Medication Errors and Continuous Quality Improvement

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Disclosure

- Authors have no financial relationships to disclose with regards to this presentation

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Objectives

- Define medication errors and describe patient safety strategies that can decrease medication errors and improve the quality of pharmacy health care delivery
- Given a scenario, be able to categorize and/or report medication errors utilizing the National Coordination Council for Medication Error Reporting and Prevention (NCCMERP) scale
- Discuss basic error mitigation strategies utilized to reduce errors and improve patient safety
- Review methods to evaluate healthcare organizations to improve processes and prevent medication errors
- Explain how root cause analysis and failure mode & effects analysis can be utilized to determine the underlying cause of medication errors
- Identify strategies, the role of technology, and the importance of a non-punitive approach for handling medication errors after errors have occurred
- Use the CQI process to encourage a culture of safety and of providing feedback and assistance to effectively minimize patient risk
- Florida law stipulates requirements for a Continuous Quality Improvement plan: Outline steps required for a successful CQI Plan incorporating the State's requirements

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Objectives - Part I

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What is a Medication Error?

According to National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP):

"A medication error is **any preventable** event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer"

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Medication Errors May Be Related To:

- Professional practice
- Health care products
- Procedures and systems
- Compounding
- Dispensing
- Distribution
- Administration
- Education
- Monitoring
- Use

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Types of Medication Errors:

- Incorrect Medication
- Incorrect Strength
- Incorrect Route
- Incorrect Duration
- Incorrect Preparation
- Incorrect Rate
- Incorrect Timing
- Distortions
- Expired Product
- Distractions
- Abbreviations

Medication errors:
- Responsible for
  - **5% to 41.3%** hospital admissions
  - **22%** readmissions
- Incidence is
  - **30%** higher in patients taking >5 drugs
  - **38%** higher in those >75 years old

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Prevalence

Incidence in acute hospitals	Deaths annually	Injuries in outpatient clinics	Added health care costs, disability, and lost productivity
6.5 per 100 admissions	**7000-9000**	**530,000**	**37.6 to 50 billion dollars**

Most common type of medication error:
Prescribing error (dosing errors)- 41%

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In the News:

Medication mix-up blamed for death of a patient at Lexington hospital

https://www.lex18.com/news/lex-18-investigates/medication-mix-up-blamed-for-death-of-a-patient-at-lexington-hospital

As a nurse faces prison for a deadly error, her colleagues worry: Could I be next?

MARCH 22, 2022 · 5:00 AM ET FROM KFF Health News

https://www.npr.org/sections/health-shots/2022/03/22/1087903348/as-a-nurse-faces-prison-for-a-deadly-error-her-colleagues-worry-could-i-be-next

Medication dispensing error nearly cost a woman her life. I-Team discovers it's not rare

by Lisa Fletcher | Thu, February 9th 2023 at 5:58 PM
Updated Tue, February 14th 2023 at 11:51 AM

https://wjla.com/features/i-team/medication-dispensing-errors-capitol-city-rehab-healthcare-center-southeast-dc-answers-long-term-healthcare-facility-dmv-tips-pharmacist-medical-error-centers-for-medicare-and-medicaid-services-cms-records+rating

Lawsuit alleges medical mistake at AZ imaging center caused life-threatening overdose

Records show patient was accidentally given a sedative during MRI scan

https://www.abc15.com/news/local-news/investigations/lawsuit-alleges-medical-mistake-at-az-imaging-center-caused-life-threatening-overdose

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Pharmacy Medication Errors in the News:

Mistakes at work happen. For pharmacists, it can end their career

By Nicole Goodkind, CNN
8 minute read · Published 9:01 AM EST, Sun December 17, 2023

https://www.cnn.com/2023/12/17/economy/pharmacists-cvs-walgreens-errors/index.html

Workers at chain pharmacies across the US have told CNN that increased demand for prescriptions, shots and other services without sufficient staff to fulfill those orders has made it nearly impossible for the workers to do their jobs properly and has created potentially unsafe conditions for customers.

https://www.cnn.com/2023/12/17/economy/pharmacists-cvs-walgreens-errors/index.html

Prescription for disaster: America's broken pharmacy system in revolt over burnout and errors

Emily Le Coz
USA TODAY

Published 6:00 a.m. ET Oct. 30, 2023 | Updated 9:36 p.m. ET Oct. 30, 2023

https://www.usatoday.com/story/news/investigations/2023/10/26/pharmacy-chains-dangerous-conditions-medication-errors/71152960007/

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Pharmacy Medication Errors in the News:

Medication error causes woman's skin to 'melt off'

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Quality Related Events:

Any incident involving the inappropriate dispensing or administration of a prescribed medication. This can include:

Variations from the prescriber's order

- Incorrect drug
- Incorrect drug strength
- Incorrect dosage form
- Incorrect patient
- Inadequate or incorrect packaging, labeling, or directions

Failures to identify and manage:

- Over-utilization or under-utilization
- Therapeutic duplication
- Drug-disease contraindications
- Drug-drug interactions
- Incorrect drug dosage or duration of treatment
- Drug-allergy interactions
- Clinical abuse/misuse

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Strategies to Minimize Errors:

Minimize clutter

- Basket system to keep different patients' prescriptions and drugs separate
- Clear away the bottles from prescriptions that have been completed
- Take phone calls in a quiet, distraction-free area

Verify orders

- ISMP recommends spelling drug names during read back
- Clarify online prescriptions if something doesn't seem accurate

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Strategies to Minimize Errors:

Use barcodes

- Increased operational efficiency
- Improved dispensing accuracy
- Reduced patient safety concerns
- Enhanced pharmacy staff visibility

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Strategies to Minimize Errors:

Be aware of look-alike sound-alike (LASA) drugs:

Table 1. FDA-Approved List of Generic Drug Names with Tall Man Letters

Drug Name With Tall Man Letters	Confused With
acetaZOLAMIDE	acetaHEXAMIDE
acetaHEXAMIDE	acetaZOLAMIDE
buPROPion	buPIRone
buPIRone	buPROPion
chlorproMAZINE	chlorproPAMIDE
chlorproPAMIDE	chlorproMAZINE
clemiPHENE	clemiPRAMINE
clemiPRAMINE	clemiPHENE
cycloSERINE	cycloSPORINE
cycloSPORINE	cycloSERINE
DAUNOrubicin	DOXOrubicin
dimenhyDRINATE	diphenhydAMINE
diphenhydAMINE	dimenhyDRINATE
DOBUTamine	DOPamine
DOPamine	DOBUTamine
DOXOrubicin	DAUNOrubicin

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Strategies to Minimize Errors:

Careful with high alert medications

- Bear a heightened risk of causing significant patient harm when they are used in error
- Consequences of an error are clearly more devastating to patients

How to avoid mistakes:

- Standardizing the ordering, storage, preparation, and administration
- Using auxiliary labels
- Employing clinical decision support and automated alerts
- Using redundancies such as automated or independent double checks when necessary

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Strategies to Minimize Errors:

Implementing technology

- Computerized Provider Order Entry (CPOE)
  - Standardizes orders and makes them legible
  - Can include built-in tools to check for potential errors
  - Speeds up ordering process and improves workflow
  - Integrated with electronic health records (EHRs)

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Strategies to Minimize Errors:

Effective warning systems	Involve the patient
• Hard stops • Manage alert fatigue	• Counseling • Accurate medication reconciliation

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Strategies to Minimize Errors:

Track medication errors

- Identify trends at a system level
- Encourage a safe space for peer-to-peer feedback
- Perform **continuous quality improvement**
- **Just culture** perspective

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National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP)

- Independent organization dedicated to improving medication safety
- **Mission:** To maximize the safe use of medications and to increase awareness of medications errors
- Composed of 27 national organizations including healthcare professionals, regulatory agencies, and consumer groups

NCCMERP
National Coordinating Council for Medication Error Reporting and Prevention

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NCC MERP Index for Categorizing Medication Errors

Definitions

Harm
Impairment of the physical, emotional, or psychological function or structure of the body and/or pain resulting therefrom.

Monitoring
To observe or record relevant physiological or psychological signs.

Intervention
May include change in therapy or active medical/surgical treatment.

Intervention Necessary to Sustain Life
Includes cardiovascular and respiratory support (e.g., CPR, defibrillation, intubation, etc.)

Hartwig, S.C., Denger, S.D., & Schneider, P.J. (1991) Severity-indexed, incident report-based medication error-reporting program. Am J Hosp Pharm, 48: 2611-2616

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Categories Explained

Category A
No Error
No Harm

Definition: Incident that has the capacity to cause an error, but no error occurs

Example: Nicardipine and nifedipine tablets are stocked in adjacent ADC cells. Despite automated dispensing, these medications have similar names and indication, therefore, they should be separated to avoid confusion

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Failure Points:

- **LASA medications:** Nicardipine and nifedipine are both calcium channel blockers with similar names, increasing the risk of selection errors
- **Proximity in storage:** Storing these medications next to each other can lead to accidental selection of the wrong drug, especially under time pressure or in high-stress situations
- **Human factors:** Fatigue, distractions, and interruptions can exacerbate the risk of selecting the wrong medication, even with automated system

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Categories Explained

Category B
Error
No Harm

Definition: Error that occurred but did not reach the patient

Example: A pharmacist enters a prescription for **clonidine** instead of **clonazepam,** but the error is detected during the final check before the medication is given to the patient

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Failure Points:

- **Data entry**: The pharmacist entered the incorrect drug into the EHR, which could have been due to a typo, misunderstanding of the prescription, or lack of familiarity with the medications
- **Verification process**: If the pharmacy verification process wasn't thorough, the error might not have been caught. This includes checking the medication against standard guidelines and the patient's medical history
- **Workload and environment**: High workload, time pressure, or a distracting environment could contribute to mistakes in data entry and verification

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Categories Explained

Category C
Error
No Harm

Definition: Error that reached the patient but did not cause harm

Example: A patient is prescribed 50 mg of losartan, but the pharmacy dispenses 25 mg tablets. The patient takes the incorrect dosage for a few days before the error is noticed

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Failure Points:

- **Prescription accuracy:** The prescription might have been unclear or incorrectly written, leading to confusion about the correct dosage
- **Dispensing process:** The pharmacy staff may have misread the prescription or selected the wrong strength of the medication during the dispensing process
- **Verification:** There might have been a lack of thorough verification by the pharmacist to ensure the correct dosage was dispensed

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Categories Explained

Category D
Error No Harm
Monitoring required

Definition: Reaches the patient and requires monitoring or intervention to prevent harm

Example: A patient was prescribed **diazepam** instead of **diltiazem** due to a misreading of the medication name and the patient takes the wrong medication, requiring monitoring

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Failure Points:

- **Prescribing error:** The healthcare provider may have misread or misinterpreted the medication name due to similar spelling
- **Transcription error:** If the prescription was handwritten, poor handwriting could have led to the wrong medication being transcribed into the patient's records
- **Administration errors**: Nurses or caregivers administering the medication might not notice the discrepancy, especially if they are not familiar with the patient's usual medications or if the error is not flagged in the patient's records

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Categories Explained

Category E
Error Harm
Intervention required

Definition: Results in temporary harm to the patient and requires intervention

Example: A patient receives an overdose of insulin, resulting in hypoglycemia. The patient requires glucose administration to stabilize blood sugar levels

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Failure Points:

- **Dosage calculation:** Errors in calculating the correct insulin dose can lead to overdosing. This might occur due to misreading the prescription or misunderstanding the patient's needs
- **Monitoring and adjusting:** Inadequate monitoring of blood glucose levels and failure to adjust insulin doses based on these readings can contribute to overdosing
- **Communication breakdown:** Poor communication between healthcare providers, or between providers and patients, can lead to misunderstandings about insulin dosing and administration

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Categories Explained

Category F
Error Harm
Hospitalization required

Definition: Results in temporary harm to the patient and requires initial or prolonged hospitalization

Example: Digoxin is prescribed and dispensed without considering the patient's impaired renal function, leading to digoxin toxicity and hospitalization for cardiac monitoring and management

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Failure Points:

- **Lack of renal function assessment**: Lack of evaluation of the patient's renal function before prescribing digoxin. Impaired renal function can significantly affect digoxin clearance, increasing the risk of toxicity
- **Verification:** The pharmacist may not have reviewed the patient's renal function or question the appropriateness of the prescribed dose
- **Lack of follow-up**: Lack of regular monitoring of digoxin levels and renal function after initiation of therapy. Monitoring is essential to detect early signs of toxicity and adjust the dose accordingly

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Categories Explained

Category G
Error
Permanent Patient Harm

Definition: Results in permanent harm to the patient

Example: A patient is prescribed an immunosuppressant medication at one-fourth the required dose. This underdosing could lead to the patient's body rejecting a transplanted organ, causing permanent damage

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Failure Points:

