—built into EMR
 - Facility P&T- track adoption

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A	B	C	D	E	F	G	H	I	J	K	L	M	N
DRUG CLASS	DRUG ORDERED	BRAND	DOSE/FREQ	DRUG SUBSTITUTED	BRAND	DOSE/FREQ	SFHE	SAND	SUAR	SMNC	SPNC	SMNC	
lipid lowering	Fluorostatin	Lescol	20.4mg/day	pravastatin	Practol	10.2mg/day				X			X
lipid lowering	Fluorostatin XL	Lescol XL	80mg/day	pravastatin	Practol	40mg/day				X			X
lipid lowering	Losartan/atorvastatin ER/Mezacor/Acoser		10.8mg/day	pravastatin	Practol	10.8mg/day				X			X
lipid lowering	Rosuvastatin	Crestor	10.4mg/day	atorvastatin	Lipitor	20.8mg/day	X			X	X		

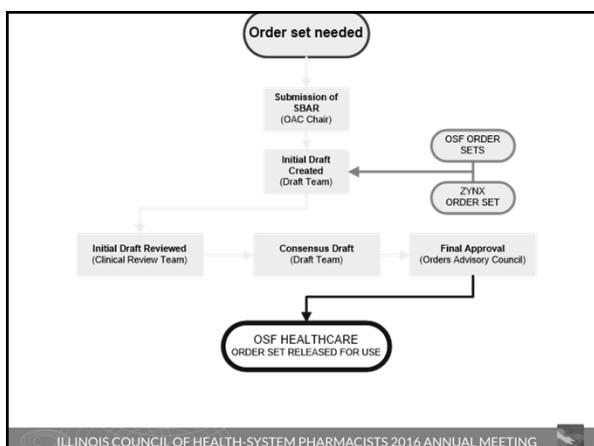
(Vithouse Status: Lipitor for higher LDL level lowering and Pravastatin for everything else except Simvastatin containing drugs (due to less drug interactions than Simvastatin). Orders for Simvastatin and/or Vytorin will be filed as ordered.)

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Order Sets

- Evidence Based
- System Wide
- Started Work prior to changing EMR (third party) pneumonia, basal bolus, NICU
- NOT facility specific
- NOT physician specific
- Use of Subject Matter Experts

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What Else

- To truly standardize the order sets, needed to standardize drip concentrations, IVPB volumes
- Easy transition to one standard system wide smart pump library
 - Same meds
 - Same concentrations
- Standard formulary in enterprise ADS

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How We Stay There

- New Facility (currently 11)
 - Scan inventory
 - Compare to OSF Formulary
 - VLOOKUP
 - Adopt Therapeutic Interchanges
 - Enforce Formulary Compliance
 - Transition to Smart Pump Library
 - Goal is BEFORE EMR go live

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Formulary Compare New Facility

DOCUSATE CALCIUM 240 MG PO CAPS	2565 auto sub exists
ENOFIBRATE 145 MG PO TABS	40010 auto sub exists
ENOFIBRATE 48 MG PO TABS	40009 auto sub exists
SUAIFENESIN-CODEINE 100-10 MG/5ML PO SOLN	79194 auto sub exists
INSULIN ASPART 100 UNIT/ML SC SODN	120948 auto sub exists

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Hosting—When Our Standard Isn't Their Standard

- Own Formulary
- Own Therapeutic Interchanges
- Own Concentrations
- Impacts:
 - Order Sets
 - Medication Records
 - Automated Therapeutic Interchanges

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Which of the following processes would aid in developing a formulary to meet system needs:

- A. Use formulary of the largest hospital
- B. Remove anything never ordered
- C. Combine all the formularies of the system hospitals so no facility loses anything they may need.
- D. Use a systematic approach of review of all formularies and usage that takes specialized populations served into consideration.

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What needs to be considered when a new facility becomes part of a healthcare system in regards to standardized formulary?

- A. Current medication administration times
- B. Medical Staff by-laws
- C. Hours of the pharmacy
- D. Profile or non-profile of ADS machines

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Which of the following technologies would not benefit from or be impacted by formulary standardization?

- A. Smart Pumps
- B. Automated Dispensing Systems
- C. Nurse Call System
- D. Provider Order Entry

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Questions



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Understanding Recent Advances in PAH Management
< A Practical Guide for Clinical Pharmacists >

Supported by educational grants from
 Actelion Pharmaceuticals and United Therapeutics

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ACTIVITY DESCRIPTION

Target Audience

This continuing pharmacy education activity is planned to meet the needs of pharmacists in a variety of practice settings, including large and small healthcare systems, outpatient clinics, managed care organizations, long-term care facilities, and academia. This program targets health-system pharmacists who are responsible for the safe and effective use of medications utilized for the treatment of patients with PAH.

Learning Objectives

Upon completing this activity, participants will be able to:

- Utilize evidence-based treatment algorithms to guide therapeutic approaches for PAH based on disease classification and prognostic factors
- Evaluate the role of the various therapeutic classes, as monotherapy or combination therapy, in the treatment of PAH as a means to individualize therapy based on disease severity and patient factors
- Discuss the role of pharmacists as part of the multiprofessional healthcare team in ensuring the safe and effective use of PAH medications

ACCREDITATION

Pharmacists
 Center for Independent Healthcare Education is accredited by the Accreditation Council for Pharmacy Education as a provider for continuing pharmacy education. Center has assigned 1.0 contact hour (0.1 CEUs) of continuing pharmacy education credits for participating in this activity.

ACPE UAN: 0473-9999-16-004-L01-P
 Activity type: Knowledge-based

To receive a Certificate of Credit, participants must complete and return the Activity Evaluation Form.

The information that you participated will be uploaded to CPE Monitor within 4 weeks and you will be able to access your credits from the profile you set up with NABP. For more information, please visit <http://www.nabp.net/>.

For questions regarding accreditation, please contact info@jointsponsor.com.

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Burden of Pulmonary Arterial Hypertension

- Sustained PAH leads to right heart failure, the leading cause of death in this population
- Associated with 1-year mortality up to 10–15%
- Rare disease, affects 15 to 26 people per million
- True burden may be underestimated:
 - Under diagnosis
 - Misdiagnosis

Benza, et al. *Chest*. 2012;142(2):448-456.
 Therioula, et al. *Eur Respir J*. 2007;30(6):1103-1110.
 Peacock, et al. *J Respir Crit Care Med*. 2011;104:3-9.
 Humbert, et al. *Am J Respir Crit Care Med*. 2006;73:1023-30.
 Badescu, et al. *Chest*. 2010;137:376-87.

Complex Therapy Management

- **General**
 - Accurate diagnosis
 - Initiation of therapy
 - Medication availability
 - Education and training
 - Staff
 - Patients
 - Cost and reimbursement
 - Limited distribution
 - Small populations
 - Contraindications
- **Prostacyclins (infused and inhaled):**
 - Unique devices and supplies
 - Complex dosing and titrations
 - Profound pharmacological effects
 - Specially-trained HCPs
- **Oral targeted therapies**
 - REMS
 - Drug interactions

Multidisciplinary Management

UI Health PAH Team

- Program Director
- PAH Nurse Coordinator
- Clinical Pharmacists
- Clinic Support Staff

Health-System Approach

- Physicians: pulmonary, critical care, cardiology
- Nurses: clinical and research
- Pharmacists: dispensing, clinical and research
- Research personnel
- Specialty services: rheumatology, hematology, hepatology, sleep medicine and cardiovascular imaging

Hemodynamic Definition of PH/PAH

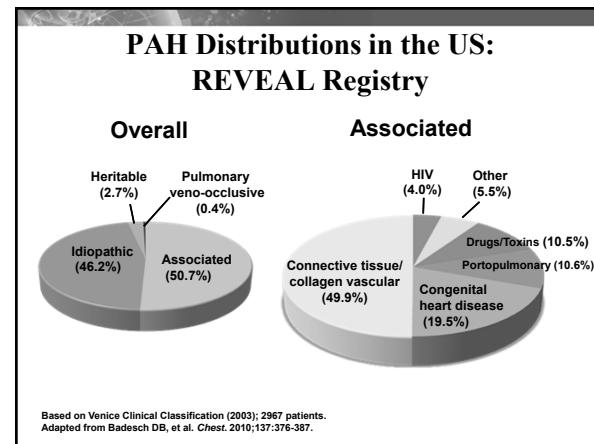
PH	Mean PAP ≥ 25 mm Hg
PAH	Mean PAP ≥ 25 mm Hg <i>plus</i> PCWP/LVEDP ≤ 15 mm Hg
ACCF/AHA includes PVR > 3 Wood Units	

LVEDP, left ventricular end diastolic pressure
Badesch D, et al. J Am Coll Cardiol. 2009;54:S55-S66.
Gaine N, et al. Eur Heart J. 2009;30:2493-257.
McLaughlin VV, et al. J Am Coll Cardiol. 2009;53:1573-1619.

5th World Symposium on PH: Modified Classification of PH

1. Pulmonary arterial hypertension <ul style="list-style-type: none"> 1.1 Idiopathic PAH 1.2 Heritable PAH 1.2.1 BMPR2 1.2.2 ALK1, ENG, SMAD9, CAV1, KCNK3 1.2.3 Unknown 1.3 Drug- and toxin-induced 1.4 HIV-associated 1.4.1 Connective tissue disease 1.4.2 HIV infection 1.4.3 Portal hypertension 1.4.4 Congenital heart diseases (update) 1.4.5 Schistosomiasis 1.4.6 Chronic hemolytic anemia 	3. PH due to lung diseases and/or hypoxia <ul style="list-style-type: none"> 3.1 COPD 3.2 Interstitial lung disease 3.3 Other pulmonary diseases with mixed restrictive and obstructive features 3.4 Sleep-disordered breathing 3.5 Alveolar hypoplasia/obstruction disorders 3.6 Chronic exposure to high altitude 3.7 Developmental lung diseases (update) 	4. CTEPH
1'. Pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis	5. PH with unclear/multifactorial mechanisms	
1'' PHN		
2. PH due to LHD <ul style="list-style-type: none"> 2.1 LV systolic dysfunction 2.2 LV diastolic dysfunction 2.3 Valvular disease 2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies 		

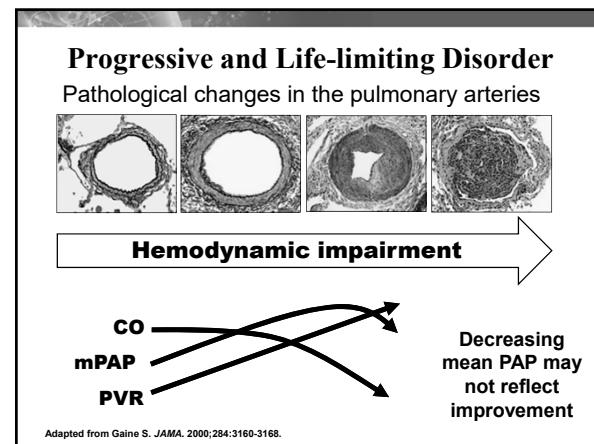
Simonneau G, et al. JACC. 2013;62:D34-D41.

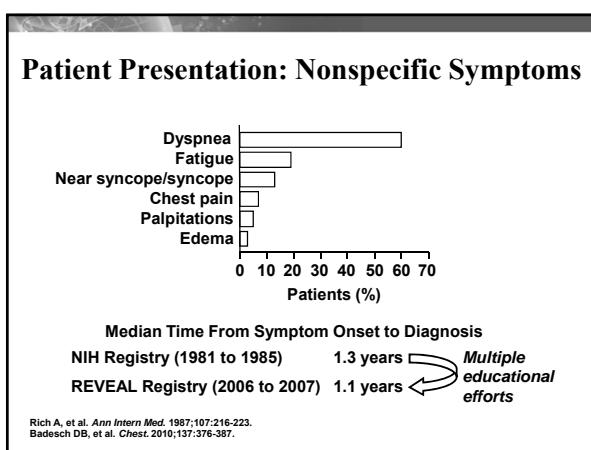


Hemodynamic-Clinical Classification Relationships

Definition	Hemodynamic Characteristics	WHO Clinical Groups
PH	mPAP > 25 mm Hg CO normal, reduced, or ↑	ALL
Pre-capillary PH	PCWP/LVEDP ≤ 15 mm Hg TPG $\geq 12-15$ mm Hg	1. PAH 3. PH due to lung disease and/or hypoxemia 4. CTEPH 5. PH with unclear or multifactorial mechanisms
Post-capillary PH	PCWP/LVEDP > 15 mm Hg TPG < 12 mm Hg	2. PH owing to LHD
Mixed PH Reactive Non-reactive/fixed	PCWP/LVEDP > 15 mm Hg TPG $\geq 12-15$ mm Hg	2. PH owing to LHD

Adapted from Hoeper M, et al. Eur Heart J. 2009;30:2493-2537.





Diagnostic and Monitoring Evaluation	
Test	Assessment/Finding
Physical examination and history	For suspected PH
Chest x-ray electrocardiography	For suspected PH
Echocardiogram	Evaluation of right ventricular function and screening tool
Ventilation perfusion scan	Screen for CTEPH
Oxygen saturation	Screen for sleep disorder or nocturnal hypoxia
Pulmonary function tests	Screen for obstructive/restrictive diseases Diffusing capacity
Blood work: ANA, LFT, HIV, BNP, UA, troponin	Screen for associated with: Connective tissue disease Liver disease Human immunodeficiency disease BNP: measure of RV failure and prognosis UA, troponin: prognosis
6-minute walk distance	Baseline exercise capacity, prognosis, response to treatment
Right heart catheterization	Used to confirm diagnosis Obtain baseline and ongoing hemodynamic profile Acute vasodilator response for CCB Determination of CO/Cl, PCWP, RAP
CTEPH, chronic thromboembolic pulmonary hypertension; PH, pulmonary hypertension; ANA, antinuclear antibody; BNP, B-type natriuretic peptide; CCB, calcium channel blocker; CO, cardiac output; Cl, cardiac index; LFT, liver function tests; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure; UA, uric acid.	
McLaughlin VV, et al. <i>J Am Coll Cardiol.</i> 2009 Apr 28;53(17):1573-619. McGoon MD, Kane GC. <i>Mayo Clinic Proc.</i> 2009;84(2):191-207.	
Vachery JL, et al. <i>Eur Respir Rev.</i> 2012;2(123):40-7.	

Gold Standard for Diagnosis of PAH

- Pulmonary artery pressure can be estimated on echocardiogram
- Right heart catheterization **required for confirmation**
 - mPAP >25 mm Hg
 - LVEDP/PCWP ≤15 mm Hg
 - “Acute Vasodilator Response”**
 - Fall in mPAP ≥10 mm Hg
 - + mPAP (absolute) <40 mm Hg
 - + Normal CO
- Provides data needed to classify type of PAH

McLaughlin VV, et al. *J Am Coll Cardiol.* 2009;53(17):1573-619.

PAH Determinants of Risk

LOWER RISK	DETERMINANTS OF RISK	HIGHER RISK
No	Clinical evidence of RV failure	Yes
Gradual	Progression of symptoms	Rapid
II, III	WHO class	IV
Longer (>400 m)	6MWD	Shorter (<300 m)
Peak VO ₂ >10.4 mL/kg/min	CPET	Peak VO ₂ <10.4 mL/kg/min
Minimal RV dysfunction	Echocardiography	Pericardial effusion, significant RV enlargement/dysfunction; RA enlargement
RAP <10 mm Hg; CI >2.5 L/min/m ²	Hemodynamics	RAP >20 mm Hg; CI <2.0 L/min/m ²
Minimally elevated	BNP	Significantly elevated

CPET, cardiopulmonary exercise testing; BNP, B-type natriuretic peptide
McLaughlin VV, et al. *J Am Coll Cardiol.* 2009;53:1573-619.

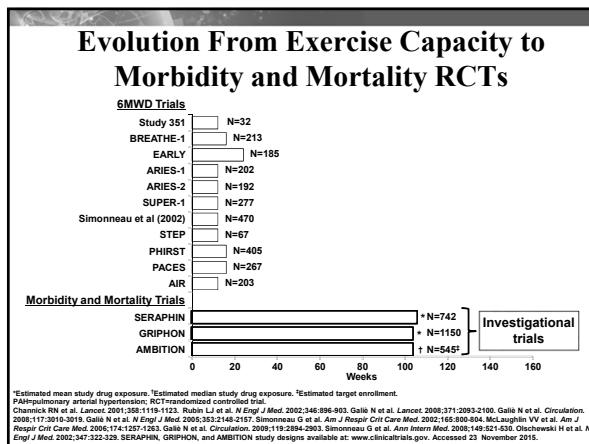
5th World Symposium on PH Goals of Therapy: Setting the Bar Higher

Functional Class	• I or II
Hemodynamics	• Normalization of RV function (RAP <8 mm Hg and CI >2.5–3.0 L/min/m ²)
Echocardiography/ MRI	• Normal/near normal RV size and function
BNP level	• ‘Normal’
6MWD	• 380–440 m, may not be aggressive enough
CPET	• Peak VO ₂ >15 mL/kg/min • VE/VCO ₂ @ AT <45

McLaughlin VV, et al. *J Am Coll Cardiol.* 2013;62:D73-81.

Initial Therapy: Making the Right Decision

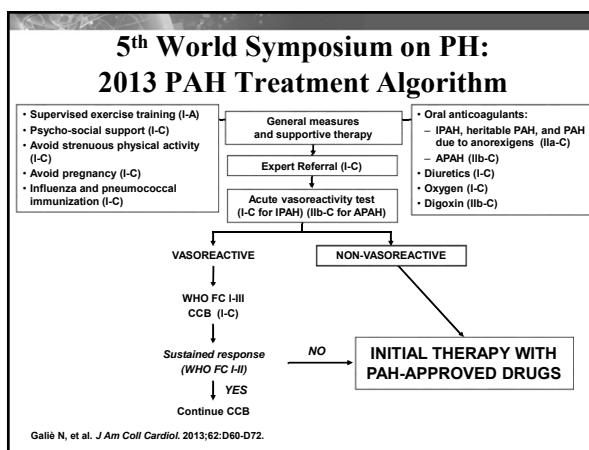
- Severity of disease
- Patient preference
- Trying to weigh the data
- When “comparing” trials, examine:
 - objective baseline characteristics of participants (age, functional class, 6MWD, hemodynamics)
 - outcome measures (6MWD, time to clinical worsening)



Time to Clinical Worsening: The Spectrum in PAH Trials

	Death	Hospital	Lung Tx	AS	Symptom	No Δ	Add therapy
BREATHE-1	X	X	X	X	X	X	X
EARLY	X	X	-	-	X	X	-
ARIES-1	X	X	X	X	X	X	X
ARIES-2	X	X	X	X	X	X	X
SERAPHIN	X	X	X	X	X	X	X
SUPER-1	X	X	X	-	-	-	X
PHIRST	X	X	X	X	X	-	X
TRIUMPH	X	X	X	-	-	-	X
PATENT-1	X	X	X	X	X	-	X
STEP	X	X	X	-	-	X	X
PACES	X	X	-	-	-	-	X
GRIPHON	X	X	X	X	X	-	X

Rubin L et al. N Engl J Med. 2002;346:200-203. Channick RN et al. Lancet. 2001;358:1119-1123. Galiè N et al. Lancet. 2008;371:2093-2100. Galiè N et al. Circulation. 2008;117:2810-2819. Rubin T et al. N Engl J Med. 2002;346:203-207. McLaughlin VV et al. Am J Respir Crit Care Med. 2006;174:1257-1263. Simonneau G et al. Ann Intern Med. 2009;149:521-530. Erratum: Ann Intern Med. 2009;150:63; 2009;151:435. McLaughlin VV et al. J Am Coll Cardiol. 2015;65(10_S): doi:10.1016/S0735-1097(15)61538-8.

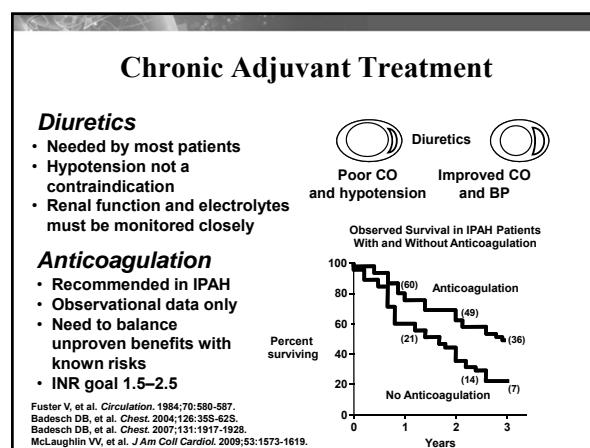
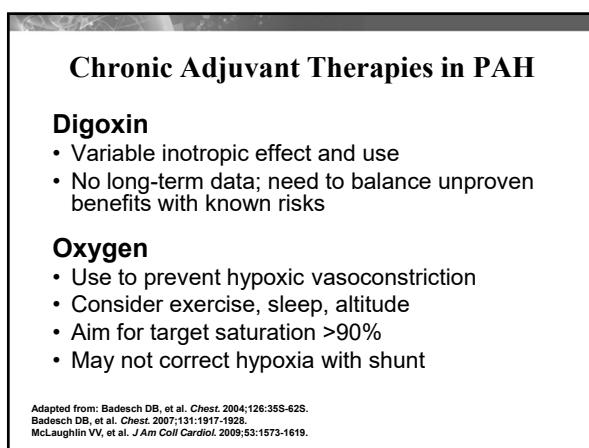


ESC/ERS 2015 Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension

Important 2015 updates:

- New parameters for definition of post-capillary PH subgroups
- Adult and pediatric common clinical classification
- Updated diagnostic algorithm and screening recommendations
- Recommendations for referral to centers of excellence
- Treatment recommendations/goals based on risk and severity**
- Combination therapy
- Additional recommendations in Groups 2–5 PH

Galiè N, et al. Eur Heart J. 2016;37:67-119.



Other Management Issues

- Encourage exercise and activity within the limits of disease and ability to maintain O₂ levels
- Consider enrollment in a pulmonary rehabilitation program
- Immunizations
- Contraception
- Psycho-social support; role of support groups

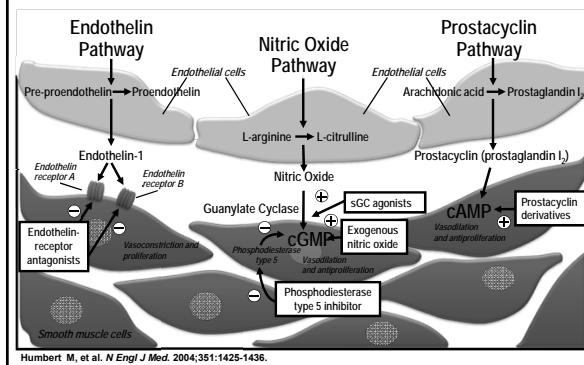
5th World Symposium on PH: 2013 PAH Treatment Algorithm

INITIAL THERAPY WITH PAH-APPROVED DRUGS				
		WHO FC II	WHO FC III	WHO FC IV
Recommendation	I A or B	<ul style="list-style-type: none"> Ambrisentan, Bosentan Macitentan Riociguat Sildenafil Tadalafil Treprostин SC, inh 	<ul style="list-style-type: none"> Ambrisentan, Bosentan, Epoprostenol IV Iloprost inh Macitentan Riociguat Sildenafil Tadalafil Treprostин SC, inh 	Epoprostenol IV
	IIa C		<ul style="list-style-type: none"> Iloprost IV*, Treprostин IV 	<ul style="list-style-type: none"> Ambrisentan, Bosentan, Iloprost inh and IV* Macitentan Riociguat Sildenafil, Tadalafil Treprostин SC, IV, Inh*
	IIb B		<ul style="list-style-type: none"> Beraprost* 	<ul style="list-style-type: none"> Initial Combination Therapy
	C		<ul style="list-style-type: none"> Initial Combination Therapy 	<ul style="list-style-type: none"> Initial Combination Therapy

Galie N, et al. *J Am Coll Cardiol.* 2013;62:D60-D72.

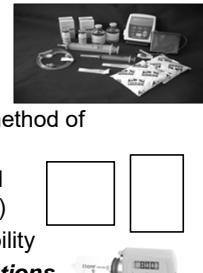
*Not approved in US.

Therapeutic Targets for PAH

Humbert M, et al. *N Engl J Med.* 2004;351:1425-1436.

Prostacyclin General Characteristics

- Often considered gold standard for advanced disease
- Unique administration devices
- Interruptions must be avoided
- Differ in stability, half-life, and method of delivery
- Available only through restricted drug distribution system (RDDS)
- Titrated to response and tolerability
- **High-risk, error-prone medications**



Prostacyclin Analogues: IV and SQ Formulations					
How Supplied	Administration	FC	Dose	Properties	Cl/P/Misc
Epoprostenol Sodium Generic, Fiofan® or Veletri® 0.5mg, 1.5mg	Continuous IV infusion via infusion pump. Requires tunneled CVC. Fiofan requires use of ice packs. Requires reconstitution.	III, IV	Initiated at 2 ng/kg/min and titrated based on response. Ongoing: 1-2 ng/kg/min q1-2 wk.	T _{1/2} <6 min. Temp and light sensitive. Reconstituted stability dependent on formulation. Rapidly hydrolyzed in the blood.	CHF due to severe LVD. Avoid abrupt withdrawals or interruption in infusion: may result in rebound PH or death.
Treprostин Sodium Remodulin® 1mg/mL, 2mg/mL, 5mg/mL, 10mg/mL in 20mL vials	Continuous IV or SubQ infusion via infusion pump. IV requires tunneled CVC.	II-IV	Initiated at 1.25 ng/kg/min and titrated based on response. Ongoing: 1.25 ng/kg/min every week or as tolerated	T _{1/2} ~4 hours. Metabolized by CYP 2C8. Diluted: 48-hour infusion duration. Undiluted: 72-hour infusion duration.	Initiated in controlled setting. Monitor for signs of BSI.

Veletri® (epoprostenol) US Prescribing Information. Actelion Pharmaceuticals US, Inc. June 2012.

Remodulin® (treprostин) US Prescribing Information. United Therapeutics Corp. December 2014.

Prostacyclin Analogues: Pivotal Trials for IV and SC Formulations

Study Name / Drug	N / Etiol / Class	Design	Positive Results
TRUST IV treprostин vs placebo	44 PAH III	Double-blind, placebo-controlled 12-week	• 6MWD • Symptoms
IV epoprostenol vs conventional Rx	81 IPAH/FPAH III,IV	Open-label 12-week	• 6MWD • Symptoms • Hemodynamics • Survival
IV epoprostenol vs conventional Rx	111 APAH SSc III,IV	Open-label 12-week	• 6MWD • Hemodynamics • Symptoms
SC treprostин vs SC placebo	470 PAH II-IV	Double-blind 12-week	• 6MWD • Symptoms • Hemodynamics

Hiremath J, et al. *J Heart Lung Transplant.* 2010;29:137-149.Barst RJ, et al. *N Engl J Med.* 1996;334:296-301.Badesch D, et al. *Ann Intern Med.* 2000;132:425-432.Simonneau G, et al. *Am J Respir Crit Care Med.* 2002;165:800-804.

Oral and Inhaled Prostacyclins					
How Supplied	Administration	FC	Dose	Properties	Cl/P/Misc
Iloprost Ventavis® 10 mcg/mL and 20 mcg/mL unit dose ampules	Intermittent inhalation via dedicated inhalation device	III, IV	2.5 mcg once, then 5 mcg per dose if tolerated for 6 to 9 x/day	T _½ ~20 to 30 min.	Caution if underlying lung disease or symptomatic hypotension. Bronchospasm Store at RT Discard unused solution One ampule used per treatment session (20 mcg/mL = 5 mcg dose only!)
Treprostинil Tyvaso® for inhalation 0.6 mg/mL in 2.9 mL ampules	Intermittent inhalation via dedicated inhalation device	III	3 breaths QID, titrated to goal 9 breaths QID	T _½ ~4 hours. Metabolized by CYP 2C8.	One inhaled ampule provides multiple doses/day Once opened: discard remaining solution after 24 hours, protect ampules from light during storage
Treprostинil Orenitram® 0.125 mg, 0.25 mg, 1 mg and 2.5 mg ER tablets	Oral extended release osmotic tablets	II, III	Initial: 0.25 mg BID or 0.125 mg TID, titrate every 3 to 4 days	T _½ ~4 hours. Metabolized by CYP 2C8. Food increases bioavailability	Abrupt discontinuation, Diverticulitis Severe hepatic impairment Avoid alcohol

Ventavis® (ilo-prost) US Prescribing Information. Actelion Pharmaceuticals US, Inc. November 2013.
Tyvaso® (treprostinil) US Prescribing Information. United Therapeutics Corp. August 2014.
Orenitram® (treprostinil) US Prescribing Information. United Therapeutics Corp. October 2014.

Prostacyclin Analogue: Pivotal Trials for Inhaled and Oral Formulations

Study Name / Drug	N / Etiol / Class	Design	Positive Results
AIR Inhaled iloprost vs placebo	203 PH III-IV	Double-blind 12-week	• Composite end point • 6MWD • Symptoms • Hemodynamics
TRIUMPH 1 Inhaled treprostинil vs placebo*	235 PAH III-IV*	Double-blind 12-week on background oral Rx	• 6MWD
FREEDOM-M Oral treprostинil vs placebo	228 PAH II-III	Double-blind, placebo-controlled 12-week	• 6MWD

*Approved for class III only. *Included background therapy with ERA or PDE-5i.

Olschewski H, et al. *J Engl J Med*. 2002;347:322-329.

McLaughlin VV, et al. *J Am Coll Cardiol*. 2012;55:1915-1922.

Hilleman J, et al. *J Heart Lung Transplant*. 2010;29:137-149.

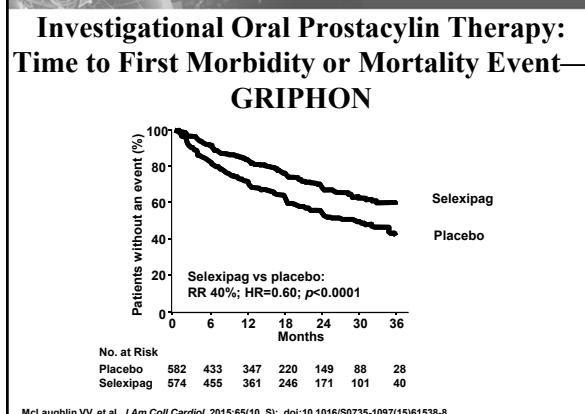
Jing Z-C, et al. *Circulation*. 2013;127:624-633.

IP Agonist

- Novel mechanism
- Oral, selective prostacyclin receptor (IP) agonist
- Structurally distinct from prostacyclin
- Studied in combination therapy
- Available only through RDDS

Selexipag			
How Supplied	REMS	Properties	Cl/P
Uptravi® 200 mcg, 400 mcg, 600mcg, 800mcg, 1000 mcg, 1200 mcg, 1400 mcg, 1600 mcg	N/A	T _½ ~6 to 13.5 hrs for active metabolite	Cl: none Caution with moderate liver disease (dose adjustment may be necessary). Avoid with severe liver disease
Administration	FC	Dose	
Oral tablets	Mostly II-III	Start at 200 mcg BID, titrate by 200 mcg BID once weekly to highest tolerated dose (max 1600 mcg BID)	Substrate of 2C8, 3A4, P-gp, BRCP, UGT1A3, UGT2B7, OATP1B1, OATP1B3

Uptravi® (selexipag) US Prescribing Information. Actelion Pharmaceuticals. January 2016.



Management of Prostacyclin-Related Effects

Adverse Effect	Management Strategy
Headache	OTC analgesics, Tramadol, opiates if severe
Diarrhea	Loperamide, Lomotil, adjust titrations
Nausea	Ondansetron or other anti-emetics, food (oral formulation)
Hypotension Dizziness	Adjust antihypertensive drugs, diuretics. Adjust titrations
Jaw Pain	Start first meal with bland food, "exercise jaw"
Leg Pain	Elevate legs, gabapentin, pregabalin, amitriptyline, other pain meds
Flushing	Adjust titrations

Management of SC Prostacyclin Effects

- Topical Agents
- Systemic Management
 - H1 and H2 blockers
 - OTC analgesics, opioids if severe
 - GABA analogs
 - Others
- Non-pharmacologic management
 - Catheter dwell times
 - Catheter type
 - Dry insertion
- Other strategies:
 - Pre-medicate
 - Rapid titration
 - Increase concentration

Bosentan			
How Supplied	REMS	Properties	Cl/P
Tracleo® 62.5 mg, 125 mg tablets	Teratogenicity, liver toxicity. Must enroll in Tracleer REMS Program	T _{1/2} ~5 hours Metabolized and strong inducer of CYP3A4 and CYP2C9, possibly CYP2C19; Caution with liver disease.	Cl: Pregnancy and use of cyclosporine or glyburide. Caution with liver disease.
Administration	FC II-IV	Dose	
Oral tablets. Can be dissolved into soln.	Initial: 62.5 mg BID x 4 weeks, then increase to 125 mg BID thereafter if tolerated and wt >40 kg.		
Amlodipine			
How Supplied	REMS	Properties	Cl/P
Letaire® 5 mg, 10 mg tablets	Teratogenicity. FRP must enroll in Letaire REMS Program	T _{1/2} up to ~15 hours Metabolized by CYP3A4 and CYP2C19, substrate of P-glyco-protein	Cl: pregnancy and IPF. Caution with anemia, fluid retention, PVOd.
Administration	FC II-III	Dose	
Oral tablets	Initial: 5 mg daily, increase to 10 mg daily if tolerated		
Macitentan			
How Supplied	REMS	Properties	Cl/P
Opsumit® 10 mg tablets	Teratogenicity. FRP must enroll in Opsumit REMS Program	T _{1/2} ~16 hrs (48 hrs for active metabolite) Metabolized by CYP3A4 and CYP2C19; active metabolite contributes ~40% of activity.	Cl: pregnancy Caution with anemia, liver disease.
Administration	Mostly II-III	Dose	
Oral tablets	10 mg po daily		

Endothelin Receptor Antagonists: Pivotal Trials

Study Name Drug	N Etiology Class	Design	Positive Results
BREATHE-1 Oral bosentan* vs placebo	213 PAH III, IV	Double-blind 16-week	• 6MWD • Delay clinical worsening • Symptoms
EARLY Oral bosentan vs placebo	185 PAH II	Double-blind 6-month	• Delay clinical worsening • Hemodynamics
ARIES-1&2 Oral ambrisentan‡ vs placebo	394 PAH II, III	Double-blind 12-week	• 6MWD • Delay clinical worsening
SERAPHIN Oral macitentan† vs placebo	742 PAH II, III	Double-blind Event-driven morbidity/mortality	• Delay disease progression • 6MWD • Symptoms

*Bosentan = Tracleo®. Approved for FC II-IV. 62.5-125 mg po bid.

†Ambrisentan = Letaire®. Approved for FC II-III. 5-10 mg po qd.

‡Macitentan = Opsumit®. Approved for FC II-III. 10 mg po qd.

Rubin L, et al. *N Engl J Med.* 2002;346:898-903. Channick RN, et al. *Lancet.* 2001;358:1119-1123. Galie N, et al. *Lancet.* 2008;371:2093-2100. Galie N, et al. *Circulation.* 2008;117:3010-3019. Pulido T, et al. *N Engl J Med.* 2013;369:809-818.

Guanylate Cyclase Stimulator

- Novel mechanism
- First non-WHO Group 1 approved indication
- Available only through RDDS
- Risk Evaluation and Mitigation Strategies (REMS) for teratogenicity
- Requires blood pressure monitoring and titration

Riociguat			
How Supplied	REMS	Properties	Cl/P
Adempas® 0.5 mg, 1 mg, 1.5 mg, 2 mg, 2.5 mg tablets	Teratogenicity. FRP must enroll in Adempas REMS Program	T _{1/2} ~12 hrs in PAH pts. Substrate of P-gp and BCRP, metabolized by CYP-1A1, 3A, 2C8, 2J2.	Cl: Pregnancy, nitrates, PDE-5i. Caution with hypotension, PVOd, bleeding, smokers.
Administration	II-III	Dose	
Oral tablets	0.5 to 1 mg TID, titrated q2weeks to max 2.5 mg TID		

Adempas® (riociguat) US Prescribing Information. Bayer Healthcare. September 2014.

sGC Stimulator Pivotal Trials

Study Name Drug	N Etiology Class	Design	Positive Results
PATENT-1 Oral riociguat* vs placebo	278 PAH I-IV	Double-blind 12-week	• 6MWD • Symptoms • Hemodynamics • Delay clinical worsening
CHEST-1 Oral riociguat vs placebo	261 CTEPH I-IV	Double-blind 16-week	• 6MWD • Symptoms • Hemodynamics

*Riociguat = Adempas®. Approved for WHO Group 1; persistent CTEPH (WHO Group 4) after surgical treatment, or inoperable CTEPH; titrated to maximum 2.5 mg po tid.

Ghofrani HA, et al. *N Engl J Med.* 2013;369:319-329.

Ghofrani HA, et al. *N Engl J Med.* 2013;369:330-340.

Sildenafil			
How Supplied	REMS	Properties	Cl/P
generic Revatio® 20 mg tablets	n/a	T _{1/2} ~4 hours Metabolized by CYP3A4 and CYP2C9 (minor)	Cl: use with organic nitrates. Increased mortality risk in ped. Caution with SCD, PVOd. Post marketing AE: NAION
Revatio® 10 mg/12.5 mL soln for injection	FC	Dose	
Powder for suspension			
Administration	Mostly II-III	Oral: 20 mg TID Inj.: 10 mg TID	
Oral tablets or suspension. Solution for injection used for NPO.			
Tadalafil			
How Supplied	REMS	Properties	Cl/P
Adcirca® 20 mg tablets	n/a	T _{1/2} ~35 hrs Metabolized by CYP3A4	Cl: use with organic nitrates Caution with SCD, PVOd.
	FC	Dose	
Administration	II-III	40mg daily	
Oral tablets			
Revatio® (sildenafil) US Prescribing Information. Pfizer Labs. January 2014.			
Adcirca® (tadalafil) US Prescribing Information. Eli Lilly and Company. April 2015.			

PDE-5 Inhibitor Pivotal Trials

Study Name Drug	N Etiology Class	Design	Positive Results
SUPER-1 Oral sildenafil* vs placebo	278 PAH I-IV	Double-blind 12-week	• 6MWD • Symptoms • Hemodynamics
PHIRST-1 Oral tadalafil§ vs placebo	405 PAH I-IV	Double-blind 16-week	• 6MWD • Delay clinical worsening • Hemodynamics • HRQoL

*Sildenafil = Revatio®. Approved for FC II-III. 20 mg po tid.

§Tadalafil = Adcirca®. Approved for FC I-IV. 40 mg po qd.

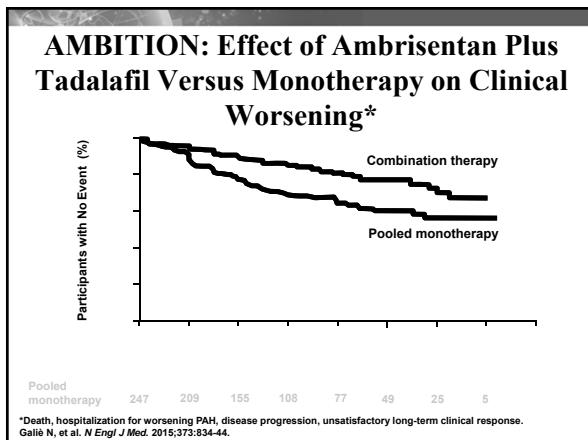
Galie N, et al. *N Engl J Med.* 2005;353:2148-2157.

Galie N, et al. *Circulation.* 2009;119:2894-2903.

Management of Oral Therapy Effects	
Adverse Effect	Management Strategy
Headache	OTC analgesics, Tramadol, opiates if severe
Peripheral Edema	Add or adjust diuretics, salt and fluid restrictions
Anemia	Periodic CBC monitoring Reduce dose or discontinue drug
Hemorrhagic events Epistaxis (sildenafil)	Caution with anticoagulants Monitor for bleeding/bruising
Nausea	Anti-emetics
Hypotension, Dizziness	Monitor BP in between dose titrations Adjust antihypertensive drugs, diuretics Reduce dose or hold titration if needed (riociguat)
Dyspepsia	PRN OTC agents if infrequent H2 blocker or PPI
Nasal congestion	Saline nasal spray
Teratogenicity	Obtain negative pregnancy test monthly for women of reproductive age Contraception mandatory
Elevated LFT's	Monitor LFT's monthly (bosentan) Reduce dose or discontinue drug

Recently Completed or Ongoing Clinical Trials of Combination Therapy					
	Current Therapy	Added Therapy	Patients (n)	Study Duration	Primary Endpoint
AMBITION	Ambrisentan/ tadalafil/ combo	Combo vs mono	500	Event-driven	Morbidity/mortality event
Pfizer	Bosentan	Sildenafil	104	12 weeks	6MWD
COMPASS-2	Sildenafil	Bosentan	250	Event-driven	Morbidity/mortality event
ATPAHSS	Ambrisentan/ tadalafil/ combo	Combo vs mono	63	36 weeks	RV mass/PVR
GRIPHON	ERA, PDE-5i, or both	Selexipag	1156	Event-driven	Morbidity/mortality event
Ikaria	≥1 current therapies	Inhaled NO	78	16 weeks	PVR
FREEDOM-EV	PDE-5i or ERA	Oral treprostinil	858	24 weeks (6MWD)/event driven	6MWD/ 1st clinical worsening event

<https://clinicaltrials.gov/>



- ### Combination Therapy Caveats
- Experience evolving
 - Most data from 'add-on' - ? De novo? Order?
 - More drugs available
 - more options
 - more ways to get it wrong
 - More questions than answers
 - Costs/expenditures; third-party hurdles
- Taichman DB. *Ann Intern Med.* 2008;149:583-585.

Transitioning Therapy

Rationale

- Recurrent bacteremia
- Clinical deterioration
- Profound improvement (benefits vs. risks)

Potential concerns

- Intermittent vs. continuous dosing of prostacyclin
- Dose limitations with inhaled therapy
- Patient compliance
- Follow-up
- Patient selection

Types

- Transitioning parenteral prostacyclins
 - Titration
 - Rapid
- Transitioning inhaled prostacyclins
- Parenteral to or from inhaled prostacyclin
- Prostacyclin to oral

Targeted Therapies: Use With Caution

Other drugs

- Multiple anti-hypertensive drugs
- Anti-platelet or anti-coagulants
- Sympathomimetic agents
- Strong inhibitors or inducers of specific CYP P450 enzymes

Co-Morbidities

- Liver or renal impairment
- Congestive heart failure
- Depression
- Cognitive impairment
- Substance abuse disorder
- Dexterity/mobility impairment
- Significant hypotension
- Immunosuppression

Transitions in Care

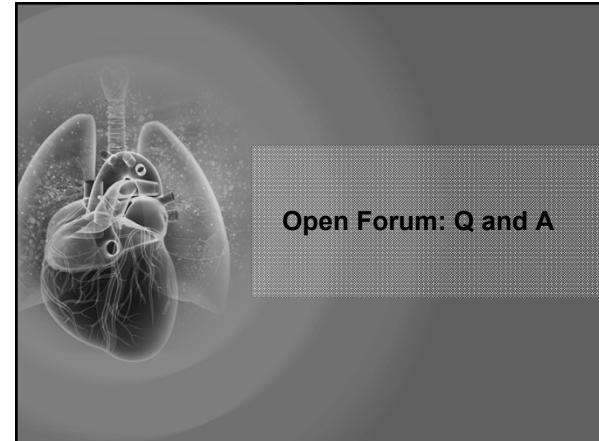
- Know your institution's policies and procedures
 - Be prepared and prioritize patient safety
 - Discharge planning
 - Contacting PAH specialists and specialty pharmacy
- Special enrollments and medication access process
 - REMS requirements
- Be familiar with significant drug interactions and AEs
- Engage the patient and caregiver, they are very well-trained and knowledgeable
 - Most patients carry backup meds/devices with them

Opportunities for Pharmacists

- Comprehensive medication reconciliation and history
- Education and training on targeted therapies and devices
- Participation in therapy selection and therapeutic alternatives
- Policies and procedure development
- Coordinate medication access
- Program enrollment for REMS or restricted distribution therapies
- Ongoing safe-use monitoring
- Dose verification, order entry and drug interactions
- Health maintenance
- Medication titration and adverse effect management
- Resource for other healthcare providers

Summary

- PAH-specific therapies promote vasodilation, leading to reduction in pulmonary vascular resistance and improved RV function
- Therapies are highly individualized and require a multi-disciplinary team of healthcare providers with specialized training
- Selection of initial therapy largely depends upon severity of disease at diagnosis
 - low-risk patients can be treated with oral agents
 - high-risk patients require parenteral prostacyclins
- Lack of improvement or worsening of parameters should trigger escalation of therapy
- There are a number of challenges associated with these complex therapies
- Pharmacists are an important part of the PAH therapy team and many opportunities are available to promote improved patient care



Venous Thromboembolism Management: Bridging the Gap Between Inpatient and Outpatient

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September 16, 2016

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Disclosure

- Both presenters have nothing to disclose

Pharmacist Objectives

- Compare and contrast the updated CHEST Guideline and Expert Panel Report for prevention and treatment of venous thromboembolism to previous CHEST guidelines
- Discuss the recently published Anticoagulation Forum guidance document on VTE and its impact on clinical practice
- Design optimal inpatient to outpatient transitions of care for patients with venous thromboembolism

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Technician Objectives

- List recommendations in the updated CHEST Guideline and Expert Panel Report for prevention and treatment of venous thromboembolism
- Discuss the recently published Anticoagulation Forum guidance document on VTE and its impact on clinical practice
- Define optimal inpatient to outpatient transitions of care for patients with venous thromboembolism

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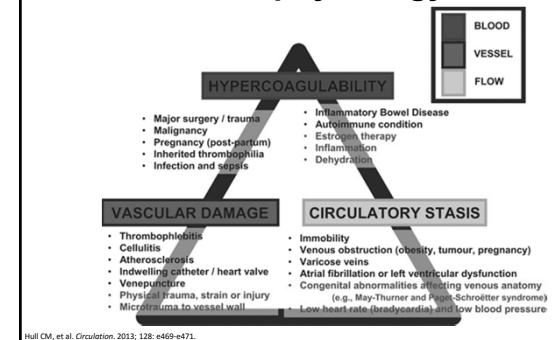
Epidemiology

- 300,000-600,000 new cases of VTE annually
- 60,000-100,000 deaths annually
 - 10 to 30% of people will die within one month of diagnosis
 - Sudden death occurs in 25% of PE
- 50% will have long-term complications after DVT
- 1/3 will have VTE recurrence within 10 years

Beckman MG, et al. Am J Prev Med. 2010;38(4S):S495-S501.

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Pathophysiology



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Pathophysiology

The diagram shows two main sections. On the left, under 'Deep Vein Thrombosis (DVT)', there are three vertical illustrations of a leg's deep veins: 'Normal' showing normal blood flow; 'DVT' showing a 'Detached blood clot' blocking the lumen; and another 'DVT' showing 'Blood clots' within the lumen. On the right, under 'Pulmonary Embolism (PE)', there is a diagram of lungs showing an 'Infarction' (area of tissue death) and an 'Embolus in lungs'. Below these is a grayscale axial CT scan of a human torso with a white arrow pointing to an embolus in the pulmonary artery.

<http://cardiosimo.wordpress.com/pulmonary-embolism/>
<http://kierdesthi.blogspot.com/2011/03/how-does-professional-athlete-get.html>
www.besttreatment.com/blog/right-the-silent-killer-with-vvc-during-dvt-awareness-month/

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VTE Prophylaxis Importance

- The Agency for Healthcare Research and Quality calls thromboprophylaxis against VTE the most important patient safety practice
- PE is the number one preventable cause of death in the hospital
- Almost 2/3 of all VTE episodes result from hospitalizations with a resultant
- CMS paying less for hospital-acquired VTE

Hicks LA, et al. *Arch Intern Med.* 2003;162(11):1245-1248.
 Sander DA, et al. *J R Soc Med.* 1989;82(4):203-205.
 Shojania KG, et al. *Evid Rep Technol Assess (Summ).* 2001;4(3):i-x, 1-668.

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Treatment of VTE

- Anticoagulation
 - Parenteral
 - UFH
 - LMWH
 - Fondaparinux
 - Direct Thrombin Inhibitors
 - Enteral
 - Warfarin
 - Dabigatran
 - Rivaroxaban
 - Apixaban
 - Edoxaban
- Thrombolysis
 - Systemic
 - Catheter-directed
 - Other
 - IVC Filters
 - Compression Stockings

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CHEST Guidelines Background

- Series of guidelines on VTE
 - Prevention
 - Medical
 - Surgery
 - Orthopedic Surgery
 - Diagnosis
 - Treatment →
 - Anticoagulants

15 updates/new additions to 10th Edition:

- Choice of anticoagulant
- Aspirin for extended prophylaxis
- Anticoagulation of subsegmental PE
- Treatment of acute PE out of the hospital
- Compression stockings to prevent PTS
- Systemic thrombolytic therapy for PE

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Recommendation Quality

- Strength
 - Grade 1: Strong
 - Grade 2: Weak
- Quality of Evidence
 - Grade A: High
 - Grade B: Moderate
 - Grade C: Low (or Very low)

Kearon C, et al. *CHEST.* 2016;149(2):315-52.

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CHEST Guidelines Changes

<p>9th Edition</p> <ul style="list-style-type: none"> For patients with DVT and no cancer who are not treated with VKA therapy, we suggest LMWH over dabigatran or rivaroxaban for long-term therapy (Grade 2C) 	<p>10th Edition</p> <ul style="list-style-type: none"> In patients with DVT of the leg or PE and no cancer, as long-term (first 3 months) anticoagulant therapy, we suggest dabigatran, rivaroxaban, apixaban, or edoxaban over vitamin K antagonist (VKA) therapy (all Grade 2B)
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Kearon C, et al. *CHEST.* 2012; 141(2)(Suppl):e195-e494S.
 Kearon C, et al. *CHEST.* 2016;149(2):315-52.

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History of Anticoagulation

Timeline of Anticoagulants:

- 1909: Hirudin Used for Anticoagulation
- 1937: Purified Heparin First Used in Humans
- 1939: Vitamin K Antagonists Discovered
- 1954: Warfarin
- 1980: LMWHs
- 1990: IV Direct Thrombin Inhibitors
- 2001: Fondaparinux
- 2010: Dabigatran
- 2011: Rivaroxaban
- 2012: Apixaban
- 2014: Edoxaban

Mardrop D, et al. Br J Haematol. 2008;141(6):757-62.
Gomez-Qutes A, et al. Curr Drug Discov Technol. 2012;9(2):83-104.

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DOAC VTE Trials

	RECOVER 1 & 2 Pooled Analysis (n=5107)	EINSTEIN Pooled Analysis (n=8282)	AMPLIFY (n=5395)	HOKUSAI-VTE (n=8240)
Agent	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Primary Outcome*	1.09 (0.76-1.57)	0.89 (0.66-1.19)	0.84 (0.60-1.18)	0.89 (0.70-1.13)
Major Bleeding	0.73 (0.48-1.11)	0.54 (0.37-0.79)	0.31 (0.17-0.55)	0.84 (0.59-1.21)
Intracranial Hemorrhage	2 dabigatran vs. 9 VKA	5 rivaroxaban vs. 13 VKA	3 apixaban vs. 6 VKA	5 edoxaban vs. 18 VKA
GI Bleed	10 dabigatran vs. 68 VKA	1 rivaroxaban vs. 3 VKA [†]	7 apixaban vs. 18 VKA	1 edoxaban vs. 2 VKA [†]

*Dabigatran, apixaban and edoxaban data represents rate of recurrent VTE or VTE-related death; rivaroxaban data represents recurrent VTE Only fatal events reported

Schulman S, et al. Circulation. 2014;129(7):764-72.
Prins MH, et al. Thromb J. 2013;11(1):21.
Agnelli G, et al. N Engl J Med. 2013;369(9):799-808.
The Hokkaido-VTE Investigators. N Engl J Med. 2013;369(15):1406-15.

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CHEST Guidelines Changes

9th Edition

- In patients with DVT of the leg and cancer, we suggest LMWH over VKA therapy (Grade 2B)
- In patients with DVT and cancer who are not treated with LMWH, we suggest VKA over dabigatran or rivaroxaban for long-term therapy (Grade 2B)

10th Edition

- In patients with DVT of the leg or PE and cancer, as long-term (first 3 months) anticoagulant therapy, we suggest LMWH over VKA therapy (Grade 2C), dabigatran (Grade 2C), rivaroxaban (Grade 2C), apixaban (Grade 2C), or edoxaban (Grade 2C)

Kearon C, et al. CHEST. 2012; 141(2)(Suppl):e495-e494S.
Kearon C, et al. CHEST. 2016;149(2):315-52.

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Anticoagulant Therapy In Cancer

- Recurrent VTE risk reduction with DOACs appears to be similar to warfarin in all patients
- In cancer patients, risk reduction for recurrent VTE is greater with LMWH than with warfarin – CLOT trial (HR, 0.48; P=0.002)
- No direct comparison with DOACs and LMWH – Indirect comparisons: LMWH likely more effective

Kearon C, et al. CHEST. 2016;149(2):315-52.
Lee YY, et al. N Engl J Med. 2003; 349:146-53.

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Anticoagulant Comparison

Factor	Preferred Anticoagulant
Cancer	LMWH
Avoiding Parenteral Therapy	Rivaroxaban; Edoxaban
Once Daily Dosing	Rivaroxaban; Edoxaban; VKA
Liver Disease/Coagulopathy	LMWH
Severe Renal Impairment	VKA
Coronary Artery Disease	VKA; Rivaroxaban; Apixaban; Edoxaban
Dyspepsia or GI Bleed History	VKA; Apixaban
Poor Compliance	VKA
Thrombolytic Therapy Use	UFH infusion
Reversal Agent Needed	VKA; UFH; Dabigatran
Pregnancy or Pregnancy Risk	LMWH

Adapted from Kearon C, et al. CHEST. 2016;149(2):315-52.

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CHEST Guidelines Changes

9th Edition

- Not Addressed

10th Edition

- In patients with an unprovoked proximal DVT or PE who are stopping anticoagulant therapy and do not have a contraindication to aspirin, we suggest aspirin over no aspirin to prevent recurrent VTE (Grade 2B)

Kearon C, et al. CHEST. 2012; 141(2)(Suppl):e495-e494S.
Kearon C, et al. CHEST. 2016;149(2):315-52.

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Aspirin Prophylaxis in VTE

	ASPIRE (n = 822)	WARFASA (n = 402)	Aggregate (n = 1,224)	
Study Design	DB, PC, RCT	DB, PC, RCT	N/A	
Intervention	ASA 100 mg vs Placebo	ASA 100 mg vs Placebo		
Median Follow-up Period	37.2 Months	24 Months		
Quality of Evidence	Low			
All Cause Mortality	Moderate			
Recurrent VTE	Moderate			
Major Bleeding	Moderate			
All Cause Mortality	3.9% vs 4.4 %	1.04 (0.32–3.42)	HR 0.82 (0.45–1.52)	
Recurrent VTE	0.74 (0.52–1.05)	0.58 (0.36–0.93)	HR 0.65 (0.49–0.86)	
Bleeding	1.73 (0.72–4.11)	0.98 (0.24–3.96)	HR 1.31 (0.48–3.53)	
Major vascular event, major bleeding, or death from any cause	0.67 (0.49–0.91)	N/A	N/A	

Becattini C, et al. *J Am Coll Cardiol*. 2012; 56(16):1569–67.
Binghton TA, et al. *N Engl J Med*. 2012;367(15):1579–87.
Kearon C, et al. *CHEST*. 2016;149(2):315–52.

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CHEST Guidelines Changes

9th Edition

- In patients with acute symptomatic DVT of the leg, we suggest the use of compression stockings (Grade 2B)
 - 2 years

10th Edition

- In patients with acute DVT of the leg, we suggest not using compression stockings routinely to prevent post thrombotic syndrome (PTS) (Grade 2B)

Kearon C, et al. *CHEST*. 2012; 141(2)(Suppl):e419s–e494s.
Kearon C, et al. *CHEST*. 2016;149(2):315–52.

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Post-Thrombotic Syndrome

- 40% of patients after DVT develop PTS
- Most symptoms occur within 6 months
- Symptoms include
 - Edema
 - Pain/aching
 - Discomfort
 - Venous stasis ulcers
 - Cellulitis
- Costs ~75% of DVT itself
- Compression stockings

Bergqvist D, et al. *Ann Intern Med*. 1997;126(6):454–7.

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Compression Stocking to Prevent PTS

	SOX Trial
Study Design	Multicenter, randomized, placebo-controlled
Intervention	30–40 mm Hg graduated ECS or placebo stockings with less than 5 mm Hg compression at the ankle
Follow-up Period	2 Years
Primary Endpoint	Incidence of PTS 6–24 months after index event
Secondary Endpoints	PTS severity, leg ulcers, recurrent VTE, death, QOL
Statistics	800 patients for 80% power, mITT, Cox regression
Baseline Characteristics	Well matched between cohorts

Khan SR, et al. *Lancet*. 2014;383(9920):880–8.

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SOX Trial

Outcome	Active Stockings (n = 409)	Placebo Stockings (n = 394)	Hazard Ratio (95% CI)
PTS (Ginsberg criteria)	14.2%	12.7%	1.13 (0.73–1.76)
PTS (Villalta criteria)	52.6%	52.3%	1.00 (0.81–1.24)
Villalta Severity			
None	51.3%	51.4%	
Mild	33.0%	32.1%	
Moderate	8.3%	10.7%	
Severe	7.5%	5.8%	
Ipsilateral Leg Ulcer	4.2%	4.1%	N/A
Recurrent VTE	8.1%	9.6%	N/A
Recurrent Ipsilateral VTE	3.9%	4.3%	N/A
Death	8.8%	9.1%	N/A

Khan SR, et al. *Lancet*. 2014;383(9920):880–8.

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CHEST Guidelines Changes

9th Edition

- Not Addressed

10th Edition

- In patients with subsegmental PE and no proximal DVT in the legs who have:
 - (i) low risk for recurrent VTE, we suggest clinical surveillance over anticoagulation (Grade 2C)
 - (ii) high risk for recurrent VTE, we suggest anticoagulation over clinical surveillance (Grade 2C)

Kearon C, et al. *CHEST*. 2012; 141(2)(Suppl):e419s–e494s.
Kearon C, et al. *CHEST*. 2016;149(2):315–52.

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Recurrent VTE Risk Factors

Patient Related

- Active malignancy
- Hereditary or Acquired Thrombophilia
- Male gender
- Age
- Antiphospholipid syndrome
- Pregnancy and puerperium
- Hormonal therapies
- Obesity
- Presence of IVC filter
- Polycythemia vera and essential thrombocythemia (JAK2 V617F)

Thrombosis Related

- Unprovoked event
- Non-surgical transient versus surgical risk factor associated with the first event
- Proximal (especially if iliofemoral) versus distal DVT
- Pulmonary embolism
- Persistence of residual vein thrombosis

Palareti G. *Scientifica* (Cairo). 2012;2012:391734.

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CHEST Guidelines Changes

9th Edition

- In patients with low-risk PE and whose home circumstances are adequate, we suggest early discharge over standard discharge (eg, after first 5 days of treatment) (Grade 2B)

10th Edition

- In patients with low-risk PE and whose home circumstances are adequate, we suggest treatment at home or early discharge over standard discharge (eg, after the first 5 days of treatment) (Grade 2B)

Kearon C, et al. *CHEST*. 2012; 141(2)(Suppl):e419S-e494S.

Kearon C, et al. *CHEST*. 2016;149(2):315-52.

At Home PE Treatment

Potential Candidates

- Clinically stable with good cardiopulmonary reserve
- No contraindications such as recent bleeding, severe renal or liver disease, or severe thrombocytopenia (ie, <70,000/mm³)
- Expected to be compliant with treatment
- Patient feels well enough to be treated at home
- **Pulmonary Embolism Severity Index (PESI)**
 - Original form score <85 or simplified form score of 0
- Rivaroxaban or apixaban

Kearon C, et al. *CHEST*. 2016;149(2):315-52.

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CHEST Guidelines Changes

9th Edition

- In most patients with acute PE not associated with hypotension, we recommend against systemically administered thrombolytic therapy (Grade 1C)

10th Edition

- In most patients with acute PE not associated with hypotension, we recommend against systemically administered thrombolytic therapy (Grade 1B)

Kearon C, et al. *CHEST*. 2012; 141(2)(Suppl):e419S-e494S.

Kearon C, et al. *CHEST*. 2016;149(2):315-52.

CHEST Guidelines Changes

9th Edition

- In selected patients with acute PE not associated with hypotension and with a low risk of bleeding whose initial clinical presentation or clinical course after starting anticoagulant therapy suggests a high risk of developing hypotension, we suggest administration of thrombolytic therapy (Grade 2C)

10th Edition

- In selected patients with acute PE who deteriorate after starting anticoagulant therapy but have yet to develop hypotension and who have a low bleeding risk, we suggest systemically administered thrombolytic therapy over no such therapy (Grade 2C)

Kearon C, et al. *CHEST*. 2012; 141(2)(Suppl):e419S-e494S.

Kearon C, et al. *CHEST*. 2016;149(2):315-52.

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Bleeding Risk

Anticoagulant Therapy

- Age >65 y
- Previous bleeding
- Cancer
- Metastatic cancer
- Renal failure
- Liver failure
- Thrombocytopenia
- Previous stroke
- Diabetes
- Anemia
- Antiplatelet therapy
- Poor anticoagulant control
- Comorbidity and reduced functional capacity
- Recent surgery
- Frequent falls
- Alcohol abuse
- NSAID Use

Thrombolytic Therapy

- Major Contraindications
 - Structural intracranial disease
 - Previous intracranial hemorrhage
 - Ischemic stroke within 3 mo
 - Active bleeding
 - Recent brain or spinal surgery
 - Recent head trauma with fracture or brain injury
 - Bleeding diathesis
- Relative contraindications
 - Systolic BP >180
 - Diastolic BP >110
 - Recent bleeding (nonintracranial)
 - Recent surgery
 - Recent dental procedure
 - Ischemic stroke more than 3 mo previously
 - Anticoagulated (eg, VKA therapy)
 - Traumatic cardiopulmonary resuscitation
 - Pericarditis or pericardial fluid
 - Diabetic retinopathy
 - Pregnancy
 - Age >75 y
 - Low body weight (eg, <60 kg)
 - Female
 - Black race

Kearon C, et al. *CHEST*. 2012; 141(2)(Suppl):e419S-e494S.

Kearon C, et al. *CHEST*. 2016;149(2):315-52.

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CHEST Guidelines Changes

9th Edition

- Not Addressed

10th Edition

- In patients who have recurrent VTE on VKA therapy (in the therapeutic range) or on dabigatran, rivaroxaban, apixaban, or edoxaban (and are believed to be compliant), we suggest switching to treatment with LMWH at least temporarily (Grade 2C)

Kearon C, et al. *CHEST*. 2012; 141(2)(Suppl):e419s-e494s.
Kearon C, et al. *CHEST*. 2016;149(2):315-52.

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CHEST Guidelines Changes

9th Edition

- Not Addressed

10th Edition

- In patients who have recurrent VTE on longterm LMWH (and are believed to be compliant), we suggest increasing the dose of LMWH by about one-quarter to one-third (Grade 2C)

Kearon C, et al. *CHEST*. 2012; 141(2)(Suppl):e419s-e494s.
Kearon C, et al. *CHEST*. 2016;149(2):315-52.

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Questions to Ponder: VTE & Anticoagulation

- Was LMWH being used?
 - Daily vs BID dosing
- Had anticoagulant dose been reduced?
- Was the patient adherent?
- Was VKA subtherapeutic?
- Was anticoagulant therapy prescribed correctly?
- Was the patient taking an DOAC and a drug that reduced anticoagulant effect?

Kearon C, et al. *CHEST*. 2016;149(2):315-52.

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Summary of Chest Guideline Updates

- Substantial landmark literature published since 9th edition released in 2012
- Practice has changed dramatically
- New guidelines support practice changes
 - Utilization of DOACs in non-cancer patients
 - Reduction in use of compression stockings
 - Subsegmental PE treatment recommendations

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Anticoagulation Forum

- Non-profit organization dedicated to educating healthcare professionals
- A group of 58 experts assembled to form detailed clinical guidance on VTE

Journal of Thrombosis and Thrombolysis
All Volumes & Issues

Volume 41, Issue 1, January 2016

Special Issue: Management of Venous Thromboembolism: Clinical Guidance from the Anticoagulation Forum

Issue Editors: Jack E. Ansell
ISSN: 0929-5305 (Print) 1573-742X (Online)



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Anticoagulation Forum- Background

- Incorporates evidence-based data and **consensus opinion** to provide practical guidance on real world clinical situations
 - Goal:
 - To be more user friendly and timely vs. CHEST guidelines
 - Includes the following topics:
- | | |
|----------------------------------|---|
| ✓ Epidemiology of VTE | ✓ VTE in unusual sites |
| ✓ Pharmacology of anticoagulants | ✓ Post-thrombotic syndrome |
| ✓ Treatment of VTE | ✓ Hereditary and acquired thrombophilia |
| ✓ Thrombolytic therapy | ✓ Heparin anticoagulant use in VTE |
| ✓ Cancer-associated VTE | ✓ Warfarin therapy in VTE |
| ✓ Obstetric-associated VTE | ✓ DOAC use in VTE |

Ansell J, et al. *J Thromb Thrombolysis*. 2016; 41:1-232.

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Snapshot: Guidance Questions

- When to use DOACs for VTE?
- Hospitalization vs. outpatient treatment for VTE?
- How to initiate DOACs for VTE treatment?
- How to interrupt anticoagulant therapy?
- Appropriate care transitions and follow-up strategy?
- How to enhance safety and efficacy of DOAC therapy?

Ansell J, et al. *J Thromb Thrombolysis*. 2016; 41:1-232.

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DOACs for VTE

- Generally preferred over warfarin
- Contraindications
 - Pregnancy/breastfeeding
 - Mechanical heart valves
- Recommended to avoid in:
 - Antiphospholipid syndrome
 - Extremes in weight: <50kg or >120kg
 - CrCl <30mL/min
 - Moderate-severe hepatic impairment
 - Cancer
- Need to have:
 - Good adherence
 - Ability to obtain DOAC long-term

Burnett A, et al. *J Thromb Thrombolysis*. 2016; 41:206-232.

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Dosing of DOACs for VTE

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Acute VTE	150mg BID after >5 days parenteral anticoagulation	15mg BID with food x 3 weeks, then 20mg daily with food	10mg BID x 7 days, then 5mg BID	60mg daily after >5 days of parenteral anticoagulation
Prevention of Recurrent VTE	No dose adjustment	No dose adjustment	Decrease to 2.5mg BID after >6 months	Not studied

Burnett A, et al. *J Thromb Thrombolysis*. 2016; 41:206-232. Adapted from Table 6.

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Considerations Prior to DOAC Administration

DOAC	Parenteral Lead-In	Single-Drug Approach	Switch or Dose De-escalation	Dosing Frequency	Renal Elimination
Dabigatran	x		x	BID	++++
Rivaroxaban		x	x	BID x 21 days, then daily	++
Apixaban		x	x	BID	+
Edoxaban	x		x	Daily	++

Burnett A, et al. *J Thromb Thrombolysis*. 2016; 41:206-232. Adapted from Table 5.

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Inpatient Vs. Outpatient

- Outpatient
 - Most patients with DVTs and many patients with PEs
- Determine low risk PE patients
 - PESI score, HESTIA criteria
- Check for contraindications to outpatient management

Streiff M, et al. *J Thromb Thrombolysis*. 2016; 41:32-67.

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Contraindications to Outpatient Management of VTE

Contraindications to Outpatient Management of VTE
• Active or high risk of bleeding
• Recent surgery (within 7 days)
• Cardiopulmonary instability
• Severe symptomatic venous obstruction
• High risk pulmonary embolism
• Thrombocytopenia (platelets<50,000/microliters)
• Other medical or surgical condition requiring inpatient management
• Medical non-compliance
• Poor hepatic function (INR>1.5)
• Unstable renal function
• Poor home health care support environment

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Streiff M, et al. *J Thromb Thrombolysis*. 2016; 41:32-67.

Patient Case #1 (KT)

KT is a 54yoF presents to her PCP with right lower extremity pain and erythema. Workup reveals a proximal DVT.

- PMH: Allergic rhinitis, HTN
- SH: (+) smoker, rare alcohol, good adherence, lives with husband of 10 years and 1 son
- Med: Loratadine 10mg daily, amlodipine 10mg daily
- PE: Height: 5'6", Weight: 180lbs, BP: 136/88 mmHg
- Labs: Chem 7 and CBC WNL; D-dimer ↑

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Where should KT initially be treated?

- A. Inpatient
- B. Outpatient
- C. Unable to determine

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Which of the following DOACs could be initiated without bridging with another anticoagulant?

- A. Dabigatran
- B. Rivaroxaban
- C. Edoxaban
- D. Enoxaparin

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What Type of Anticoagulation is BEST to Initiate for KT?

- A. Vitamin K antagonist (VKA)
- B. Low molecular weight heparin (LMWH)
- C. Direct oral anticoagulant (DOAC)

What drug/dose would you initiate? Why?

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Interrupting DOAC Therapy

- ~10% of VTE patients/year require temporary interruption of anticoagulant for a procedure
- In general, it's preferred to avoid **bridging** therapy
- Determine bleeding risk of procedure
 - Minimal bleeding risk: dental extraction of 1-2 teeth, cataract/glaucoma intervention
 - Low risk: dental extraction 3+ teeth, endoscopy with biopsy, cholecystectomy
 - High risk: Major surgery (>45min), coronary artery bypass, bowel resection

Burnett A, et al. J Thromb Thrombolysis. 2016;41:206-232

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Interrupting DOAC Therapy Cont.

- Determine patient specific risk factors for bleeding (ex. anemia, age>65, diabetes, hepatic/renal dysfunction)
- For minimal risk procedures, do not interrupt therapy
- For low bleeding risk procedures, stop DOAC before procedure (5 half-lives) and resume 24 hours after
 - 48-72 hours for high bleeding risk procedures
- Prophylactic UFH, LMWH, DOAC or mechanical VTE measures may be used until therapeutic doses of DOAC are resumed

Witt D, et al. J Thromb Thrombolysis. 2016;41:187-205

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Care Transitions and Follow-Up

- Each DOAC requires a dose de-escalation or switch from parenteral therapy
- Inadequate care transitions cost health-care systems \$25-\$45 billion annually
- Pharmacy-directed anticoagulation services have been shown to improve adherence, patient satisfaction, and clinical outcomes

Burnett A, et al. J Thromb Thrombolysis. 2016;41:206-232.

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DOAC Discharge Checklist

- Patient is an appropriate DOAC candidate and eligible for outpatient treatment
- Consistent access to DOAC (ex. Affordability, on formulary)
- Thorough education provided to patient and/or caregiver including safety net phone number
- Referral or handoff to appropriate provider (ex. anticoagulation clinic, PCP)
- Time of last drug administration and next scheduled dose
- Documentation and communication to next care setting (indication, intended duration, dose/time of admin)
- Follow-up arranged for periodic assessment (3-12 months)
 - Renal function, liver function, upcoming invasive procedures, new drug interactions

Burnett A, et al. J Thromb Thrombolysis. 2016;41:206-232. Adapted from Table 18.

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Enhancing Safety/Efficacy of DOAC therapy

- Use a comprehensive, multi-media educational approach
- Actively engage the patient
- Increase health literacy via education
- Provide drug-specific educational points
 - Dabigatran: store in original container
 - Dabigatran/edoxaban: do not crush
 - Rivaroxaban: take w/ food

Burnett A, et al. J Thromb Thrombolysis. 2016;41:206-232.