- **Prescription error:** The initial error is prescribing the incorrect dose, possibly due to miscalculation or misunderstanding of the required dosage
- **Lack of verification:** Failure to double-check the prescribed dose against standard dosing guidelines or the patient's specific needs
- **Communication gaps**: There may have been a lack of communication between the prescriber and the pharmacist regarding the patient's specific needs and the critical importance of accurate dosing

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Categories Explained

Category H
Error Harm
Life Sustaining
Intervention Required

Definition: Results in harm to the patient and requires intervention to sustain life

Example: A patient with epilepsy does not receive their anticonvulsant medication due to an omission in their medication orders. This could lead to a severe seizure that necessitates emergency medical intervention to stabilize the patient

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Failure Points:

- **Prescription accuracy:** The healthcare provider may have failed to include the anticonvulsant medication in the patient's orders
- **Pharmacy verification:** The transition of care pharmacist might have failed to catch the discrepancy in the medication reconciliation
- **Patient monitoring:** There might have been inadequate monitoring of the patient's condition, delaying the detection of the missing medication and the onset of the seizure

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Categories Explained

Category I
Error
Patient Death

Definition: Results in the patient's death

Example: A patient with a known severe allergy to penicillin is mistakenly administered piperacillin tazobactam. The patient develops an anaphylactic reaction, leading to respiratory failure and death

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Failure Points:

- **Allergy documentation:** Failure to properly document and communicate the patient's severe penicillin allergy in their medical records
- **Medication reconciliation:** Poor medication reconciliation processes, which should include checking for allergies and contraindications
- **Labeling and alerts:** Lack of effective labeling and alert systems in EHR or automated dispensing cabinets (ADC) to flag severe allergies

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Test Question #1

A nurse administers a dose of insulin to a patient with diabetes. However, the dose given is slightly higher than prescribed. The patient experiences no adverse effects because the error is caught early, and the patient's blood sugar levels are closely monitored and managed. According to the NCC MERP Index for Categorizing Medication Errors, which category does this error fall into?

a. Category A
b. Category B
c. Category C
d. Category D

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d. Category D

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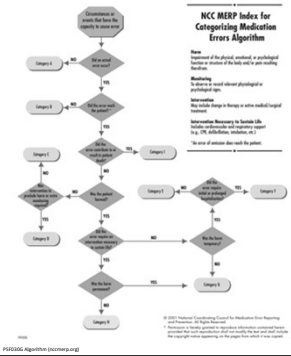

NCC MERP Index for Categorizing Medication Errors Algorithm

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How to report medication errors?

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Objectives - Part II

- Review methods to evaluate healthcare organizations to improve processes and prevent medication errors
- Explain how root cause analysis and failure mode & effects analysis can be utilized to determine the underlying cause of medication errors

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Safe Medication Practices

- The Institute for Safe Medication Practices (ISMP) is an independent, non-profit organization in the United States **devoted to <u>medication error prevention</u>**
- The cornerstone of ISMP is based on voluntary practitioner medication error reporting programs:
  - National Medication Errors Reporting Program (MERP)
  - National Vaccine Errors Reporting Program (VERP)
- Medication errors can occur at any point of the medication use system
- Safe medication practices are crucial to ensure patient safety & error reduction

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Safe Medication Practices

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Plan – Do – Study - Act

A systematic, interactive quality improvement method used to improve clinical care and practice outcomes

Plan	Do	Study	Act
Identify a Goal or Purpose & Develop Initiative	Implement the Plan	Analyze & Monitor Results	Adjust the Plan or Process

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Lean & Six Sigma

Lean

emphasizes **efficiency** by reducing waste, errors and delays

Six Sigma

prioritizes **quality** and **consistency** by involving processes and reducing variation

Lean Six Sigma

Provides high **quality** through **efficient** processes

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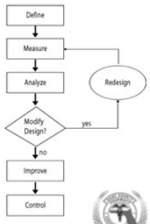
DMAIC – 5 Phases of Lean Six Sigma

- DMAIC is a problem-solving approach that drives Lean Six Sigma
- It is a data-driven quality strategy to improve existing process problems with unknown causes
  - **D**efine the problem, current processes, and ultimate goal
  - **M**easure the problem and understand the current process by collecting relevant data to understand processes
  - **A**nalyze data collected to identify root cause
  - **I**mprove the process by developing and implementing solutions
  - **C**ontrol and sustain improvements put in place



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Test Question #2

Examples of Continuous Quality Improvement (CQI) programs include Lean and Six Sigma. Six Sigma focuses on reducing defects by using the DMAIC process. What does DMAIC stand for?

a. Determine, Measure, Assess, Improve, Check
b. Define, Measure, Analyze, Improve, Control
c. Determine, Measure, Analyze, Improve, Control
d. Define, Measure, Assess, Improve, Check

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Root Cause Analysis

A **retrospective** investigation of an event that has already occurred to uncover causes of the incident, failure or problem

Root
- Define the problem & areas of improvement

Cause
- Locate the "root" cause
- Implement the Five Whys Strategy to avoid assumptions and explore the cause-and-effect relationship underlying a particular problem

Analysis
- Find corrective & preventative solutions
- Create actionable strategies to implement solutions
- Monitor solution & analyze if it helps improve

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Characteristics of a Successful RCA

- Identifies system and process changes needed to improve performance and reduce the risk for further events to occur
- Assumes that any problem is preventable
- Focuses primarily on systems and processes, not on individual performance
- Focuses on the why to understand the events being investigated to identify all root causes

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The 5 Whys Technique

- Focus on the why to understand the events being investigated to identify all root causes
  1. What happened?
  2. What normally happens?
  3. What do policies/procedures require?
  4. Why did it happen?
  5. How was the organization managing the risk before the event?

Question #2 and Question #3 help determine **reliability** of the processes

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Steps to Conduct RCA

- **Step 1.** Assemble a Team
- **Step 2.** State the Problem & Determine What Happened (through documentation and pertinent questions)
- **Step 3.** Create a Flow Chart (e.g., diagram the flow) of the Event
- **Step 4.** Identify Root Causes and Possible Contributing Factors
- **Step 5.** Write Root Cause Statements
- **Step 6.** Develop Action & Measures

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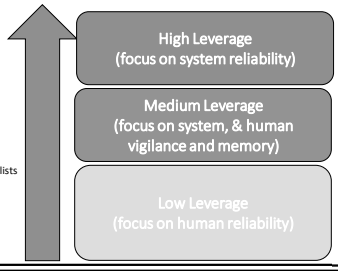
ISMP Hierarchy of Effectiveness of Risk-Reduction Strategies

Rank Order of Error Reduction Strategies:

- Forcing Functions
- Barriers & Fail Safes
- Automation & Computerization
- Standardization & Protocols
- Redundancies
- Warnings, Alerts, Reminders, & Checklists
- Rules & Policies
- Educational Programs
- Suggestions to "be more careful"



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Safety Strategies: High Leverage

Forcing Functions

- Retrieval of High-Alert Medication from Automated Dispensing Cabinet Restriction, Smart Infusion Pumps

Fail Safes & Barriers

- Fail Safes: Automated Dispensing Cabinets
- Barriers: Hard Stops (patient allergy)

Automation & Computerization

- Using computerized physician order electronic prescribing systems
- Implementing barcode technology for the preparation, dispensing, and administration of medications

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Safety Strategies: Medium Leverage

Standardization & Protocols

- Order Sets
  - Total Parenteral Nutrition Order Set
- Protocols
  - IV to PO Protocol
  - Renal Dose Adjustment Protocol
  - Therapeutic Interchange Protocol

Redundancies

- Independent double checks on dosing, infusion pump programming, and concentrations

Warnings, Alerts, Reminders, & Checklists

- Drug-Drug Interaction Alerts, High Dose Alerts, Drug Utilization Alerts

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Safety Strategies: Low Leverage

Rules & Policies

- High-Risk/High Alert Medication Policy

Educational Programs

- New employee and annual training
- Medication safety training
- Continuing education

Suggestions to be "more careful"

- Recommendations to improve

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Failure Mode and Effect Analysis (FMEA)

A **prospective** method used to evaluate the potential for failures and to determine what potential effects could occur if any change are made

Failure	Mode	Effect	Analysis
Recognize potential points where a process, product or system might fail	Specific ways in which failures can occur within a process, product or system	Effects or consequences of each failure mode on the overall process, product or system	Systematic evaluation of each failure mode to identify causes, effects and prevention strategies

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FMEA Explained

- Also called “potential failure modes and effects analysis” or “failure modes, effects and criticality analysis (FMECA)”
  - "Failure Modes“: the ways, or modes, in which something might fail
    - Failures are prioritized according to:
      - how serious their consequences are
      - how frequently they occur
      - how easily they can be detected
- "Effects Analysis“: refers to studying the consequences of those failures

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When to Use FMEA

- Evaluation of both, new and existing processes, products, or systems
  - For new products, it identifies potential falls or unintended consequences prior to their implementation
  - For existing products, it identifies how proposed changes can impact the system
- Periodically throughout the time a process, product, or systems is active
- Prior to developing control plans for a new or modified process, product, or system

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Steps to Conduct FMEA

- **Step 1.** Select a process
- **Step 2.** Recruit a team
- **Step 3.** Create a process map
- **Step 4.** Determine Failure Mode, Causes, and Effects
- **Step 5.** Determine likelihood of occurrence and detection
- **Step 6**. Assign severity and risk profile number
- **Step 7.** Solution for riskiest step
- **Step 8.** Implement solution and monitor outcomes

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Leapfrog Group

- **Nonprofit** organization dedicated to improving healthcare quality and safety in the United States
- Assigns letter grades to hospitals based on their performance in preventing **medication errors**, injuries, accidents and infections
- Conduct the Leapfrog Hospital Survey to evaluate hospitals on **safety**, quality and resource use

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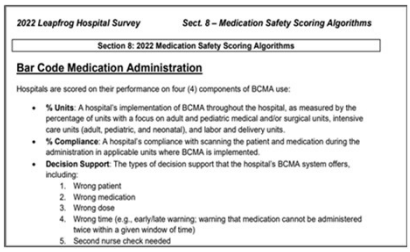
Leapfrog Hospital Survey Example



2022 Leapfrog Hospital Survey *Sect. 8 – Medication Safety Scoring Algorithms*

Section 8: 2022 Medication Safety Scoring Algorithms

Bar Code Medication Administration

Hospitals are scored on their performance on four (4) components of BCMA use:

- **% Units**: A hospital's implementation of BCMA throughout the hospital, as measured by the percentage of units with a focus on adult and pediatric medical and/or surgical units, intensive care units (adult, pediatric, and neonatal), and labor and delivery units.
- **% Compliance**: A hospital's compliance with scanning the patient and medication during the administration in applicable units where BCMA is implemented.
- **Decision Support**: The types of decision support that the hospital's BCMA system offers, including:
  1. Wrong patient
  2. Wrong medication
  3. Wrong dose
  4. Wrong time (e.g., early/late warning; warning that medication cannot be administered twice within a given window of time)
  5. Second nurse check needed

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DNV (Det Norske Veritas)

- Plays a significant role in improving medication safety in healthcare settings through its accreditation and certification programs
- DNV's NIAHO® (National Integrated Accreditation for Healthcare Organizations) standards include specific requirements for medication management
  - Ensures that hospitals have robust systems in place to manage medications safely and effectively
- Emphasizes proactive risk management
- Conducts regular surveys and assessments to ensure compliance with their standards

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Objectives - Part III

- Identify strategies, the role of technology, and the importance of a non-punitive approach for handling medication errors after errors have occurred
- Use the CQI process to encourage a culture of safety and of providing feedback and assistance to effectively minimize patient risk
- Florida law stipulates requirements for a Continuous Quality Improvement plan: Outline steps required for a successful CQI Plan incorporating the State's requirements

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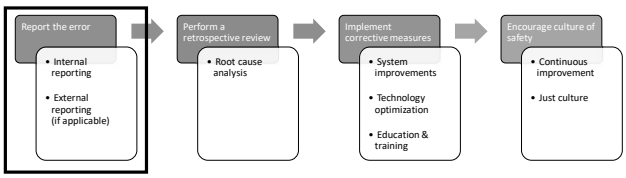
How to Address Medication Errors



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Report the Error

Internal Reporting	External Reporting
• Use institution's incident reporting system • Be detailed and objective: ○ What led to the error ○ Consequences of the error	• Depending on the type of error and the severity, may report to external bodies: ○ **FDA** (MedWatch, VAERS) ○ **ISMP** (MERP)

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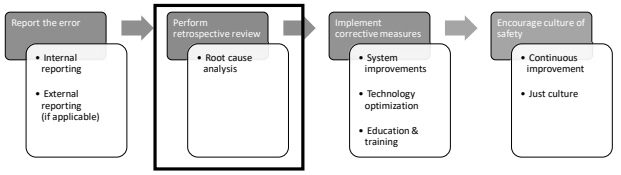
How to Address Medication Errors



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Retrospective Review

Root cause analysis (RCA)

- Uncover system-level and human factors contributing to the error
- Use data to analyze patterns in error reports, workflow, or technology that might have played a role
  - EHR issues, communication breakdowns, etc.

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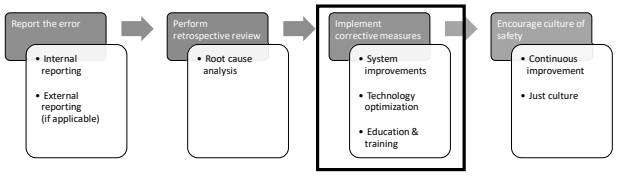
How to Address Medication Errors



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Implement Corrective Measures

- **System improvements (High Leverage, Medium Leverage)**
  - Based on the RCA, develop and implement solutions to prevent similar errors, such as revising protocols, improving alert systems, or adding redundancies like double checks
- **Technology optimization (High Leverage)**
  - Implement medication management technologies that support automation and interoperability
  - Modify decision support systems, clinical alerts, or EHR configurations to prevent medication errors
- **Education and training (Low Leverage)**
  - Reinforce education for staff about the correct procedures, potential error-prone areas, and safety precautions

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Technology Optimization

- Pharmacy Management Software
- Medication Dispensing Devices
- Workflow Management Software
- Barcode Technology
- IV Smart Pump Interoperability
- Pharmacy Clinical Surveillance Tools

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Pharmacy Management Software

Hospital	Retail
• **Cerner, Epic**	• **Enterprise, Newleaf**
• **Advantages**: ○ Electronic health record ○ Electronic prescribing software ○ Order sets ○ Alerts	• **Advantages**: ○ Electronic prescriptions ○ Organized and efficient workflow ○ Drug utilization review alerts

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Medication Dispensing Devices

Pyxis

Automated Dispensing Cabinets	Medication-filling Robot
• **Pyxis, Omnicell** o Used in hospitals • **Advantages**: o Medications available near point of care o Dispensing of right drug o Automatic drug tracking	• **Yuyama, Kirbi Lester** o Used in community pharmacies • **Advantages**: o Automated dispensing o Decreased human error o Frees staff time to focus on other activities

Kirbi Lester

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Workflow Management Software

DoseEdge

IV Verification/Tracking Software	Prescription Verification Software
DoseEdge, Medkeeper • Used in hospitals **Advantages**: • Comprehensive evaluation of the accuracy of a dose • Remote compounding verification	**Parata** • Used in community pharmacies **Advantages**: • High-speed and high-accuracy visual inspection system • Safely and efficiently verification

Parata

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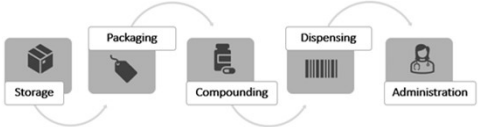
Barcode Technology



Barcode technology ensures the five rights of medication administration:

✓ Right Patient ✓ Right Drug ✓ Right Dose ✓ Right Route of Administration ✓ Right Time

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IV Smart Pump Interoperability

2020 - 2021 ISMP Targeted Medication Safety Best Practices for Hospitals

- **All IV medications should be administered through programmable IV smart pumps using dose error reduction software (DERS)**

  Most hospitals and health systems are compliant

- **Institutions should implement smart pumps with <u>bidirectional interoperability</u>* to EHRs**
  - ***Bidirectional Interoperability:*** Two-way, real-time, continuous communication between smart pump and EHR; has both of the following:
    - **Auto-programming:** Ability of EHR to transfer medication orders and infusion parameters directly to smart pump
    - **Auto-documentation:** Ability of smart pump to transfer infusion-related data to EHR

  Implementation lagging in many hospitals and health systems

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IV Smart Pump Interoperability

Cedars-Sinai. Enhancing Patient Safety Through EHR and Infusion Integration [Video]. YouTube. Published November 9, 2016. Accessed November 20, 2024. https://www.youtube.com/watch?v=-tBYYAgBRR.

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Pharmacy Clinical Surveillance Tools

Examples:
- Sentri7
- Vigilanz

Common clinical uses

Clinical Action	Description	Impact
IV to oral conversion	Alerts pharmacist to a patient on IV medication who is a candidate for conversion to oral medication	• Reduced exposure to nosocomial pathogens via intravenous access site • Reduced risk of phlebitis • Increased patient mobility • Improved patient comfort and convenience • Potential decreased length of stay • Lowered direct and indirect costs
Renal dose adjustment	Alerts pharmacist to a patient on a medication that needs to be evaluated for appropriateness of dose and/or frequency	• Optimized medication benefits • Reduced risk of serious adverse effects
Antimicrobial stewardship	Alerts pharmacist to a patient with specific combinations of culture and sensitivity results and antimicrobial therapy (de-escalation or therapy optimization opportunity)	• De-escalated or optimized medication regimen • Decreased antimicrobial resistance and multi-drug resistant organisms • Reduced waste • Avoided harm
Anticoagulation monitoring	Alerts pharmacist to patients on anticoagulant(s) to ensure appropriate use and monitoring of high-risk medications	• Improved appropriate use of anticoagulant medications • Enhanced monitoring and management of anticoagulant therapy in accordance with evidence-based guidelines, regulatory requirements, and national patient safety goals

Impact on inpatient care

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Test Question #3

The Institute for Safe Medication Practices (ISMP) created the hierarchy of effectiveness for risk-reducing strategies, which of the following is considered a medium leverage strategy?

a. Having an in-service event on how to properly document rate changes on intravenous infusion
b. Using technology with advanced analytics that identifies unusual behavior and flags individuals when it comes to dispensing and administration of controlled substances
c. System requiring an independent double check when administering a paralytic to a critically ill patient
d. A system wide protocol on how to dose and monitor patients on vancomycin

82

Test Question #3

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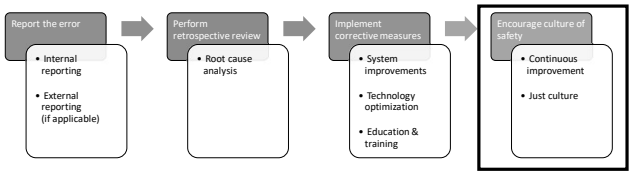
How to Address Medication Errors



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Encourage Culture of Safety: Continuous Improvement

Continuous Improvement

- Regularly review medication safety policies, analyze trends, and engage staff in proactive risk assessments
- Florida law outlines the steps required for a continuous quality improvement plan
  - **64B16-27.300 Standards of Practice - Continuous Quality Improvement Program**

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Encourage Culture of Safety: Continuous Improvement

64B16-27.300 Standards of Practice - Continuous Quality Improvement Program

1. **Establish the CQI Program Framework**
   - Define the CQI system for identifying and evaluating quality-related events (QREs) to enhance patient care
   - Identify QREs, including medication errors, dosage issues, and critical patient risks
2. **Form a CQI Committee**
   - Create a committee with pharmacists, interns, technicians, and relevant staff
   - Define roles and responsibilities for regular engagement in CQI activities

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Encourage Culture of Safety: Continuous Improvement

64B16-27.300 Standards of Practice - Continuous Quality Improvement Program

3. **Implement Regular QRE Reviews**
   - Conduct quarterly reviews of QREs to analyze issues and recommend improvements
   - Document each QRE in a dedicated record or database, recorded by the pharmacist on the reporting day
4. **Develop Procedures for Analyzing Quality**
   - Include detailed descriptions for each QRE to support analysis and corrective actions
   - Focus on process improvements related to staffing, workflow, and technology

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Encourage Culture of Safety: Continuous Improvement

64B16-27.300 Standards of Practice - Continuous Quality Improvement Program

5. **Address QREs Promptly**
   - Outline immediate corrective actions and long-term measures to resolve QREs and prevent recurrence

6. **Maintain Confidential, HIPAA-Compliant Records**
   - Ensure all CQI records are confidential and do not include patient or employee names
   - Retain summaries of QRE analyses and remedial actions for four years, adhering to peer-review protections

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Encourage Culture of Safety: Just Culture

Just Culture

- A philosophy that emphasizes accountability & learning over punishment in response to errors and near-miss events
  - **Non-punitive environment**
- Seeks to establish environment where staff feel safe to report mistakes and system vulnerabilities
  - **Promotes culture of trust and continuous improvement**
- Recognizes that human errors mainly arise from system flaws rather than individual negligence
  - **Separates events resulting from flawed system design or unintentional human error from those caused by reckless behavior**

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Encourage Culture of Safety: Just Culture

Human Error	At-Risk Behavior	Reckless Behavior
Inadvertent action (slip, lapse, mistake)	**Choice or action that increases risk (shortcuts, workarounds)**	**Conscious disregard of a substantial & unjustifiable risk**
"I forgot to enter a patient's amikacin dose"	*"I dosed a patient's amikacin using a historical weight from 2011"*	*"I purposely avoided dosing a patient's amikacin because it was hard and time-consuming"*
Manage through changes in: • Processes • Procedures • Training • Design • Environment	Manage by: • Removing incentives for at-risk behaviors • Creating incentives for healthy behaviors • Increasing situational awareness	Manage through: • Remedial action • Disciplinary action
CONSOLE	TRAIN & COACH	DISCIPLINE

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Encourage Culture of Safety: Just Culture

Second Victims

- Healthcare providers involved in unanticipated adverse patient event, medical error and/or a patient-related injury who become traumatized and become victims of their own emotions
- Often feel personally responsible as if they have failed their patients, second-guessing their clinical skills and knowledge base
- They can be overcome by feelings of guilt, depression, sleep disturbances, anxiety, suicidal ideation, burnout/turnover, PTSD, distraction, or lack of confidence
  - **May affect medical judgment and lead to further medical errors**

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Encourage Culture of Safety: Just Culture

- **Five rights of second victims (TRUST)**
  - **T**reatment that is just
  - **R**espect
  - **U**nderstanding and compassion
  - **S**upportive care
  - **T**ransparency and opportunity to contribute
- **Safety actions to consider:**
  - Instill a just culture
  - Establish a second victim response team
  - Offer immediate peer-to-peer emotional support or buddy programs

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Conclusion

- Implementing high leverage strategies can effectively reduce medication errors in healthcare settings
- Continuous improvement of healthcare processes are essential to identify weaknesses and enhance systems to prevent future errors
- Root cause analysis (RCA) and failure mode and effects analysis (FMEA) are critical methodologies for uncovering the underlying causes of medication errors, facilitating targeted interventions
- Adopting a non-punitive approach, combined with technology integration, plays a vital role in effectively managing medication errors and encouraging reporting
- Developing a Continuous Quality Improvement (CQI) Plan is necessary to meet regulatory requirements and foster an environment focused on patient safety and quality enhancement
- Cultivating a culture of safety that emphasizes "Just Culture" is crucial for minimizing medication errors and ultimately improving patient outcomes

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Take Home Points

- Medication errors can occur at any stage of the medication process
- Serious patient harm, including adverse drug events, prolonged hospital stays, and increased healthcare costs can result from medication errors
- Implementing strategies such as electronic prescribing, barcoding systems, double-checking procedures, and continuous education for healthcare professionals can significantly reduce the risk of medication errors
- Encouraging a culture where healthcare professionals feel comfortable reporting errors without fear of punishment is essential. Promoting teamwork and open communication is key to fostering this environment

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Thank You!