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Comparison to CHEST 10th Edition

CHEST	Anticoagulation Forum
DOAC preferred over warfarin in VTE and no cancer as long-term anticoagulant	Same
LMWH preferred over DOAC or warfarin in VTE patients with cancer	Same
Use aspirin in patients with unprovoked VTE stopping anticoagulant therapy	Same
Do not routinely use compression stockings to prevent PTS	Same
Subsegmental PE and no proximal DVT Low risk: clinical surveillance High risk: anticoagulation	Individualize therapy
Low-risk PE, treat at home or early discharge	Same

Ansell J, et al. J Thromb Thrombolysis. 2016; 41:1-232.

Kearon C, et al. CHEST. 2016;149(2):315-52.

Comparison to CHEST 10th Edition

CHEST	Anticoagulation Forum
Use of thrombolytic therapy in PE -Specific recommendations for higher risk vs. lower risk patients	Individualize therapy based on clinical presentation with cardiac biomarkers, chest CT and echocardiography
Switch to LMWH when DOAC or warfarin is ineffective at therapeutic dose	Warfarin: Increase the target INR range or switch to an alternative anticoagulant DOACs: not addressed
Increase LMWH by 1/2 to 1/3 if recurrent VTE on long-term treatment	Not addressed

Ansell J, et al. J Thromb Thrombolysis. 2016; 41:1-232.
Kearon C, et al. CHEST. 2016;149(2):315-52.

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Anticoagulation Forum VTE Summary

- Summarizes the literature to come up with recommendations
- Provides “guidance” vs. “guidelines”
- Stresses individualized treatment
- Contains useful clinical tools and covers a wide area of clinical topic related to VTE
- Place in clinical practice
 - A nice supplement to the gold standard CHEST guidelines
 - How often will it be updated??

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CASE DISCUSSION

Designing Optimal Transitions of Care

<https://connect.curaspan.com/>

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KT is switched to dabigatran. One month later, she needs surgery for her wrist. What is the best way to manage her anticoagulation?

- A. Continue dabigatran without regard to surgery
- B. Hold dabigatran (4 doses) prior to surgery
- C. Hold dabigatran (6 doses) prior to surgery
- D. Hold dabigatran (6 doses) prior to surgery and switch to IV heparin until the procedure

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Case #2 (GE)

- CC: I can't breathe
- HPI: GE is a 38 year old female with PMH of GERD and B12 deficiency who presents with SOB and substernal chest pain. She says it is not like her previous GERD symptoms and it's getting harder for her to breathe.
- SH: (-) smoker, good adherence; does not like injections
- Med: Vit B₁₂ 1 mg daily, Pantoprazole 40mg daily, Yasmin daily
- PE: Height: 5'7", Weight: 80kg, BP: 116/74 mmHg, O₂ sat: 94%
- Labs: Chem7 WNL, WBC: 12; Troponin: 0.27
- Imaging:
 - CT-PE: Filling defect in the right main stem bronchus suggestive of PE
 - Duplex Ultrasound: No deep venous thrombosis noted
 - TTE: EF 55-60%, no valvular abnormalities, RVSP 45 mmHg

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Patient Case #1 (KT) Continued

KT is a 54yoF presents to her PCP with right lower extremity pain and erythema. Workup reveals a proximal DVT.

- PMH: Allergic rhinitis, HTN
- SH: (+) smoker, rare alcohol, good adherence, lives with husband of 10 years and 1 son
- Med: Loratadine 10mg daily, amlodipine 10mg daily
- PE: Height: 5'6", Weight: 180lbs, BP: 136/88 mmHg
- Labs: Chem 7 and CBC WNL; D-dimer ↑

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If KT weighed 120 lbs and not 180 lbs and wanted a once daily VTE treatment option which would be the BEST recommendation?

- A. Rivaroxaban 15 mg daily
- B. Edoxaban 30 mg daily
- C. Edoxaban 60 mg daily
- D. Apixaban 10 mg daily
- E. Dabigatran 150 mg daily

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What is the Best Initial Treatment Option?

- A. Initiate dabigatran 150mg BID
- B. Initiate enoxaparin 80mg BID and bridge to warfarin 5mg
- C. Initiate apixaban 10mg BID
- D. Initiate edoxaban 60mg daily

Should GE be treated as an inpatient or outpatient?

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GE is Discharged after 2 days. What are Treatment Instructions?

- A. Continue this regimen at home
- B. After 5 days, decrease dose
- C. After 5 days, increase dose
- D. After 5 days, change to once daily

What are Important Counseling Points Prior to Discharge?

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Conclusion

- The initial treatment of VTE has begun to move from the inpatient to outpatient arena
- DOAC use is increasing and pharmacists need to be familiar with aspects of utilization
- Guidelines and guidance documents exist, but should not supersede clinical judgment
- Anticoagulation clinics likely to begin seeing more DOAC patients creating more transitions of care opportunities

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Questions?

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Original illustration by David Wink

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Venous Thromboembolism Management: Bridging the Gap Between Inpatient and Outpatient

Diana Isaacs, PharmD, BCPS, BC-ADM, CDE & Alex Kantorovich, PharmD, BCPS

Learning Objectives:

1. List recommendations in the updated CHEST Guidelines and Expert Panel Report for prevention and treatment of venous thromboembolism.
2. Discuss the recently published Anticoagulation Forum guidance document on venous thromboembolism and its impact on clinical practice.
3. Define optimal inpatient to outpatient transitions of care for patients with venous thromboembolism.

Technician Self-Assessment Questions

1. Which of the following is a recommendation in the CHEST 10th edition regarding venous thromboembolism (VTE) treatment that was not in the previous version? (Objective 1)
 - A. Dabigatran is preferred over other direct oral anticoagulants (DOAC's) for VTE since it is the oldest and most studied.
 - B. DOAC's are preferred over warfarin for VTE in patients without cancer.
 - C. Warfarin is preferred over low molecular weight heparin (LMWH) for VTE in patients with cancer.
 - D. Patients with low risk PE should be treated inpatient for 5 days.
2. Which of the following is a listed contraindication to outpatient management of VTE listed in the Expert Panel Report? (Objective 1)
 - A. Poor hepatic function
 - B. Chronic kidney disease
 - C. Cancer
 - D. Diabetes
3. All of the following are ways that the recently published Anticoagulation Forum guidance document on VTE may impact clinical practice EXCEPT: (objective 2)
 - A. Provides a checklist for patients being discharged on DOACs
 - B. Offers guidance on which patients should be treated inpatient vs. outpatient
 - C. Offers guidance on interrupting DOAC therapy for procedures
 - D. Replaces the CHEST guidelines, since it is the most up-to-date resource
4. Which of the following DOACs could be initiated within the inpatient setting for an acute VTE and be continued in the outpatient setting? (objective 3)
 - A. Dabigatran
 - B. Rivaroxaban
 - C. Edoxaban
 - D. Enoxaparin

New Antibiotics for the Post-Antibiotic Era

Eric Wenzler, PharmD, BCPS
Infectious Diseases Pharmacotherapy Fellow
University of Illinois at Chicago
September 16, 2016

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Disclosures

- I have no conflicts of interest relative to the content of this presentation

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Objectives for Pharmacists

- Review recently approved antimicrobials including their spectrum of activity and potential place in therapy
- Discuss the pertinent antimicrobial stewardship implications of newly approved agents
- Identify antimicrobial agents in the advanced stages of the drug development pipeline and assess their potential implications for infectious diseases pharmacotherapy

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Objectives for Technicians

- Review recently approved antimicrobials including their spectrum of activity and potential place in therapy
- Discuss the pertinent antimicrobial stewardship implications of newly approved agents
- Identify antimicrobial agents in the advanced stages of the drug development pipeline.

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220/146 mmHg

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KLEBSIELLA PNEUMONIAE		
Drug	VITEK Interp	VITEK MIC
Amikacin	Intermediate (c)	32 (c)
Ampicillin		
Ampicillin/Sulbactam	Resistant (c)	>=32/16 (c)
Cefazolin	Resistant (c)	>=64 (c)
Cefepime	Resistant (c)	>=64 (c)
Ceftazidime	Resistant (c)	>=64 (c)
Ceftriaxone	Resistant (c)	>=64 (c)
Imipenem	Resistant (c)	8 (c)
Levofloxacin	Resistant (c)	>=8 (c)
Nitrofurantoin	Intermediate (c)	64 (c)
Piperacillin/Tazobactam	Resistant (c)	>=128 (c)
Tobramycin	Resistant (c)	>=16 (c)
Trimeth-Sulfamethox	Resistant (c)	>=320 (c)

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"We're here. We're in the post-antibiotic era. There are patients for whom we have no therapy, and we are literally in a position of having a patient in a bed who has an infection, something that five years ago even we could have treated, but now we can't...."

- Arjun Srinivasan, MD
Associate Director for Healthcare Associated Infection Prevention Programs, Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases

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The Problem¹

HAZARD LEVEL URGENT

Clostridium difficile (*C. difficile*), Carbapenem-resistant Enterobacteriaceae (CRE), Drug-resistant *Neisseria gonorrhoeae* (cephalosporin resistance)

HAZARD LEVEL SERIOUS

These are significant antibiotic-resistant threats. For varying reasons (e.g., low or declining incidence or favorable availability of therapeutic agents), they are not urgent threat, but their threat will increase and may become urgent without ongoing public health monitoring and prevention activities.

HAZARD LEVEL CONCERNING

These are bacteria for which the threat of antibiotic resistance is low and/or there are multiple therapeutic options for resistant infections. These bacterial pathogens cause severe illness. Threats in this category require monitoring and in some cases rapid incident or outbreak response.

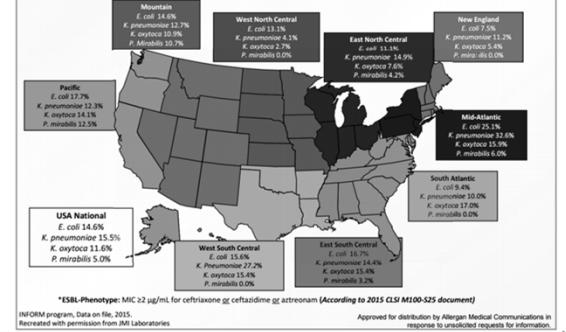
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The Illinois Problem

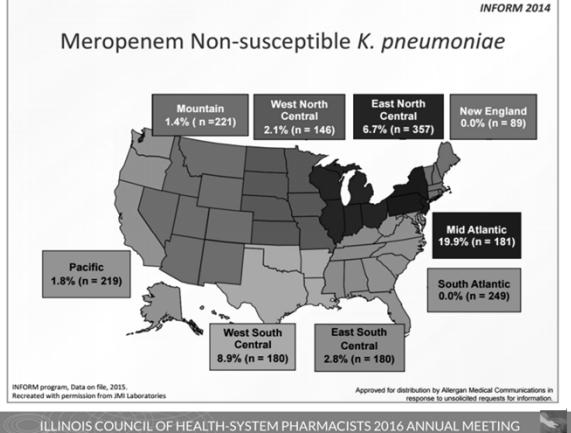
- What % of Gram negative *Enterobacteriaceae* are ESBL + across the continental United States?
• ~15%
- What % of Gram negative *Enterobacteriaceae* are ESBL + in the Illinois region?
• ~15%

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ESBL-phenotype Rates by USA Census Region and Organism Species

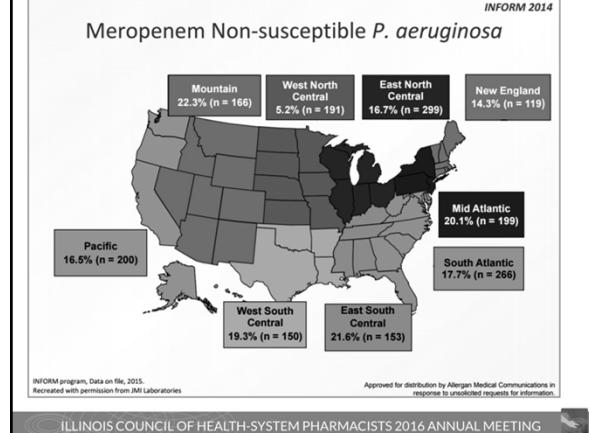


Meropenem Non-susceptible *K. pneumoniae*



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Meropenem Non-susceptible *P. aeruginosa*



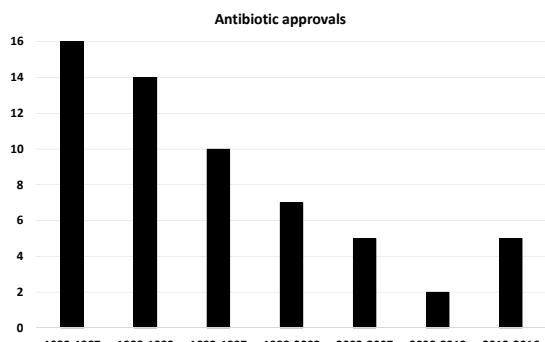
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The Health-System Problem

- **Antibiogram**
- UIC resistance rates
 - ESBL
 - *E. coli* ~ 10%
 - *K. pneumoniae* ~ 15%
 - CRE ~ 9%
 - MDR *P. aeruginosa* ~ 20%

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(Part of) The Solution



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Recently approved antimicrobials

- Dalbavancin – May 2014
- Tedizolid – June 2014
- Oritavancin – August 2014
- Ceftolozane-tazobactam – December 2014
- Ceftazidime-avibactam – February 2015

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Ceftolozane-tazobactam

- Ceftolozane:
 - Oxyimino cephalosporin with excellent affinity for PBPs of *Pseudomonas* spp.
- Tazobactam:
 - β -lactamase inhibitor
 - Activity against Ambler class A, C, and some D enzymes²
 - Mediocre activity against ESBLs and AmpCs
 - No activity against carbapenemases

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Ceftolozane-tazobactam

- ESBL activity is unreliable
 - 58% ESBL *K. pneumoniae* from pneumonia patients³
 - 78% ESBL from abdominal and urinary isolates⁴
- Pseudomonal susceptibilities 86-95%^{5,6}
 - 60-80% against ceftazidime and meropenem resistant strains
 - 92% against meropenem-resistant strains

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Ceftolozane-tazobactam

- Primary *in vitro* activity is aerobic Gram negative bacilli
 - Poor Gram positive and anaerobe activity⁷
 - Combine with metronidazole and/or Gram positive agent
- Not reliable against *Acinetobacter* or *Stenotrophomonas* spp.²

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Ceftolozane-tazobactam

- Approved dose-1.5g Q8 hours⁸⁻¹⁰
- Adjusted for renal function
- Non-inferiority established in:
 - ASPECT cUTI: phase II+III cUTI¹¹
 - vs levofloxacin
 - ASPECT cIAI: phase II cIAI¹², two phase III cIAI trials¹³
 - vs meropenem
- Numerically lower cure rates in mild renal dysfunction
- AEs were mild and reversible

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Stewardship considerations

- Primary place in therapy is MDR *Pseudomonas aeruginosa*
 - Check local resistance rates
- Primary need is off-label for serious infections
 - May decrease carbapenem use
- Existing resistance limits use
 - Need susceptibility testing
- Extended infusion?

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Stewardship considerations

- Likely need to restrict to prior authorization
- Cost:
 - 1.5g vial - \$109.61
 - ~\$2,300 for 7 day course
- 3g dose being studied in VAP vs meropenem
- Needs to be given with metronidazole and/or Gram positive agent if used empirically
- Potential option for PCN allergies

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Ceftazidime-avibactam

- Oxyimino cephalosporin
- Non-β-lactam β-lactamase inhibitor
- Inhibits class A, C, and D β-lactamases¹⁴
- High threshold to resistance in *Enterobacteriaceae*¹⁵⁻²¹
- Variable *P. aeruginosa* activity²²⁻²⁴
- Limited Gram positive and anaerobic activity²⁵

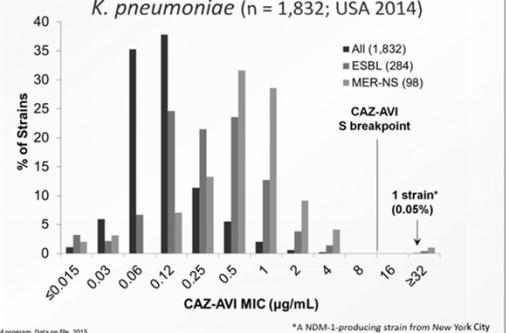
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Ceftazidime-avibactam²⁶

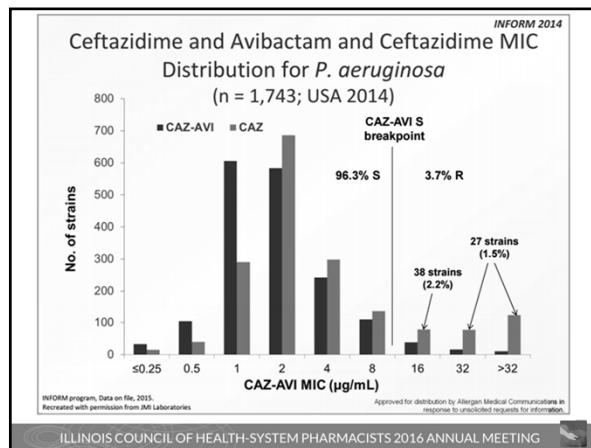
β-Lactamase	Avibactam	Clavulanic Acid	Tazobactam
Class A (Serine)	TEM, SHV and ESBLs	Yes	Yes
	CTX-M and ESBLs	Yes	Yes
	PER, VEB, GES	Yes	Yes
	KPC	Yes	No
Class B (Metallo)	IMP, VIM, NDM	No	No
Class C (Serine)	Chromosomal <i>Enterobacteriaceae</i> AmpC	Yes	No
	Chromosomal <i>Pseudomonas</i> AmpC	Yes	No
	Plasmidic ACC, DHA, FOX, LAT, MIX, MIR, ACT	Yes	No
Class D (Serine)	Penicillinase-type OXA-1, -31, -10, -13	Variable	Variable
	Carbapenemase-type OXA-23, -40, -48, -58	Variable	Variable

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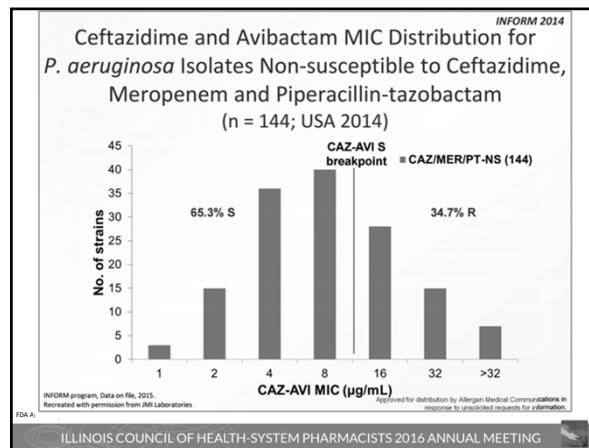
INFORM 2014 Ceftazidime and Avibactam MIC Distribution for *K. pneumoniae* (n = 1,832; USA 2014)



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Ceftazidime-avibactam

- Approved dose is 2.5g Q8 hours
- Adjusted for renal function
- Non-inferiority established in:
 - 2 phase II cUTI trials²⁷
 - 1 phase II cIAI²⁸
- RECLAIM 1+2: phase III cIAI trials²⁹

Table 14: Clinical Cure Rate at TOC by Baseline Renal Function (mITT Population) – Phase 3 cIAI Trial

Baseline Renal Function	Ceftazidime-avibactam + Metronidazole	Meropenem
CrCL >50 mL/min	322/379 (85%)	321/373 (86%)
CrCL > 30 to ≤ 50 mL/min	14/31 (45%)	26/35 (74%)

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Ceftazidime-avibactam²⁶

Table 2: Initially Proposed Dosage Regimen and Used in Phase 3 Trial

Estimated CrCL (mL/min)	Proposed Dosage Regimen
> 50	2.5 g IV (over 2 hours) every 8 hours
≥ 31 to ≤ 50	1.25 g IV (over 2 hours) every 12 hours
≥ 16 to ≤ 30	1.25 g IV (over 2 hours) every 24 hours
≥ 6 to ≤ 15	0.625 g IV (over 2 hours) every 24 hours
≤ 5	0.625 g IV (over 2 hours) every 48 hours

Table 3: Predicted Exposure in Simulated cIAI Patients with Varying Degree of Renal Function Resulting Using the Initially Proposed Dosing Regimen

Renal Function	Proposed Dose Regimen	Ceftazidime		Avibactam	
		Cmax,ss (µg/mL)	AUC0-24,ss (µg·h/mL)	Cmax,ss (µg/mL)	AUC0-24,ss (µg·h/mL)
NORM	2000 mg CAZ + 500 mg AVI q8h	47.2±13.4	542±161	9.31±1.87	93.5±21.3
MILD	2000 mg CAZ + 500 mg AVI q8h	59.9±17.1	828±260	11.2±2.37	131±36.4
MOD	1000 mg CAZ + 250 mg AVI q12h	33.5±9.6	448±142	6.84±1.48	80.3±22.8
SEV1	1000 mg CAZ + 250 mg AVI, q24h	33.9±10.2	400±136	7.61±1.85	82.8±26.7
SEV2	500 mg CAZ + 125 mg AVI q24h	27.0±9.03	455±180	6.79±2.07	116±47.6
ESRD	500 mg CAZ + 125 mg AVI q48h	45.7±22.9	898±527	5.26±1.04	75.6±16.8

NORM (CrCL > 80 mL/min); MILD (CrCL 51 mL/min to ≤ 80 mL/min); MOD (CrCL 31 mL/min to ≤ 50 mL/min); SEV1 (CrCL 16 mL/min to ≤ 30mL/min); SEV2 (CrCL 6 mL/min to ≤ 15 mL/min); ESRD End-stage renal disease (CrCL 0 mL/min to ≤ 5 mL/min).

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Ceftazidime-avibactam²⁶

Table 6: Revised/Newly Proposed Dosing Regimen for Ceftazidime-Avibactam

Estimated CrCL (mL/min) ^a	Recommended Dosage Regimen for Ceftazidime-Avibactam
Greater than 50	2.5 grams (2 grams/0.5 grams) intravenously (over 2 hours) every 8 hours
31 to 50	1.25 grams (1 grams/0.25 grams) intravenously (over 2 hours) every 8 hours
16 to 30	0.94 grams (0.75 grams/0.19 grams) intravenously (over 2 hours) every 12 hours
6 to 15 ^b	0.94 grams (0.75 grams/0.19 grams) intravenously (over 2 hours) every 24 hours
Less than or equal to 5 ^b	0.94 grams (0.75 grams/0.19 grams) intravenously (over 2 hours) every 48 hours

^aAs calculated using the Cockcroft-Gault formula. ^bBoth ceftazidime and avibactam are hemodialyzable; thus, ceftazidime-avibactam should be administered after hemodialysis on hemodialysis days.

Table 7: Predicted Exposures for the Revised Dosing Regimens in Patients with Varying Degrees of Renal Function

Renal Function	Revised Dosing Regimen	Ceftazidime		Avibactam	
		Cmax,ss (µg/mL)	AUC0-24,ss (µg·h/mL)	Cmax,ss (µg/mL)	AUC0-24,ss (µg·h/mL)
NORM	2000 mg CAZ + 500 mg AVI, q8h	45.5 (63)	518 (63)	9.17 (62)	91.2 (62)
MILD	2000 mg CAZ + 500 mg AVI, q8h	57.6 (63)	783 (64)	11.0 (62)	126 (63)
MOD	1250 mg CAZ + 250 mg AVI, q12h	31.6 (63)	643 (64)	7.32 (62)	11.6 (63)
SEV1	750 mg CAZ + 188 mg AVI, q12h	31.6 (63)	571 (64)	7.61 (62)	118 (63)
SEV2	750 mg CAZ + 188 mg AVI, q24h	38.6 (64)	628 (65)	9.70 (63)	158 (66)
ESRD	750 mg CAZ + 188 mg AVI, q48h	59.6 (67)	1120 (69)	7.78 (62)	111 (62)

CAZ = ceftazidime; AVI = avibactam; NORM (CrCL > 80 mL/min); MILD (CrCL 51 mL/min to ≤ 80 mL/min); MOD (CrCL 31 mL/min to ≤ 50 mL/min); SEV1 (CrCL 16 mL/min to ≤ 30mL/min); SEV2 (CrCL 6 mL/min to ≤ 15 mL/min); ESRD End-stage renal disease (CrCL 0 mL/min to ≤ 5 mL/min).

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RECAPTURE 1 and 2³⁰

- Ceftazidime-avibactam 2.5g Q8h vs. doripenem 500mg Q8h for cUTI and AP
 - Possible switch to PO after 5 days
- 1033 patients
- Primary endpoints:
 - Patient reported symptomatic resolution at day 5
 - Combined symptomatic resolution and microbiological eradication at TOC

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RECAPTURE 1 and 2³⁰

- Non-inferiority was achieved
 - Superiority with ceftazidime-avibactam in micro eradication at TOC
- No reduction in efficacy in renal impairment
 - 1250 mg Q12h regimen was used for CrCl <50 mL/min
- No new safety concerns identified

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Ceftazidime-avibactam²⁶

Table 4: Percentage of Simulated Patients with cIAI Achieving PK/PD* Target Ceftazidime-Avibactam (5000 Simulated Subjects per Group)**

Renal Function	Proposed Dosing Regimen	% of Simulated Patients Achieving PK/PD Target
CAZ-AVI MIC=4 µg/mL		
NORM	2000 mg CAZ + 500 mg AVI, q8h	98.9
MILD	2000 mg CAZ + 500 mg AVI, q8h	99.9
MOD	1000 mg CAZ + 250 mg AVI, q12h	98.9
SEV1	1000 mg CAZ + 250 mg AVI, q24h	97.8
SEV2	500 mg CAZ + 125 mg AVI, q24h	100
ESRD	500 mg CAZ + 125 mg AVI, q48h	100
CAZ-AVI MIC=8 µg/mL		
NORM	2000 mg CAZ + 500 mg AVI, q8h	98.1
MILD	2000 mg CAZ + 500 mg AVI, q8h	99.9
MOD	1000 mg CAZ + 250 mg AVI, q12h	95.7
SEV1	1000 mg CAZ + 250 mg AVI, q24h	85.9
SEV2	500 mg CAZ + 125 mg AVI, q24h	94.4
ESRD	500 mg CAZ + 125 mg AVI, q48h	99.9

CAZ = ceftazidime; AVI = avibactam; NORM (CrCL > 80 mL/min); MILD (CrCL 51 mL/min to ≤ 80 mL/min); MOD (CrCL 31 mL/min to ≤ 50 mL/min); SEV1 (CrCL 16 mL/min to ≤ 30mL/min); SEV2 (CrCL 6 mL/min to ≤ 15 mL/min); ESRD End-stage renal disease (CrCL 0 mL/min to ≤ 5 mL/min).

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REPRISE³¹

- Ceftazidime-avibactam 2.5g Q8h vs. best available therapy
- Patients with cUTI or cIAI d/t ceftazidime non-susceptible Gram negative pathogens
 - 97% received carbapenem
 - Pts with ongoing S&S could have received any treatment
 - Those who received effective therapy had to be clinically worsening
- Exclusion was CrCl <6 mL/min

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REPRISE³¹

- >90% had cUTI in both groups
- >80% had CrCl >50
- 80-90% of pathogens were *E. coli* or *K. pneumoniae*
- 4/266 (1.5%) *Enterobacteriaceae* isolates ceftazidime-avibactam resistant
 - 9/14 (64%) *P. aeruginosa* resistant
- Clinical cure at TOC was identical at 91%
 - Micro response was 18% higher in ceftazidime-avibactam group

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REPURPOSE^{32,33}

- Phase III trial vs meropenem for HAP/VAP
 - 2.5g Q8h over 2 hours vs. 1g Q8h over 30 min
 - 879 patients
- Non-inferior at 21 day TOC visit
- All-cause 28 day mortality similar
- Approved by EMA on 6/24 for HAP/VAP, cUTI, cIAI

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Stewardship considerations

- Primary need is off-label for serious infections
- CRE is currently most urgent threat
 - Local resistance rates
 - In vitro* activity, safety profile, and clinical experience with ceftazidime provide promise
 - Need additional clinical data for CRE
 - Allow for avoidance of polymyxins and aminoglycosides in CRE?
 - Combo therapy?

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Stewardship considerations

- Likely need to restrict to prior authorization
- Cost:
 - 2.5g vial - \$359.10
 - \$7,541.10 for 7 day course
- Needs to be given with metronidazole and/or Gram positive agent if used empirically
 - Compatibility with vancomycin
- Manufacturing issue has caused shortage
 - Drug not available until March

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Stewardship considerations

	Ceftolozane-Tazobactam	Ceftazidime-Avibactam
Spectrum		✓
Dose	✓	✓
Clinical trial data		✓
Safety	✓	✓
Cost	✓	

Other formulary concerns?

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Pipeline antimicrobials

- Currently in/completed phase III trials
 - Meropenem/vaborbactam
 - Eravacycline

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Meropenem-vaborbactam

- Vaborbactam is cyclic boronic acid based non β -lactam β -lactamase inhibitor
- Potent activity against class A and C β -lactamases
 - Including serine carbapenemases, especially KPC
- Vaborbactam shown to improve activity against CRE by over 64 fold³⁴
- No activity against MBLs

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Meropenem-vaborbactam

- PK of vaborbactam shown to match meropenem extremely well^{35,36}
- ELF penetration 63% and 53%³⁵
- Currently in Phase III trials as fixed dose combination of 2g meropenem/2g vaborbactam Q8h as 3 hour infusion
 - cUTI and AP vs piperacillin-tazobactam
 - CRE infections vs. best available therapy

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Meropenem-vaborbactam

- cUTI and AP study completed June 2016³⁷
 - Compared to piperacillin-tazobactam
 - Step-down to PO therapy
 - Met FDA and EMA non-inferiority endpoint
 - Superior to piperacillin-tazobactam in FDA endpoint
 - 188/192 (98.4%) vs. 171/182 (94%)
 - Microbiological eradication 66.7% vs. 57.7%
 - No unanticipated adverse events

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Meropenem-vaborbactam

- Stewardship considerations
 - Active against CREs
 - When approved will have only clinical data in patients with CRE infections
 - Will begin HAP/VAP trial soon vs. piperacillin-tazobactam
 - Price?
 - Susceptibility testing?

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Eravacycline

- Novel, synthetic fluorocycline^{38,39}
 - Active against ESBL, CRE, *A. baumannii*, MRSA, and VRE
 - No *P. aeruginosa* activity
- Compared to tigecycline, improved:
 - PK
 - Tolerability
 - *in vitro* CRE activity

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Eravacycline

- IGNITE 1⁴⁰
 - Phase III study vs ertapenem for cIAI
 - Met FDA and EMA primary endpoint of non-inferiority in clinical response at TOC in MITT group
 - 95% CI bounds -7.1%-5.5%
 - No serious adverse events
- IGNITE 2
 - Phase III trial in cUTI vs levofloxacin

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Eravacycline

- IGNITE 2⁴¹
 - 1.5 mg/kg daily followed by 200 mg PO Q12h vs levofloxacin 750 mg daily
 - Minimum of 3 IV days
 - Did not achieve either FDA or EMA non-inferiority endpoint
 - Not able to push dose to PO 400 mg due to adverse events
 - N/V similar to tigecycline

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Eravacycline

- Stewardship considerations
 - 1 mg/kg IV Q12h dose only going forward
 - PO dosage form?
 - Extremely broad activity
 - VRE and *Acinetobacter* spp.
 - Bacteriostatic
 - Tetracycline analogue
 - Pregnancy, pediatrics...

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Summary

- Resistance among Gram negative pathogens will continue to increase
- Two new antimicrobials are promising although they do not address all relevant pathogens and clinical data in target infections are lacking
- Meropenem-vaborbactam should close some of the existing gaps in available agents

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New Antibiotics for the Post-Antibiotic Era

Eric Wenzler, PharmD, BCPS
Infectious Diseases Pharmacotherapy Fellow
University of Illinois at Chicago
September 16, 2016

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New Antibiotics for the Post-Antibiotic Era

Eric Wenzler, PharmD, BCPS

Self-Assessment Questions

1. According to the 2013 Center for Disease Control and Prevention Antibiotic Resistance Threat Report, which of the following pathogens is categorized as a threat level of "urgent"?
 - A. Multidrug-resistant *Pseudomonas aeruginosa*
 - B. Extended spectrum β-lactamase producing (ESBL) *Enterobacteriaceae*
 - C. Carbapenem-resistant *Enterobacteriaceae* (CRE)
 - D. Vancomycin-resistant *Enterococcus* (VRE)
2. Resistant Gram negative pathogens are not a substantial problem in the Illinois region as local resistance rates are far less than national rates
 - A. True
 - B. False
3. Which of the following agents would be the most appropriate therapeutic option to treat a 67 year old patient with no known drug allergies and a CrCl of 52 mL/min with a complicated intra-abdominal infection (cIAI) due to carbapenem-resistant *K. pneumoniae*?
 - A. Ceftazidime-avibactam 2.5g every 8 hours
 - B. Meropenem 2g every 12 hours
 - C. Ceftolozane-tazobactam 1.5g every 8 hours
 - D. Fosfomycin 6g IV every 6 hours
4. Once FDA approved, which of the following agents will have the only in-human randomized controlled trial data to support its use for patients with serious infections due to carbapenem-resistant organisms?
 - A. Eravacycline
 - B. Ceftaroline-avibactam
 - C. Delafloxacin
 - D. Meropenem-vaborbactam
5. Which of the following agents has reliable activity against *Acinetobacter spp*?
 - A. Meropenem-vaborbactam
 - B. Ceftolozane-tazobactam
 - C. Eravacycline
 - D. Ceftazidime-avibactam
 - E. None of the above

Answer key:

1. C
2. B
3. A
4. D
5. C

Pharmacy Audits – How Can the Pharmacy Staff Get Involved?

Thomas Wheeler, PharmD, BCPS, CPHIMS

Sima Shah, PharmD, MPH

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Learning Objectives

1. Review main Joint Commission (TJC) and 340B Medication Management standards and requirements
2. Outline the preparatory process and identify strategies for successful TJC and 340B audits
3. Discuss potential roles pharmacy technicians can play in the preparation for an audit
4. Recognize how the "lessons learned" from the audit can be used to improve compliance with the set standards

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Things Fall Apart

- **Second Law of Thermodynamics - Increased Entropy**

The Second Law of Thermodynamics is commonly known as the Law of **Increased Entropy**. While quantity remains the same (First Law), the **quality** of matter/energy deteriorates gradually over time.

*As usable energy is irretrievably lost, disorganization, randomness and **chaos increases***

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Chaos Increases



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So it's not our fault !

- It's a universal law of physics that left alone, processes, and organization fall apart.
- TJC prep should not be just before the survey, but should be a continual state of readiness- so that patient care is provided at a high level.
- Safe and efficient systems
- **Happy pharmacy staff** (or at least less stressed).



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What it feels like when TJC arrives- ZOMBIE APOCALYPSE



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The Joint Commission Audits

- Tom Wheeler- PharmD, BCPS, CPHIMS
- Corporate Director of Pharmacy Rush University Medical Center- Chicago



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Gap Analysis

- Current practice- top deficiencies are technical not clinical- lending them selves to pharmacy tech leadership.
- Best Practice- continual state of readiness. Think aircraft carrier.
- Education Need- what is the area to focus on, what documentation is necessary.
- Learning objective- how to get to full and continual compliance.

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Med Errors- How Can We Provide Safe and Efficient Care?

- Our drugs can Cure and Kill.
- Medication Management standards- are termed MM .
- 8 different areas.
- TJC Standards are in place to provide a framework for an effective and SAFE medication management system.

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What are the Areas?

- Planning
- **Selection and procurement**
- Storage
- Ordering
- Preparing and dispensing
- Administration
- Monitoring
- Evaluation

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Needs Assessment

- What do you need to know?
- Readiness is not just for pencil pushing coffee drinking directors and managers.
- Some of the section is higher level planning.
- **Most involve front line pharmacy technicians and pharmacists.**
- An engaged staff is a compliant and safe department.

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What is TJC

- A. New frozen yogurt franchise
- B. Non binding Quality Agency
- C. Government Agency
- D. Accrediting organization –for Medicare and Medicaid

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The Joint Commission

- Established in 1951.
- Focus on safety and quality.
- Deemed status accrediting agency- Medicare doesn't have inspectors.
- Located in Oakbrook.
- Once was the only game in town, now DNV, etc.