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Medication Errors and Continuous Quality Improvement

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Slide 1

How much is Enough: Medication Dosing in Obesity

Resident Name: Giselle Amago
Residency Program: Miami VA Healthcare System
Residency Program Location: Miami, Florida
Date of CE: 01/25/2025

Slide 2

Abbreviations

- aPTT: Activated partial thromboplastin time
- BMI: Body Mass Index
- CrCl: Creatinine Clearance
- CRP: C-reactive protein
- dL: Deciliters
- eGFR: Estimated glomerular filtration rate
- Ht: Height
- IBW: Ideal Body Weight
- IL: Interleukin
- GERD: Gastroesophageal Reflux Disease
- GI: Gastrointestinal
- Kg: Kilograms
- M: Meter
- Mg: Milligrams
- Min: Minutes
- mL: Milliliters
- US: United States
- PPI: Proton-Pump Inhibitor
- Scr: Serum Creatinine
- TBW: Total Body Weight
- TNF: Tumor Necrosis Factor
- VTE: Vein Thromboembolism
- Wt: Weight

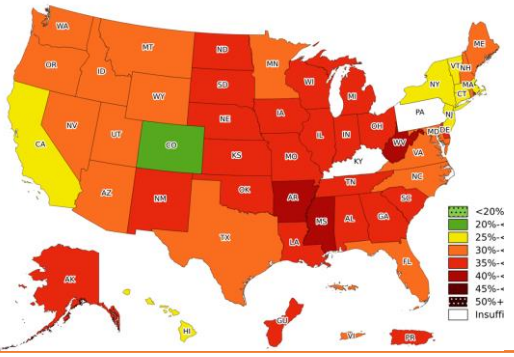
Slide 3

Objectives

1. Describe obesity's pathophysiology and classification
2. Summarize impact of obesity in the pharmacokinetic profile of medications
3. Identify body size descriptors to guide medication dosing
4. List examples of weight-based medications
5. Discuss scenarios where obesity complicates medication dosing

Slide 4

Obesity Facts



- Obesity prevalence in the US continues to rise from 15% in the 1980's to 35% or greater in 2023

Slide 5

Obesity Facts

Per CDC:

- 1/5 children and 2/5 adults in the United States have obesity
- 2023 data shows that in 23/48 states more than 1/3 adults (35%) has obesity
- Higher prevalence in Non-Hispanic African Americans and lower literacy groups
- Obesity cost the US healthcare system almost $173 billion/year in 2019

Slide 6

Obesity Pathophysiology

Energy imbalance:

calories expended < calories supplied

Genetic predisposition and chronic low-grade inflammation

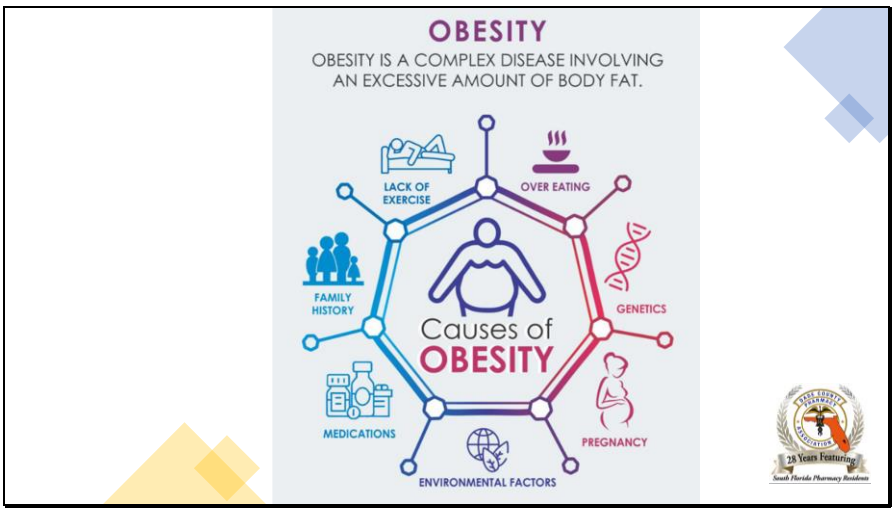
Pro-inflammatory cytokines (TNF, IL) and markers (CRP) are more elevated in obesity

Visceral adipose tissue seems to be more inflammatory versus subcutaneous fat tissue

Can lead to non-alcoholic steatohepatitis and cirrhosis = affects metabolism/elimination

Adipose tissue accumulation → Weight increased → Physiological changes → Main phases of pharmacokinetics of drugs → Inappropriate doses

Slide 7



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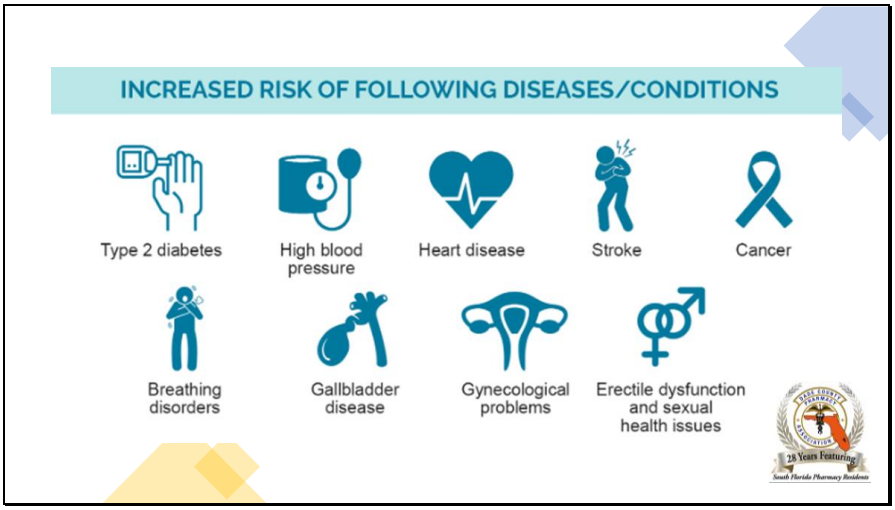

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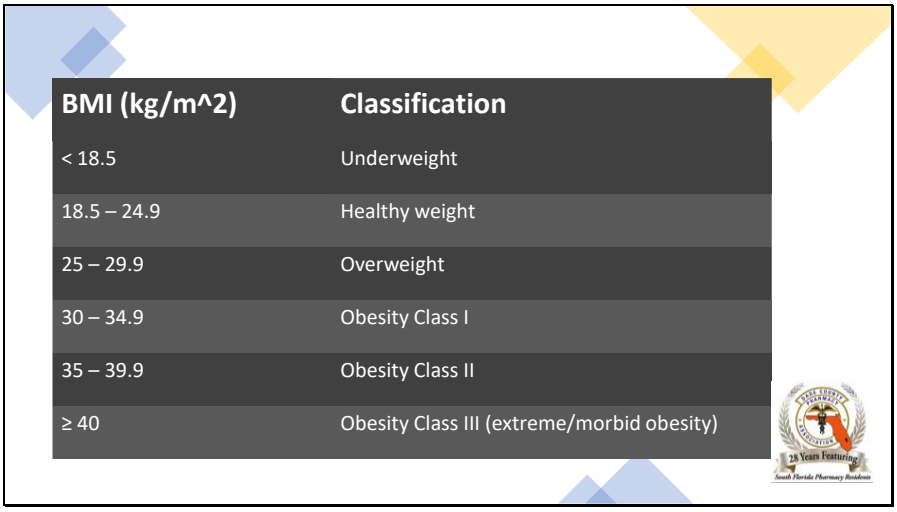


BMI (kg/m^2)	Classification
< 18.5	Underweight
18.5 – 24.9	Healthy weight
25 – 29.9	Overweight
30 – 34.9	Obesity Class I
35 – 39.9	Obesity Class II
≥ 40	Obesity Class III (extreme/morbid obesity)

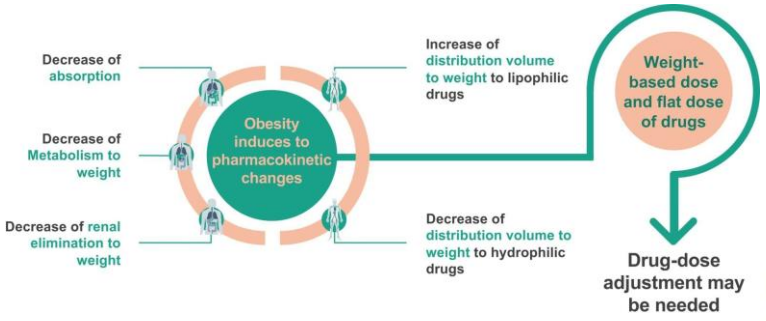
Slide 10

Pathophysiological Modifications in Obesity

- Increased blood flow and GI transit
- Changes in body composition
- Hepatomegaly
- Liver and kidney impairment

Slide 11

Pharmacokinetic Changes in Obesity



Slide 12

Absorption

- Oral absorption depends on:
  - GI pH
  - Gut motility
- Transdermal and subcutaneous absorption depends on:
  - Adipose tissue
  - Gastric retention time

Slide 13

Absorption

- GI pH affects ionization state
  - Alkaline molecules are ionized in acidic environment = more soluble
  - Many patients with obesity have GERD → more PPI → higher pH → decrease absorption of medications like tyrosine kinase inhibitors (needs acidic pH)
- Gut motility and gastric retention time
  - Studies' results differ but show trends favoring gastric emptying acceleration = less gastric retention

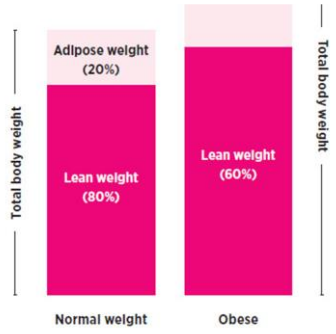
GI transit ↑ and gastric retention ↓ = ↓ Absorption

- Contraceptive/Nicotine patches consistently show lower mean concentration in obesity

Slide 14

Distribution

- Depends on body composition which affects volume of distribution of drugs
- Total body weight is composed by fat mass (20%) and lean body weight (80%)
  - Lean body weight changes with age, physical activity, and ethnicity = interindividual variability between patients with obesity



Slide 15

Distribution

- Liver and adipose tissue volume and mass increase significantly with body weight increase
  - Expansion of lipophilic compartment
- Blood volume and flow increases to compensate for the metabolic demand
  - Still adipose tissue's blood flow is about 20 times lower than muscle's blood flow = difficult access for drugs

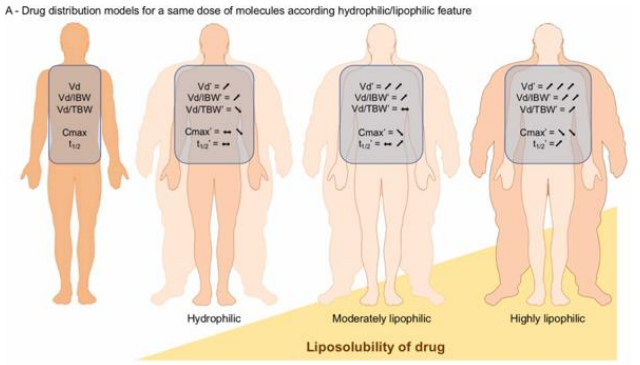
Slide 16

Distribution

- Volume of distribution does not proportionally increase with body weight
  - Depends on amount of water in adipose tissue and severity of obesity
  - Less severe obesity = more water in adipose tissue = better penetration of hydrophilic drugs
  - Studies suggest that aminoglycosides' volume of distribution is reduced in morbid obesity
  - Lipophilic drugs' volume of distribution is higher = less exposure/concentration
    - ❖Benzodiazepines and verapamil accumulate in fat tissue = prolonged half-life, longer time to steady state

- In Obesity: **Fat mass ↑ and Lean Body Weight ↓**
  - **Volume of distribution of lipophilic drugs ↑↑↑ = underdosing**
  - Volume of distribution of hydrophilic drugs ↓ = overdoses with total body weight
  - Influences half-life, peak concentrations, and steady state concentrations of drugs

Slide 17



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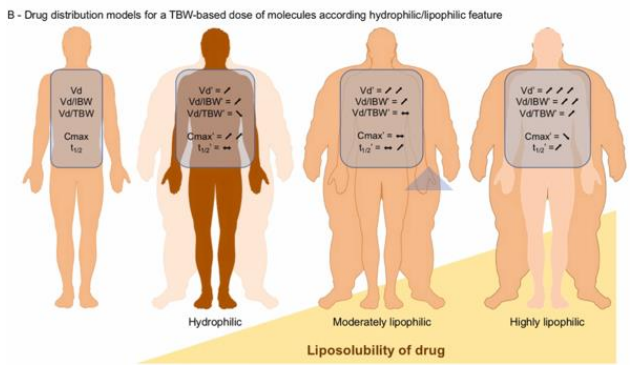
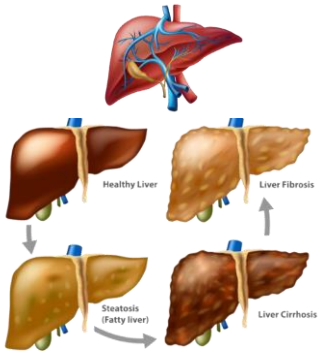


Slide 19

Metabolism



- Hepatic clearance depends on:
  - Hepatic extraction
  - Liver blood flow

Slide 20

Metabolism

- In obesity:
  - Higher hepatic blood flow due to higher blood volume → enhances hepatic metabolism
- Liver undergoes fatty infiltration → Non-alcoholic fatty liver disease
  - Ranges from liver steatosis to cirrhosis = decrease metabolism
  - Changes to Phase I metabolism (CYP450- enzymes)
  - Changes to Phase II metabolism (glucuronidation)

Slide 21

Changes to CYP450-Enzymes in Obesity

- Reduced CYP3A4/ CYP2C19 expression = ↓ active metabolites for prodrugs and ↑ some active drugs = under/overdose
  - Less metabolism of benzodiazepines (midazolam, alprazolam), carbamazepine = less extraction/clearance
  - Clopidogrel resistance associated to obesity and higher BMI
  - Pantoprazole shows 50% less clearance = enhanced exposure in obesity
  - CYP3A4 could be affected by weight loss and bariatric surgery → increasing the hepatic extraction
    - ❖Requires higher doses of medications like tacrolimus, sirolimus, and mycophenolic acid

Slide 22

Changes to CYP450-Enzymes in Obesity

- Increased CYP2D6 metabolism but studies do not associate activity with BMI
- Trend suggest increased CYP2C9 metabolism, but studies show no significant correlation with activity and BMI
  - Phenytoin and ibuprofen have higher clearance in obesity
  - Not enough known to verify impact of obesity on CYP2C9 metabolism

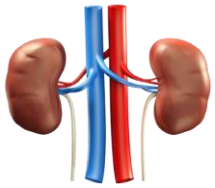
Slide 23

Changes to Glucuronidation in Obesity

- Increased glucuronidation
  - Acetaminophen has increased elimination correlated to BMI
  - Morphine has ↑ active metabolite concentrations, but formation is similar to that of non-obese patients
    - ❖Accumulation attributed to decreased clearance and impairment of transporters
- Limited studies - unable to make conclusions

Slide 24

Renal Extraction



- Main route of drug elimination
  - Depends on renal elimination capacity and muscle mass
- Creatinine: metabolite produced by muscle, exclusively eliminated by kidneys
- Multiple formulas to determine eGFR
  - **Cockcroft & Gault**
    - ❖Uses TBW → overestimates clearance → potential overdose
    - ❖Using theoretical weight **(Lean body weight)** is most accurate
      - ➢Creatinine clearance is closely related to lean body weight
  - MDRD4 (Modification of Diet in Renal Disease)
    - ❖Underestimates clearance
    - ❖Preferred in patients with renal impairment
  - Chronic Kidney Disease Epidemiology (CKD-Epi)

Slide 25

Renal Elimination in Obesity

- Obesity associated with diabetes, hypertension, hyperlipidemia, and overactivation of renin-angiotensin system leads to glomerular hyperfiltration
- Age
- As body size increases, clearance increases
- Lean body weight is the preferred descriptor for estimation of clearance

Slide 26

Impact in Medication Dosing

- **Recommended doses of medications are based on pharmacokinetic data from individuals with normal weights**
  - Difficult for providers to determine appropriate dose
  - Understanding drugs' pharmacokinetic properties and pathophysiologic changes are essential when deciding dosing regimen

Slide 27

Body Size Descriptors

Name of Descriptor	Formula
Total body weight (kg)	-
Ideal body weight (kg)	Male: 50 kg + 2.3 x (inches > 60) Female: 45.5 kg + 2.3 x (inches > 60)
Lean body weight (kg)	Male: $\frac{9270 \times TBW}{6680 + 216 \times BMI}$ Female: $\frac{9270 \times TBW}{8780 + 244 \times BMI}$
Adjusted body weight (kg)	IBW + 0.4 (TBW – IBW)
Body Surface Area (m^2)	$\sqrt{\frac{height\ (cm) x\ TBW}{3600}}$

Slide 28

Total Body Weight

- Assumes linear pharmacokinetic behavior of drugs from normal-weight patients to patients with obesity
- Problems wit assumption:
  - Cannot assume that a 150 kg patient eliminates a drug twice as fast as a patient of 75 kg and double the dose
  - Higher doses = more toxicity
    - ❖Nephrotoxicity, neurotoxicity with antibiotics
    - ❖Bleeding with anticoagulants
- Solution: dose reductions/ "caps" to doses
  - Problem: can lead to subtherapeutic exposure and treatment failure

Slide 29

Ideal Body Weight

Male: 50 kg + 2.3 x (inches > 60)
Female: 45.5 kg + 2.3 x (inches > 60)

- Does not account for body composition
- Assumes that all patients of same height and sex should receive same dose
- Problem with assumption:
  - Inaccurate in practice, can lead to underdosing
  - A male with TBW of 150 kg and height of 170 cm has same ideal body weight as a male who is 80 kg and 170 cm tall
  - Both could potentially receive a mg/kg dose based on 65 kg (ideal body weight)

Slide 30

Lean Body Weight

Male: $\frac{9270 \times TBW}{6680 + 216 \times BMI}$

Female: $\frac{9270 \times TBW}{8780 + 244 \times BMI}$

- Reflects weight of all "non-fat: body components (muscle/vascular organs like liver and kidneys)
- It contributes to **~99% of drug's clearance** = **Useful for guiding dosing in obesity**
- Most commonly cited formula
  - Not optimal and can produce a negative result
  - The new Janmahasatian formula is preferred
    - ❖ More stable across body sizes, especially in morbid obesity
- Problem: numerical complexity with clinician's limited time

Slide 31

Adjusted Body Weight

IBW + 0.4 (TBW – IBW)

- Mainly used in aminoglycoside antibiotic dosing with the correction factor
- Accounts for adipose tissue, but does not affect drug clearance
- Rarely used, but some evidence for use in antibiotics in morbid obesity

Slide 32

Body Surface Area

$$\sqrt{\frac{height\ (cm) x\ TBW}{3600}}$$

- Mainly used to dose chemotherapeutic drugs
- Correlates with cardiac output, blood volume, and renal function
- Controversial in patients at extremes of body sizes → does not account for varying body composition
  - Why older drugs (cyclophosphamide, paclitaxel, and doxorubicin) were capped (2 m^2) → could result in subtherapeutic treatment
- Unless reduced dose is required (renal disease), total body weight should be used in calculation
- Minimal research on its use with other medications

Slide 33

Main Points for Medication Dosing with Size Descriptors

- Estimation of optimal dose for obese patients is difficult
- Use of total body weight will not provide comparable drug response across different body sizes
  - Can lead to underdosing or toxicity
- Individualized dosing based on **lean body weight** is recommended due to its correlation with **drug clearance**
  - Along with therapeutic drug monitoring and clinical response

Slide 34

Examples of Weight-Based Medications

Disclaimers:
- Not all inclusive list
- Recommendations have limitations and do not apply to all patients
- Clinical judgement and personalized therapy should guide dosing in practice

Slide 35

Anticoagulants	Dosing Recommendations	Notes
Enoxaparin	Usually: Treatment: Capped at 100 mg in patients over 100 kg Prophylaxis: 20-40 mg daily Suggestion: Treatment VTE: 1.5 mg/kg (lean body weight) Prophylaxis: 30-40 mg twice daily	Hydrophilic drug → increased clearance in obesity Subtherapeutic concentrations
Unfractionated heparin	Usually dosed based on total body weight (units/kg or units/kg/hour) and aPTT: Cap dose varies by institution Prophylaxis: 5000 units twice or three times a day Suggestion for prophylaxis: 5000 units three times a day	Hydrophilic drug → increased clearance in obesity Subtherapeutic concentrations
Direct Oral Anticoagulation (Apixaban, Rivaroxaban, Dabigatran, Edoxaban)	Apixaban: no dose adjustment (changes not expected to be clinically meaningful) 5 mg every 12 hours Rivaroxaban: no dose adjustment (low Volume of distribution) 20 mg daily with food Dabigatran: studies shown subtherapeutic levels/thromboembolism → switch to alternative Edoxaban: concerns with increased clearance in obesity → use alternative	Each may have different outcomes Low-quality data supports avoiding Dabigatran or considering Apixaban/Rivaroxaban Lack of data for Edoxaban

Slide 36

Antibiotics/Antiviral/ Antifungal	Dosing Recommendations	Notes
Vancomycin	Loading dose: 20-25 mg/kg (max: 3 grams)	Use total body weight Adjust based on clinical response, therapeutic drug monitoring (peak and trough)
Gentamicin	Use adjusted body weight	Adjust based on clinical response, therapeutic drug monitoring
Cefepime	Up to 2 grams every 8 hours extended infusion	Extended infusion preferred in critically ill patients to overcome variability in serum concentration
Acyclovir	5 mg/kg IV x 1	Use ideal or adjusted body weight in obesity Renal function is the most important consideration for dosing
Fluconazole	Loading dose: 12 mg/kg x 1 Maintenance: 6 mg/kg every 24 hours	Use total body weight Variable exposure in obesity, data is limited and shows worse outcomes in obesity

Slide 37

Sedation	Dosing Recommendations	Notes
Propofol	Induction: IBW 0.5-2.5 mg/kg Maintenance: TBW or IBW 50-200 mcg/kg/minute	Highly lipophilic but does not accumulate in obesity Requires large doses, unclear effects (deleterious cardiovascular effects) Adjust based on clinical response
Dexmedetomidine	Use IBW or Adjusted body weight	Limited data in obesity Studies show significantly lower clearance in obesity: careful
Midazolam	Initial Doses/continuous infusions: IBW or Adjusted body weight	Highly lipophilic = increased volume of distribution, may benefit from larger initial doses Clearance does not seem to change with BMI = possible accumulation Supplemental doses as needed until desired effect is achieved

Slide 38

Scenarios with Challenging Medication Dosing

Disclaimers:
- Recommendations have limitations and do not apply to all patients
- Clinical judgement and individualized therapy should guide dosing in practice

Slide 39

Scenario 1:
Antimicrobial medication dosing for patient with septic shock

- Patient: 35-year-old man, BMI = 50 kg/m^2
- With life-threatening infection in septic shock
- No knowledge of pharmacokinetic/pharmacodynamic changes or impact of antimicrobial medication dosing
- Team wants to start empiric therapy with Piperacillin/Tazobactam, but unsure of what dosing method to use

Slide 40

Scenario 1:
Antimicrobial medication dosing for patient with septic shock

- Dosing Options: traditional infusion method versus extended infusion method
- Recommendation: Extended infusion method
  - Piperacillin/Tazobactam 4.5 grams every 8 hours infused over 4 hours
    - ❖Per Stanford Antimicrobial Safety and Sustainability Program Dosing Guide for Obesity
    - ❖Preferred in critically ill, treating pathogen with MIC ≥ 8 mg/dL, or CrCl > 100 mL/min
- Reasoning: increases drug concentration early = increased likelihood of target concentration at site of infection = improved outcomes

Slide 41

Scenario 2:
VTE prophylaxis dosing

- Patient: 69 year-old man, BMI = 44.8 kg/m^2 (Ht: 67 inches, Wt: 130 kg)
- In ICU after motor vehicle accident with pelvic and multiple rib fractures
- Scr = 1.1 mg/dL, CrCl = 72.9 mL/min
- Recommendations for VTE prophylaxis?

Slide 42

Scenario 2:
VTE prophylaxis dosing

- <u>VTE prophylaxis:</u> Enoxaparin have shown to be superior in this population
  - One study by Scholten showed a lower incidence of VTE in patients using enoxaparin 40 mg twice daily
  - Clearance increases with body size

Slide 43

Slide 44

1. Fill in the Blank

As the fat mass increases at the expense of the lean body weight, the volume of distribution for lipophilic drugs ___increases_____.

Slide 45

2. True or False

True

Medication dosing recommendations are based on pharmacokinetic data from individuals with normal weights making it challenging for providers to make dosing decisions for obese patients

Slide 46

3. Multiple Choice

Drug Clearance is greater in obesity and correlates with:

a) Total body weight
b) Adipose body weight
c) Lean body weight

Slide 47

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Slide 48

Thank you

Breathe Easy: Asthma Guideline Updates

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January 25th, 2025

1

Objectives

- Review the epidemiology, pathophysiology, and diagnosis of asthma
- Discuss the 2024 GINA guideline update for the adult and pediatric populations
- Evaluate the role of AIRSUPRA® in the treatment of asthma

2

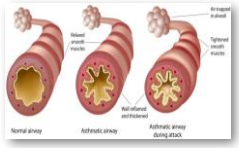
What is Asthma?

- Asthma is defined as:
  - History of respiratory symptoms
  - Airflow limitation
  - Severity that varies over time

3

Pathophysiology

- Asthma is a chronic disease of the lungs that causes bronchoconstriction, due to
  - Airway inflammation
  - Airway hyperresponsiveness
  - Mucous secretion
- Inflammation and hyperresponsiveness of the airway is a result of allergens and triggers in the airway epithelium that lead to IgE release



4 Journal of Allergy and Clinical Immunology. 2020;145(6):1983-1995. The Lancet. 2018;391(10131):783-800. IgE: Immunoglobulin E

4

Pathophysiology

- While bronchoconstriction is reversible, inadequate treatment and triggers can lead to irreversible airway remodeling
- Airway remodeling consists of:
  - Epithelial damage
  - Airway smooth muscle hypertrophy
  - Subepithelial fibrosis
  - Reticular basement membrane thickening

5 The Lancet. 2018;391(10131):783-800.

5

Clinical Presentation

Chest tightness	Cough
Wheezing	Shortness of breath

6 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2024.

6

Epidemiology - 2021

- A total of **4,700,000** children and **20,300,000** adults were diagnosed with asthma nationally
- A total of 9,900,000 children and adults experienced an asthma attack
- Approximately 100,000 children and adults required an emergency visit, with about 2.9% requiring hospitalization
- A **10.6%** mortality rate per million was recorded across both children and adults

7 Most Recent National Asthma Data. Centers for Disease Control and Prevention.

7

Asthma Guidelines

8

GINA

- GINA was established in 1993 by the National Heart, Lung, and Blood Institute, National Institutes of Health, and the World Health Organization to spread awareness to healthcare providers
- Collaborates with healthcare professionals, patient representatives, and public health officials worldwide to help reduce the prevalence, mortality, and morbidity of asthma
- GINA updates The Global Strategy for Asthma Management and Prevention yearly
  - Used by healthcare professionals for guidance for the management of asthma

9 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2024.