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If TJC walked into 4 of your med rooms

- A. Unlikely to find unsecured meds
- B. Possible to find unsecured meds
- C. Likely to find unsecured meds
- D. We are in trouble

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What are the standards ?

- MM – The goal is to provide a framework for an effective and safe medication management system
- Very little clinical requirements
- 8 different sections

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MM I-VIII

- Planning
- Selection and Procurement
- Storage
- Ordering and Transcribing
- Preparing and Dispensing
- Administration
- Monitoring
- Evaluation

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What does TJC State Should Be Done?

- Reduce variation, errors and misuse.
- Evidence Based Practice.
- Manage CRITICAL processes to promote safe medication management.
- Standardize , standardize, standardize.
- Monitoring the medication management process for efficiency, quality and safety.

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Medication Management- Top NonCompliant Standards/NPSGs for Hospitals (Jan-Dec, 2015)

Standard/NPSG	% Non - compliant
MM.03.01.01	Storage and Security of Meds
MM.04.01.01	Medication Orders
MM.05.01.01	Medication Order Review
NPSG.03.04.01	Labeling in OR/procedures
MM.05.01.07	Preparing medications
NPSG.03.06.01	Reconciling Medications
MM.05.01.09	Labeling medications
MM.01.02.01	Look alike sound alike Med
MM.01.01.03	High alert /Hazardous Meds

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MM.01.01.03**High Alert and Hazardous Drugs**

- And yes- you will probably get a raise if you go to your director and quote the standard number.
- This standard – high-alert and hazardous meds.
- If you think you know of a better way to minimize admin errors for these SPEAK UP.

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What are your High alert and Hazardous meds**Audience Participation**

- Each site must have a list?

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High alert Medications MM 01.01.03

- We define them ☐ yes- you and I
- Do you know what your site strategy is
- Audience participation- name some
- Does everyone at your site know? How is this communicated?

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SALAD**Look Alike Sound Alike Medication Strategies (MM.01.02.01)**

- Consider multiple concentrations of the same medication.
- Have you defined policy on ordering LASAs?
- Recommendation: Address display of LASA via TALLman lettering, use of brands or indications; address storage via restrictions preparation, labeling.

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The Hospital Selects and Procures Medications MM 02.01.01

- Standardize and limits concentrations- why?
- Need a formulary- and it needs to be “readily available”
- Non formulary meds
- Drug Shortages
- substitutions

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MM.03.01.01 Medication Storage and Security ☆ Problematic EPs

EP 2: medications are stored according to manufacturer's recommendations –
 EP 3: all medications and biologicals are stored in secure areas to prevent diversion and locked when necessary, in accordance with law and regulation –
 Failure to address diversion –
 EP 6: the hospital prevents unauthorized individuals from obtaining medications in accordance with law and regulation –
 EP 7: all products are labeled with contents, expiration date (Bulk Packaging-Imaging) –
 EP 8: removes expired, damaged, and/or contaminated meds/stores separately

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MM 03.01.03

- The hospital safely manages emergency medications.
- Readily available.
- Whenever possible in unit –dose age-specific.
- When used- they are replaced promptly.

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MM 04.01.01

- Medication orders are clear and accurate.

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MM 05.01.01

- A Pharmacist reviews the appropriateness of all medication orders for medications to be dispensed in the hospital

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MM 05.01.07

- The hospital safely prepares medications.
- This is entirely within the scope of the day to day activities.
- Do you speak up if there is a problem?
- Do you speak up if a coworker isn't measuring up?

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Remember NECC

- New England Compounding
- 800 sickened , 52 died
- Pharmacy preparation errors happen
- Complex processes, different staff, ever changing formulas and drugs

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MM 05.01.09

- Medications are labeled
- What needs to be on the label?

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MM 05.01.11

- The hospital safely dispenses medications
- Anti-diversion strategies
- How many of you have been around narcotic diversion

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MM 05.01.17

- The hospital follows a process to retrieve recalled or discontinued medications

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MM 07.01.03

- The hospital responds to actual or potential adverse drug events, significant adverse drug reactions and medications errors.

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Post test questions

1. What is the most common TJC citation?
2. What are the two letters which identify pharmacy oriented sections in TJC accreditation manual
3. How often should you prepare for TJC visits?
4. Managing emergency medications is not covered by TJC ?

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Resources

- **The Joint Commission**
- https://www.jointcommission.org/facts_about_joint_commission_accreditation_standards/

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340B Audits

Sima Shah, Pharm.D, MPH
 University of Illinois Hospital &
 Health Sciences System
 September 17, 2016

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Statement of Conflicts of Interest

I have no actual or potential conflict of interest in relation to this presentation.

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I am familiar with the 340B Drug Discount Program (340B Program).

- A . Yes
- B . No

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I am involved with the 340B program.

- A. Yes
- B. No

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340B Program

- Provides **covered outpatient drugs** to eligible health care organizations at significantly reduced prices¹
- Administered by **Office of Pharmacy Affairs (OPA)** within the Health Resources and Services Administration (HRSA)¹
- Mandated for **drug manufacturers** who participate in the Medicaid Drug Rebate Program¹
- The 340B Program enables covered entities to stretch scarce Federal resources, reaching more eligible (underserved) patients and providing more comprehensive services²

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340B Controversies

Different interpretations of the 340B regulations³

Management of 340B program varies, lack consistency³

HRSA begins conducting audits in 2012²

Negative publicity and lobbying to scale down⁴

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340B Program Regulations⁵

Requirement	Definition	Operational
OPA Database	Maintain <u>accurate covered entity information in OPA database</u>	Review database periodically
Duplicate Discount Prohibition	Cannot use upfront discounted 340B priced drugs and back-end Medicaid rebate on the <u>same claim</u>	Billing restrictions/requirements with Medicaid fee-for-service claims
Diversion Prohibition	Law prohibits the resale or transfer of 340B drugs to <u>anyone other than a patient of the covered entity</u>	340B drugs may only be dispensed to 340B eligible patients. Maintain accurate 340B drug inventory

All covered entities have to follow these three regulatory requirements

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Inventory Management of 340B Drugs⁶

<i>Separate dual physical inventory</i>	Replenishment (Single inventory)
<ul style="list-style-type: none"> Purchase directly from 340B account Non-340B and 340B medications have two different stock bottles 	<ul style="list-style-type: none"> Non-340B account= Initial purchase of 11-digit NDC Split-billing software maintains tally of credits. 

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Cover slide 3 – put title here

University of Illinois Hospital & Health Sciences System

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University of Illinois Hospital & Health Sciences System

Background:

- Academic teaching hospital: 7 health science colleges
- 495-bed tertiary care hospital, 22 outpatient clinics and 1 FQHC with 11 satellite locations
- Outpatient payor mix: Medicare (22%); Medicaid (16%); Medicaid Managed Care (23%) and self-pay (2%)
- Demographics: African American (48%); Hispanic (6%) and Caucasian (16%)

340B Participation:

- University of Illinois Hospital (DSH) and Mile Square Health Center (FQHC).
- The University of Illinois Ambulatory Care Pharmacies are contract pharmacies for the UI Health covered entities (6 ambulatory pharmacies).
- 340B participation audited by HRSA in October 2015

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340B at UI Health

- Unique to our health system...
 - Contract pharmacy arrangement
 - Access to the EMR
 - Work closely with the clinics
 - Decision to fill a prescription with 340B is prospective and is made at the pharmacy level
 - Split-billing system is a combination of homegrown and outside vendor.

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HRSA Audit

Audit notice	Audit Documentation Request		
Authorizing official will receive the audit notification	Past six month of dispense data	Request Policy & Procedure and other documents	On-site Audit
	Review of prescriptions for 340B eligibility	Site visits of hospital and pharmacies	HRSA Findings
			1. No findings OR 2. Findings. Either appeal the findings <u>or</u> accept and provide corrective action plan

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Preparatory process for successful 340B audits

Establish comprehensive teams (across the health system and within the pharmacy)

Review 340B Policy and Procedures

340B patient definition eligibility- how is a dispense eligible?	Examine and define system flows and work flows	Inventory management of drugs
--	--	-------------------------------

Educate key stakeholders, providers and staff members

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Identify strategies for successful 340B audits

Create a 340B compliance plan

- Use 340B regulation requirements and policy and procedures
- Review 340B claims and 340B purchases
- Audit 340B dispenses for 340B patient definition
 - Review Medicaid FFS and Managed Care Claims and split-billing system
- Review information in the OPA database
- Review the policies and procedures
 - Educate staff with new updates and a review of the 340B Program
- Split-Billing system and accumulators: test the anomalies each time change is made to the logic

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Role pharmacy technicians can play in the preparation for an audit

- Assure appropriate inventory management
- Provide insight on workflow practices
- Administer self-audits with pharmacist oversight
- Compile self-audit findings
- Assist with dissemination of audit findings

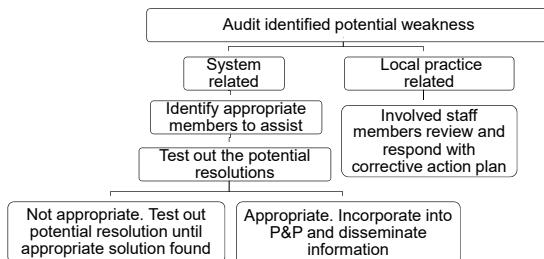
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“Lessons learned” from the audit can be used to improve compliance

- Strong audits = identify potential weaknesses
- Identify appropriate team members to resolve the problem
- Document problem and resolution
- Incorporate practice changes into policy and procedures and educational modules
- Disseminate and review information with other departments within the institution

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Corrective Feedback Mechanism



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Case Study

Elizabeth picked up a prescription from one our pharmacies on 1/8/16; the fill was a 340B drug. This dispense was randomly selected on our monthly 340B audit. The information below is populated from our prescription data entry system. The QI technician reviews the dispense to ensure that it was appropriate to dispense 340B (Diversion Prohibition).

Rx#	Written	Name	DOB	ITEM	MD
12345	1/7/2016	Bennet, Elizabeth	10/3/1971	Dark Chocolate 100mg	Tolstoy, Leo

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Case Study

The QI technician will review and collect information from the EMR to ensure that prescription was an eligible 340B dispense. The information below is completed by the technician and reviewed by the 340B pharmacist.

Rx Clinic originated?	Is the clinic an approved 340B clinic?	Established Patient established with clinic?	Protocol or Other	Meet 340B Criteria?	AB Comments	SS comments	Staff Comments
gen med	yes	6/2/16	n/a	yes	med list original order entered and electronically signed by R. Waters on 11/24/2013 at 2:44pm.	Continuation of 11/24/2013 gen med Int-General Medicine Note September 9, 2013, R. Welch Prescription is 340B eligible.	

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Conclusion

For a successful 340B Program:

- Understand the 340B regulations and maintain a compliance plan
- Conduct self-audits to help ensure the system is working
- Technicians have an integral role in maintaining compliance
- Use self-audit findings to correct potential weaknesses

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Which 340B Program regulation requires accurate management of 340B drugs inventory?

- A. OPA Database Review
- B. Duplicate Discount Prohibition
- C. Diversion Prohibition
- D. Drug Management Requirement

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Establishing a 340B compliance plan should be based on two key components, the 340B regulation requirements and:

- A. Inventory Management Regulation
- B. Feedback from key stakeholders, providers and staff
- C. 340B Policy and procedures
- D. 340B split-billing system

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Pharmacy technicians should be involved in the 340B audit process. One example of the role taken by the technician is:

- A. Assisting with inventory management
- B. Overseeing the audits
- C. Act as the authorizing official

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Self-audits are an integral part of 340B compliance, the best use of audits findings is:

- A. Maintain records in 3 ring binders
- B. Assist with identifying system weaknesses
- C. Send to HRSA
- D. Review findings but do not disseminate

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Resources

- HRSA
– <http://www.hrsa.gov/opa/>
- Apexus
– <https://www.apexus.com>
- 340B Health
– <http://www.340bhealth.org>

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Cultivating Safety in the Pharmacy

Adam Bursua, PharmD, BCPS

Medication Safety and Quality Coordinator, UI Health
Clinical Assistant Professor, University of Illinois College of Pharmacy

The speaker has no conflicts to disclose.

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Objectives

- Describe the link between Just Culture and error prevention
- Recognize the culpability of various types of errors
- Order the effectiveness of process improvement strategies from most to least effective
- Identify techniques to improve “high-stakes” communication

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1999 - Institute of Medicine Report - To Err is Human

- Watershed moment for our approach to building a safer health system
- Majority of medical errors do not result from individual recklessness or the actions of a particular group
 - “not a bad apple problem”
- More commonly caused by faulty systems, processes, and conditions that lead people to make mistakes

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Faulty systems, Processes, Conditions

- How does our health system learn from itself?
 - Critical role of voluntary error reporting

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Avoiding the Shame and Blame Culture

- Recent error in which an IV pump was used incorrectly
 - Resulted in the infusion of 25,000 units of heparin in < 30 minutes
- Safety software on the infusion pump would have prevented the error, but it was not enabled by the administering nurse

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After the Error

- People expect change after an error
 - Disciplining individuals for error they were involved in is an easy way for managers show they run a tight ship
 - The “tough” response is not always the most effective response
 - “I can assure you, this won’t happen again”

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Pharmacy Example

- A pharmacist is checking an oral morphine dose prepared by her technician. When looking at the stock bottle, she notices that the 20 mg/mL stock solution was used instead of the 2 mg/mL stock solution.
- The pharmacist notes that this is the 2nd time this technician has made this error.

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Scenario

- The error is reported to the pharmacy manager
- You are the Lead Technician, and the pharmacy manager comes to you and says they do NOT want to hear about an error like this happening again. They want RESULTS!

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What Do You Do?

- No other technicians have had a problem filling morphine Rx's
- This technician has worked in your department for 10 years
 - Reputation for being slow
 - Some of their peers have complained that they aren't a team player

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Different Approaches

Blame and Shame

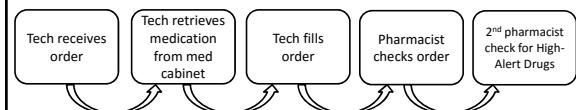
- The technician is blamed and disciplined for the error
- They are no longer allowed to work with controlled substances
 - Leads to a demotion and subsequent reduction in pay

Just Culture

- An investigation is performed into the Root Causes of the error
- Focus is on faulty systems, processes, conditions
- Reservation of judgment and blame

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High Level of Workflow



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Root Cause Analysis

Tech retrieves medication from Med Cabinet

- The stock solutions of morphine 2mg/mL and 20 mg/mL are kept in a secure medication cabinet
- The cabinet is re-stocked using a barcode system
- The two concentrations were correctly stored prior to the error

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Latent Conditions

Please select the appropriate item:

Available Products
morphine (bulk btl) 2mg/1mL 100mL soln
morphine (bulk btl)20mg/1mL 100mL soln
morphine "EXTENDED" release 100mg tab
morphine "EXTENDED" release 15mg tab
morphine "EXTENDED" release 30mg tab
morphine "EXTENDED" release 60mg tab

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Latent Conditions

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Identifying the root cause/latent condition for error

Before	After
morphine (bulk btl) 2mg/1mL 100mL soln	morphine (bulk btl) 2mg/1mL 100mL soln
morphine (bulk btl)20mg/1mL 100mL soln	morphine "EXTENDED" release 100mg tab
morphine "EXTENDED" release 100mg tab	morphine "EXTENDED" release 15mg tab
morphine "EXTENDED" release 15mg tab	morphine "EXTENDED" release 30mg tab
morphine "EXTENDED" release 30mg tab	morphine "EXTENDED" release 60mg tab
morphine "EXTENDED" release 60mg tab	morphine [high conc bulk btl] 20mg/1mL 30mL soln

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Different Outcomes

Shame and Blame	Just Culture
<ul style="list-style-type: none"> The technician feels tremendous guilt/stigmatized <ul style="list-style-type: none"> Reduced satisfaction The root cause(s) are never identified <ul style="list-style-type: none"> Latent conditions for error remain Next time the error happens, there is a reluctance to report <ul style="list-style-type: none"> Remember what happened last time? 	<ul style="list-style-type: none"> Staff are more likely to recover after making a mistake <ul style="list-style-type: none"> Also more likely to self report errors Faulty processes, latent conditions that lead to error are discovered <ul style="list-style-type: none"> Corrective actions can be implemented Error reporting is encouraged <ul style="list-style-type: none"> You don't feel like someone is getting fired every time you report an error

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Just Culture and Accountability

- Just Culture does not mean that individuals are not accountable for their actions
- Shifts focus from the individual to the system
- The outcome of the error should not determine the need for discipline
- Reckless or malicious acts should be disciplined
- Other high risk behavior, especially if repeated, may also be grounds for discipline
 - It is important that staff understand the difference
 - punished for making mistakes vs. disciplined for not following appropriate work procedures

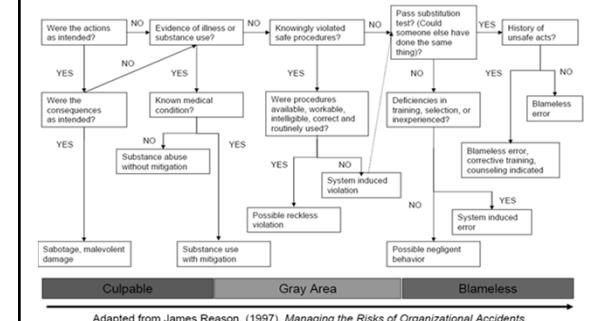
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Which of the following describe an advantage of adopting a “just culture” response to errors in a pharmacy?

- A. Improved identification of individuals that have a high rate of error in their work
- B. More sensitive detection of reckless behavior
- C. Provides an anonymous outlet for staff to report individuals that ignore department policies
- D. Preservation of a robust voluntary error reporting

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Just Culture – Knowing How to React

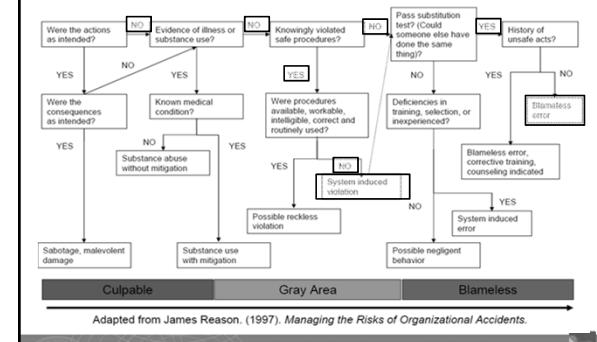
Adapted from James Reason. (1997). *Managing the Risks of Organizational Accidents*.

Heparin Error, Revisited

- The nurse didn't use the IV pump with the safety functions enabled, which led to an adverse drug event
- Policy in unit states that nurses MUST use the library with the safety functions enabled
- This nurse was never trained on how to use the safety functions (usually works on a different unit)
- Audits suggest that safety features on pumps are only correctly utilized ~ 80% of the time on this unit

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Just Culture – Knowing How to React

Adapted from James Reason. (1997). *Managing the Risks of Organizational Accidents*.

Just Culture – Culture of Safety

- Better identification of system induced errors (lack of proper training) that may have otherwise been deemed to be “bad apple” problems
- Preserves a safety culture that promotes error reporting

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- Culture of Safety Survey
- Community Pharmacy Culture of Safety Survey
 - Available at AHRQ website

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AHRQ Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

Community Pharmacy Culture of Safety Survey

	Strongly Disagree	Disagree	Neither Agree nor Disagree	Agree	Strongly Agree
1 Staff are treated fairly when they make mistakes	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2 When a mistake happens, we try to figure out what problems in the work process led to the mistake	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3 This pharmacy places more emphasis on sales than on patient safety	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4 This pharmacy helps staff learn from their mistakes rather than punishing them	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5 When the same mistake keeps happening, we change the way we do things	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6 This pharmacy is good at preventing mistakes	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7 We look at staff actions and the way we do things to figure out what mistakes happen in this pharmacy	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8 Staff feel like their mistakes are held against them	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9 The way we do things in this pharmacy reflects a strong focus on patient safety	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10 Mistakes have led to positive changes in this pharmacy	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

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According to the Just Culture algorithm of unsafe acts, which of the following characteristics of a medication error should most clearly result in disciplinary action of the pharmacist or technician involved?

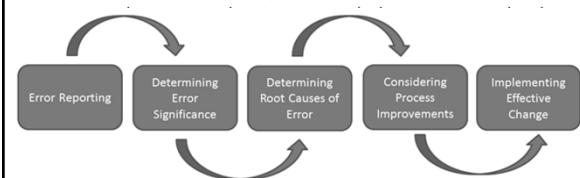
- A. The error resulted in harm
- B. The individual involved was knowingly engaging in reckless behavior
- C. The error resulted from a breach in policy
- D. The same individual has made the same mistake repeatedly

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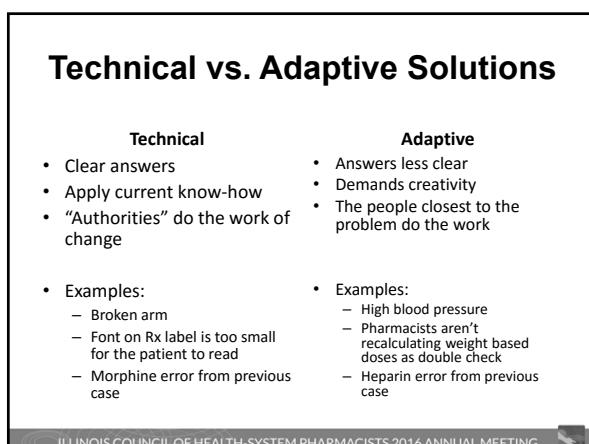


Considering Process Improvements

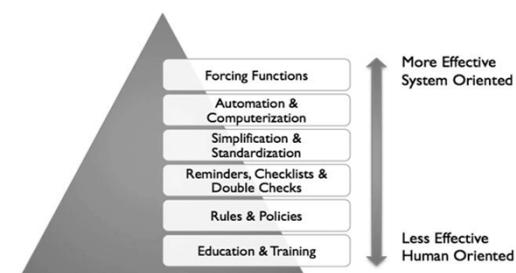
- A key question in considering potential process improvements is whether there are primarily **technical** or **adaptive** solutions to a problem.



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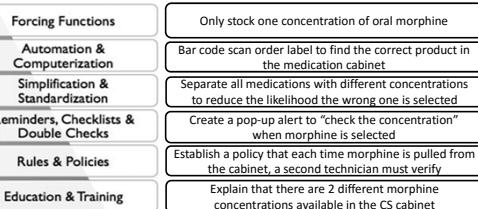
Hierarchy of Intervention Effectiveness



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Hierarchy of Intervention Effectiveness

Example: Morphine Error



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Promethazine is an anti-emetic drug that has been associated with severe tissue injury when administered intravenously. The Institute for Safe Medication Practices recommends implementing interventions that reduce the risk of these injuries. Which of the following interventions would be expected to most effectively prevent this adverse drug event?

- Educating staff about the risk of intravenous administration
- Forcing SC or IM ordering of promethazine by removing the IV route from the promethazine order form or computerized physician order entry system
- Developing a policy and procedure that describes methods for administering promethazine that reduce the potential for tissue injury
- Creating a pop up alert for nurses who administer promethazine, reminding them of the potential for severe adverse events that can result from IV administration

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Avoid Assumptions and Make it Structured IMPROVING COMMUNICATION

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Paper Folding Exercise

- This exercise requires listening to and following directions.
- As you hear the oral instructions, perform the requested task.
- No one may ask questions during this activity.
- You may use only the materials given to you for the exercise.
- You must close your eyes during the activity — no peeking!

- Fold your sheet of paper in half.
- Tear off the upper right-hand corner.
- Fold your paper in half again.
- Tear off the lower right-hand corner.
- Fold your paper in half.
- Tear off the upper left-hand corner.
- Fold in half a final time.
- Tear off the lower left-hand corner.
- Unfold your paper and hold it up.
- Open your eyes, look at the product and compare it with the other participants' products."

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Communication Errors in the Pharmacy

- Example:**
 - You are working in the OR pharmacy in the hospital. The anesthesiologist request a vial of cisatracurium for a case.
 - The pharmacist looks in the refrigerator, but there is no supply remaining.
 - The pharmacists tells the technician to go to central pharmacy to retrieve the cisatracurium.
 - The technician returns with cisatracurium, gives it to the pharmacist, who gives it to the anesthesiologist.

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Making Incorrect Assumptions



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Continued

- The anesthesiologist drew up 6 mL to get a 12 mg dose and administered it to the patient
 - Unfortunately this was 60 mg, instead of 12 mg

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Miscommunication

- The anesthesiologist didn't even know that a 10 mg/mL product exists
- The pharmacist didn't specify the concentration of cisatracurium to procure
- The technician didn't ask for clarification
- Every handoff of the medication was an opportunity to catch the error, simply by stating the product and concentration that was handed off

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Other Error Prone Communication Examples

- Draw up 5 of lasix
 - 5 mg? 5 mg/kg? 5 mL
- Order 100 of albumin
 - 100 gm? 100 mL?
 - 5%? 25%?
- Tell them to take one teaspoon of the amoxicillin three times a day
 - What concentration of amoxicillin?
 - Does the patient know how much a teaspoon is?
- The patient is on 3 and 3
 - Referring to 3 mg IV morphine Q 3 hours scheduled and 3 mg IV morphine Q 3 hours PRN breakthrough pain
 - Don't get me started

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Avoiding Miscommunication

- Never allow for assumptions when communicating drug data
- Always state the full drug details during handoffs
- Agree to a standardized method for giving and receiving communication
 - SBAR
 - Checklists

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SBAR

- The Joint Commission has recognized SBAR as a best practice for standardized communication in healthcare
 - S** – Situation
 - B** – Background
 - A** – Assessment
 - R** – Recommendation

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SBAR Background

- Developed by the US Navy to improve high stakes communication nuclear submarines
- Adopted by healthcare in the 1990's
 - Primarily used by nursing
- Studies suggest SBAR
 - Reduces the omission of critical information
 - Makes handoffs more concise
 - Enables assertiveness

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How SBAR Works

- Requires a cultural change
- Both parties of the communication should have a clear understanding of the SBAR structure
- Steps:
 - Organize the four elements of the briefing information in your head or on paper
 - Only include relevant and important data
 - Present your briefing
 - The recipient confirms, clarifies, or enhances your communication and carries out the necessary actions

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SBAR example

- Without SBAR:
 - Hi, I just got that vancomycin order for patient Johnson, did you mean to enter the 2 gram Q12 dose?
- With SBAR:
 - **S**-A dose of 2 grams Q12 hours was entered for patient Johnson
 - **B**-Vancomycin dosing is weight based at ~15 mg/kg, and the dosing interval is determined by renal function
 - **A**-The dose you entered appears too high @ 22 mg/kg, and the interval is too close, since the patients CrCl is 24 mL/min
 - **R**-Reduce the dose to 1250 mg, and extend the interval to Q 24 hours

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Other Methods to Improve Communication

- Employ the read back method
- Use structured handoff tools
- When working in a team, ALWAYS start with introductions
 - Checklist example
- Create space for communication (daily huddles)
- Ensure that clear procedures for escalation are in place

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Which of the following methods can reduce the incidence of miscommunication of “high stakes” information?

- A. Employing a form of structured communication, like SBAR
- B. Ensuring there are clear procedures for escalation when individuals cannot agree on a safe way to proceed
- C. When working in teams, always start by having each team member introduce themselves
- D. All of the above methods can reduce the risks of miscommunication

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Summing It Up

- Just Culture is an important part of cultivating a safe pharmacy environment
 - Focus on systems solutions, avoid blaming individuals
 - Encourages error reporting
- When implementing process improvements some strategies are more effective than others
 - Aim for higher level strategies when serious errors are likely or have already occurred
- Communication errors are common
 - Structuring communication can be more efficient and less susceptible to error

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Resources

- AHRQ
 - Safety surveys
 - Tools to improve communication
- ISMP
 - Safety action agendas
 - Decades of publications on improving safety in the pharmacy environment
- IHI
 - Courses on patient safety and quality improvement

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Thank you,

Stay safe!



The Expanding Role of Pharmacy Technicians - Investigational Drug Service

Margie Villarreal-Flores, CPhT
 Pharmacy Technician Specialist
 University of Illinois Hospital & Health Sciences System

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The Expanding Role of Pharmacy Technicians – Investigational Drug Service

I have no Financial Conflict of Interest to declare.

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Learning Objectives

1. Review goals and structure of the Investigational Drug Service (IDS).
2. Review Good Clinical Practice (GCP) and other guidelines.
3. Identify IDS technician responsibilities and job requirements.

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Specialty Areas

- Automation
- Controlled Substance
- Quality Assurance
- Sterile Compound
- Medication Reconciliation
- Check Tech Check
- IDS

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Investigational Drug Service

Goals:

- To assist and support investigators in meeting their obligations in conducting clinical drug research at the University of Illinois Hospital and Health Sciences System
- To help ensure the delivery of high quality health care, while minimizing the risks associated with participation in an investigational drug trial.

Structure and Staff:

- Approximately 100 drug studies
- 2 pharmacists, 1 technician

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IDS Services

Research Activities:

- Meet with investigators
- Site Selection Visits
- Site Initiation Visits
- Study Monitor Visits

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IDS Services

Special Compounding and other support:

- Provide blinded medication dosage forms
 - Utilizing a capsule filling system
- Develop randomization tables
- Provide customized dispensing packages if needed (blistercards, pill boxes)

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IDS Services

Drug Handling:

- Procurement – IDS assumes responsibility for ordering investigational agents when required.
- Storage – IDS provides the proper storage conditions, including segregation, security, light, temperature and humidity.
- Destruction – IDS performs on site destruction on study medication when requested by the study sponsor.

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IDS Services

Record Keeping:

- Maintains accurate records all drugs received and dispensed.
- Inventory and dispensing records are audited on a regular basis.
- Archives all Pharmacy records after study has final close out visit.

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IDS Technician Job Requirements

- Assist Pharmacists in daily operations of IDS.
- Must be accurate, detail-oriented, able to multitask, maintaining a clean, organized work environment.
- Must be a licensed and certified pharmacy technician (CPhT).
- Complete Continuing Education (CE) courses for recertification as required by the Department of Financial and Professional Regulation.
- Complete Mandatory CE, Net Learning Modules and training sessions deemed necessary by the department as assigned.

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IDS Technician Job Requirements (cont.)

- Complete the Collaborative Institutional Training Initiative (CITI) Good Clinical Practice (GCP) every 2 years for research.
- Completion of five years of progressively more responsible work experience that is comparable to that gained at the Pharmacy Technician III level
- Prepare sterile compounds per the department's policies and procedures for sterile product preparation.
- Able to navigate and utilize the pharmacy information system.

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Job Responsibilities

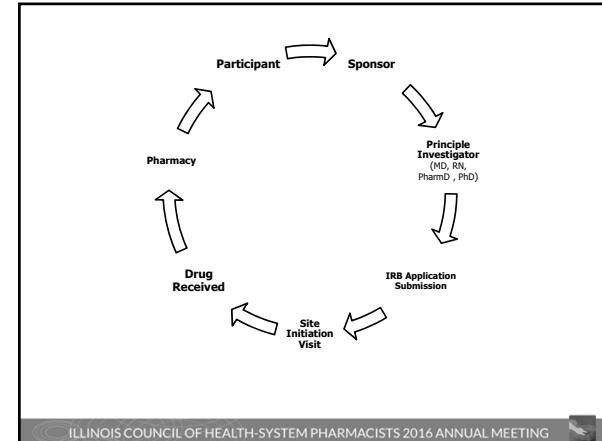
- Assure proper handling, storage, disposition record of investigational drugs in accordance with the hospital policy, Joint Commission, state and federal standard guidelines.
- Maintain accurate accountability of all drugs, shipping receipts, dispensation, maintain inventory and expiration, destruction and returns of sponsor supplied agents.
- Drug handling and preparation specifically, assist in the dispensing process including packaging, compounding, labeling and delivery.
- Ensure drug segregation, security and temperature, light, moisture and sanitation control.
- Maintain records all IRB approvals, patient orders and consent forms.

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Job Responsibilities

- Responsible for billing of Investigator quarterly or when deemed appropriate for IDS services.
- Maintain all new and old accounts with investigators.
- Updating investigator drug registration database and IDS activity study report.
- Must be able to work unsupervised and prioritize workflow.
- Assists with teaching and training of rotating P4 students and residents.
- Attendance and participation with scheduled meetings and in-services are required.

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GCP and IDS

- Good Clinical Practice (GCP, ICH E6)
 - an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve the participation of human subjects.

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Other IDS Guidelines

- Institutional Review Board (IRB)
 - to protect the rights and welfare of study participants. 21CFR§56
- Illinois Pharmacy Practice Act (Section 1330.530.c.4)
 - investigational drugs are to be stored, dispensed and properly labeled by the department of pharmacy.

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Other IDS Guidelines

- Hematology/Oncology Pharmacy Association (HOPA)
 - IDS Best Practice Standards

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A goal of the IDS is to assist and support investigators in meeting their obligations in conducting clinical drug research.

- A. True
B. False

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Good Clinical Practice (GCP) is:

- A. An International ethical and scientific quality standard
- B. Concerned with designing, conducting, recording & reporting trials
- C. Applied to animal & human participation subjects
- D. All of the above
- E. A & B

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Job requirements/responsibilities for an IDS technician include:

- A. Accurate and detail oriented
- B. Completion of CITI and GCP training every 2 years
- C. Ability to navigate pharmacy information system
- D. Maintain records of all IRB approvals
- E. Updating investigator drug registration database
- F. All of the above

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Glossary

- Principle Investigator - is the holder of an independent grant administered by a university and the lead researcher for the grant project, usually in the sciences, such as a laboratory study or a clinical trial.
- Protocol - a formal or official record of scientific experimental observations. A procedure for carrying out a scientific experiment or a course of medical treatment.
- Informed Consent- Patient Consent- Informed consent is the process of communication between a patient and physician that results in the patient's authorization or agreement to undergo a specific medical intervention.
- Clinical Trials- research studies that explore whether a medical strategy, treatment, or device is safe and effective for humans. These studies also may show which medical approaches work best for certain illnesses or groups of people.
- Study Monitor - make sure that the primary data are collected and recorded properly. They meet periodically with research coordinators and review their study records. They ensure that the reporting of adverse events is complete

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http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf (Accessed on 8/17/2016).
- Hematology/Oncology Pharmacy Association IDS Best Practice Standards.
http://www.hopax.org/uploads/files/2016/HOPA16_IDS_Guidelines.pdf (Accessed on 8/17/2016).
- Institutional Review Boards, 21CFR§56. http://www.ecfr.gov/cgi-bin/text-idx?SID=3ee286332416f26a91d9e6d786a604ab&mc=true&tpl=/ecfrbrowse/Title21/21tab_02.tpl (Accessed on 8/24/2016)
- Illinois Administrative Code, Section 1330.520.
<ftp://www.ilga.gov/JCAR/AdminCode/068/068013300E05300R.html> (Accessed on 8/24/2016)

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Pharmacy Technician- Acquired Medication Histories in the ED: A Path to Higher Quality of Care

David Huhtelin, PharmD

Emergency Medicine Clinical Pharmacist

SwedishAmerican Hospital–A Division of UW Health

September 17, 2016

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Disclosure

- Author of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation: None

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SwedishAmerican Hospital – A Division of UW Health

- Located in Rockford, IL
- 333 bed community hospital
- Level II Trauma Center
- Emergency Department
 - ~70,000 visits annually
 - Clinical Pharmacist and Medication History Technician coverage 10 hours a day, 7 days per week
 - Added PGY2 Emergency Medicine Program June 2016



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Learning Objectives

- Identify opportunities for expanded pharmacy technician roles in obtaining accurate, timely medication histories in the emergency department (ED)
- Describe the components and value of a pharmacy technician driven medication history program

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Medication History

- What is a medication history (MH)?
- Is it performed the same everywhere?
- What are the sources of information?
- How long should it take to complete each MH per patient?
- Is the quality of MH the same across providers?
- Is this an important part of workflow during an admission?