9

Diagnosis of Asthma

10

Diagnostic Tools

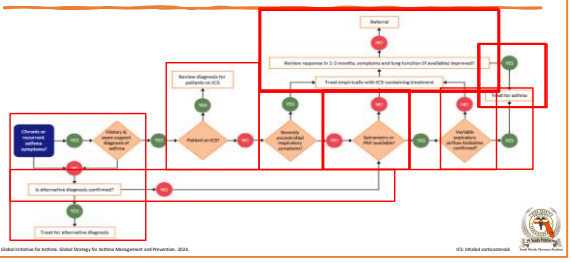
- Spirometry
  - Previously the only tool recommended for the diagnosis of asthma
  - Measures how much air can be inhaled and exhaled
  - Diagnosis: FEV_1 or FVC ≥ 12% and ≥ 200 mL
- PEF
  - May be used if spirometry not possible
  - Measures the airflow out of the lungs
  - Diagnosis:
    - Adults: PEF ≥ 20%
    - Pediatrics: PEF ≥ 15%

11 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2024.

FEV$_1$, Forced expiratory volume in one second
FVC: Forced vital capacity
PEF: Peak expiratory flow

11

Diagnostic Flowchart



12 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2024.

ICS: Inhaled corticosteroid

12

Diagnosing Patients on ICS

- ICS dose should be reduced by 25-50%
  - Asthma control and lung function should be reassessed within 2-4 weeks following the reduction
- If variable expiratory limitation and worsening symptoms are observed, asthma diagnosis is confirmed
- If symptoms remain stable and no variable expiratory limitation is noted, the ICS-containing product should be discontinued
  - Asthma control and lung function tests should be reassessed in another 2-3 weeks

13 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2024.

13

Diagnosis for 5 Years & Younger

- Diagnosis can be difficult in this population
- Various tests are used to assist in the diagnosis of asthma in this population, such as:
  - Therapeutic trials
  - Allergic sensitization tests
  - Chest radiographs
  - Lung function test
  - Exhaled nitric oxide

14 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2024.

14

Knowledge Check

PEF can be used as a diagnostic tool instead of spirometry

A. True

B. False

15

15

Knowledge Check

PEF can be used as a diagnostic tool instead of spirometry

A. True

B. False

16

16

Diagnostic Tools

- Spirometry
  - Previously the only tool recommended for the diagnosis of asthma
  - Measures how much air can be inhaled and exhaled
  - Diagnosis: FEV_1 or FVC ≥ 12% and ≥ 200 mL
- PEF
  - May be used if spirometry not possible
  - Measures the airflow out of the lungs
  - Diagnosis:
    - Adults: PEF ≥ 20%
    - Pediatrics: PEF ≥ 15%

17 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2024.

FEV$_1$: Forced expiratory volume in one second
FVC: Forced vital capacity
PEF: Peak expiratory flow

17

Adult and Adolescent Populations

18

Track 1 versus Track 2

- For adult and adolescent asthma management, two tracks can be used
- The GINA guidelines recommend the use of track 1 over track 2
  - Track 1 consists of the use of ICS-formoterol inhaler for AIR therapy and MART
    - AIR therapy is considered for steps 1-2
    - MART is considered for steps 3-5
  - Track 2 uses PRN ICS + SABA or SABA alone for rescue therapy
    - AIR therapy is considered at all steps

AIR: Anti-inflammatory reliever
MART: Maintenance-and-reliever therapy
PRN: As needed
SABA: Short-acting beta-agonist

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AIR versus MART

- AIR therapy involves the use of an inhaler containing a low-dose ICS and a rapid-acting bronchodilator as needed
- MART involves the use of a daily ICS-formoterol inhaler in addition to an as needed reliever treatment
- Both AIR therapy and MART have been associated with a reduction in severe exacerbations

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Treatment for ≥ 12 Years of Age

Steps 1-2: Symptoms ≤ 3-5 days per week and normal/mildly reduced lung function

Track 1 – Steps 1-2 PRN low-dose ICS-formoterol	**Track 2 – Step 1** ICS when SABA is taken	**Track 2 – Step 2** Low-dose ICS
Alternative – Steps 1-2 Low-dose ICS when PRN SABA taken OR LTRA OR HDM SLIT		

SABA: Short-acting beta-agonist
LTRA: Leukotriene-receptor antagonist
HDM: House-dust mite
SLIT: Sublingual immunotherapy

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Treatment for ≥ 12 Years of Age

Step 3: Symptoms most days or nighttime awakening ≥ 1 per week or low lung function

Track 1 Low-dose ICS-formoterol	**Track 2** Low-dose ICS-LABA

Alternative
Medium-dose ICS OR LTRA OR HDM SLIT

LABA: Long-acting beta-agonist

22

Treatment for ≥ 12 Years of Age

Step 4: Daily symptoms, awakening at night ≥ 1 per week, and low lung function or recent exacerbation

Track 1 Medium-dose ICS-formoterol	**Track 2** Medium/high-dose ICS-LABA

Alternative
High-dose ICS OR LAMA OR LTRA OR HDM SLIT

LAMA: Long-acting muscarinic antagonist

23

Treatment for ≥ 12 Years of Age

Step 5: Persistent symptoms or exacerbations despite adherence and correct use of inhaler

Track 1 LAMA/refer for phenotype assessment OR high-dose **ICS-formoterol** ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP	**Track 2** LAMA/refer for phenotype assessment OR high-dose **ICS-LABA** ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

Alternative
Azithromycin OR LTRA OR low-dose oral corticosteroids

IL5: Interleukin-5
IL5R: Interleukin-5 receptor
IL4Rα: Interleukin-4 receptor alpha
TSLP: Thymic stromal lymphopoietin

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Recommended AIR & MART

ICS-formoterol Inhaler for ≥ 18 Years of Age	Dosing
Budesonide-formoterol 160/4.5 mcg per inhalation (DPI, pMDI)	**Steps 1-2**: 1 inhalation PRN **Step 3**: 1 inhalation BID (or daily) + 1 inhalation PRN **Steps 4-5**: 2 inhalations BID + 1 inhalation PRN **Max: 12 inhalations per day**
Budesonide-formoterol 80/2.25 mcg per inhalation (pMDI)	**Steps 1-2**: 2 inhalations PRN **Step 3**: 2 inhalations BID (or daily) + 2 inhalations PRN **Steps 4-5**: 4 inhalations BID + 2 inhalations PRN **Max: 24 inhalations per day**
Beclomethasone-formoterol 100/6 mcg per inhalation* (DPI, pMDI)	**Steps 1-2**: 1 inhalation PRN **Step 3**: 1 inhalation BID (or daily) + 1 inhalation PRN **Steps 4-5**: 2 inhalations BID + 1 inhalation PRN **Max: 12 inhalations per day**

***Not studied for AIR therapy, may be suitable due to effectiveness observed for MART**

DPI: Dry powder inhaler; pMDI: Pressurized meter-dosed inhaler; PRN: As needed; BID: Twice-daily

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Recommended AIR & MART

ICS-formoterol Inhaler for 12-17 Years of Age	Dosing
Budesonide-formoterol 160/4.5 mcg per inhalation (DPI, pMDI)	**Steps 1-2**: 1 inhalation PRN **Step 3**: 1 inhalation BID (or daily) + 1 inhalation PRN **Steps 4-5**: 2 inhalations BID + 1 inhalation PRN **Max: 12 inhalations per day**
Budesonide-formoterol 80/2.25 mcg per inhalation (pMDI)	**Steps 1-2**: 2 inhalations PRN **Step 3**: 2 inhalations BID (or daily) + 2 inhalations PRN **Steps 4-5**: 4 inhalations BID + 2 inhalations PRN **Max: 24 inhalations per day**

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ICS Dose Options

ICS Inhaler	Low (mcg)	Medium (mcg)	High (mcg)
Beclometasone dipropionate (standard particle, pMDI HFA)	200-500	> 500-1000	> 1000
Beclometasone dipropionate (extra-fine particle, DPI or pMDI, HFA)	100-200	> 200-400	> 400
Budesonide (standard particle, DPI or pMDI, HFA)	200-400	> 400-800	> 800
Ciclesonide (extra-fine particle, pMDI, HFA)	80-160	> 160-320	> 320
Fluticasone furoate (DPI)	100		> 200
Fluticasone propionate (DPI, standard particle pMDI, HFA)	100-250	> 250-500	> 500
Mometasone furoate (standard particle, pMDI, HFA)	200-400		> 400

Displayed is the total daily ICS dose alone or in combination with LABA
Potency equivalence is not implied between inhalers

HFA: Hydrofluoroalkane propellant

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Different Types of Inhalers

- DPI
  - Active ingredient is stored as a dry powder within a capsule
  - Once inhaler is prepared, a quick forceful inhalation ensures proper delivery of the medication
- pMDI/HFA
  - Medication is stored in a pressurized canister; active ingredient is released as an aerosol or mist once canister is pressed
  - Inhalation should be slow and steady to ensure proper delivery of the medication

28 How to use a dry-powder inhaler. National Heart, Lung, and Blood Institute. 2021.
How to use a metered-dose inhaler. National Heart, Lung, and Blood Institute. 2021.

28

Knowledge Check

Which of the following is an inhaler that can be used for AIR therapy using track 1 management?

A. Budesonide-formoterol pMDI

B. Fluticasone DPI

C. Mometasone-formoterol HFA

D. Fluticasone-salmeterol pMDI

29

29

Knowledge Check

Which of the following is an inhaler that can be used for AIR therapy using track 1 management?

A. Budesonide-formoterol pMDI

B. Fluticasone DPI

C. Mometasone-formoterol HFA

D. Fluticasone-salmeterol pMDI

30

30

Recommended AIR & MART

ICS-formoterol Inhaler for ≥ 18 Years of Age	Dosing
Budesonide-formoterol 160/4.5 mcg per inhalation (DPI, pMDI)	**Steps 1-2**: 1 inhalation PRN **Step 3**: 1 inhalation BID (or daily) + 1 inhalation PRN **Steps 4-5**: 2 inhalations BID + 1 inhalation PRN **Max: 12 inhalations per day**
Budesonide-formoterol 80/2.25 mcg per inhalation (pMDI)	**Steps 1-2**: 2 inhalations PRN **Step 3**: 2 inhalations BID (or daily) + 2 inhalations PRN **Steps 4-5**: 4 inhalations BID + 2 inhalations PRN **Max: 24 inhalations per day**
Beclomethasone-formoterol 100/6 mcg per inhalation* (DPI, pMDI)	**Steps 1-2:** 1 inhalation PRN **Step 3:** 1 inhalation BID (or daily) + 1 inhalation PRN **Steps 4-5:** 2 inhalations BID + 1 inhalation PRN **Max: 12 inhalations per day**

*Not studied for AIR therapy, may be suitable due to effectiveness observed for MART

DPI: Dry powder inhaler PRN: As needed
pMDI: Pressurized meter-dosed inhaler BID: Twice daily

31

Pediatric Population

32

Treatment for 6 – 11 Years of Age

Step 1: Symptoms < 2 days per week

PRN SABA

Low-dose ICS when SABA is taken

33

Treatment for 6 – 11 Years of Age

Step 2: Symptoms 2-5 days a week

Low-dose ICS

Alternative
LTRA OR low-dose ICS when SABA taken

PRN SABA

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34

Treatment for 6 – 11 Years of Age

Step 3: Symptoms most days or waking up at night ≥ 1 per week

Low-dose ICS-LABA OR medium-dose ICS OR very low dose ICS-formoterol (MART)

Alternative
Low-dose ICS + LTRA

PRN SABA or ICS-formoterol

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35

Treatment for 6 – 11 Years of Age

Step 4: Symptoms most days, waking up at night ≥ 1 per week, and low lung function

Refer for expert advice OR medium-dose ICS-LABA OR low-dose ICS-formoterol (MART)

Alternative
Tiotropium OR LTRA

PRN SABA or ICS-formoterol

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36

Treatment for 6 – 11 Years of Age

Step 5: Persistent symptoms or exacerbations despite adherence and correct use of inhaler

Refer for phenotype assessment ± higher dose ICS-LABA/anti-IgE, anti-IL4Rα, anti-IL5

Alternative
Low-dose oral corticosteroids

PRN SABA

37

ICS Dose Options

ICS Inhaler	Low (mcg)	Medium (mcg)	High (mcg)
Beclometasone dipropionate (standard particle, pMDI HFA)	100-200	> 200-400	> 400
Beclometasone dipropionate (extra-fine particle, pMDI, HFA)	50-100	> 100-200	> 200
Budesonide (standard particle, DPI or pMDI, HFA)	100-200	> 200-400	> 400
Budesonide (nebules)	250-500	> 500-1000	> 1000
Ciclesonide (extra-fine particle, pMDI, HFA)	80	> 80-160	> 160
Fluticasone furoate (DPI)	50		-
Fluticasone propionate (DPI, standard particle, pMDI, HFA)	50-100	> 100-200	> 200
Mometasone furoate (standard particle, pMDI, HFA)	100		200

Displayed is the total daily ICS dose alone or in combination with LABA
Potency equivalence is not implied between inhalers

38

Recommended MART

Inhaler	Dose
Budesonide-formoterol 80/4.5 mcg per inhalation (DPI)	**Step 3:** 1 inhalation daily + 1 inhalation PRN **Step 4:** 1 inhalation BID + 1 inhalation PRN **Max: 8 inhalations per day**

39

Treatment for 5 Years & Younger

Step 1: Infrequent viral wheezing and no or few interval symptoms

Insufficient evidence for the use of a daily controller

Alternative
Short course ICS at onset

PRN SABA

40 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2024.

40

Treatment for 5 Years & Younger

Step 2: Inconsistent asthma symptoms requiring SABA ≥ 3 per year, symptoms indicating asthma is not well controlled or experiencing ≥ 3 exacerbations per year

Low-dose ICS

Alternative
LTRA OR intermittent short course ICS at onset

PRN SABA

41 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2024.

41

Treatment for 5 Years & Younger

Step 3: Asthma diagnosis & not controlled on low-dose ICS

Double 'low-dose' ICS

Alternative
Low-dose ICS + LTRA OR specialist referral

PRN SABA

42 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2024.

42

Treatment for 5 Years & Younger

Step 4: Asthma not well-controlled on double 'low-dose' ICS

Continue controller & refer to specialist

Alternative
LTRA OR increase ICS frequency
OR intermittent ICS

PRN SABA

43 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2024.

43

ICS Dose Options

ICS Inhaler	Total daily low dose (mcg)
Beclometasone dipropionate (pMDI, standard particle, HFA)	100 (≥ 5 years of age)
Beclometasone dipropionate (pMDI, extrafine particle, HFA)	50 (≥ 5 years of age)
Budesonide nebulized	500 (≥ 1 year of age)
Fluticasone propionate (pMDI, standard particle, HFA)	50 (≥ 4 years of age)
Mometasone furoate (pMDI, standard particle, HFA)	100 (≥ 5 years of age)

Potency equivalence is not implied between inhalers

44 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2024.

44

Knowledge Check

A 7-year-old female presents with asthma symptoms 3 days per week with no nighttime awakenings. Which is the recommended initial treatment for this patient?

A. Medium-dose ICS
B. Low-dose ICS + PRN SABA
C. SABA PRN
D. Low-dose ICS + LABA + LAMA

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45

Knowledge Check

A 7-year-old female presents with asthma symptoms 3 days per week with no nighttime awakenings. Which is the recommended initial treatment for this patient?

A. Medium-dose ICS

B. Low-dose ICS + PRN SABA

C. SABA PRN

D. Low-dose ICS + LABA + LAMA

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Treatment for 6 – 11 Years of Age

Step 2: Symptoms 2-5 days a week

Low dose ICS

Alternative
LTRA OR low dose ICS when SABA taken

PRN SABA

47 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2024.

47

Newly FDA-Approved Inhaler: AIRSUPRA®

48

AIRSUPRA®

- FDA-approved combination inhaler consisting of SABA plus ICS for adults
- Components: albuterol and budesonide
- Strength: 90/80 mcg per inhalation
- Dosing: Two inhalations every 4 hours PRN for asthma symptoms (max: 12 inhalations in 24 hours)

49 U.S Food and Drug Administration. 2023.

49

MANDALA Trial

Study Design	Methods	Intervention	Outcomes	Results
• Phase 3 • Randomized • Double-blinded • Multinational • Event-driven	**Inclusion:** • Age ≥ 4 years with at least one exacerbation • On medium-high dose ICS-LABA for ≥ 3 months • FEV_1 40-90% with a 12% reversibility **Exclusion:** • COPD • Systemic glucocorticoid • Biologic treatment	• Albuterol-budesonide 90/80 mcg vs albuterol 90 mcg: 2 inhalations as needed in response to symptoms (max: 12 inhalations/day) • Albuterol-budesonide 90/40 mcg vs albuterol 90 mcg: 2 inhalations as needed in response to symptoms (max: 12 inhalation/day)	**Primary Outcome:** • First event of severe asthma exacerbation in a time-to-event analysis	**Primary Outcome:** • Albuterol-budesonide 180/160 mcg vs albuterol 180 mcg: HR, 0.74; 95% CI: 0.62-0.89; **P=0.001** • Albuterol-budesonide 180/80 mcg vs albuterol 180 mcg: HR, 0.84; 95% CI: 0.71-1; **P=0.05**

Statistically significant reduction in the risk of experiencing a severe asthma exacerbation was observed in individuals with controlled moderate-to-severe asthma who were treated with albuterol-budesonide compared to albuterol alone

50 *The New England Journal of Medicine*. 2022;386(21):2071-2083.

COPD: Chronic obstructive pulmonary disease
CI: Confidence interval
HR: Hazard ratio

50

DENALI Trial

Study Design	Methods	Intervention	Outcomes	Results
• Phase 3 • Randomized • Double-blinded • Multicentered	**Inclusion:** • Age ≥ 4 years with mild-moderate asthma • On PRN SABA or low-dose ICS plus • PRN SABA • FEV_1 50-85% with a 15% reversibility **Exclusion:** • COPD • Systemic corticosteroid in the last 3 months • Recent asthma hospitalization	• Albuterol-budesonide 90/80 mcg: 2 inhalations QID • Albuterol-budesonide 90/40 mcg: 2 inhalations QID • Albuterol 90 mcg: 2 inhalations QID • Budesonide 80 mcg: 2 inhalations QID • Placebo: 2 inhalations QID	**Primary Outcome:** • Change from baseline FEV_1 AUC from 0-6 hours averaged over 12 weeks to assess the contribution from albuterol and change from baseline in trough FEV_1 at week 12 to assess the contribution of budesonide on the lung function efficacy of each individual component	**Primary Outcome:** • **Change from baseline FEV_1 AUC from 0-6 hours averaged over 12 weeks** o Albuterol 180 mcg vs placebo: LSM 60.5 mL; 95% CI 7.7-113.4, **P=0.025** o Albuterol-budesonide 180 mcg vs placebo: LSM 161.9 mL; 95% CI 109.4-214.5, **P<0.001** o Albuterol-budesonide 180/160 mcg vs budesonide 160 mcg: LSM 80.7 mL; 95% CI 28.4-132.9, **P=0.003** • **Change from baseline in trough FEV_1 at week 12** o Budesonide 160 mcg vs placebo: LSM 73.3 mL; 95% CI 4.4-142.2, **P=0.037** o Albuterol-budesonide 180/160 mcg vs placebo: LSM 99.9 mL; 95% CI 30.9-168.8, **P=0.005** o Albuterol-budesonide 180/80 mcg vs placebo: LSM 87.9 mL; 95% CI 18.8-156.9, **P=0.013** o Albuterol-budesonide 180/80 mcg vs albuterol 180 mcg: LSM 120.8 mL; 95% CI 51.5-190.1, **P<0.001**

Each component of AIRSUPRA® contributed to the lung function efficacy, complying with the FDA requirements prior to approval of combination products

51 *Chest Journal*. 2023;164(4):585-595.

LSM: Least square mean

51

Knowledge Check

What type of inhaler is AIRSUPRA®?

A. LAMA

B. SABA

C. ICS

D. ICS + SABA

52

52

Knowledge Check

What type of inhaler is AIRSUPRA®?

A. LAMA

B. SABA

C. ICS

D. ICS + SABA

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Adult and Pediatric Adjunct Therapies

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Allergen Immunotherapy

- Considered add-on therapy for those who experience allergy symptoms to aeroallergens
- De-sensitization process is performed when allergens are identified
- Available approaches for allergen immunotherapy are SCIT and SLIT

SCIT: Subcutaneous immunotherapy
SLIT: Sublingual immunotherapy

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SCIT

- Allergen extracts are administered gradually over a course of three to five years
- Each injection is tailored specifically to each patient's allergens
- SCIT should not be initiated until asthma symptoms have been controlled
- Monitoring for 30 minutes post-injection is required due to risks of reactions

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SLIT

- Allergen extracts are provided as sublingual tablets or drops
- Duration of therapy for SLIT depends on the type of allergen
  - HDM is used in adults whose asthma symptoms are driven by HDM
  - Ragweed is used in children that have been identified to have allergic rhinitis due to sensitivity to ragweed

HDM: House dust mite

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Immunizations

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Recommended Coverage

- Immunizations can prevent respiratory infections, such as:
  - COVID-19
  - Influenza
  - Pertussis
  - Respiratory syncytial virus
  - *Streptococcus pneumoniae*

59 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2024.

59

Asthma Remission

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Remission in Adult Asthma

- Clinical or complete remission off treatment can occur spontaneously or after discontinuation of treatment
- Remission off treatment can be observed in those whose asthma symptoms are due to occupational allergens, with removal of exposure inducing remission
- Remission on treatment has been observed in those with severe symptoms treated with biologics

61 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2024.

61

Remission in Pediatric Asthma

- Individuals who experience remission during childhood may face a higher risk of lung function decline and airflow limitation in adulthood compared to those who do not experience childhood remission
- Caregiver should be advised of recurrence possibility during adulthood

62 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2024.

62

Conclusions - Updates in Asthma

- Asthma diagnostic tools were updated to include the use of PEF if spirometry is unavailable or use is not feasible
- The 2024 GINA guideline updates recommend the use of ICS-formoterol as a rescue and maintenance inhaler
- AIRSUPRA® was recently approved by the FDA in 2023 as the first ICS-SABA inhaler
- The immunization information has been updated to provide additional details on protection against respiratory syncytial virus
- Emphasis placed on importance of caregivers knowing that remission does not mean asthma is cured as it can resurface in adulthood

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Chronic Kidney Disease: Update on Guidelines, Management, and New Treatments

Stephanie Mourino, PharmD
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Miami, Florida
January 25, 2025

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Disclosure

All authors have no financial relationships to disclose with regards to this presentation.

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Objectives

- Provide an overview of chronic kidney disease (CKD), including pathophysiology, diagnosis and staging, prevalence, and risk factors.
- Summarize the KDIGO guidelines for the pharmacological and non-pharmacological management of CKD.
- Review common CKD complications and approaches to their management.

KDIGO: Kidney Disease: Improving Global Outcomes

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Abbreviations

ACC: American College of Cardiology
ACEi: Angiotensin-converting enzyme inhibitors
ACR: Albumin-to-creatinine ratio
AHA: American Heart Association
AKI: Acute kidney injury
AKD: Acute kidney disease
ARB: Angiotensin receptor blocker
BMI: Body mass index
BP: Blood pressure
CBC: Complete blood count
CI: Contraindicated
CKD: Chronic kidney disease
CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration
CPS: Calcium polystyrene sulfonate
CVD: Cardiovascular disease
CV: Cardiovascular
DASH: Dietary approaches to stop hypertension
DHP-CCBs: Dihydropyridine calcium channel blockers
eGFR: Estimated glomerular filtration rate
eGFRcr: Estimated glomerular filtration rate creatinine
eGFRcys: Estimated glomerular filtration rate cystatin
eGFRcr-cys: Estimated glomerular filtration rate creatinine cystatin
EKG: Electrocardiogram
EPO: Erythropoietin
ESA: Erythropoiesis-stimulating agent
GFR: Glomerular filtration rate
GLP-1 RA: Glucagon-like peptide-1 receptor agonists
Hgb: Hemoglobin
Hct: Hematocrit
HCTZ: Hydrochlorothiazide
HTN: Hypertension
KDIGO: Kidney Disease: Improving Global Outcomes
LFT: Liver function tests
MDRD: Modification of diet in renal disease
MRA: Mineralocorticoid receptor antagonist
NSAIDS: Nonsteroidal anti-inflammatory drugs
ns-MRA: Non-steroidal mineralocorticoid receptor antagonist
PTH: Parathyroid hormone
RAAS: Renin-angiotensin-aldosterone system
RASi: Renin-angiotensin system inhibitors
SCr: Serum creatinine
SE: Side effects
SGLT2i: Sodium-glucose cotransporter-2 inhibitors
SOB: Shortness of breath
SHPT: Secondary hyperparathyroidism
SPS: Sodium polystyrene sulfonate
SZC: Sodium zirconium cyclosilicate
T2D: Type 2 Diabetes
TSAT: Transferrin saturation
XOI: Xanthine oxidase inhibitors

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eGFR Equations

CKD-EPI

$eGFR_{cr} = 142 \times \min(S_{cr}/\kappa, 1)^{\alpha} \times \max(S_{cr}/\kappa, 1)^{-1.200} \times 0.9938^{Age} \times 1.012$ [if female]

$eGFR_{cys} = 133 \times \min(S_{cys}/0.8, 1)^{-0.499} \times \max(S_{cys}/0.8, 1)^{-1.328} \times 0.996^{Age} \times 0.932$ [if female]

$eGFR_{cr\text{-}cys} = 135 \times \min(S_{cr}/\kappa, 1)^{\alpha} \times \max(S_{cr}/\kappa, 1)^{-0.544} \times \min(S_{cys}/0.8, 1)^{-0.323} \times \max(S_{cys}/0.8, 1)^{-0.778} \times 0.9961^{Age} \times 0.963$ [if female]

MDRD

$eGFR = 175 \times (S_{cr})^{-1.154} \times (age)^{-0.203} \times 0.742$ [if female] $\times 1.212$ [if Black]

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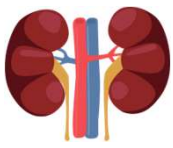
Introduction

- **Chronic Kidney Disease (CKD):** gradual decline in kidney function lasting 3+ months, resulting from structural or functional abnormalities of the kidneys.
  - Urine sediment abnormalities
  - Persistent hematuria
  - Electrolyte disturbances
  - Histology or imaging abnormalities
  - History of kidney transplantation
  - GFR < 60 mL/min/1.73 m^2



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Epidemiology

- Approximately **1 in 7 adults** in the US (about 14%) are estimated to have CKD.
  - CKD is more common in women (14%) than men (12%).
  - CKD is more common among non-Hispanic Black adults (20%) compared to non-Hispanic Asian adults (14%) and non-Hispanic White adults (12%).
- **Diabetes** and **hypertension** are the two leading causes of CKD worldwide.
- CKD prevalence **increases** with age, affecting approximately 34% of individuals aged 65 years or older.