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Medication History

- First use of term “Medication History” in 1972
- The process of collecting a patient’s allergies, medications, compliance, and most recent doses
- Medication information gathered:
 - Formulation
 - Dose
 - Route
 - Frequency
 - Indication

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Sources of Information

- Patient
- Medication Vials
- Medication Lists
- Family Member
- Care Giver
- Pharmacy
- Primary Care Office
- Discharge Instructions
- Assisted Living Facility
- Insurance Claim History
- Veterans Affairs

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Length of History

- Multiple studies have shown the average MH performed by a technician takes 30 minutes
- Depending on complexity, a range of 10 minutes to 3 hours has been documented
- Depends largely on baseline information and how many sources have to be explored

Cater SW et al. J Emerg Med. 2015;48:230-238.

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Joint Commission

- 2005 National Patient Safety Goal #8
- Goal #8a and b: This requires hospitals to accurately and completely reconcile medications across the care continuum.
- #8a: The JCAHO will fully implement by January 2006 this requirement to develop a process for involving the patient upon admission in obtaining and documenting a complete list of his or her current medications. This process includes comparing the medications that the organization provides with those on the list.
- #8b: This requires organizations to communicate the patient's complete list of medications to the next provider of service whenever referring or transferring the patient to another setting, service, practitioner, or level within or outside the organization.

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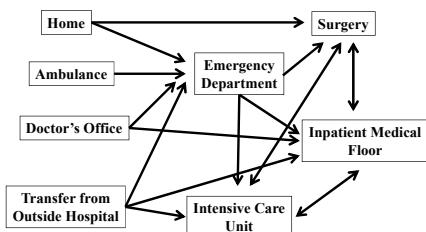
Impact of Medication Histories

- When performed by a pharmacist, one of two variables shown to significantly reduce medical errors that affected patient outcomes
- Medication error rates between 45%-76%
 - Most errors occur during admission
- Average cost of preventable medication error \$3,511
- Each error increased length of stay 3.37 days
- Pharmacist conducted results in a decrease of 128 deaths/year/hospital

Bond CA et al. Pharmacotherapy. 2002;22:134-147.
Sen S et al. Am J Health Syst Pharm. 2014;71:S1-S6.Hug BL et al. Jt Comm J Qual Patient Saf. 2012;38:120-126.
Bond CA et al. Pharmacotherapy. 1999;19:556-564.

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Patient Flow into Hospital



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Impact of Medication Histories in the ED

- Factors affecting medication accuracy range from patient ability to communicate to time restraints
- ED patients were missing at least one medication on 56% of histories
- ED patients had at least one dosage error on 80% of histories

Caglar S et al. J Emerg Med. 2011;40:613-616.

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Pharmacist vs. Other Providers

- Physicians had a 21% rate of discrepancy vs. pharmacist conducted medication history
- Patients less often had allergy and medication details documented with physician history
- ED provider entered medications were incomplete 78% of the time and corrected by a pharmacist
- Pharmacists had the least amount of discrepancies of any provider in one study:

	Pharmacist	Technician	RN
Discrepancies per Medication	0.16	0.36	0.59

*All values statistically significant

Reeder TA et al. Am J Health Syst Pharm. 2008;65:857-860.
Carter MK et al. Am J Health Syst Pharm. 2006;63:2500-2503.
Kramer JS et al. Hosp Pharm. 2014;49:826-838.

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Medication History Technician (MHT) vs. Other Providers

- No significant difference between technician and pharmacist acquired medication histories in the ED
- In the ED, MHTs were accurate 88% of the time vs. RNs at 57%
- High risk medications and anticoagulant last administration times were more frequently documented for MHTs

Johnston R et al. Can J Hosp Pharm. 2010;63:359-365.
Hart C et al. P T. 2015;40:56-61.

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Medication History Technician vs. Other Providers

- Counterpoint – The Med “Wreck” Tech
 - One study found that MHT performed histories did not result in a significant reduction of unjustified medication errors
 - Academic medical center
 - No pharmacy trained investigator on study
 - Physicians could have not looked at MHT list
 - Only allowed 2 hours after medication collection for admit orders, any changes after not counted

Cater SW et al. J Emerg Med. 2015;48:230-238.

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Metrics

- It can be difficult with limited resources to evaluate the effectiveness of your program
- Multiple factors involved including the experience of technician, ability to re-interview the patient, and how history is documented
- Classifying the severity and cost of an intercepted error can be difficult

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Metrics - Personnel

- Technician verifies another technician
- Technician verifies RN/other staff
- Pharmacy student verifies technician
- PGY-1 Resident verifies technician
- Pharmacist verifies technician

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Metrics - Data

- Length of history
- Sources used
- Prescription vs. OTCs
- Class of medication
- Comparison of providers
- Time from admission to completion of medication history
- Immunizations
 - pneumonia and influenza
- Data Collection
 - Medication Omission
 - Medication Commission
 - Incorrect/Missing Frequency
 - Incorrect/Missing Dose
 - Incorrect/Missing Formulation
 - Incorrect Drug
 - Incorrect/Missing Allergies
 - Incorrect/Missing Route

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Establishing A Program

- Provider buy-in
- Supplies (computer, cell phone, contact cards, etc.)
- Create a template indicating required fields for what the technician is to collect every interview
- Consider sample patient cases or test for competency
- Hire technicians that already have experience and familiarity with medications, strengths, frequencies, and dosage forms
- Supplement with pharmacy students

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Technician Work Space in ED



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Establishing A Program

- How will list be entered into EMR
 - Include your IT department and Nursing
- Decision on whether or not a pharmacist must sign off on accuracy of history
- How to report/pass off complex scenarios and regimens to pharmacist team
- How to notify providers a history is complete
- Quality assurance program

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3. Sen S, Siemianowski L, Murphy M, McAllister SC. Implementation of a pharmacy technician-centered medication reconciliation program at an urban teaching medical center. *Am J Health Syst Pharm.* 2014;71:51-56.
4. Hug BL, Keohane C, Seger DL, Yoon C, Bates DW. The costs of adverse drug events in community hospitals. *Jt Comm J Qual Patient Saf.* 2012;38:120-126.
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10. Johnston R, Saulnier L, Gould O. Best possible medication history in the emergency department: comparing pharmacy technicians and pharmacists. *Can J Hosp Pharm.* 2010;63:359-365.
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If I have funding for only one Medication History Technician, one of the most beneficial areas for the technician to staff would be:

- A. Same Day Surgery
- B. Intensive Care Unit
- C. Emergency Department
- D. Pharmacy

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Which of the following would not be collected during a medication history interview?

- A. Medication formulation
- B. Allergies
- C. Last taken dose
- D. Surgical history
- E. Frequency

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Which of the following is not a component of establishing a medication history technician program?

- A. Creating an interview template
- B. Administer patient cases/tests for competency
- C. Provider buy-in
- D. Supplement with pharmacy students
- E. Hire a new pharmacy technician graduate

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Questions?



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Residency Project Pearls

Michael Beshir, PharmD
Anne Misher, PharmD
Jasmine Shah, PharmD

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CONFLICTS OF INTEREST

The speaker and authors of this study have no actual or potential conflicts of interest

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OBJECTIVES

- Recognize the true cross-reactivity between penicillins, cephalosporins, and carbapenems in β -lactam antibiotics.
- Identify patients with reported β -lactam allergies who can safely tolerate β -lactam antibiotics

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THE IMPACT OF IMPLEMENTING A β -LACTAM ALLERGY GUIDELINE AT A LARGE ACADEMIC MEDICAL CENTER

Michael Beshir, PharmD
Rush University Medical Center

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RUMC POST-GUIDELINE STUDY

- Setting
 - Rush University Medical Center
 - Chicago, IL
 - 664-bed Academic Medical Center
- Intensive care units
 - Medical: 24 beds
 - Cardiac: 28 beds
 - Surgical: 22 beds
 - Neuroscience: 28 beds



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BACKGROUND

- β -Lactam class - most commonly reported medication allergies¹
 - 10% of patients report an allergy to penicillin²
- 80-90% of reported PCN allergies:
 - Negative PCN skin test suggesting PCN tolerance.²
- If PCN skin test positive → Likely IgE mediated → Life-threatening

1. Macy E, Contreras R. Health care use and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: A cohort study. J Allergy Clin Immunol. 2014;133(3):790-6.

2. Drug allergy: an updated practice parameter. Annals of allergy, asthma & immunology: official publication of the American College of Allergy, Asthma, & Immunology. Oct 2010;105(4):259-273.

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TYPES OF REACTIONS

Type I IgE-Mediated	Type II Cytotoxic (IgG, IgM-complement)	Type IV Cellular/delayed (T lymphocytes)
Severe -Immediate (<1 hr) -Anaphylaxis, angioedema, bronchospasms	Hemolysis, thrombocytopenia, neutropenia, or interstitial nephritis	-Contact dermatitis -Delayed non-urticarial rashes
Non-Severe -Delayed onset (1-72 hrs) -Rash, urticaria, wheezing -No anaphylaxis or angioedema	Type III: Immune complex (IgG, IgM immune complex)	Idiopathic -Serum sickness -Fever, rash, urticaria, lymphadenopathy, and arthralgias -Onset 7-14 days

Coombs R et al. *Clinical Aspects of Immunology*. 3rd ed. Oxford: Blackwell; 1975:671.

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PENICILLIN SKIN TEST

- Gold standard for ruling out IgE-mediated reactions
 - Negative predictive value: 97-99%
- Safe, with minimal discomfort
- Rapid → Less than one hour
- Drawbacks
 - Costly
 - Requires special technique

1. Park M, Markus P, Matesic D, Li JT. Safety and effectiveness of a preoperative allergy clinic in decreasing vancomycin use in patients with a history of penicillin allergy. *Ann Allergy Asthma Immunol* 2006; 97:681

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CROSS-REACTIVITY

- Cephalosporins
 - Historically: 10% reaction risk if allergic to PCN
 - 2/5 major reports were from the 1970's
 - Contaminated with trace amounts of PCN
 - Not PCN skin tested
 - Cross-reactivity risk ~2% when adjusted for reports prior to 1980.

Joint Task Force on Practice Parameters. *Ann Allergy Asthma Immunol*. 2010;105(4):259-273.

Dickson SD et al. *Clin Rev Allergy Immunol*. 2013;45(1):131-142.

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CROSS-REACTIVITY

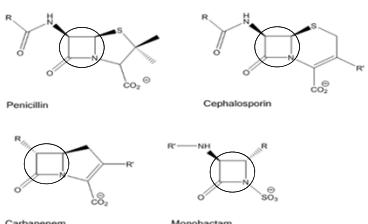
- Carbapenems
 - Limited data
 - Presumed high** due to structural similarity to PCN
 - 1988 study:
 - 20-40% correlation¹
 - 2014 systematic review²
 - 854 PCN allergic patients → Cross-reactivity < 1%

1. Saxon A, Adelman DC, Patel A, et al. Imipenem cross-reactivity with penicillin in humans. *J Allergy Clin Immunol* 1988; 82:213.

2. Kula B, Djordjevic G, Robinson JL. A systematic review: can one prescribe carbapenems to patients with IgE-mediated allergy to penicillins or cephalosporins? *Clin Infect Dis* 2014; 59:1113.

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β-LACTAM CHEMICAL STRUCTURE

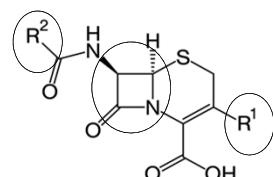


- Share a four-membered cyclic amide (lactam)

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β-LACTAM CHEMICAL STRUCTURE

- Cephalosporins



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CLINICAL IMPLICATIONS

- Patients with penicillin allergies are more likely to:
 - Receive broad spectrum antibiotics²
 - Experience antibiotic resistance¹
 - Greater drug toxicity
 - Suboptimal therapy
 - Higher costs

1. Macy E, Contreras R. Health care use and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: A cohort study. *J Allergy Clin Immunol.* 2014;133(3):790-6.
 2. Lee CE, Zembower TR, Fotis MA, et al. The incidence of antimicrobial allergies in hospitalized patients: implications regarding prescribing patterns and emerging bacterial resistance. *Arch Intern Med.* 2000;160:2819.

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RUMC DATA

- Prevalence of reported β -lactam allergies
 - 5808 of 93,854 (**6.2%**) patients admitted from 1/2011 to 12/2014
- Reported allergens

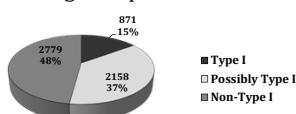


O'Driscoll T, Hanson A, Segreti J, Tobin M, Wang S. Implementation of β -Lactam Allergy Guidelines at a Large Academic Medical Center. ICAAC 2015 (Abstract S-1343).

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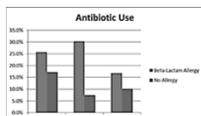
RUMC DATA

- Types of allergies reported



- Use of broader spectrum antibiotics

Antibiotic	RR	95% CI	P
Levofloxacin	1.6	1.53-1.68	<0.0001
Clindamycin	3.81	3.67-3.96	<0.0001
Vancomycin	2.03	1.93-2.14	<0.0001



O'Driscoll T, Hanson A, Segreti J, Tobin M, Wang S. Implementation of β -Lactam Allergy Guidelines at a Large Academic Medical Center. ICAAC 2015 (Abstract S-1343).

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OF PATIENTS WHO REPORT ALLERGY TO β -LACTAM ANTIBIOTICS, WHAT PERCENTAGE IS EXPECTED TO SAFELY TOLERATE THESE ANTIBIOTICS?

- $\geq 90\%$
- 60 – 80%
- 20 – 40%
- $\leq 10\%$

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A PATIENT ALLERGIC TO PENICILLIN IS _____ % LIKELY TO REACT TO CEFTRIAXONE.

- $\geq 50\%$
- 15-25%
- 10%
- $\leq 5\%$

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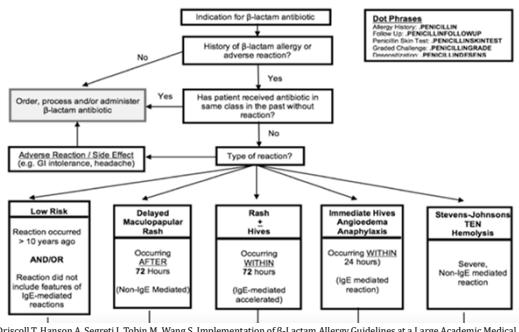
ADDRESSING THE PROBLEM

- What we know
 - Prevalence of *true* type 1 allergy \rightarrow low
 - Cross-reactivity of PCN and β -lactams \rightarrow low
 - PCN skin test reliable, but widespread use impractical

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RUMC GUIDELINE

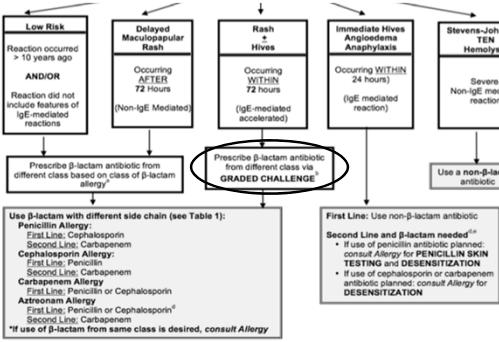
Figure 1. β -Lactam Allergy Practice Parameter Algorithm (Adapted from UV Health)



O'Driscoll T, Hanson A, Segreti J, Tobin M, Wang S. Implementation of β -Lactam Allergy Guidelines at a Large Academic Medical Center. ICAAC 2015 (Abstract S-1343).

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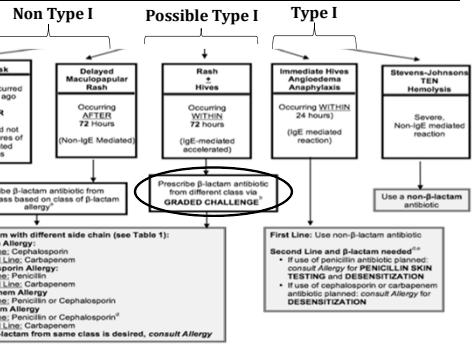
RUMC GUIDELINE



O'Driscoll T, Hanson A, Segreti J, Tobin M, Wang S. Implementation of β -Lactam Allergy Guidelines at a Large Academic Medical Center. ICAAC 2015 (Abstract S-1343).

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RUMC GUIDELINE



O'Driscoll T, Hanson A, Segreti J, Tobin M, Wang S. Implementation of β -Lactam Allergy Guidelines at a Large Academic Medical Center. ICAAC 2015 (Abstract S-1343).

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RUMC GUIDELINE

β -lactam Side Chain Table

Beta-Lactams with Similar Side Chains									
	Side Chain								
	Penicillins	Cephalosporins	Carbapenems	Monobactams	Monocyclic Lactams	Dihydro- β -lactams	Thienamycin	Other Beta-Lactams	None
Penicillins G, V	Penicillin G, V	Ampicillin	Carbenicillin	Amoxicillin	Acidophilus	Orfloxacin	Cephalexin	Cefotaxime	None
Ampicillin		100%	100%	100%	100%	100%	100%	100%	100%
Aztreonam						100%	100%	100%	100%
Cephalosporins									
Pip/Taze (Zervex)									
1 st	Cephalexin								
Cephalexin	100%	100%	100%	100%	100%	100%	100%	100%	100%
Cefaclor									
Cefaclor									
2 nd	Cefuroxime								
Cefuroxime	100%	100%	100%	100%	100%	100%	100%	100%	100%
Cefuroxime									
Cefuroxime									
3 rd	Cefoperazone								
Cefoperazone									
Cefoperazone									
Cefoperazone									
4 th	Cefotaxime								
Cefotaxime									
Cefotaxime									
5 th	Ceftriaxone								
Ceftriaxone									
Ceftriaxone									
Monobactams									
Mono									

Guide: Lactic acid-forming agent on vertical axis

Legend: \square Least likely to cause an allergic reaction (similar side chain)

\blacktriangle Intermediate option

\blacktriangledown Least likely to cause an allergic reaction (dissimilar side chain)

\square Use if no alternatives

\blacktriangle Most likely to cause an allergic reaction (dissimilar side chain)

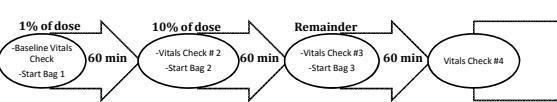
\blacktriangledown Avoid use

Bridged Agents: On RUMC Recommended

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GRADED CHALLENGE

- Cautious administration of medication to patient who is *unlikely* to be allergic
- Choose antibiotic with *dissimilar* side chain
- Process



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WHICH OF THE FOLLOWING PATIENTS IS THE BEST CANDIDATE FOR A CEFTRIAXONE GRADED CHALLENGE?

A.	Patient	Allergy	Reaction
A.	A	Penicillin	Nausea and Headache
B.	B	Penicillin	Rash
C.	C	Penicillin	Anaphylaxis and hives
D.	D	Penicillin	Rash, but tolerated ceftriaxone during previous admission

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GUIDELINE OBSTACLES

- Staff awareness and compliance
- Ambiguity in classifying type of allergy
- Increased liability and apprehension of reaction
- Ordering and preparation
- Requirement to consult Allergy and Immunology (A&I) prior to graded challenge attempt

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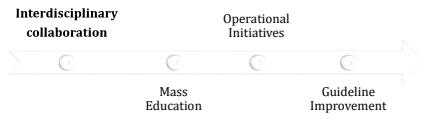
GUIDELINE IMPLEMENTATION



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PROMOTING GUIDELINE USE

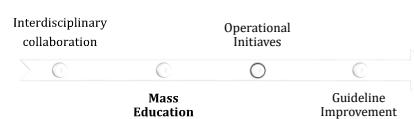
- Interdisciplinary collaboration
 - Allergy and Immunology (A&I)
 - Infectious Diseases (ID)
 - Nursing



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PROMOTING GUIDELINE USE

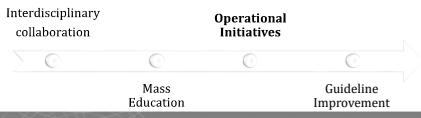
- Education
 - House-staff
 - ID Grand Rounds
 - Internal Medicine Noon Conference
 - Pharmacy
 - Pharmacy Grand Rounds
 - Nursing
 - In-services provided to different units



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PROMOTING GUIDELINE USE

- Operational Initiatives
 - Order-set development and optimization
 - November 2015
 - Technician instructions for IV preparation
 - On-going. Ex Ceftaroline added in March, 2016
 - Infusion pump library update
 - November 2015



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GRADED CHALLENGE ORDER SET



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GRADED CHALLENGE ORDER SET

Beta-Lactam Graded Challenge Module

- Vital Signs
 - Vital Signs - During Graded Challenge Process
- Nursing
 - Call Physician - Graded Challenge
- Medications - Treatment of Mild and Systemic Symptoms
 - epinephrine (ADRENALIN) injection 0.3 mg
 - epinephrine (ADRENALIN) 0.1 mg/mL (10,000) injection syringe 0.3 mg
 - epinephrine (ADRENALIN) 0.1 mg/mL (10,000) injection starting Today at 0046 until Thu 12/31/2045, Other, Systemic symptoms - see Admin instruction
 - diphenhydramine (BENADRYL) injection 25 mg
 - diphenhydramine (BENADRYL) injection 50 mg
 - methylprednisolone sodium succinate (SOLU-MEDROL) injection 125 mg

MAINTAIN starting Today at 0047 Until Specified. ** If patient requires Epinephrine or diphenhydramine, immediately stop protocol and call the primary service, and Allergy/Immunology fellow refers to plan of care instructions. ** If patient has a severe reaction, immediately stop protocol and call the primary service, and Allergy/Immunology fellow refers to plan of care instructions. ** Mild symptoms, such as new onset runny nose, itchy eyes, sneezing, mild rash, hives, and/or mild swelling of the lips, tongue, and/or throat, do not require stopping protocol. However, if these symptoms are severe enough to interfere with the patient's ability to tolerate the challenge, then stop protocol and call the primary service. ** Severe symptoms, such as difficulty breathing, hives, severe nausea, vomiting, diarrhea, chest pain, shortness of breath, and/or hypotension, do not require stopping protocol. Difficulty breathing and confusion are indicative of anaphylaxis and require Epinephrine. ** If the systolic blood pressure is less than 90 mmHg or the diastolic blood pressure is less than 60 mmHg, immediately give diphenhydramine intravenously (125 mg IV for adults). If necessary, repeat epinephrine and diphenhydramine every 15 minutes until the blood pressure is restored to greater than 90 mmHg. If these medications are required, then stop protocol and call the primary service. ** If the systolic blood pressure is less than 90 mmHg or the diastolic blood pressure is less than 60 mmHg, immediately give diphenhydramine intravenously (125 mg IV for adults). If necessary, repeat epinephrine and diphenhydramine every 15 minutes until the blood pressure is restored to greater than 90 mmHg. If these medications are required, then stop protocol and call the primary service.

MAINTAIN starting Today at 0047 Until Specified. The nurse is to provide the patient with their cell phone and explain possible allergic reactions. If the patient has any of the following symptoms: runny nose, itching, congestion, mild rash/red/crunch, hives, full body hives, difficulty breathing, shortness of breath, wheezing, hoarseness, and/or cramps.

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PROMOTING GUIDELINE USE

- Guideline Improvements
 - Removing A&I consult requirement for graded challenges
 - Elucidating definition of allergy type
 - Redesigning of β-Lactam Side Chain Chart

The diagram consists of four circles arranged horizontally. The first circle is labeled "Interdisciplinary Collaboration". The second circle is labeled "Operational Initiatives". Below these two is a horizontal arrow pointing right, containing the text "Mass Education". At the end of the arrow is a third circle labeled "Guideline Improvements".

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RUMC POST-GUIDELINE STUDY

- Purpose
 - Assess β-Lactam Allergy guideline implementation and impact of educational interventions
- Outcomes
 - Primary Endpoint
 - Number of **Graded Challenges**
 - Secondary Endpoint
 - Use of broad-spectrum antibiotics
 - (vancomycin, levofloxacin, clindamycin) and aztreonam
 - Use of β-Lactams

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RESULTS

Types of Allergies

Pre-guideline Jun - Dec 2014 N=200	Post-guideline Jun - Dec 2015 N=200												
<table border="1"> <tr> <td>Type 1</td> <td>39%</td> </tr> <tr> <td>Non-Type 1</td> <td>28%</td> </tr> <tr> <td>Possible Type 1</td> <td>34%</td> </tr> </table>	Type 1	39%	Non-Type 1	28%	Possible Type 1	34%	<table border="1"> <tr> <td>Type 1</td> <td>34%</td> </tr> <tr> <td>Non-Type 1</td> <td>36%</td> </tr> <tr> <td>Possible Type 1</td> <td>31%</td> </tr> </table>	Type 1	34%	Non-Type 1	36%	Possible Type 1	31%
Type 1	39%												
Non-Type 1	28%												
Possible Type 1	34%												
Type 1	34%												
Non-Type 1	36%												
Possible Type 1	31%												

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RESULTS

- Graded Challenge Attempts

Number of Graded Challenges

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RESULTS

- Primary Outcome
 - 12 Graded Challenges
 - 7 of 12 → Jan - March 2016
 - 6 of last 7 *without* A&I consult
 - With the exception of 1 patient, all were able to safely tolerate graded challenge
 - Deviation from protocol
 - Allergy documentation updated to allow future use of tolerated agent

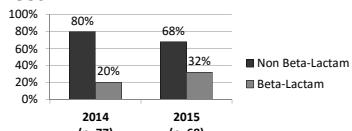
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RESULTS

- Secondary Endpoints
 - Use of **broad-spectrum** antibiotics

Outcome N (%)	Jun - Dec 2014 (N=200)	Jun - Dec 2015 (N=200)	P
Composite Use of Broad Spectrum Use	198 (99)	187 (94)	.58
• Vancomycin	79 (40)	53 (27)	< 0.05
• Levofloxacin	81 (41)	77 (39)	0.75
• Clindamycin	101 (51)	110 (55)	0.53
• Aztreonam	12 (6)	4 (5)	< 0.05

- β-Lactam Use



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CONCLUSION

- Implementation of a β-Lactam allergy guideline at a Large Academic Medical Center
 - Complex, multifaceted process
 - Requires
 - Strong collaboration
 - Education
 - Ongoing process improvement

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CONCLUSION

- Implementation of a β-Lactam allergy guideline at a Large Academic Medical Center
 - Correction of allergy history encouraging
 - Impact on **patient outcomes** → potential area of future study
 - Late surge in graded challenge attempts
 - Underscores importance of educational efforts and interdisciplinary collaboration

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CONCLUSION

- Ongoing Process
 - Protocol/operational improvements
 - Team education by pharmacists
 - Inter-professional collaboration
 - Next steps...
 - Multi-annual, retrospective review → Patient outcome focus

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WHICH OF THE FOLLOWING IS A CORRECT STATEMENT?

- Education is instrumental to the compliance and success of implementing a β-Lactam Guideline
- Interdisciplinary collaboration is an important early step in the process of guideline implementation
- Developing a β-Lactam Allergy Guideline is a must in order to increase use of β-Lactam antibiotics in penicillin-allergic patients
- A and B only
- All of the above

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ACKNOWLEDGEMENTS

- Shayna Ravindran, MD
- Sheila Wang, Pharm.D., BCPS AQ-ID
- Amy Hanson, Pharm.D., BCPS
- Christy Varughese, Pharm.D., BCPS
- Tristan O'Driscoll, Pharm.D.
- Mary Tobin, MD
- Sarah Won, MD, MPH

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1. Macy E, Contreras R. Health care use and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: A cohort study. *J Allergy Clin Immunol.* 2014;133(3):790-6.
2. Drug allergy: updated practice parameter. Annals of allergy, asthma & immunology: official publication of the American College of Allergy, Asthma, & Immunology. Oct 2010;105(4):259-273.
3. Coombs R et al. *Clinical Aspects of Immunology.* 3rd ed. Oxford: Blackwell; 1975:671.
4. Park M, Markus P, Matesic D, Li JT. Safety and effectiveness of a preoperative allergy clinic in decreasing vancomycin use in patients with a history of penicillin allergy. *Ann Allergy Asthma Immunol.* 2006; 97:681
5. Saxon A, Adelman DC, Patel A, et al. Imipenem cross-reactivity with penicillin in humans. *J Allergy Clin Immunol.* 1988; 82:213.
6. Kula B, Djordjevic G, Robinson JL. A systematic review: can one prescribe carbapenems to patients with IgE-mediated allergy to penicillins or cephalosporins? *Clin Infect Dis.* 2014; 59:1113.
7. Lee CE, Zembower TR, Fotis MA, et al. The incidence of antimicrobial allergies in hospitalized patients: implications regarding prescribing patterns and emerging bacterial resistance. *Arch Intern Med.* 2000; 160:2819.
8. O'Driscoll T, Hanson A, Segreti J, Tobin M, Wang S. Implementation of β-Lactam Allergy Guidelines at a Large Academic Medical Center. *ICAAC 2015 (Abstract S-1343).*

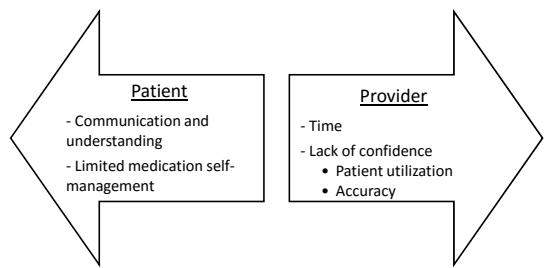
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Objectives

- Identify barriers to medication list utilization for physicians and other healthcare professionals
- Describe preliminary pilot data on understanding patient utilization of their medication list

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Limitations to Medication List Utilization



Leonhardt K, et al. Agency for Healthcare Research and Quality (US); 2008.

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Preferences for Patient Medication List Structure to Optimize Utilization

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University of Georgia
College of Pharmacy
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The speaker has no actual or potential Conflict of Interest in relation to this presentation.

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Medication Errors

- ≥ 6 medications can lead to medication errors¹
- Regimen complexity decreases adherence²
- The Joint Commission: 2008 National Patient Safety Goals³⁻⁴
 - Prioritized medication reconciliation
 - Patients should be provided with a medication card with a list of all medication
- 48-98% of medication lists contain discrepancies³

1. Leonhardt K, et al. Agency for Healthcare Research and Quality (US); 2008.
2. Nezi L, Martin A, Andreucci VE, et al. *Am J Nephrol.* 2011;34(1):171-6.
3. Chae SY, Chae MH, et al. *J Am Board Fam Med.* 2009;22:677-685.
4. <http://www.jointcommission.org/patientsafety/nationalpatientsafetygoals>

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Literature Review: Provider Perspective

Author	Objective	Study Outcomes
Rahmner et al.	General practitioners perspective	Prescribers feel responsible only for their own prescriptions
Leonhardt et al.	Interventions can improve medication list accuracy	Medication list accuracy improves with both patient and provider involvement

Leonhardt K, et al. Agency for Healthcare Research and Quality (US); 2008.
Rahmner P, et al. *Ann Fam Med.* 2010;8:40-46.

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Literature Limitations

- How can providers utilize the medication list to improve communication?
 - What aspects of the medication list are utilized for patient care activities?
- Do all healthcare providers utilize the same information from the medication list?
 - What variations exist between different healthcare providers?

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Pilot Study

- Survey conducted at Dreyer Medical Clinic and Midwestern University
 - Patients
 - Healthcare professionals
 - Physicians
 - Nurses
 - CMAs
 - Pharmacists
- Patient focus group
 - Patient insight in to medication utilization and contents

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Pilot Study

Healthcare Professionals (n=24)

- List used to know:
 - Which medications
 - When medication taken
- Preferred contents:
 - Brand/generic
 - Indication
 - Prescriber
 - Date medication started
 - Allergies/intolerances

Patients (n=41)

- Survey
 - Use list to know indication
 - Preferred contents:
 - When to seek care
 - Directions
- Focus Group
 - Format of medication list could be improved

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Survey Expansion

Improve Survey

Question wording

Single Clinic Site

Outpatient health professionals only

Sample Size

Few physician responses with pilot study

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Primary Aim

Primary Aim 1

- Determine how physicians utilize medication lists generated by the electronic health record (EHR)

Hypothesis

- Medication lists are not being utilized to the fullest potential

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Primary Aim

Primary Aim 2

- To identify physician desired content and formatting of an optimal medication list in order to assist in defining a standard

Hypothesis

- Desired content will vary among physicians; however, it is anticipated common themes in design will emerge

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Study Methods

- Study Design
 - Cross-sectional Survey
 - Physicians
 - Email distribution of survey
- Distributed throughout Illinois

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Criteria

Inclusion

- Active Illinois license
- Email listed within database provided by 3rd party affiliate of American Medical Association

Exclusion

- Unable to complete survey in English

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Survey Procedures

- Estimated sample size: ~5000 physicians
 - Completion rate: 24%
 - Anticipated completed: 1200 surveys
- Incentive
 - 1 of 3 \$10 gift cards

Cook JV et al. BMC Health Serv Res. 2009;9:160.
Sheehan KB. J Comput Mediat Commun. 2006;6(2).

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Study Methods

- Obtain contact information for physicians across the state of Illinois
- Send surveys via email link to SurveyMonkey.com
- Send reminder to participants one week after initial email

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Survey

- Estimated time to complete: 5-10 minutes
- Revisions incorporated based on pilot study results
- Demographics
- Section 1: Medication list utilization
 - Which
 - When
 - How
 - Why

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Survey

- Section 2: Preferred medication list characteristics
 - 13 Questions:
 - Brand/generic
 - Prescriber
 - Adverse effects
 - Start date
 - Date of next refill
 - Efficacy
- Section 3: How medications are arranged
 - Alphabetical
 - Indication
 - Time of day
 - Start date

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Statistical Analysis

- Descriptive statistics

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Results

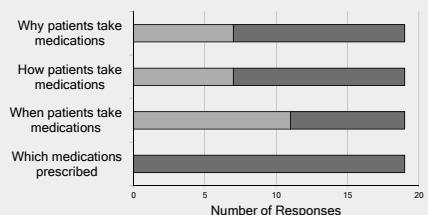
Characteristics of Survey Respondents
n=18

Male, (%)	68
Average age, years	52
Average years in practice	21
Ethnicity	
White, (%)	61
Black, (%)	5.6
Asian, (%)	22.2
Hispanic, (%)	11.1
Area of Practice	
Internal Medicine, (%)	11
Family Practice, (%)	17
Specialty, (%)	72

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Results

What type of information do you gain from medication lists provided by patients?
n=18



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Results

Characteristic	Likert Scale Response n=18
Medication allergies	2.89
Indication	2.72
Intolerance to medications	2.72
Start date of medication	2.61
Adherence rate of medication	2.61
Reasons of discontinuation of previous medications	2.50
Medication generic name	2.44
Anticipated duration of therapy	2.39
Prescribing provider	2.34
Medication brand name	2.28
How medication is taken	2.28
When medication is taken	2.22
Goal of therapy	2.17
History of previous medications	2.17
Next refill date	2.11

* Likert scale response of 1 indicates Not at all helpful, 2 Somewhat helpful and 3 Very helpful

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Limitations

- Low response rate
- Limited external validity
 - Limited to those listed within registries
- Survey not validated
- Response bias
- Physicians only

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Future directions

- Increase survey distribution
 - Other healthcare professionals
 - Patients
 - Partner with Illinois Medication Safety Coalition
- Create optimized, standardized medication list
 - Determine outcomes with various medication list formats
 - Recommend changes to EHR providers

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Research Lessons

- Survey as a research tool
 - Survey question writing
 - Sample size
 - Survey distribution method
- Creating a line of research
 - Importance of pilot data
 - End goal vs "next steps"

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Which of the following is a barrier for provider utilization of medication lists?

- A. Lack of time to verify accuracy of the medications on the patient's medication list.
- B. Understanding of the electronic health record functions, resources and capabilities.
- C. Patient utilization of medication cards to provide an accurate medication list.
- D. Patients often have an abundance of medication self-management and adherence.

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Which of the following statements is correct?

- A. Pilot data to date shows no improvements are necessary for patient medication lists.
- B. Patient focus group data demonstrates areas for improvement including formatting of the medication list.
- C. An initial pharmacist survey demonstrated that pharmacists most prefer for medications to be listed chronologically.
- D. There is an abundance of literature assessing how patients and providers are currently utilizing medication lists.

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Acknowledgements

- Jill S. Borchert, PharmD, BCPS, BCACP, FCCP
- Mary Ann Kliethermes, BS, PharmD
- Spencer Harpe, PharmD, PhD, MPH
- Midwestern University Chicago College of Pharmacy

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Optimizing Medication Batching Workflow to Reduce Waste in a Pediatric Setting

Jasmine Shah, PharmD
PGY2 Pharmacy Resident: Drug Information
Chicago, IL

The speaker and authors of this study have no actual or potential conflicts of interest

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Learning Objectives

- Describe lean methodology processes and how they can be applied to pharmacy workflow.
- Identify factors specific to the inpatient pediatric setting that can contribute to increased medication waste.

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Approximately what percentage of dispensed medications from an inpatient pharmacy are later wasted?

- A. 0% - 10%
- B. 10% - 20%
- C. 20% - 30%
- D. 30% - 40%

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Background

- Studies estimate **20-30%** of medications are wasted on average at a healthcare institution
- Given the increasing costs of healthcare, a multi-faceted approach including an efficient dispensing workflow is **necessary to reduce waste**

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Project Background

What causes medication waste?

- Potential modes of waste can occur between time of preparation of medication to time of administration:
 1. Provider could change the dose
 2. Change the route of administration
 3. Drug could be discontinued
 4. Patient could be discharged
- The longer the period of time between time of preparation to time of administration- **the more potential for waste**

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Background

- Waste potential is especially pertinent in the **pediatric population**
- Majority of pediatrics dosing is **weight-based** and thus medications prepared are **patient-specific doses**
 - Require individual drawing up in pharmacy
 - Drawn up drug cannot be re-used
 - Short expiration
- Pediatric patients' weight and fluid status are more frequently changing, often requiring dose adjustments

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Background

Methods of getting the medication to the floor:

- **Just-in-time Dosing:** Each medication dose is dispensed from pharmacy right before scheduled administration time
- **Automated Dispensing Cabinets:** Medications are stocked on nursing unit and released at administration time of order
- **Cart-fill/Batch:** Scheduled medications are prepared and delivered in batches in advance based on scheduled due times

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Which of the following is a disadvantage of "just-in-time" preparation?

- A. Increased amounts of expired medications on the floor
- B. Can result in delays getting the medication to the floor
- C. Often requires keeping high amounts of inventory on hand to supply large batches
- D. Increased amount of medications being wasted

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Study Objective

- To construct a multiple-batch medication preparation schedule in the pediatric setting and evaluate its impact on medication waste outcomes

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Study Design

- Post-implementation case study
- Study Setting: Rush University Medical Center Pediatric Satellite
- Study Period: Pre-intervention: 07/2015 - 10/2016; Intervention: 12/2015
- Inclusion Criteria: All pediatric oral and IV medications prepared in the batch

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Rush University Medical Center:

- 664 bed tertiary care academic medical center located in Chicago
- Pediatric pharmacy section within a large hospital that serves only the pediatric floors
- Floors covered:
 - Peds Psych - 15 beds
 - PICU - 18 beds
 - Gen Peds - 22 beds
 - Mother/Baby - 23-34 beds
 - Labor & Delivery - 10 beds



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Methods

- Step 1: Analysis of current data and resources to determine an optimum new batching schedule
- Step 2: Implementation of new batching schedule
- Step 3: Analysis of post-implementation data collection

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Methods – Step 1: New Batch

- An optimum batching schedule was determined based upon the following data points retrieved from EPIC
 - Medication ordering times
 - Medication administration times
- Current workflow and resources were also taken into account to determine feasible schedule

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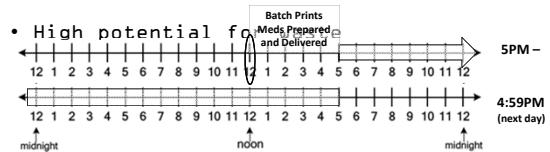
Pre-Implementation Workflow

- Pediatric satellite open from 7:00 - 20:30
- 7:00 - 15:30: AM pediatric pharmacist and AM pediatric technician
- 12:00 - 20:30: PM pediatric pharmacist and PM pediatric technician
- Rounding generally occurs from 08:00-12:00
- Consult services round in afternoon

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Pre-Implementation Workflow

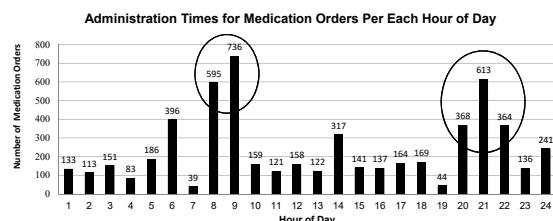
- Pre-implementation: one batch for pediatric medications that need to be compounded
- Batch prints at noon with all oral and IV pediatric medications that are scheduled for 24 hour period



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Pre-Implementation Workflow

- Peak administration times: 9AM, 9PM



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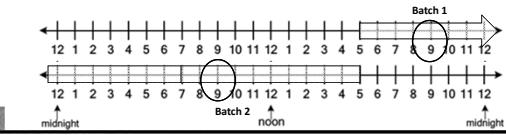
Methods – Step 2: Implementation

Current Batch

Batches	Print Time	Admin Time of Meds
Peds Batch 1	12:00	17:00 – 16:59(next day)

New Batch Times

Batches	Print Time	Admin Time of Meds
Peds Batch 1	12:00	17:00 – 06:59(next day)
Peds Batch 2	17:30	07:00(next day) – 16:59(next day)



Methods – Step 2: Implementation

- Implemented a 10-day pilot with the new batch on weekdays only
- Updated technician and pharmacist workflows
- Education and training for affected groups
 - Pharmacy Technicians
 - Pharmacists

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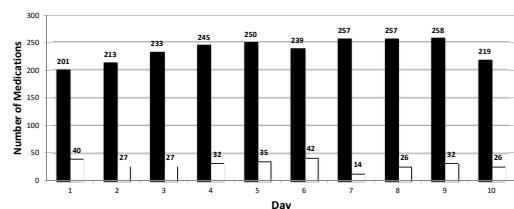
Methods – Step 3: Post- Implementation

- Primary outcome:** Percentage of batched medications being wasted per day
 - Waste: defined as medications that were discontinued before being given, data from EPIC
- Secondary outcomes:**
 - Reasons for discontinuation
 - Medications/classes that were discontinued
 - Times of discontinuation

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Results – Primary Outcome

Total Number of Medications in Batch Made vs Wasted



% of Medications Wasted Per Day

- Ranged 5% - 20%
- Average = 13%

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Results – Primary Outcome

- Post-Intervention vs. Historical Data

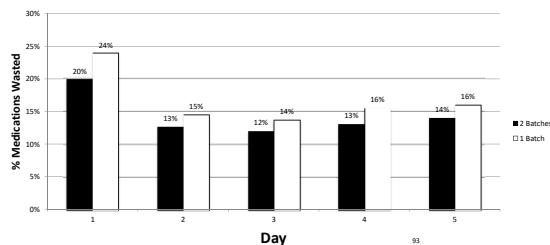
Month	% Wasted Medications (average)
December Pilot	13.01%
October	14.96%
September	14.87%
August	15.20%
July	15.10%

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Pilot Results

Post-Intervention (2 Batches) vs. Pre-Intervention (1 Batch) Workflow
Range: 2-4% difference

% of Medications Wasted

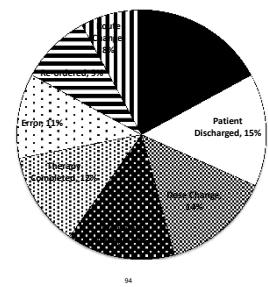


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Pilot Results

Discontinuation Reasons

Reason	# Meds
Unknown Reason	28
Patient Discharged	24
Dose Change	23
Frequency Change	23
Therapy Completed	20
Error	18
Re-ordered	15
Route Change	13



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Pilot Results

- Medications Wasted - Highest Quantity

Medication	Dosage Form
Chlorothiazide	Injection
Furosemide	PO Suspension
Hydrocortisone	Injection
Piperacillin/Tazobactam	Injection
Hydrochlorothiazide	PO Suspension
Methylprednisolone	Injection

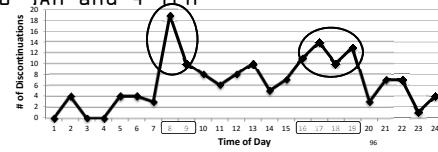
- Most common classes: diuretics, anti-hypertensives, steroids, and antibiotics

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Pilot Results

- ~1/3 of discontinued doses were discontinued 3 hours or less before the due time

- Most common discontinuation periods of time for wasted medications were 8-9 AM and 4-5 PM



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Challenges/Limitations

- Small sample size
- Fluctuating number of doses
- Only estimating waste based on medications discontinued early
 - many other forms of waste
- Feasibility of "ideal" batch times
- Inability to separate P0 batch from IV batch
- Labor cost was not collected

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Conclusion

- Implemented a two-batch workflow which resulted in a 2-4% decrease in medication waste and an associated relative reduction in cost of ~14%
- For our institution, inefficiencies in process and increase in technician/pharmacist work time outweighed medication waste reduction with this workflow
- Collected data used to determine future approaches to reduction in waste

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Future Directions

- Target IV only
- High-cost medication classes
- Frequently adjusted medication classes
- Adjustment in batch times
- Standardized dosing
- Expanding use of Automatic Dispensing Cabinets

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Advice for Future Implementers:

- Important factors to consider:
 - Pediatric bed census
 - Current batch size
 - Current number of returns/wasted medications
 - Number of available technicians
 - IT ability
 - High cost waste
- Daily evaluation once implementation is started

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Acknowledgements

- Beth S. Shields, PharmD
Associate Director, Pharmacy Operations
- Jessica Jacobson, PharmD, BCPPS
Clinical Pharmacist, Pediatrics
- Kristen Welsh, PharmD, BCPPS
Clinical Pharmacist, Pediatrics

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Questions for Panel?

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Supporting Literature

STUDY: Effects of a new sterile product preparation and delivery process on operational efficiency and cost

- **Pre-implementation:** preparing ~853 doses per day using two batches; wasting 26% of meds in every batch
- **Post-implementation:** increased to four batches a day
- Reduction of wasted medications from 26% to 18% resulting in a **28% reduction of total cost of waste**

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Advice for Future Implementer:

- Potential **benefits** of multiple batches:
 - Less first doses will need to be made, as they will just default to part of the batch
 - Better allocation of technician time during in-between batch hours
 - Less potential for medication errors because possibly incorrect doses not being sent up 24 hours in advance and staying in Pyxis until removed

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Advice for Future Implementer:

- Potential **disadvantages** of multiple batches:
 - Lack of efficiency in terms of doubling up on set-up, preparation, delivery, checking times
 - Single dose vials (<24 hr expiration): may be better to draw up all doses at once instead of use multiple vials
 - Drawing up from extended-use batched bags may limit cost savings, no need for new vial every time

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Pilot Results

- ~1/3 of discontinued doses were discontinued 3 hours or less **before** the due time

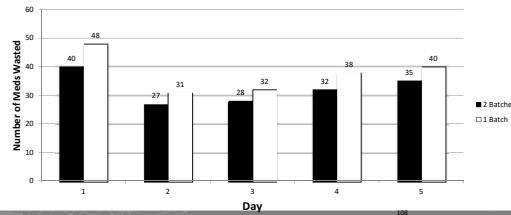
- Most common discontinuation periods of time for **wasted medications** were 8-9AM and 4-7PM



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Pilot Results

- Post-Intervention Workflow vs Pre-Intervention Workflow
- Absolute Number of Medications Wasted in New (2 Batches) vs. Simulated Old (1 Batch) Workflow



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Background

- **Just-in-time Dosing:** Each medication dose is dispensed from pharmacy right before scheduled administration time
 - **Advantage:** minimize waste, minimize expired medications on floor
 - **Disadvantage:** time intensive and labor intensive
- **Automated Dispensing Cabinets:** Medications are stocked on nursing unit and released at administration time of order
 - **Advantage:** time and labor efficient, no delay in medication
 - **Disadvantage:** need for increased stock, expired meds, limited meds
- **Cart-fill/Batch:** Scheduled medications are

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Supporting Literature

STUDY:

- **Hospital setting:** 205-bed children's center, ~1850 doses/day
- **Pre-Implementation:** One Batch
- **Post-Implementation:** Three Batches
- **Results:**
 - Waste reduction: 28.7% per batch → 19.7% per batch
 - Net annual savings: \$97,940
- **Conclusion:** 3 batches reduced waste; greater than 3 batches per day would not be cost-effective due to increased labor costs

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Innovative Pharmacy Services: Boldly Going Where No Pharmacist Has Gone Before

Julio Rebollo, PharmD, BCPS, AE-C
Jennifer Mazan, PharmD
Lisa Palmisano, PharmD, BCACP

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Learning Objectives

- Examine the role of the pharmacist in collaborative care clinics
- Discuss the development of a pharmacy consult service within interprofessional sites
- Explore methods to enhance student learning in a collaborative setting
- Identify metrics used to track the impact of collaborative efforts on patient outcomes

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Pharmacists Walking on New Territory to Save Limbs: The Collaboration Between Pharmacists and Podiatrists

Julio A. Rebollo Pharm.D., BCPS, BC-ADM, AE-C
ICHP 2016 Annual Meeting
September 17, 2016

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Disclosures

- I have no actual or potential conflict of interest in relation to this presentation.

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Wound Healing Center (WHC)

- Located within a safety-net hospital
- 12 beds
- 20-30 patients per day
- Outpatient/inpatient wound management:
 - Diabetic foot ulcers (DFU)
 - Neuropathic
 - Venous stasis
 - PVD
 - Decubitus ulcers

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WHC

- Wound management team
 - Doctors of podiatric medicine (DPMs)
 - Physicians
 - Surgeons (vascular)
 - Physical therapists
 - Nurses
 - Wound specialists
 - Wound care technicians
 - Pharmacy
 - Medication delivery

DPM: Doctor of podiatric medicine

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Patient case

- 63 y/o HM, Spanish speaking, newly diagnosed diabetic, malnourished, not seen a physician in past 15 yrs
- Recently d/c from hospital, no PCP
- DFU, OM, HBV, current smoker (~5/d)
- Pain: 5-10/10, unable to walk 50 ft.
- No surgeries



HM: Hispanic male; PCP: primary care provider; OM: osteomyelitis; HBV: Hepatitis B virus

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Case

- Medications
 - Metformin 1000 BID
 - Ertapenem 1 g IV daily
 - Outpatient infusion clinic
 - Hydrocodone/APAP 7.5mg/325 mg PRN
- Monitors BG QID
 - Per granddaughter- FBG ~280s and PPBG 350s despite diet changes (lots of fruit)
- Laboratory results from admission
 - A1C:14.5%; LDL:37, TG: 50; HDL:7; TC: 74; Alb: 1.0



FBG: Fasting blood glucose; PPBG: Post prandial blood glucose

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What is the most appropriate intervention a pharmacist can do at this time?

- A. Order an A1C, CMP, pre-albumin and another fasting lipid panel to confirm current results
- B. Obtain immunization history and administer the recommended vaccinations per CDC
- C. Add insulin, an ACEI/ARB, a high-intensity statin and aspirin to his current diabetes treatment
- D. Counsel the patient and family and schedule an appt. with the next available PCP asap

CMP: comprehensive metabolic panel; CDC: Centers for disease control

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Background

- DFUs; major medical, social and economic problem
- >25% of the patients with diabetes will develop a foot ulcer and have a 40% higher 10-year mortality
- ~90% of amputations are preceded by foot ulcers that could potentially be prevented
- >70,000 non-traumatic lower-limb amputations in 2010
- ~50% who had a major limb amputation will die within 5 years
- Recurrence >50%

1. Centers for Disease Control and Prevention. National diabetes statistics report: Estimates of diabetes and its burden in the United States, 2014. Atlanta, GA: U.S. Department of Health and Human Services; 2014.
2. Diabetes Care 2010; 33(10):2292-2293.
3. Int Wound J 2007; 4: 286-287.
4. JAMA 2005; 293:217-228.

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Guideline recommendations

- A foot specialist and a “multidisciplinary” team approach:
 - Decrease the risk of foot infections
 - Decrease complications
 - Optimize glycemic control
 - Educate patient
 - Diabetes education, smoking cessation, nutrition
 - Prevent recurrence!

1. JAMA 2005; 293:217-228
2. Wound Rep Reg 2006; 14:680-692.
3. Diabetes Care 2016;39(Suppl 1):S1-S2.

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Role of the pharmacist in a WHC

- Medication optimization
- Education
 - Patient, podiatrist and physician
- Monitoring
- Coordination of care
- Immunizations!!!

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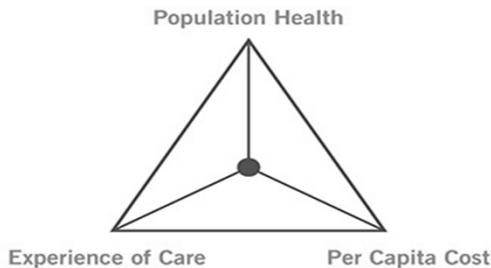
Assessment question

When initiating new clinical pharmacy services the following should be considered:

- A. Patient demographics such as age, sex, race and insurance
- B. How to improve patient outcomes, experience and decrease costs
- C. Location of the clinic, access and the cost of services to be provided
- D. Developing a collaborative practice agreement and define roles

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The IHI Triple Aim



Institute for Healthcare Improvement. Available at: http://www.ihi.org/Engage/Initiatives/TripleAim/Documents/Triple-Aim-Triangle_withTitle%20while%20background%20v3.jpg. Accessed August 9, 2016.

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Establishing clinical pharmacy services in a WHC

- Identify your population of care and measures
- Form a team
- Test your idea
- Monitor outcomes

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An efficient way pharmacists can evaluate and implement a new clinical service in a clinic is by:

- A. Performing a retrospective chart review to obtain a baseline
- B. Performing patient satisfaction surveys before and after a service
- C. Using a model for improvement such as the Plan-Do-Study-Act (PDSA)
- D. Forming a team that includes pharmacy students on rotation

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Establishing clinical pharmacy services in a WHC

- Identify your population of care
 - Ambulatory care services
 - WHC was not part of the original plan
 - Work with IT
 - ~~1600 admissions related to diabetes!
 - Setting goals
 - Time frame
 - How to measure improvement (Triple Aim)
 - A1C, BP, LDL, medication adherence...
 - Readmissions, amputations, reinfections...
 - Patient satisfaction,

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Establishing clinical pharmacy services in a WHC

- Form a team
 - Physician champion
 - Support services
 - Promote services
 - Net-work
 - Other clinicians?
 - Involve IT
 - Engage your leadership
 - Pharmacy director/manager
 - Anyone from the C-suite!

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Establishing clinical pharmacy services in a WHC

- Testing the idea
 - Plan, Do, Study and Act
 - A1C screening-inpatient
 - Provide DM education during admission
 - Diabetes education group/individual-outpatient
 - Missing appointments
 - Transportation issues
 - Costs
 - Promote pharmacy services among physicians/clinics
 - Pre-filled referral DM forms
 - Wound clinic!

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Establishing clinical pharmacy services in a WHC



Institute for Healthcare Improvement. Available at: <http://www.ihi.org/resources/Pages/HowtoImprove/ScienceofImprovement/HowtoImprove.aspx>. Accessed August 9 2016.

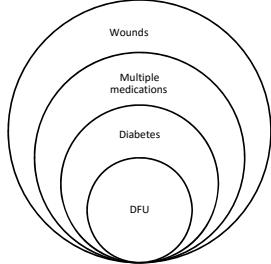
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Establishing clinical pharmacy services in a WHC

- WHC
 - About 90% appt show rate
 - Transportation provided
 - About 70% diabetes
 - Ulcer recurrence/reinfection
 - Multiple readmissions
 - Multiple medications/comorbidities
 - Lack of primary care provider f/u or multiple providers
 - Polypharmacy

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Establishing clinical pharmacy services in a WHC



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Establishing clinical pharmacy services in a WHC

- More PDSA cycles!
 - Laboratory monitoring
 - Medication optimization
 - Challenging- Need a PCP
 - Patient education (empower)
 - Disease state, medication, nutrition...
 - Follow up
 - How often?
 - Communication with PCP
 - Challenges: unable to contact or no PCP

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Establishing clinical pharmacy services in a WHC

- Monitoring outcomes
 - Assess your progress
 - How many patients have you seen?
 - What services have you provided?
 - Are your measures improving?
 - A1Cs
 - BP
 - Medication adherence
 - Readmissions
 - Patient satisfaction
 - Do you need to add new/tailor services?
 - Patient-centered care

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Patient case- A month later

- Pt has now a PCP, next appt in 4 wks
- Pain 2-3/10, able to walk
- Still smoking
- BG monitoring log
 - FBG:180s
 - 2Hr PPBG 200s
- Two new medications added



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Patient case- A month later

- Medications:
 - Metformin 1000 BID
 - Ertapenem 1 g IV daily
 - Outpatient infusion clinic
 - Hydrocodone - Acetaminophen 7.5mg/325 mg PRN
 - Lantus 15 units QHS
 - Lisinopril 20 mg



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What is the most appropriate intervention a pharmacist can do during this encounter?

- A. Assess diabetes control, and adjust insulin after discussing with PCP
- B. Refer to a smoking cessation specialist or the quit line; pt ready to quit
- C. Recommend walking 20-30 min per day at least 5 days per week
- D. Measure BG, blood pressure and discuss medication adherence

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Integrating pharmacy students and enhancing learning in a WHC

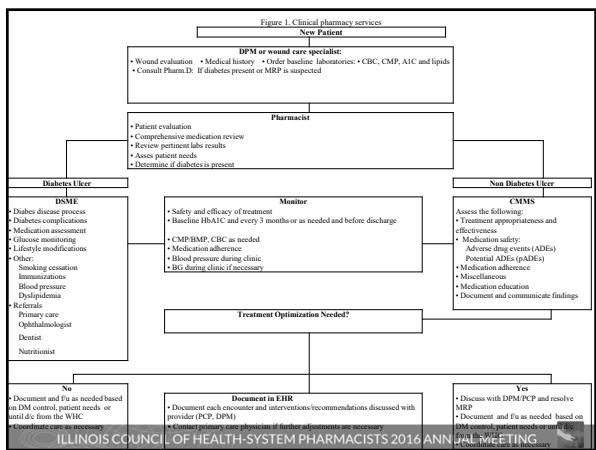
- Ambulatory care rotation
 - Description of rotation
 - Patient population
 - You will see blood!
 - Interdisciplinary team
 - DPMs, PTs, MDs, surgeons, MD students/residents
 - Common disease states
 - All chronic conditions!
 - DM→ ulcer
 - Student references
 - ADA standards of care

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Integrating pharmacy students and enhancing learning in a WHC

- Role of the pharmacy student
 - Optimize medications
 - SOAP format!
 - Monitoring
 - Drug safety
 - » Adjusting, stopping, adding, refilling meds
 - Drug efficacy
 - Empowering the patient!
 - Student intervention process
 - 10 patients seen at the same time
 - Average wound care visit 60-90 min
 - Population of focus

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Patient case: 6 months later

- Pt is doing well
- FBG: 120s, PPBG 150s
- During wound care appointments, pharmacy students continued to:
 - Optimize medications
 - Provide education:
 - Diabetes
 - Nutrition
 - Medication
 - Smoking cessation!
 - On NRT
 - Non-pharmacological recommendations
 - Monitor labs

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Patient case- 6 months later

- Medications:
 - Metformin 1000 BID
 - Nicotine patches
 - Lantus 30 units QHS
 - Lisinopril 20 mg
 - Aspirin 81 mg
 - Atorvastatin 80 mg
- Labs
 - A1C 6.5%; HDL 49; LDL 92; Alb 4.0

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What service can a pharmacy student provide during this visit?

- A. Administer PPSV23 and influenza vaccines today
- B. Refer the patient to the certified diabetes educator
- C. Adjust insulin based on the most recent A1C of 6.5%
- D. Refer the patient to GI to initiate hepatitis treatment

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Integrating pharmacy students and enhancing learning in a WHC

- Common clinical interventions

- Patient education

- Medication
- Diabetes
- Life style
- Smoking cessation
- Immunizations!

- Monitoring

- Labs: A1C, CMP/BMP, Lipids, BP, BG
- Medication adherence
- ADEs, pADEs

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Integrating pharmacy students and enhancing learning in a WHC

- Coordination of care

- Referrals
- Collaborating with PCP
- Transitions of care
- Communication with other clinicians, social workers, case managers

- Tracking results and interventions!

- Potential for research

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Tracking patient outcomes- Metrics used

- Back to the triple aim!

- Improve outcomes

- A1C
- ADEs, pADEs

- Improve patient experience

- Patient satisfaction
- By WHC

- Decrease cost

- Amputations \$\$\$?
- ED visits

ADE: Adverse drug events; pADEs: potential adverse drug events

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Tracking patient outcomes- Challenges

- Documentation!
 - Multiple EHRs
 - Laboratory results
 - MEDITECH
 - PCP clinics
 - » Athena
 - Outpatient WHC notes
 - MEDITECH
 - Paper charts!
 - Excel
 - No access to PCP notes
 - Did the pt f/u?

HER: Electronic health record

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Tracking patient outcomes- Challenges

- Documentation...
 - Pharmacist's notes
 - Diamed
 - Only certain providers had access to it
 - Fees to obtain certain reports
 - Fax notes, recommendations
 - Excel
 - Tracking lab values and interventions

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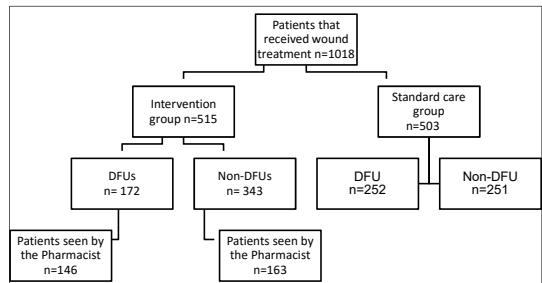
Tracking tool used

- ADE and pADEs tracking tool
 - Adapted from the University of Southern California School of Pharmacy Medication Therapy Intervention & Safety Documentation Program User Manual (v 7.0, last updated 4/6/2012)

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Table 1. Commonly Identified Medication Related Problems (MRPs) in a WHC	
Treatment Appropriateness and Effectiveness	<ul style="list-style-type: none"> Untreated medical problem Drug dosing not adequate for treatment goals Treatment not optimal based on current evidence/ guidelines Monitoring standards not being followed (for disease state)
Medication Safety (ADEs/pADEs)	<ul style="list-style-type: none"> Drug dosing excessive for treatment goals Incomplete/improper directions No indication for medication prescribed Polypharmacy- Rx not needed/duplication Contraindication Adverse Drug Reaction (ADR) Drug interaction Lab/diagnostic test indicated, not ordered Abnormal lab result not addressed Medication overuse or misuse Dose discrepancy between patient use & prescribed therapy Using expired medications
Non-adherence & patient variables	<ul style="list-style-type: none"> Medication underuse/poor adherence Dosage form not reasonable for patient Inadequate patient self-management Patient dissatisfied or refuses treatment

Retrospective chart review 2010-2015



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Patient population

Table 2. Characteristics of the Patients that Received Wound Care Treatment at the WHC		
Characteristic	Intervention Arm (2013-2015) n=515	Standard Care Arm (2010-2012) n=503
Age, mean ± S.D. yr	59±15	64±16.4
Sex (%)		
Male	307 (59.6)	308 (61.2)
Female	208 (40.4)	195 (38.8)
Race (%)		
Black	164 (31.8)	111 (22)
Hispanic	309 (60)	342 (68)
Other(White, Asian)	42 (8.2)	50 (10)
Ulcer Type (%)		
Diabetic foot ulcers	343 (66.6)	252 (50)
Non diabetic foot ulcers:	172 (33.4)	251 (50)
Traumatic	39 (7.6)	28 (5.6)
* Other	133 (25.8)	223 (44.3)
Ulcers with Initial Diameter > 20cm ²	89 (17.3)	66 (13.1)

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Interventions/recommendations conducted by pharmacists/students

Variable	Intervention Arm (n=515)
Patients seen by the pharmacist	309
Patient Encounters	888
Encounters Per Patient	2.9
MEPs encountered (%)	44.1
Adherence and Effectiveness	
Safety	138 (31.3)
ADE's	155 (35.1)
poor's	72 (16.3)
Non-Adherence and Patient Variables	83 (16.0)
Miscellaneous	99 (22.4)
Interventions (%)	49 (11.1)
Patient Education	450 (40.8%)
Monitoring	218 (19.0%)
Coordination of Care	193 (18.3%)
Medication Optimization	203 (19.2%)
Other	11 (1%)
Diabetes Initiations	
Patients with documented diabetes	146
Patients with prior DSME (%)	12 (8.2)
Patients who received DSME at the WHC (%)	146 (100)
Initial A1C % (n=129), mean ± S.D.	9.48 ± 2.4
Final A1C % (n=87), mean ± S.D.	8.30 ± 1.7
Change in A1C (%)	1.18

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Which of the following was the most common intervention performed by pharmacists/students at the WHC?

- A. Identifying medication related problems related to safety
- B. Administering influenza and pneumonia vaccines
- C. Providing patient education during each visit to the WHC
- D. Optimizing medications and monitoring laboratory values

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Questions?

- Seven months later!!!



"Common people achieve uncommon results when they work as a team..."

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Acknowledgements

- All my students who completed their rotation at the WHC and participated in this project
- Drs. Valdes, Kulekowskis, Lopez and all the WHC staff at NAH WHC
- Charlene A. Hope, MS, Pharm.D., BCPS

NAH: Norwegian American Hospital

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Clinical Pharmacy Services in a Dental Clinic – an Innovative and Dynamic Interprofessional Team

Lisa Palmisano, PharmD, BCACP
Jennifer Mazan, PharmD
ICHP 2016 Annual Meeting
September 17, 2016

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Disclosures

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

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Case

BP is 77 year old female with a history of atrial fibrillation, HTN, T2DM, COPD and osteoporosis. Current medications include:

- Albuterol
- Alendronate
- Aspirin
- Lisinopril
- Metformin
- Budesonide/formoterol
- Warfarin

HTN = hypertension
T2DM = Type 2 Diabetes Mellitus
COPD = Chronic Obstructive Pulmonary Disease

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Dental clinic - background

- 50,000 + patients/year
- Student – driven clinic
 - 150 third year and 150 fourth year dental students
- Clinic structure:
 - 12 suites (~ 16 operatory rooms)
 - Dental student teams
 - At one time approximately 150 patients at clinic

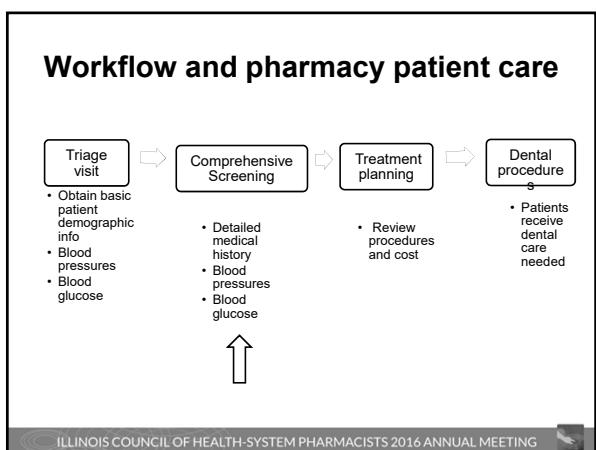


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Pharmacist role in a dental clinic

- Innovative interprofessional patient care approach
- Literature scarce/none
- Medication experts
 - Obtain additional patient medical information
 - Review medications and medical conditions
 - Identify dental medication interactions
 - Discuss recommendations to enhance dental patient care

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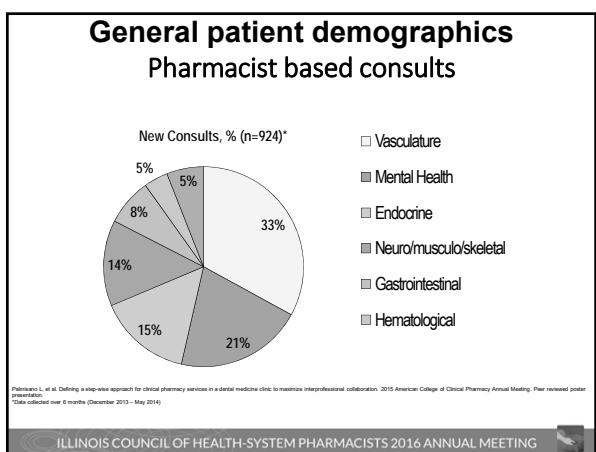


General patient demographics
Pharmacist based consults

New Consults*	Average \pm SD (range)
Number of medications average \pm SD (range)	7.4 \pm 5.4 (0 – 28)
Number of disease states average \pm SD (range)	4.0 \pm 2.7 (0 – 14)
Consult duration (min) average \pm SD (range)	8.2 \pm 4.0 (5 – 20)

Palmisano L, et al. Defining a step-wise approach for clinical pharmacy services in a dental medicine clinic to maximize interprofessional collaboration. 2015 American College of Clinical Pharmacy Annual Meeting. Peer reviewed poster presentation.
*New consults = 227. Data collected over 6 months (December 2013 – May 2014).

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BP is 77 year old female with a history of atrial fibrillation, HTN, T2DM, COPD and osteoporosis.

Current medications include:

- Albuterol
- Alendronate
- Aspirin
- Lisinopril
- Metformin
- Budesonide/formoterol
- Warfarin

HTN = hypertension

T2DM = Type 2 Diabetes Mellitus

COPD = Chronic Obstructive Pulmonary Disease

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How can the pharmacist ensure this patient is getting the best dental care?

- A. Obtaining additional patient medical information such as the value and date of last INR
- B. Assess patient's risk of developing osteonecrosis of the jaw due to bisphosphonate use
- C. Assess patient's blood pressure to ensure value is not high enough to warrant vasoconstrictor dose limit
- D. Discuss with patient the importance of rinsing mouth after using budesonide/formoterol
- E. All of the above

INR = international normalization ratio

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Establishing services...

1. Connecting between pharmacy and dental providers
2. Identify the dental patient populations of high risk needs
3. Establish a protocol of high risk dental patients
4. Determine the best process for intervention
5. Develop plans for management of the dental populations consulted
6. Evaluate the efficiency and use of the protocol

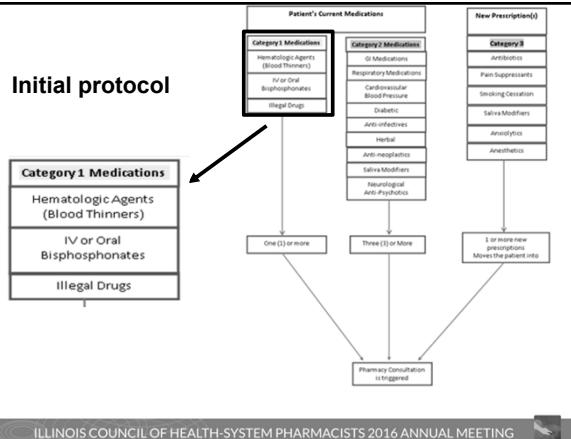
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Where to begin...

1. Connecting between pharmacy and dental providers
2. Identify the dental patient populations of high risk needs
3. Establish a protocol of high risk dental patients
4. Determine the best process for intervention
5. Develop plans for management of the dental populations consulted
6. Evaluate the efficiency and use of the protocol

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Initial protocol



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Establishing services...

1. Connecting between pharmacy and dental providers
2. Identify the dental patient populations of high risk needs
3. Establish a protocol of high risk dental patients
4. **Determine the best process for intervention**
5. Develop plans for management of the dental populations consulted
6. Evaluate the efficiency and use of the protocol

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Process of intervention

- Trial and error
- Learning the dental process of patient information intake
 - What questions does the pharmacist need to ask?
- Re-assess process of dental care during visit
- Where can pharmacy make the most impact?

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Establishing services...

1. Connecting between pharmacy and dental providers
2. Identify the dental patient populations of high risk needs
3. Establish a protocol of high risk dental patients
4. Determine the best process for intervention
- 5. Develop plans for management of the dental populations consulted**
6. Evaluate the efficiency and use of the protocol

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Dental patient - treatment protocols/recommendations

Utilizing dental resources and literature:

- American Dental Association
- American Heart Association
- American Academy of Orthopedic Surgeons
- Malamed - Handbook of Local Anesthesia. 6th ed. 2013.
- Little and Falace's - Dental management of the medically compromised patient. 8th ed. 2013.

Protocols:

- Blood pressure
- Diabetes
- Anticoagulation
- Hepatic/Renal dysfunction
- Others

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Which of the following dental patients would benefit most from screening by a pharmacist?

- A. 57 yr old with a history of anxiety and depression.
- B. 42 yr old male with well controlled HTN.
- C. 71 yr old with a history of T2DM, HTN, & CKD.
- D. 38 yr old who recently recovered from acute sinusitis.

HTN = hypertension
T2DM = Type 2 Diabetes Mellitus
CKD = Chronic Kidney Disease

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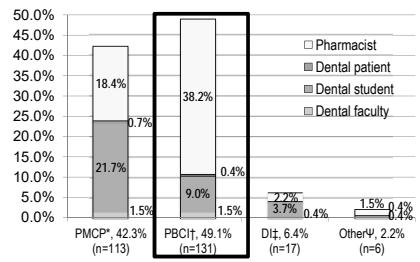
Establishing services...

1. Connecting between pharmacy and dental providers
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3. Establish a protocol of high risk dental patients
4. Determine the best process for intervention
5. Develop plans for management of the dental populations consulted
- 6. Evaluate the efficiency and use of the protocol**

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Retrospective research – chart review

What were the reasons and who prompted the consult?



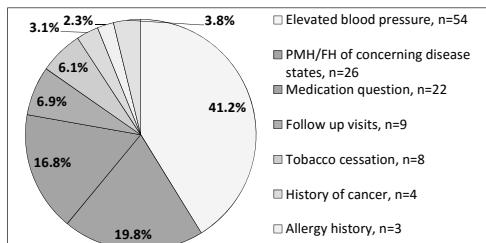
Palmarino L, et al. Defining a step-wise approach for clinical pharmacy services in a dental medicine clinic to maximize interprofessional collaboration. 2015 American College of Clinical Pharmacy Annual Meeting. Peer-reviewed poster presentation.

* PMCP=Pharmacy Medication Consult Protocol; † PBCI=Patient-based Case Inquiry; ‡ DH=Drug Information; ¶ Other reasons were due to a single follow-up visit

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Retrospective research – chart review

What were the specific triggers in the PBCI?

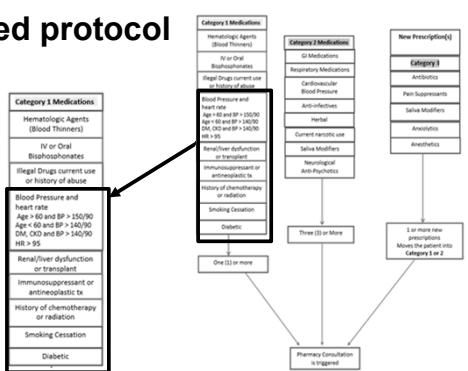


Other triggers: OGI/urea dysfunction/n implant, n=2 (1.3%); Medication non-compliance, n=2 (1.3%); illicit drug use/self-medicated, n=1 (0.8%)

Prakash L, et al. Defining a step-wise approach for clinical pharmacy services in a dental medicine clinic to enhance interprofessional collaboration. 2015 American College of Clinical Pharmacy Annual Meeting. Peer reviewed poster presentation.

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Modified protocol



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Continuous evaluation of the protocol

- Recognizing potential areas of missed patient care opportunities
- How to address the concerns
- Recurrent themes of medical conditions/medications

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Most of the pharmacy consults were being prompted by which of the following?

- A. Pharmacy medication protocols
- B. Pharmacy based case inquiries – reasons outside of the protocol
- C. Drug information questions
- D. Other

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Which condition triggered the most Patient Based Case Inquiries(PBCI) by the pharmacist?

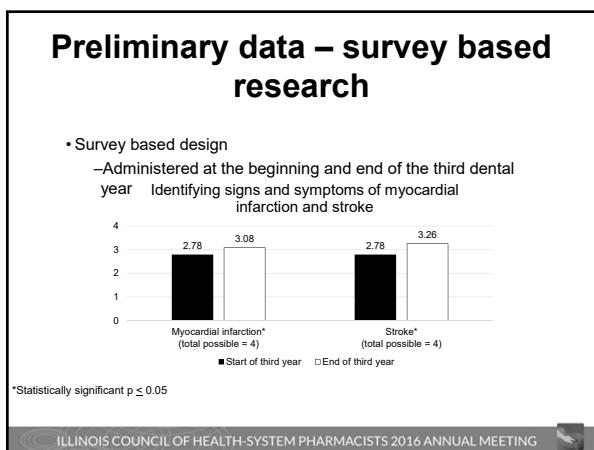
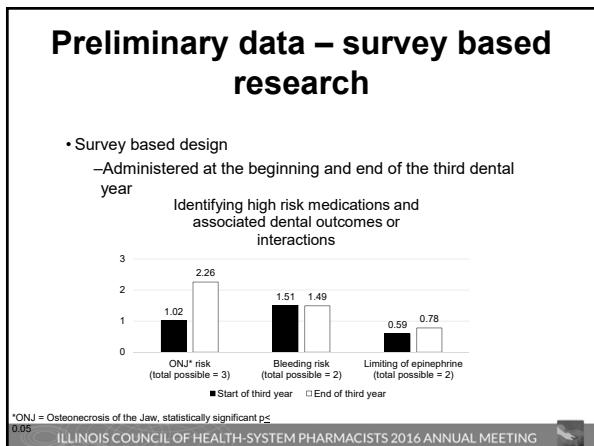
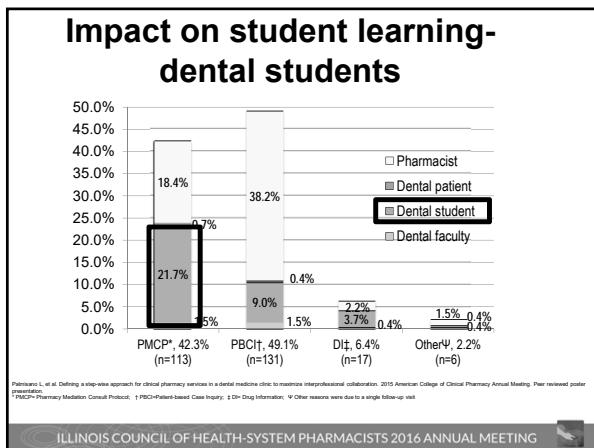
- A. Medication allergies
- B. History of cancer
- C. Elevated blood pressure
- D. Anticoagulation use

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Impact on student learning

- Dental students
- Pharmacy students

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Pharmacy Student Learning

- Ambulatory care rotation
- Interdisciplinary education
- Learning experiences
 - Medication Reconciliation
 - Review/incorporation of guidelines
 - Drug information questions from dental faculty
 - Patient Counseling
 - Communication and interviewing skills

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Pharmacy Student Learning

- Pharmacy students teach dental students
 - Chronic disease state management
 - HTN, T2DM, anticoagulation, immunosuppression, smoking cessation, osteoporosis
- Pharmacy students learn unique dental aspects
 - Local anesthetics
 - Drug interactions
 - Dental implications of medications-xerostomia

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Pharmacy Student Learning

- Get students involved in all aspects
 - Screenings
 - Patient consults
 - Dental student consults
 - In-services to dental faculty and students

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Pharmacy consults by dental students were prompted approximately _____ % of the time.

- A. 20
- B. 50
- C. 75
- D. 100

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The development of protocols in a dental clinic not only enhances patient safety but also enhances student learning. Which of the following medical conditions is most effectively managed by a protocol?

- A. Osteoporosis
- B. Smoking cessation
- C. Type 2 Diabetes Mellitus
- D. Hypertension
- E. C and D

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Tracking outcomes Challenges and methods used

- Interventions incorporated into pharmacy consult note – easy to track
- IT support
- EMR
- Support by administrators/deans/dental faculty
- Executive report completed annually

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Description of Interventions

Type	Description
1	Assessing for signs/symptoms (s/sx) of disease events (e.g. myocardial infarction (MI)/stroke, hypo/hyperglycemia, etc.)
2	Recommending specific consults to be obtain by specialists or primary care physicians
3	Recommending specific medication therapies/adjustments (e.g. pain management, lidocaine/epinephrine, antibiotics, etc.)
4	Inquiring on the safety and efficacy of the medications (i.e. side effects of local anesthetic after administration)
5	Medication review during consult or if thorough assessment of medications and oral health implications in consult form
6	Contacting the primary care provider or specialist via telephone to review the patient case (e.g. elevated blood sugars > 300)
7	Educating the patient, student , and/or faculty on monitoring and medication information (e.g. managing hypoglycemia)
8	Written/printed handouts provided (e.g. tobacco cessation products, list of free clinics, drug information, etc.)
9	Assisting in patients with high risk needs (e.g. coordinating care to the emergency room)
10	Drug information, smoking cessation, updated medication list

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Most Common Interventions

Total interventions for FY 2015-2016 = **3140**

Type 7 - Educating the patient or student on monitoring parameters (e.g. signs and symptoms of myocardial infarction/stroke), medication interactions, and disease state management and preventative measures (e.g. minimizing the risk of hypoglycemia)
—most frequently and consistently **21.7%**;

Type 3 - Recommending specific medication therapies/adjustments (e.g. pain management, etc.)
—occurred consistently **19.1%**; and

Type 1 - Assessing for signs and symptoms of myocardial infarction or stroke, hypoglycemia, depression, etc.
—occurred consistently **19.0%**.

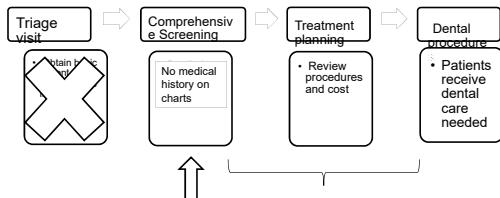
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Which of the following was the most tracked intervention?

- A. Educating the patient or student on monitoring parameters, medication interactions, and disease state management and preventative measures
- B. Recommending specific consults to be obtain by specialists or primary care physicians
- C. Medication review during consult or if thorough assessment of medications and oral health implications in consult form
- D. Drug information, smoking cessation, updated medication list

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Current challenges Change of workflow



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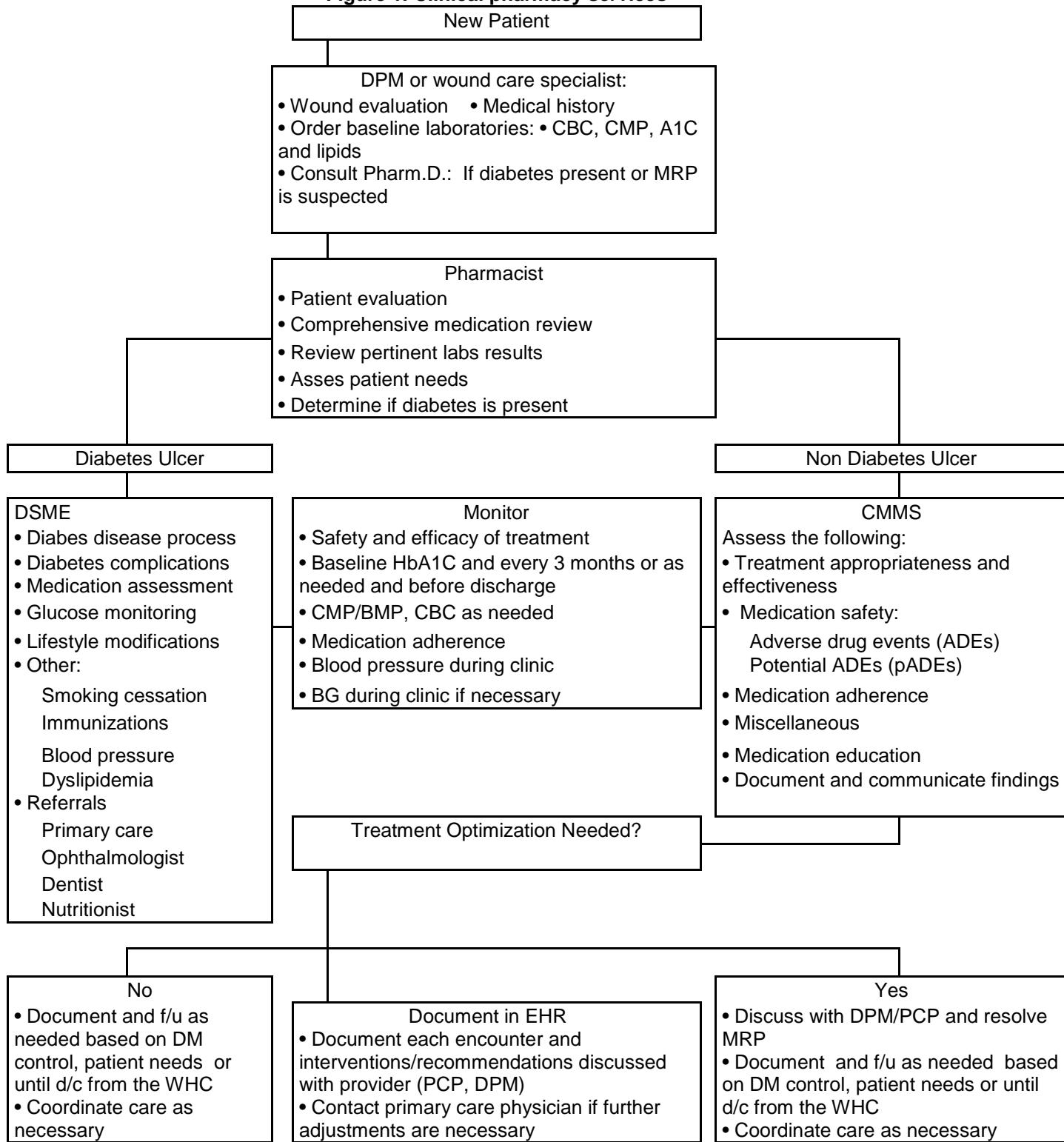
Questions



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Pharmacists Walking on New Territory to Save Limbs: The Collaboration Between Pharmacists and Podiatrists – slides 30 and 40

Figure 1. Clinical pharmacy services



* DPM: doctor of Podiatric medicine, MRP: medication related problem.....

Pharmacists Walking on New Territory to Save Limbs: The Collaboration Between Pharmacists and Podiatrists – slides 30 and 40

*Table 1. Commonly Identified Medication Related Problems (MRPs) in a WHC

Treatment Appropriateness and Effectiveness	<ul style="list-style-type: none">· Untreated medical problem· Drug dosing not adequate for treatment goals· Treatment not optimal based on current evidence/ guidelines· Monitoring standards not being followed (for disease state)
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Non-adherence & patient variables	<ul style="list-style-type: none">· Medication underuse/poor adherence· Dosage form not reasonable for patient· Inadequate patient self-management· Patient dissatisfied or refuses treatment
Miscellaneous	<ul style="list-style-type: none">· Inadequate refills between visits· Non-formulary/not cost effective drug choice· No follow-up/appointment with PCP

* Adapted from the University of Southern California School of Pharmacy Medication Therapy Intervention & Safety Documentation Program User Manual (v 7.0, last updated 4/6/2012)

Peace, Love, and Understanding Leadership

Desi Kotis Pharm.D FASHP
 Erick Borkowski Pharm.D
 Whitnee Caldwell Pharm.D
 Sharon Karina Pharm.D
 Candidate

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Conflicts of Interest

- We have nothing to disclose relating to this topic.

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Strategies for Successfully Integrating Life & Career

Sharon Karina
 P3 Pharmacy Student
 Midwestern University

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Objective

- Discuss strategies for successfully integrating life and career

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Now that we're connected 24/7, have you ever:

- Been contacted to cover someone's shift on your day off?
- Had to leave work to pick up a sick child?
- Needed to handle a work emergency during dinner?

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What about the students here?



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It's not about balance...

- We can't dedicate equal and separate time to life and career (or school)
- Striving to do this can lead to burn out



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Integration

Community

Mind, body,
spirit YOU Family

Career

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But how? The answer may surprise you!

- Identify what you're passionate about - how does it relate to other areas of your life?
- Be flexible with leaning in and out of roles
- Recognize you've likely been forced to be adaptable already

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Story time!

- 12 hours before my 7AM therapeutics final, I get a phone call...
- Dad versus final - which one did I choose?

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Integration won.

- We are all more resilient than we may give ourselves credit for
- The key to successful integration is self awareness and adaptability

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A good example of integration is turning off your work phone when you arrive at home.

- A. True
B. False

False! Integration allows you freedom to move between work and other aspects of your life.

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A good example of integration is turning off your work phone when you arrive at home.

False! Integration allows you freedom to move between work and other aspects of your life.

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Integration means you must always be available for work 24/7.

- A. True
- B. False

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Integration means you must always be available for work 24/7.

False! Boundaries are good - the point is to establish them to your comfort level.

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A good way to start integrating is to first identify what you're passionate about in each area of your life.

- A. True
- B. False

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A good way to start integrating is to first identify what you're passionate about in each area of your life.

True! Knowing what you love about each aspect can show parallels between different areas - and make things 'click'.

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Integrating life instead of separating and balancing can lead to a happier and healthier you.

- A. True
- B. False

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Integrating life instead of separating and balancing can lead to a happier and healthier you.

True! And without the added stress of trying to give 100% to every area, you may even find you perform better.

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Peace, Love, and Understanding Leadership

Desi Kotis Pharm.D FASHP
Director, Pharmacy
Northwestern Medicine

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Objective

- List Barriers to recruiting and retaining women leaders as well as solutions to these barriers

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Fostering Women Leaders

The challenges are well known: women in business continue to face a formidable gender gap for senior leadership positions. Moreover, there are fewer and fewer women at each step along the path, although they represent the majority of entry level employees. Barriers are too well known: cultural factors, ingrained mindsets and mind locks, and stubborn forms of behavior, including a tendency to tap a much narrower band of women leaders than is possible given the talent pool.

McKinsey & Company, "Women in the Workplace," June 2015

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Why Focus on Developing Women Leaders?

- Talent
- Demographics
- Pragmatic realities



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Women Continue to be Underrepresented as Senior Leaders



Sources: Bureau of Labor Statistics (2011), EEOC Employer Information Report for Hospitals (2011), American Hospital Association (2010), American College of Healthcare Executives (2013).

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Is There Still a Glass Ceiling?



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Have you experienced or observed the glass ceiling phenomena in your career?

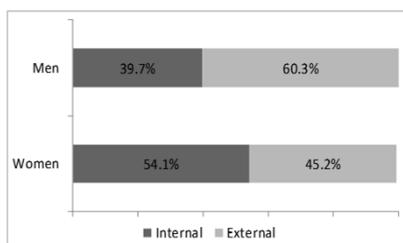
A. YES

B. NO

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Career Paths

Women are more likely to be promoted internally than hired externally.



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Factors Valuable to Career Success

Women cited specific factors as more helpful to their careers than men did, including:

- Leadership abilities
- Involvement in professional or community organizations
- Networking within their organizations
- Having sponsors to endorse them
- Access to flexible work practices
- Support from family

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Challenges to Career Advancement

Women identified challenges to career advancement:

- Lack of supportive supervisors
- Exclusion from informal networks
- Lack of senior role models "like me"
- inhospitable culture/biased attitudes
- Failure of senior leadership to help advance someone "like me"
- The need to prioritize family over work

Men identified different challenges to career advancement:

- Unwillingness to change organizations / companies
- Having an ineffective leadership style
- Lack of significant general or line management experience

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What? More Women?

Many factors you might think would be predictive of group performance were not. Group intelligence had little to do with individual intelligence.

Women's social sensitivity is higher. And team diversity - of every type -- is essential.



What Makes a Team Smarter?
More Women ...
Wolff & Malone, HBR
Jun 2011

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A Fitness Test for Your Top Team

- Where are the women in our talent pipeline?
- What skills are we helping women build?
- Do we provide sponsors along with role models & mentors?
- Are we rooting out unconscious biases?
- Are our policies helping or hurting?

Mckinsey & Company. Women Matter: a fitness test for your top team. January 2015

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How We Encourage Inspiring Women Leaders . . .

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“

There is a special place in hell for women who don’t help other women.”

Madeleine Albright

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Recruiting and Retaining Women Leaders



- Is the role a defining issue?
- Do women bring a different mindset to negotiation?
- Salary Issues
 - Fair market value
 - The process .
- Benefit issues

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LEADERSHIP

INTENTION . ATTENTION . RETENTION



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Dual Career Issues

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Succession Planning



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Mentors vs. Sponsors

Whitnee Caldwell, PharmD
Clinical Pharmacist
Northwestern Memorial Hospital

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Learning Objective

Describe examples of mentors versus sponsors and the differences between them

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Mentors vs. Sponsors

A coach talks to you
A mentor talks with you
A sponsor talks about you



http://content.presentermedia.com/file/u/10sp/1000000/16094/coach_wth_wht_hnd_01_01_01_01.jpg



http://happy-human.com/wp-content/uploads/2014/10/CoachHelp_ppt_02.ppt



<http://tinyurl.com/oytqjzg>

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Functions of Sponsors and Mentors

Sponsors

- Powerfully positioned champions
- 2 Principle functions
 - Puts own reputation on the line
 - Takes responsibility for protégé's promotion

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Mentors

- Experienced advisors
- Many functions
 - Sounding board & shoulder to cry on
 - Supplier of solicited advice
 - Provider of support and guidance as

Identifying a Sponsor

- 3 "MUSTS" for every sponsor
 - High-level contacts for strategic introductions
 - Stretch assignments that will advance your career
 - A broad perspective



<http://eloborit.com/wp-content/uploads/2014/08/business-opportunity-seeker1.jpg>

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Sponsors

- Two-way street
 - Deliver outstanding performance
 - Consistently make your sponsor look good

Beware!!

Skill set of Sponsor vs Role Model
Anonymous Sponsors



http://www.clipartbest.com/cliparts/b1y/gM/vsgaM4L.jpg

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Mentor: Sounding Board

- One-way street
 - Expect very little in return
 - Behind the scenes
 - Less emphasis on making someone else look good



https://image.sproutsitemedia.images/v2/images/21201774.width%20178.height%20178.png

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Mentors vs. Sponsors

- Provide emotional support → **Mentor**
- Senior manager with influence → **Sponsor**
- Fights to get their people promoted → **Sponsor**
- Provides exposure to contacts who may help their career → **Mentor**
- Focus on increasing personal and professional development → **Mentor**

Can exist at any level within

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Gender Differences in Leadership?

Erick J. Borkowski, PharmD
Pharmacy Manager
Northwestern Medicine Lake Forest Hospital

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Objective

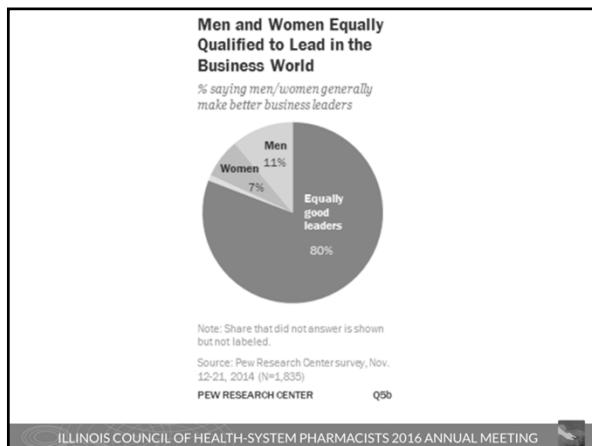
- Discuss Gender Differences in Leadership and how to successfully incorporate into management style.

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Is There a Gender Advantage In Leadership?

- WHO DO YOU THINK WOULD MAKE A BETTER BUSINESS LEADER?
 - Men?
 - Women?
 - Equal?

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Is There a Difference?

Gender Strength	Nine Leadership Strengths
Women>>Men	People Development Expectations and Rewards Role Modeling Inspiration Participative Decision Making Intellectual Stimulation Efficient Communication
Women>Men	Individual Decision Making Control and Corrective Action
Women=Men	
Men>>Women	

"Female Leadership, A Competitive Edge for the Future," McKinsey & Company, 2007.

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Is There a Difference?

Leadership Competencies	Male	Female	t	Sig.
Takes Initiative	49.8	56.4	-13.67	0.00
Displays High Integrity and Honesty	49.9	54.7	-9.78	0.00
Drives for Results	50.6	55.2	-9.53	0.00
Practices Self-Development	51.3	56.0	-9.51	0.00
Develops Others	51.1	55.1	-8.14	0.00
Inspires and Motivates Others	51.6	55.1	-7.35	0.00
Builds Relationships	51.2	54.5	-6.70	0.00
Collaboration and Teamwork	52.1	54.5	-4.96	0.00
Champions Change	51.6	54.0	-4.96	0.00
Establishes Stretch Goals	51.7	54.1	-4.77	0.00
Solves Problems and Analyzes Issues	52.0	52.7	-1.38	0.17
Communicates Powerfully and Prolifically	52.9	53.4	-1.14	0.26
Connects the Group to the Outside World	52.3	52.1	0.34	0.73
Innovates	52.6	52.2	0.96	0.34
Technical or Professional Expertise	52.1	51.1	2.10	0.04
Develops Strategic Perspective	53.7	51.2	5.06	0.00

Zenger/Folkman, 2011

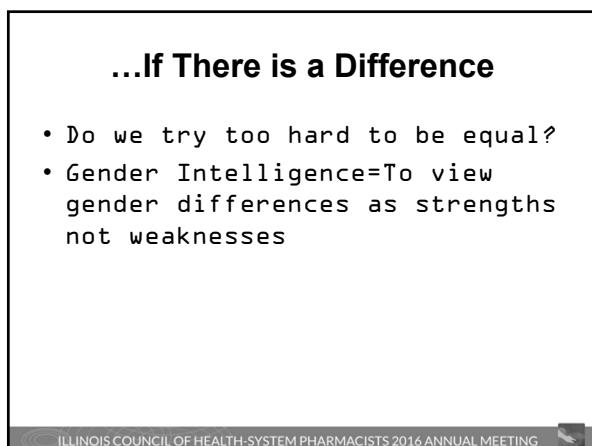
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Gender Blind Spots?

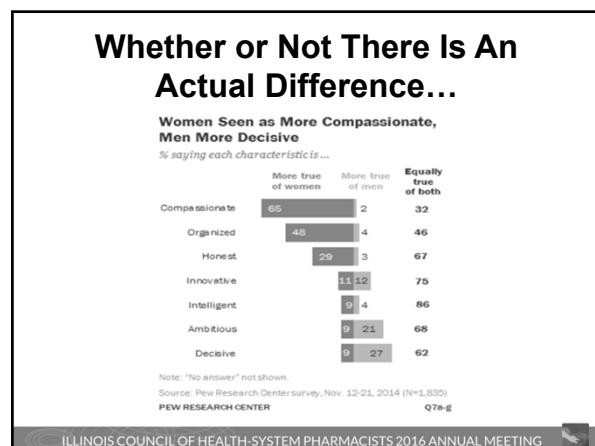
Women	Men
There's room for improvement.	If it isn't broken, why fix it?
Recognize me for my effort.	Recognize me for my results.
Let's solve this as a team.	Let me work independently on this task.
Give me direct feedback.	I feel like I am on egg-shells with you.
Allow me to ask questions.	Let's not slow our progress down.
Listen to me.	I am listening to you.
I'll express my emotions freely.	I'll keep my emotions hidden.
You're too insensitive.	No I'm not.

Annis B., Gray J. *Work With Me: The Eight Blind Spots Between Men and Women in Business*; 2013.

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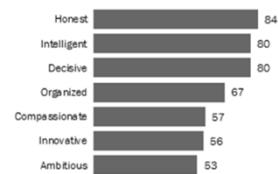
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Which Traits Matter Most?

Which Leadership Traits Matter Most? % saying it is absolutely essential for a leader to be ...



Source: Pew Research Center survey, Nov. 12-21, 2014 (N=1,835)
PEW RESEARCH CENTER Q25e-g

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The Personal Side...

- Practice Coordinator position approved by hospital leadership
- 3 of the 4 applicants were women
- Promoted from within
- Ultimately candidate selected balanced my leadership style

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Conclusions

- Men and Women may have different inherent strengths in leadership qualities
- Cannot oversimplify the debate and claim that one sex makes a superior leader
- Organizational performance relies on complimentary and diversity of behaviors

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Questions?

New Drug Updates

Lalita Prasad-Reddy, PharmD, MS, BCACP, BCPS, CDE
 Clinical Assistant Professor
 Chicago State University College of Pharmacy

Diana Isaacs, PharmD, BCPS, BC-ADM, CDE
 Clinical Pharmacy Specialist
 Cleveland Clinic Diabetes Center

September 16, 2016

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Disclosures

- Both presenters have nothing to disclose.

Pharmacist Objectives

- Describe the place in therapy and mechanisms of action of newly approved drugs in the last 15 months.
- Compare newly approved agents from current agents utilized in the management of disease.
- Describe newly approved agents in terms of their place in therapy, effectiveness, safety, and patient administration.
- Summarize important patient counseling pearls for newly approved agents for the management of disease.

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Technician Objectives

- Describe the place in therapy and mechanisms of action of newly approved drugs in the last 15 months.
- Compare newly approved agents from current agents utilized in the management of disease.
- Describe newly approved agents in terms of their place in therapy, effectiveness, safety, and patient administration.

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New Drug Stats

- From 2006-2014
 - Average 28 novel drugs approved/year
- In 2015, 45 novel drugs approved
 - 16 (36%) are first-in-class (ex. Praxbind®)
 - 21 (47%) to treat rare/orphan diseases (ex. Kanuma®)
 - 29 (64%) approved in the US before other countries (ex. Entresto®)
- In 2016 (as of July)
 - 16 novel drugs approved

Novel Drugs Summary 2015. Available at: <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugInnovation/ucm474696.htm>. Accessed August 8th, 2016

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New Drugs & Disease States

- Diabetes
 - Insulin degludec (Tresiba®)
 - Lixisenatide (Adlyxin®)
- Gout
 - Lesinurad (Zurampic®)
- Bleeding reversal
 - Idarucizumab (Praxbind®)
- Hyperlipidemia
 - Evolocumab (Repatha®)
 - Alirocumab (Praluent®)
- Heart Failure
 - Sacubitril/valsartan (Entresto®)
 - Ivabradine (Corlanor®)
- Asthma
 - Reslizumab (Cinqair®)
 - Mepolizumab (Nucala®)
- Hepatitis C
 - Sofosbuvir/velpatasvir (Epclusa®)
 - Elbasvir/grazoprevir (Zepatier®)
 - Daclatasvir (Daklinza®)

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The Ideal Basal Insulin

- Possess a peakless profile _____
- Deliver a consistent and reliable rate of absorption _____
- Provide less variability in coverage among all populations _____
- Cause no weight gain or hypoglycemia _____
- Provide a true 24 –hour coverage following a single injection _____
- Allow mixing of basal/bolus insulins in same injection syringe _____

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Insulin Degludec (Tresiba®)

- Indications for Insulin Degludec (Ideg)
 - Improve glycemic control in adults with diabetes mellitus
- FDA approved September, 2015
- Specifics
 - After injection, Ideg dihexamers join together creating long, soluble multihexamer chains that prolong duration of action
 - Compared to glargine, exhibits equivalent or even superior glycemic control
 - Available in U-100 and U-200 formulations

Tresiba Package Insert, NovoNordisk, 2015

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A Comparison of Kinetics

Property	Glargine (U-300)	Glargine (U-100)	Degludec
Onset (hours)	6	4-5	1 – 2
Duration of Action (hours)	24-36	24	> 42
Half-life (T1/2)	~ 19 hours	~ 12 hours	25 hours
Time to Steady State	5 days	24 hours	3 days

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Tresiba® Clinical Data

Study Design	Intervention	Results: Efficacy
Fifty-two weeks, randomized, controlled, open-label, multi-national, parallel design, treat-to-target, non-inferiority trial	Adults with type 2 diabetes inadequately controlled with oral glucose lowering agents were randomized to insulin degludec ($n = 773$) or insulin glargine ($n = 257$) once daily, both in combination with metformin.	Insulin degludec and insulin glargine decreased mean A1C concentrations from baseline by 1.06 and 1.19%, respectively, with an estimated treatment difference of 0.09% (95% CI -0.04 to 0.22%), indicating that degludec was noninferior to insulin glargine. Rates of hypoglycemia were similar, with nocturnal hypoglycemia and severe hypoglycemia occurring less frequently ($p < 0.05$) with degludec.
Fifty-two weeks, randomized, controlled, open-label, treat-to-target, multi-national, non-inferiority trial	Study B: Adults with type 2 diabetes inadequately controlled with insulin +/- oral agents were randomized to degludec ($n = 755$) or insulin glargine ($n = 251$) in combination with aspart before meals, +/- metformin and/or pioglitazone.	Insulin degludec and insulin glargine decreased mean A1C concentrations by 1.10 and 1.18%, respectively, with an estimated treatment difference of 0.08% (95% CI -0.05 to 0.21%), meeting criteria for noninferiority for degludec. Rates of overall hypoglycemia and nocturnal hypoglycemia were lower in those treated with insulin Degludec, while rates of severe hypoglycemia were similar between groups.

Diabetes Care 35:2464–2471, 2012
doi:10.2337/dc12-2013

Degludec vs. Glargine

Degludec	Glargine
Can be mixed in one injection syringe with rapid-acting insulin	Should not be mixed in one injection syringe with rapid-acting insulin
Day-to-day variability of absorption is significantly lower than glargine	Day-to-day variability with glargine seen in multiple patient populations
Flexibility in dosing	Requires once to twice daily administration
Overall, Degludec is associated with improved glycemic control overall with less hypoglycemia	

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Patient Populations who may Benefit from Tresiba®

- Elderly
- Learning difficulties
- Dependent on caretakers or healthcare professionals for insulin administration
- Unable to achieve glycemic control despite optimized glycemic regimens

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Which of the Following is a Difference Between Insulin Degludec and Insulin Glargine?

- A. Insulin degludec can be mixed with insulin aspart in a syringe
- B. Insulin degludec can be inhaled
- C. Insulin glargine causes less hypoglycemia
- D. Insulin glargine offers more flexibility in dosing

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Lixisenatide (Adlyxin®)

- FDA approved: July, 2016
- Glucagon-like-peptide receptor agonist (GLP-1 RA)
- MOA: improves glycemic control through effects on glucose-dependent insulin secretion, glucagon secretion, gastric emptying, and satiety
- Shorter half-life (2-5 hours), more impact on PPG compared with other GLP-1 RAs

Universalis. Micromedex 2.0. Available at: <http://www.micromedexsolutions.com>. Accessed August, 2016

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Lixisenatide: A Me Too Drug?

- Safety/effectiveness evaluated in 10 clinical trials including 5400 patients with type 2 diabetes
 - Superior to placebo
 - Non-inferior to exenatide BID and insulin glulisine

Study	Study Design	Results
GetGoal X	634 patients, open-label, randomized to lixisenatide 20mcg daily or exenatide 10mcg bid.	After 24 weeks, similar reductions in A1C and FBG. More weight loss with exenatide (-3.98 vs. -2.96kg) and fewer GI events with lixisenatide.
GetGoal-Duo2	896 patients on basal insulin randomized to lixisenatide or insulin glulisine.	After 26 weeks, lixisenatide non-inferior to glulisine in A1C reduction (-0.6% vs. -0.8%) and superior in weight loss (LS mean difference: -1.99kg).

Rosenstock et al. Diabetes Care. 2013 Oct; 36(10):2945-51. Anderson et al. Ther Adv Chronic Dis. 2016 Mar; 7(1):4-17

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GLP-1 RA Comparison

GLP-1 RA	Dosing Schedule (SC)	CrCl Renal Dose Adjustments	A1c Lowering
Albiglutide (Tanzeum®)	30mg-50mg weekly	None	~1%
Dulaglutide (Trulicity®)	0.75-1.5mg weekly	None	~1.5%
Exenatide (Byetta®)	5mg-10mg BID 1-60 minutes before meals	30-50: use caution <30: not recommended	~1%
Exenatide extended release (Bydureon®)	2mg weekly	30-50: use caution <30: not recommended	~1.5%
Liraglutide (Victoza®)	0.6mg daily x1 week, then 1.2-1.8mg daily	Mild to severe renal impairment: not recommended	~1.5%
Lixisenatide (Adlyxin®)	10mcg daily x 2 weeks, then 20mg daily, 1 hour before breakfast	30-50: use caution <30: not recommended	~0.9%

R. Dolito. Document: Comparison of GLP-1 Agonists. Pharmacist Letter/Prescriber's Letter. December 2014

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In the Pipeline: iGlarLixi

- Lixisenatide + insulin glargine in a fixed-ratio pen
- Daily dose range: 10-60 units corresponding to lixisenatide 5-20mcg

Lixisenatide and Insulin Glargine/Unisodas Briefing Document. Available at: <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteeMeetingMaterials/Drugs/EndocrinologicAndMetabolicDrugsAdvisoryCommittee/UCM505559.pdf>. Accessed August 11th, 2016

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Which of the Following is an Important Patient Counseling Point for Lixisenatide?

- A. Take with food to avoid upset stomach
- B. Do not use if you are already taking insulin
- C. Common side effects include nausea and diarrhea
- D. Only needs to be injected once weekly

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Lesinurad (Zurampic®)

- FDA approved December, 2015 for hyperuricemia in gout
- MOA: reduces serum uric acid by inhibiting transporter proteins involved in uric acid reabsorption including uric acid transporter 1 (URAT1) and organic anion transporter 4 (OAT4)
- Dose: 200mg QAM with food and in combo with a xanthine oxidase inhibitor
- Adverse Effects: headache, Scr increase, GERD
- Place in therapy: add on to allopurinol or febuxostat in patients not at target uric acid levels

Lesinurad package insert. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/207988bl.pdf Accessed August 12th, 2016

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Zurampic® Clinical Trials

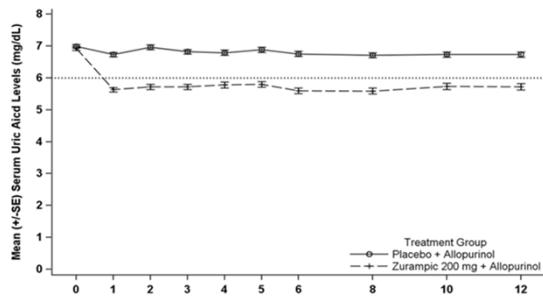
- 3 randomized, placebo-controlled studies

Drugs	Design	Results
Zurampic® + allopurinol vs. allopurinol alone	2 randomized 12 month trials (n=1213)	A greater proportion of patients treated with Zurampic® combination achieved UA<6mg/dL compared with allopurinol alone (54 vs 28% and 55 vs 23%). No major differences in gout flares from 6-12 months.
Zurampic® + febuxostat vs. febuxostat alone	1 randomized 12 month trial	More uric acid lowering with Zurampic® combination. No significant difference in the rate of gout flares.

Zurampic package insert. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/207988bl.pdf Accessed August 12th, 2016

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Uric Acid Lowering



Lesinurad package insert. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/207988bl.pdf Accessed August 12th, 2016

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Other Chronic Gout Drugs

Drug	MOA	Usual Dose	Place in Therapy	Comments
Allopurinol	Xanthine oxidase inhibitor (XOI)	100-800mg PO daily	1 st line	Generic/cheap
Febuxostat	Xanthine oxidase inhibitor (XOI)	40-80mg PO daily	1 st line	Brand/expensive
Probenecid	Uricosuric	250-1000mg PO BID	Alternative 1 st line if CI or intolerance to XOI	Many drug interactions
Colchicine	Anti-inflammatory	0.6mg PO daily or BID for prophylaxis	1 st line for acute gout attacks and gout prophylaxis with uric acid lowering therapy	Many drug interactions/expensive
Pegloticase	Catalyzes the oxidation of uric acid to allantoin	8mg IV infusion q 2 weeks	Gout refractory to conventional therapy	Many adverse effects/expensive

Fleischmann et al. *Rheumatology* (2014) 53 (12): 2167-2174.
Khanna et al. *Arthritis Care & Research* Vol. 64, No. 10, October 2012, pp 1431-1446

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Zurampic®-Clinical Pearls

- Avoid if CrCL<45 ml/min
- Take with food at the same time as xanthine oxidase inhibitor
- Black box warning: acute renal failure
- Monitor uric acid, renal function
- Advise patients to drink 2L of fluid daily
- Max out allopurinol or febuxostat before adding

Lesinurad package insert. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/207988bl.pdf Accessed August 12th, 2016

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Which of the Following Drugs/Doses is Most Appropriate to Combine with Zurampic® for Gout Treatment?

- Colchicine 0.6mg PO daily
- Probenecid 500mg PO BID
- Allopurinol 100mg PO daily
- Febuxostat 80mg daily

Assume normal renal function

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Idarucizumab (Praxbind®)

- Bleeding reversal for dabigatran (Pradaxa®) due to uncontrolled life-threatening bleeding or a need to undergo emergency surgery
- FDA approved October, 2015
- First and only DOAC reversal agent
- MOA: humanized monoclonal antibody fragment-binds to dabigatran and its metabolites with higher affinity than dabigatran to thrombin, neutralizing its anticoagulant effects

Praxbind package insert. Available at <http://docs.bmsboehringer-ingelheim.com/PrescribingInformation/Ps/Praxbind/Praxbind.pdf>. Accessed Aug 11th, 2016.

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Praxbind®: Important Points

- Supplied: 2.5 GM/50 ML
- Dose: 5g (2 vials) IV 1 time dose
- Keep refrigerated, unopened vials protected from light may be stored at room temp up to 48 hours, 6 hours if in light
- Use solution within 1 hour of removing from vial
- Most common adverse effects (>5%): hypokalemia, constipation, fever, delirium
- Increases thromboembolic risk**
- May restart dabigatran 24 hours later

Praxbind package insert. Available at <http://docs.bmsboehringer-ingelheim.com/PrescribingInformation/Ps/Praxbind/Praxbind.pdf>. Accessed Aug 11th, 2016.

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Praxbind®: Clinical Trials

- Approved based on 3 clinical trials in healthy volunteers
 - Patients given dabigatran and then various amounts of Praxbind® to establish effective dose and side effects
 - Median age: 36 years
- Accelerated FDA approval
- Ongoing trial in patients with life-threatening or uncontrolled bleeding or who need emergency surgery/urgent procedures

<http://www.praxbind.com/clinical/trial-archives>. Accessed August 12th, 2016.

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Praxbind®: Clinical Trials (Cont)

Goal: Determine safety/efficacy of idarucizumab

Study	Study Design	Results
RE-VERSE AD	<ul style="list-style-type: none"> 2 arms of dabigatran: <ul style="list-style-type: none"> Group A (51 patients): life-threatening bleeding Group B (39 patients): invasive surgery required that could not be delayed Over 90% received dabigatran for stroke prevention in atrial fibrillation All patients received 5g of IV idarucizumab 	<ul style="list-style-type: none"> Median age: 76.5 years Median hospitalization: 8 days Dilute thrombin time was normalized in 98% of patients in group A and 93% of patients in group B Ecarin clotting time normalized in 89% of group A and 88% group B 18 deaths overall (9 in each group) 5 thrombotic events 21 patients with severe adverse events <p>Interim Analysis: plan to enroll ~300 patients</p> <p>Summary: Idarucizumab rapidly and completely reversed the anticoagulant activity of dabigatran in 88 to 98% of patients</p>

Polisick CV et al. N Engl J Med. 373:1588-1595

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Praxbind® is Used to Reverse Which Anticoagulant(s)?

- Warfarin only
- Dabigatran only
- Rivaroxaban only
- Any of the DOAC's
- Enoxaparin

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PCSK9 Inhibitors

- Indications:
 - Treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease
- Place in therapy:
 - Those who need additional LDL lowering despite maximally tolerated statin

Effects on cardiovascular mortality have NOT been determined!

N Engl J Med. 2015; 373:1588-1595

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PCSK-9 Pharmacology

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A Comparison of Agents

Evolocumab (Repatha®)

- FDA Approved August, 2015
- Reduced LDL ~ 55 – 75%
- 140 mg SUB-Q every 2 weeks
- Associated with angioedema

Alirocumab (Praluent®)

- FDA Approved July, 2015
- Reduced LDL 46 – 60%
- 75 mg SUB-Q every 2 weeks
- Associated with drug-neutralizing antibodies

N Engl J Med 2015; 373:1588-1595

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Which of the Following Statements is True Regarding PCSK-9 Inhibitors?

- A. They are less effective than statins at LDL lowering
- B. They are dosed via a weekly IV infusion
- C. They are associated with angioedema and drug-neutralizing antibodies
- D. They reduce cardiovascular mortality

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Ivabradine (Corlanor®)

- FDA Approved April, 2015
- Indications
 - To reduce the risk of hospitalization for worsening heart failure in patients with stable, symptomatic chronic heart failure
 - Left ventricular ejection fraction $\leq 35\%$
 - Sinus rhythm with resting heart rate ≥ 70 beats per minute
 - Must be on maximally tolerated doses of beta-blockers or have a contraindication to beta-blocker use

Corlanor® package insert, Amgen, 2015

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Ivabradine

- Mechanism of action
 - Selectively and specifically inhibits the cardiac pacemaker current within the SA node that regulates heart rate
 - Administration results in a dose-dependent reduction in heart rate
 - Cardiac effects are specific to SA node
 - No effect on blood pressure
 - No effect on myocardial contractility
 - No effect on intra-cardiac conduction
- Does not exhibit negative inotropic effects!!!

Corlanor® package insert, Amgen, 2015

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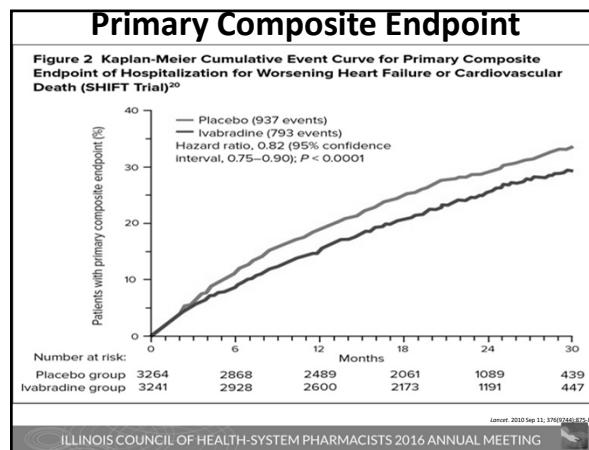
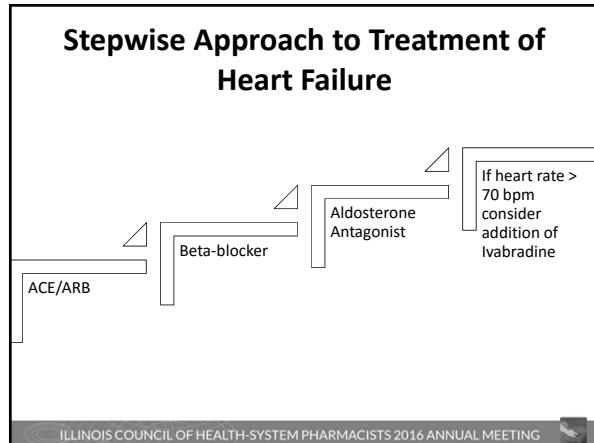
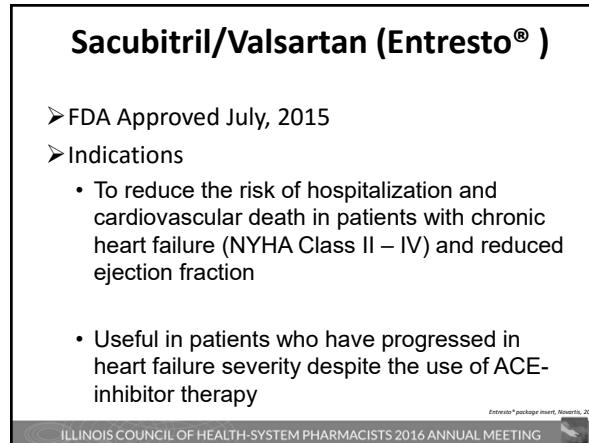
Ivabradine Dosing and Monitoring

Initial Dose	Dose Adjustments for Heart Rate	Dosage Adjustments
5 mg twice daily with meals	If heart rate > 60 bpm: 7.5 mg BID If heart rate < 50 bpm: 2.5 mg BID	Dosage adjustments are required in patients at risk for hemodynamic compromise, heart conduction defects, sinus node dysfunction, and elderly patients
Efficacy monitoring: Blood pressure, heart rate, heart rhythm		
Safety monitoring: Heart rate, dizziness, fatigue, syncope If heart rate < 50 bpm on 2.5 mg dose, Corlanor® should be discontinued		

Corlanor® package insert, Amgen, 2015

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Clinical Data: SHIFT Study			
Study Design	Intervention	Results: Efficacy	Results: Safety
Randomized, double-blind, placebo-controlled, parallel group study in patients with systolic HF, NYHA class II, III, IV symptoms, in a stable condition for ≥4 weeks, on guideline-based medical therapy with unchanged HF medications and doses for ≥4 weeks, and with a documented hospital admission for worsening HF within the previous 12 months	<p>Patients were randomized to ivabradine 5mg BID (titrated to max 7.5mg BID) or matching placebo</p> <p>Background medications were continued which included beta-blockers, ACE-inhibitors, diuretics, and aldosterone antagonists</p>	<p>Ivabradine was associated with a significant reduction in the primary outcome (24% in the ivabradine group vs. 29% in the placebo group) (95% CI 0.75–0.90; $p<0.0001$)</p> <p>Cardiovascular deaths & all cause deaths were not significantly reduced in the ivabradine group ($p=0.128$) but death due to HF (3% ivabradine vs. 5% placebo; $p=0.014$) & hospital admissions for worsening heart failure decreased significantly (16% ivabradine vs. 21% placebo; $p<0.0001$)</p>	<p>Ivabradine was associated with fewer serious adverse events in the ivabradine group (45% ivabradine vs. 48% placebo; $p=0.025$)</p>

Lancet. 2010 Sep 11; 376(9745):875-85.ILLINOIS COUNCIL OF HEALTH-SYSTEM PHARMACISTS 2016 ANNUAL MEETINGILLINOIS COUNCIL OF HEALTH-SYSTEM PHARMACISTS 2016 ANNUAL MEETINGILLINOIS COUNCIL OF HEALTH-SYSTEM PHARMACISTS 2016 ANNUAL MEETING

Sacubitin/Valsartan

- Mechanism of action due to combination neprilysin inhibitor (sacubitin) + ARB
- Cardiovascular effects
 - Enhanced levels of peptides due to inhibition of peptide degradation
 - Vasodilation
 - Sodium loss
 - Decrease in cardiac and vascular remodeling
 - Inhibition of the effects of angiotensin II
 - Vasodilation
 - Inhibits aldosterone release

Entresto® package insert, Novartis, 2015

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PARADIGM Study

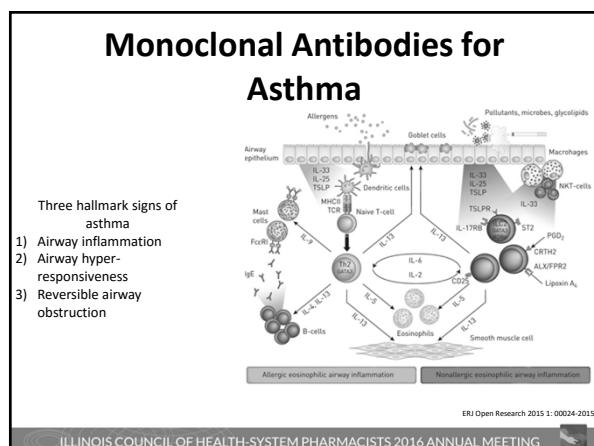
Study Design	Intervention	Results: Efficacy	Results: Safety
Randomized, double-blind, phase 3 trial comparing Entresto® to enalapril in patients with chronic heart failure with a reduced ejection fraction currently on a beta-blocker and ACE-inhibitor therapy	Patients were randomized to Entresto® 200 mg vs. enalapril 10 mg BID	Patients who were randomized to Entresto® had a significant reduction in the incidence of death from cardiovascular causes, hospitalization due to heart failure, and death from any cause	Entresto® was associated with an increased incidence of hypotension, although enalapril was associated with an increased incidence of hyperkalemia, and serum creatinine increase

N Engl J Med 2014; 371:993-1004

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Dosing and Monitoring		
Initial Doses	Target Dose	Dosage Adjustments
Previous ACE-I or ARB – 49/51 mg bid	Titrate after 2 – 4 weeks to 97/103 mg bid as tolerated by the patient	Dosage adjustments are required in severe renal and moderate hepatic impairment Use is not recommended in severe hepatic impairment
No ACE-I or ARB or low doses – 24/26 mg bid		
If switching from another ACE/ARB therapy, 36 hour washout period is recommended		
Efficacy monitoring: Blood pressure		
Safety monitoring: Serum creatinine, Electrolytes		

Erlotinib® package insert, Novartis, 2015



Which of the Following Agents Requires Monitoring in a Physician's Office After Administration Due to Anaphylaxis Concerns?		
A. Xolair®		
B. Nucalla®		
C. Cinquair®		
D. All of the above		

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What is the Mechanism of Action of Ivabradine?		
A. Improves glycemic control in adults with diabetes mellitus		
B. Inhibits the cardiac placement current within the SA node that regulates heart rate		
C. Reduces LDLR degradation and increases LDLR reutilization		
D. Binds to dabigatran neutralizing its anticoagulant effects		

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ASTHMA MONOCLONAL ANTIBODIES			
	Omalizumab (Xolair®)	Reslizumab (Cinquair®) (March 2016)	Mepolizumab (Nucala®) (November 2015)
Mechanism of action	IgE antibody	Interleukin-5 antagonist monoclonal antibody (IgG1 kappa)	Interleukin-5 antagonist monoclonal antibody (IgG1 kappa)
Indications	Moderate to severe persistent asthma in patients 6 years of age and older with a positive skin test to aeroallergen inadequately controlled on ICS	Add-on maintenance treatment of patients with severe asthma aged ≥18 years with an eosinophilic phenotype	Add-on maintenance treatment of patients with severe asthma > 12 years
Dosing	75 to 375 mg SC every 2 or 4 weeks (dependent on IgE level and weight)	3 mg/kg IV q4wk infused over 20-50 minutes	100 mg SQ q 4 weeks
Adverse effects	Arthralgias, myalgias, headache, viral infections, injection site reactions	Myalgias, elevated CPK, oropharyngeal pain	Headache, injection site reactions, back pain, and fatigue
Anaphylaxis reactions are possible, and have occurred with all of the above!!!			

Nucala® package insert, GlaxoSmithKline, 2015.
Cinquair® package insert, Teva Pharmaceuticals, 2016.
Xolair® package insert, Novartis, 2015.

NOVEL APPROACHES TO HEPATITIS C VIRUS (HCV)			
	Epcisa® (sofosbuvir/velpatasvir) (June 2016)	Zepatier® (elbasvir-grazoprevir) (January 2016)	Daklinza® (dasabuvir) (July 2016)
Indications	Indicated for adults with HCV infection genotypes 1, 2, 3, 4, 5, and 6 with and without cirrhosis	Indicated for adults with HCV with or without ribavirin for treatment of chronic HCV genotypes 1 or 4 infection in adults	Indicated for adults with HCV genotypes 1 or 3
Concomitant therapy	Approved for use in combination with the drug ribavirin	Does not need to be administered with interferon and ribavirin	Must be taken with sofosbuvir, or with sofosbuvir + ribavirin
Adverse Effects	Headache, fatigue	Fatigue, headache, nausea, anemia*	Headache, fatigue, nausea, anemia
Dosing	One tablet (400 mg of sofosbuvir and 100 mg of velpatasvir) taken orally once daily with or without food (Tablets: 50 mg elbasvir and 100 mg grazoprevir)	One tablet taken orally once daily with or without food (Tablets: 50 mg elbasvir and 100 mg grazoprevir)	60 mg once daily
Clinical Pearls	First drug available that treats all major genotypes of HCV Bradycardia is a concern; Epcisa® should not be used with amiodarone	Breakthrough therapy for patients with hepatitis C genotype 1 disease who have ESRD or HD, and for patients with hepatitis C genotype 4	Dose adjustments necessary for CYP3A medications

Daklinza® package insert, BMS, 2015.
Epcisa® package insert, Gilead Sciences, 2016.
Zepatier® package insert, Merck, 2016.

Which of the Following Agents Can be Administered Without Ribavirin for Treatment of HCV?

- A) Epclusa®
- B) Daklinza®
- C) Zepatier®
- D) All must be administered with ribavirin

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Other Notable New Agents

Drug Name	Generic	Approval Date	Indication
Xiidra®	lifitegrast ophthalmic solution	7/11/16	Dry eye disease
Zinbryta®	Daciluzumab	5/27/16	Multiple sclerosis
Nuplazid®	Pimavanserin	4/29/16	Hallucinations/delusions associated with Parkinson's Disease
Defitelio®	defibrotide sodium	3/30/16	Hepatic veno-occlusive disease s/p stem cell transplant
Taltz®	ixekizumab	3/22/16	Plaque psoriasis
Anthim®	oblitoxaximab	3/18/16	Inhalational anthrax
Briviact®	brivaracetam	2/18/16	Partial onset seizures
Uptravi®	Selexipag	12/22/15	Pulmonary arterial hypertension
Kanuma®	Sebelipase alfa	12/8/15	Lyosomal acid lipase (LAL) deficiency
Veltassa®	Patiromer	10/21/15	Hyperkalemia
Vraylar®	Cariprazine	9/17/15	Schizophrenia/bipolar disorder

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Summary

- Several groundbreaking new drugs for chronic disease states over the past year
- Most clinic guidelines not updated yet to reflect new drug choices
- Knowledge of new agents and clinical judgment is essential when treating patients

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Questions?

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PGY1 Residency Programs

Pharmacy

Jennifer Ellison, PharmD

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Examples of PGY1 Pharmacy Residency Learning Experiences

- Orientation
- General Medicine
- Infectious Disease
- MICU
- Pediatrics
- Administration
- Research project month
- SICU/CVICU
- Electives—cardiology, ED, oncology, anticoagulation, NICU, pediatrics oncology
- Longitudinals—staffing, project, precepting/drug information/med safety/informatics

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Different settings

- Settings
 - Hospital
 - Ambulatory care/acute care combination
 - College based
- Different populations
 - VA/geriatric
 - Pediatric
 - Ambulatory/outpatient

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Common Components of PGY1 Programs

- Staffing component
 - Varies by program
- Teaching
 - Some require completion of teaching certificate
 - College based may differ from non-college based
- Direct Patient Care

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What To Look For

- Consider your patient care interests
 - Do you want to do a PGY2?
 - What electives are offered?
 - What resources are available?

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PGY1 Residency Options: Ambulatory Care

Nadine Isho, Pharm.D.

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Residency program types

- Postgraduate Year 1 (PGY1)
 - Provides general training
 - 3 types
 - Health System
 - Managed care
 - Community
 - Focuses include clinical judgment and problem-solving skills
- Postgraduate Year 2 (PGY2)
 - Focused area of training
 - Ambulatory care, Cardiology, pharmacy administration, drug information, etc
 - Focuses include using prior skills to allow independent professional functioning

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Why choose an ambulatory care residency?

- Enhance communication skills
- Sharpen critical thinking
- Leadership opportunities
- Work as part of an interdisciplinary patient care team
- Networking
- Specialization in a field

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Opportunities

- Direct patient care
 - Free up physician time
 - Increase patient access to care
 - Enhance clinical and economic outcomes
- Practice management
- Medication management
- Trusted relationships with recurring patients
- Coordination of care
- Patient advocacy
- Wellness
- Patient education

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Ambulatory Care Core learning experiences

- Direct patient care
 - Drug therapy management
- Health education
 - Understand and teach primary literature
- Practice management
 - Manage projects to enhance leadership and independence
- Drug information
 - Practice being a resource for provider and patient questions
- Administration
 - Collaboration with pharmacy leaders to improve pharmacy services

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Ambulatory settings

- Hospital
- Community-based practice
- Patient centered Medical Homes
- Accountable care organizations
- Specialty Services/Pharmacy

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Ambulatory specialties

- Primary care
- Management of the following chronic conditions:
 - Diabetes
 - Asthma
 - Smoking cessation
 - Heart failure
 - Infectious disease
 - Anticoagulation
 - Many others
- Community based practice
 - MTM
 - Immunizations
 - Travel medicine
 - Medication management

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Preparation for Residency

- Network and research prospective programs
 - Consider Professional Organization Membership: ICHP, ASHP, APhA
- 4th Professional year
 - Draft CV
 - Draft cover letter
 - Be specific to each site
 - Letters of recommendation
 - Sign up with the National Matching Service
 - Contact prospective residency directors
 - ASHP Midyear clinical meeting
 - Residency showcase
 - Personnel Placement Service
 - Complete program applications
 - Interview
 - Submit ranking to National Matching Service

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Resources

- <http://www.ashp.org>
- <http://www.natmatch.com/ashprmp>
- <http://www.careerpharm.com>
- <http://ichpnet.org>

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Residency Interview Pearls

**Abby A. Kahaleh, BPharm, MS,
PhD, MPH**

Roosevelt University College of
Pharmacy

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Prior to the Interview (1)

- Research the program
- Familiarize yourself with the location of the interview
- Gather information from current or previous residents
- Make sure all your documents have been received
- Ask about formal presentations, number of interviewers, and expectations

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Main Goal of the Interview

- *Residency program perspective:*
 - Evaluate which candidate is 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

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Types and Format Interviews

- Individual, group, combination
- Meetings with residents, preceptors, pharmacy directors, residency directors, staff
- Presentation, clinical case
- Tour of the facility
- Breaks/meals between interviews

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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?

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The key to a top curriculum vitae and letter of intent

Karen M. Kelly, Pharm.D.
Pharmacy Manager
Evanston Hospital
NorthShore University
HealthSystem

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What to include in your CV

- **Personal information**
 - Name, address, current phone & professional email address
- **Licensure Status**
 - State & type of license
- **Education**
 - School, degree, years attended, anticipated graduation, GPA
- **Professional experience**
 - Reverse chronological order
 - Position, name & location, time frame, name of supervisor, including title
 - Description of position
 - Notable contributions to pharmacy practice

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Curriculum vitae (CV)

- Latin = course or outline of your life
- Organized list:
 - Professional qualifications
 - Education
 - Achievements & experiences
- Varies in length, more detailed than a resume
- Living document

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What to include in your CV

- **Professional & Community Service**
 - Name of group
 - Office held
 - Describe the scope of responsibility & impact
- **Membership in organizations**
- **Special experiences, skills, language**
- **References**
 - list out

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Employers look for...

- Professionalism
- Signs of achievement
- Pharmacy-related focus & career direction
- Hard worker, continued willingness to work hard
- Patterns of stability

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Tips

- Update regularly
- Use headings to identify each section
- Simple fonts
- No abbreviations
- Be honest in your content
- Focus on positive achievements
- Watch for spelling errors
- Have someone proofread it for you

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What not to include

- Personal, biographical information
- Reason for changing jobs or having no job
- Information that predates pharmacy school
 - except for education, degrees earned
- Interests and hobbies
- Photo, unless requested

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Letter of Intent

- Defines your goal of achieving a Pharmacy Residency
- Highlights your current skills, what you can contribute to benefit their patients and the organization
- Identifies what you hope to learn from that program
- Answer these questions:
 - Why you are pursuing a residency?
 - Why is this program your top choice?
 - How will the position help you develop as a professional?
 - How will your skills and experiences help you succeed?
 - What are your professional goals?

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Letter of Intent

- Format
 - Use business letter formatting
 - Limit to 1- 2 pages
 - Usually 3-5 paragraphs
 - Do not include detailed personal information
- Composition of the letter
 - Individualized focus for each site you are applying
 - What is it about this particular residency and organization that has led to you select it?
 - Include skills and interests you have that make you a good candidate

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Final Thoughts

- Be honest in your content
- Highlight your strengths & achievements - what can you contribute that would make a program select you?
- Create a good first impression
- CV and Letter of Intent are an advertisement for YOU!

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The Interview Process and How to Conduct Yourself at Interviews and at Midyear

Milena McLaughlin, PharmD, MSc, BCPS-AQ ID, AAHIVP
 Assistant Professor of Pharmacy Practice
 Midwestern University - Chicago College of Pharmacy
 HIV/AIDS Clinical Pharmacist
 Northwestern Memorial Hospital

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The Interview Process

- Apply, Interview, Rank, Match!
- Anticipate the "usual" questions
- Research different interview styles
 - Behavior-based
 - Formal
 - Casual
- If needed, take a few seconds to collect your thoughts
- This is also your time to get to know the program!

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Your CV

- Everything is fair game!
- Know something about everything on your CV
- Interviewer will take 8-12 seconds to look at your CV
 - Highlight important information!

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Before the Interview

- Do your research!
 - Program, interviewers, institution
 - Job description (rotations)
- Make a list of questions
- Plan for weather, travel, etc.
 - Allow plenty of extra time and arrive early
- Presentations
 - Bring on at least 2 forms of media and print out

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During the Interview

- You are ALWAYS being interviewed
- Be attentive and watch mannerisms
- Ask questions!
- Do not try to "overshadow" other interviewees
- Make eye contact
- Avoid any negativity or complaining
- Take notes!
 - Helpful for ranking program and writing thank you letters!

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After the Interview

- Send a follow-up thank you!
 - More important that it is personalized than hand-written vs email
- Write down any thoughts or notes
 - You will need to rank programs!

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Midyear Do's!

- Plan out the showcases
- Ask thoughtful questions
 - Avoid asking questions regarding information that can be found on the program's website
- Speak with residents
- Follow post midyear instructions

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Midyear Don'ts!

- Don't be a lingerer!
- Don't force your business card/CV!
 - Hundreds of students multiplied by hundreds of CVs...
- Don't be aggressive!
- Don't be on your phone!
- Pharmacy is a small world!
 - Seriously, we cannot say this enough...

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Resources

- GlassDoor (www.glassdoor.com)
 - https://www.glassdoor.com/Interview/pharmacist-interview-questions-SRCH_K00,10.htm
- US News and World Report
 - <http://money.usnews.com/money/careers/slideshows/the-10-most-common-interview-questions/12>
- The Pharmacy Professionals' Guide to Résumés, CVs and Interviews. 3rd Edition. Thomas Reinders.

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The Key to a Top Curriculum Vitae (CV) and Letter of Intent (LOI)

Jen Phillips, PharmD, BCPS
 Associate Professor, Midwestern University
 September 17, 2016

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Objectives

1. Identify the purpose of a letter of intent and a CV.
2. List things to include and not include in a letter of intent and a CV.

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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

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Curriculum Vitae

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Why do I need a CV?

- Highlights what you have accomplished
 - School
 - Career
 - Extra-Curricular activities

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CV: What to Include

- Header
 - Include name & contact information
- Educational experience
- Work experience
- Presentations
- Publications
- Honors
- Licensure
- Certifications
- Memberships/professional activities
- References

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CV Elements

- Contact Information
 - Business and Permanent address
 - Professional e-mail address
- Educational experiences
 - Post-secondary education
 - Degrees earned and anticipated
 - Residency, fellowship programs
 - GPA?
- Work experience
 - May list non-pharmacy employment (as a new practitioner only)
 - Brief description of duties may be included

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CV Elements

- Rotations
 - Completed and anticipated
 - List preceptors and dates
 - May include bullets summarizing details or work on special projects
- Presentations / Publications
 - Include those given at regional, state, and national meetings
 - Include title, audience, and location for presentations
 - Cite in proper format for articles

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CV Elements

- Honors
 - Dean's list, scholarships, and other special recognition
- Licensure/Certification
 - Pharmacy licensure
 - ACLS, BLS, or immunization certification
- Professional Involvement
 - Include all organizations
 - Denote status (e.g., member or officer position)

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CV: Common Errors

- Make sure that your CV:
 - Is easy to read and follow
 - Is Up-to-date
 - Has a consistent format throughout (e.g., bullets, chronological order, tense agreement, etc.)
 - Does not contain spelling errors
 - Contains the correct titles for all preceptors and references included

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Letter of Intent

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Why do I need an LOI?

- 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

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LOI: Overcoming Barriers

Issue	Recommendation
"I do not feel comfortable selling myself."	<ul style="list-style-type: none"> 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."	<ul style="list-style-type: none"> 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."	<ul style="list-style-type: none"> Seek examples from current residents, websites, etc. Refer to outside sources for suggestions (residency books, articles, this presentation, e.g.)

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LOI: 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!)

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LOI: 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

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LOI: 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

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LOI: 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"

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Additional "hints"

- Proofread, proofread, PROOFREAD!
- Spend a LOT of time thinking
 - Goals, preferences, etc.
- Customize your letter/CV by site
 - People, experiences, examples that support your skill assessment
- Send a different letter/CV to each place

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Additional Reading

- Bauman JL, Sims KA. The ACCP Field Guide to Becoming a Standout Pharmacy Residency Candidate. American College of Clinical Pharmacy. 2012. p. 161-163.
- Gallagher JC, Wodlinger Jackson AM. How to write a curriculum vitae. Am J Health-Syst Pharm. 2010;67:446-7.

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The Match Process and PhORCAS

Molly Rockstad, PharmD, BCPS, BCACP
PGY1 Residency Coordinator
John H. Stroger, Jr. Hospital of Cook County
Chicago, IL

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What is PhORCAS?

- Pharmacy Online Residency Centralized Application Service
- Provides a single platform for all aspects of residency application:
 - Applicant Portal
 - Application submission
 - NMS ("The Match") registration
 - Program Portal
 - References Portal

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Benefits of PhORCAS

- Single application for multiple programs
- Single transcript request
- Streamlined recommendation process (both requests and submissions)
- Ability to customize materials for each program
- Electronic tracking of application status
- Integration with the Match

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Application Components

- Demographics
- Transcripts
- Personal Statement/Letter of Intent
- Curriculum Vitae (CV)
 - Additional section for extracurricular and professional activities
- References
- Supplemental material (program specific)

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Initial Steps

- Demographics
 - Address, phone, citizenship, academic history, GPA
 - DOB, gender and ethnicity for ASHP data collection only
- Transcripts
 - Request official transcripts and submit to PhORCAS using the transcript request form
 - Make sure to allow sufficient time for delivery and processing

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Personal Statement/ Letter of Intent

- Uploaded as a word or PDF file
- Can (and should) be customized to each program
 - Be careful not to mix up programs
- Check program information for specific content requests and/or word limits

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CV

- Uploaded as a word or PDF file
- Can be customized to programs, but may not need to be
- Be complete but concise
- Will be prompted to enter activities separately
 - Do not skip this step even though most information will already appear on the CV
 - Allows for more detailed descriptions
 - Allows programs to filter candidates based on experience

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References

- Applicant will enter the name, email address, and phone number of each reference
- Will then enter reference requests for each program separately
 - Can send each reference writer any combination of requests (all or only a few)
 - Space for notes on each request
 - Deadlines
 - Special requests for content
 - Supplemental recommendation materials

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Reference Etiquette

- Entering a reference request prompts an immediate notification
 - No surprises!
- Allow writers sufficient time for completion
- Communicate important deadlines
- Be reasonable with special requests
 - No longer includes space for freetext
 - Additional supplemental letters discouraged by PhORCAS
 - Consider discussing goals and any hopes for content face-to-face instead

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Supplemental Information

- Check program requirements
- Supplemental information may include:
 - Additional demographic information
 - Program-specific paperwork
 - Interview availability
 - Additional transcripts
- Any supplemental material for a program should be saved as a single file

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Final Steps

- Finalize attachments for each program
 - Allows you to select the customized versions of each category as applicable
- Register and pay for the Match
- Check and re-check!
 - Silly mistakes will cost you
- Adhere to deadlines
 - Submit early. Do not tempt technology
 - PhORCAS will allow reference letters and transcripts to be added to an application after the deadline
 - However, programs may choose not to accept late submission of these items

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Good Luck!!!

Questions?

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