CDC. Chronic Kidney Disease Initiative: Data and Research.

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Evaluation of CKD

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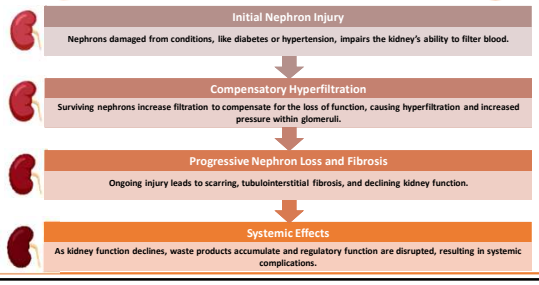
Pathophysiology of CKD



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Screening

- There is controversy and lack of consensus on the effectiveness of population-wide CKD screening.
- Screening for CKD is **cost-effective** in individuals with **diabetes and hypertension**.
- Testing of individuals with risk factors for CKD is the only method that would detect CKD at early stages and allow the initiation of appropriate treatments.
- **Early detection** of CKD can help prevent or delay CKD progression, reduce complications (such as CV events), and improve outcomes.

CKD Screening: Key Factors

WHO should be screened?

Individuals with risk factors for CKD:
- Hypertension, diabetes, CVD
- Family history of kidney disease
- Age 60 years or older
- History of AKI
- Frequent use of nephrotoxic medications

WHAT should be measured?
- Kidney function: eGFR
- Kidney injury: ACR

HOW often should screening occur?
- There are no evidence-based recommendations regarding the frequency of screening in individuals at risk of CKD.

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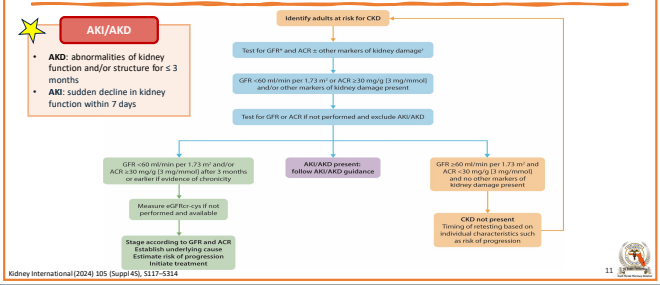
Screening Algorithm



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Risk Factors

- **Common risk factors – hypertension, diabetes, CVD, prior AKI/AKD**
- **Lifestyle risk factors – obesity, smoking**
- **Multisystem diseases/chronic inflammatory conditions**
- **Iatrogenic (Drug-induced nephrotoxicity and radiation nephritis)**
- Family history or known genetic variant associated with CKD
- Genitourinary disorders
- Gestational conditions
- Occupational exposures that promote CKD risk

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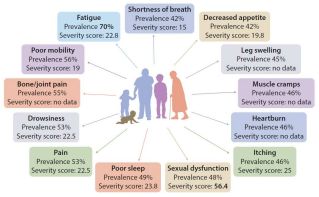
Clinical Presentation

- Most individuals with CKD are **asymptomatic** until it progresses to more advanced stages and/or complications arise.
- When symptoms do occur, they may include:
  - Fatigue
  - Poor mobility
  - Cramping or muscle/bone pain
  - Itching
  - Loss of appetite
  - Shortness of breath
  - Edema



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Diagnosis

Laboratory tests	**Blood test** (serum creatinine, eGFR) **Urine test** (albuminuria/proteinuria)
Imaging	Ultrasound, IV urography, CT kidneys ureters bladder, or MRI to assess kidney structure
Kidney biopsy	Ultrasound-guided percutaneous
Genetic testing	Evolving as a tool for diagnosis due to the growing recognition of genetic factors contributing to CKD

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Classification

CAUSE GFR ACR

- **Causes:**
  - Uncontrolled hypertension or diabetes
  - Glomerulonephritis
  - Polycystic kidney disease
  - Tubulointerstitial diseases
  - Severe or repeated AKI
  - Family history of CKD or kidney failure
- Understanding the underlying cause of CKD is critical for appropriate treatment and management.

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Classification

CAUSE **GFR** ACR

- **Glomerular Filtration Rate**
  - Rate at which the kidneys filter blood, removing waste and excess fluid
  - GFR is calculated using the MDRD and CKD-EPI equations
  - Factors used to calculate eGFR:
    - Serum creatinine (SCr)
    - Cystatin C (if available)
    - Age
    - Sex

GFR Category	GFR (mL/min/1.73 m²)	Description
G1	≥ 90	Normal or high
G2	60-89	Mildly decreased
G3a	**45-59**	**Mildly to moderately decreased**
G3b	**30-44**	**Moderately to severely decreased**
G4	**15-29**	**Severely decreased**
G5	**< 15**	**Kidney failure**

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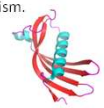
Classification

CAUSE **GFR** ACR

- **Glomerular Filtration Rate**
  - **Cystatin C** is a non-glycosylated, basic protein encoded by the CST3 gene that is found in all nucleated cells.
    - Released in the bloodstream at a constant rate and freely filtered, reabsorbed and degraded in the proximal tubules.
    - Identified as a potential biomarker for kidney function due to its consistent production, minimal dependence on external factors and complete renal metabolism.



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Classification

CAUSE **GFR** ACR

- **Glomerular Filtration Rate**

Creatinine Vs. Cystatin C		
Parameter	**Creatinine**	**Cystatin C**
Influencing Factors	Muscle mass, critically ill, elderly patients	Thyroid disease, adiposity, underlying inflammation
Early CKD Detection	Less sensitive	More sensitive
Cost	Low	Higher

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Classification

CAUSE **GFR** ACR

- **Glomerular Filtration Rate**
  - Combined **eGFRcr-cys** equation provides a more accurate assessment of kidney function compared to each biomarker alone.
  - **eGFRcr-cys** is recommended to be used in clinical situations where **eGFRcr** is less accurate and GFR is critical for guiding clinical decisions.
  - If cystatin C is available, the GFR category should be estimated from the combination of creatinine and cystatin C.

Domain	eGFRcr	eGFRcys	eGFR cr-cys
Body habitus and changes in muscle mass		✓	
Smoking	✓		
Diet	✓		
Illness other than CKD (malnutrition, cancer, heart failure, et.)			✓
Steroids (anabolic, hormone)			✓
Decreases in tubular secretion		✓	
Broad spectrum antibiotics		✓	

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Classification

CAUSE GFR **ACR**

- **Albumin-to-Creatinine Ratio**
  - **Equation:** Albumin (mg/dL) / Creatinine (g/dL)
  - Albuminuria is the presence of albumin in the urine and occurs when glomeruli in the kidneys are damaged
  - Albuminuria (ACR ≥ 30 mg/g [≥ 3 mg/mmol])

UACR Category	Range (mg/g)	Description
A1	< 30	Normal to mildly increased
A2	**30-300**	**Moderately increased**
A3	**>300**	**Severely increased**

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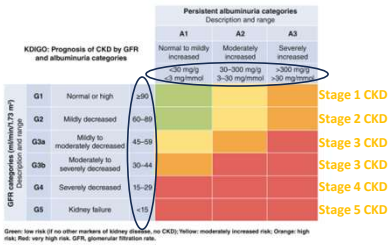
Prognosis of CKD



Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red: very high risk. GFR, glomerular filtration rate.

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Delaying CKD Progression

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CKD Treatment and Risk Modification

- Individuals with CKD should be managed with a comprehensive treatment strategy
- **Goals:**
  - Treat reversible causes of kidney failure
  - Prevent or delay the progression of kidney disease
  - Treat complications of kidney failure
  - Renally dose adjust when appropriate for the level of eGFR
  - Identify patient in whom kidney replacement therapy will be required

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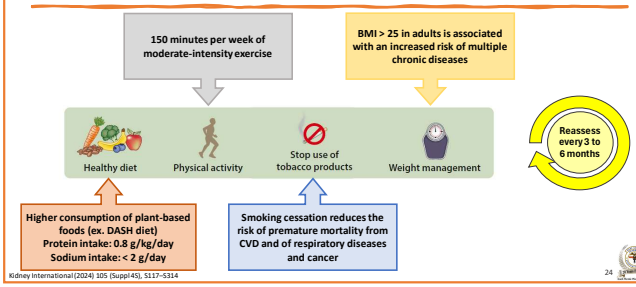
CKD Management – Lifestyle



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CKD Management – Blood Pressure

Blood pressure management

- Hypertension is present in approximately **80-85%** of patients with CKD.
- Accelerates kidney function decline and increases CV risk.
- Early detection and management can delay the progression of albuminuric CKD and reduce the rate of cardiovascular complications.

Goals

- **KDIGO:** SBP < 120 mm Hg
- **ACC/AHA:** BP < 130/80 mm Hg

Consider less intensive treatment in patients with:

- Frailty
- High risk of falls and fractures
- Limited life expectancy
- Symptomatic postural hypotension

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CKD Management – Blood Pressure

- RAS Inhibitors
- Thiazide Diuretics
- Calcium Channel Blockers
- Beta-blockers

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CKD Management – Blood Pressure

RAS Inhibitors

- **First line therapy:** ACE inhibitors and ARBs
- Both target RAAS to reduce vasoconstriction, aldosterone secretion/effects, and intraglomerular pressure.
- Start in patients with:
  - HTN
  - CKD
  - Moderately-to-severely increased albuminuria with or without diabetes

ARBs

Losartan
Valsartan
Olmesartan
Candesartan
Irbesartan

ACEIs

Lisinopril
Enalapril
Ramipril
Captopril
Quinapril

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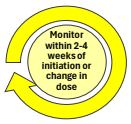
CKD Management – Blood Pressure

RAS Inhibitors

- **Monitor:**
  - BP
  - Serum creatinine
  - Potassium
- Hyperkalemia associated with the use of RASi should be **treated** rather than decreasing the dose or discontinuing RASi.
- Continue therapy unless SCr increases by more than 30% within 4 weeks.



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CKD Management – Blood Pressure

RAS Inhibitors

- Consider **reducing the dose or discontinuing RASi** in the setting of:
  - Symptomatic hypotension
  - Uncontrolled hyperkalemia despite medical treatment
  - Reduce uremic symptoms while treating kidney failure (eGFR < 15 mL/min per 1.73 m^2)
- Continue therapy even when the eGFR drops below 30 mL/min/1.73 m^2.

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CKD Management – Blood Pressure

Thiazide Diuretics

- Reduces sodium and water reabsorption in the kidneys to manage volume overload and hypertension.
- Frequently used in individuals with CKD as fluid overload often occurs.
- **Monitor:**
  - BP
  - Electrolytes
  - Serum creatinine

Diuretics
HCTZ
Chlorthalidone
Chlorothiazide
Indapamide

DHP-CCBs
Amlodipine
Nifedipine
Nicardipine
Felodipine

DHP-CCBs

- Blocks calcium entry into vascular smooth muscle cells which helps manage hypertension.
- **First-line** antihypertensive agent in adult kidney transplant recipients.
- **Monitor:**
  - BP
  - Peripheral edema

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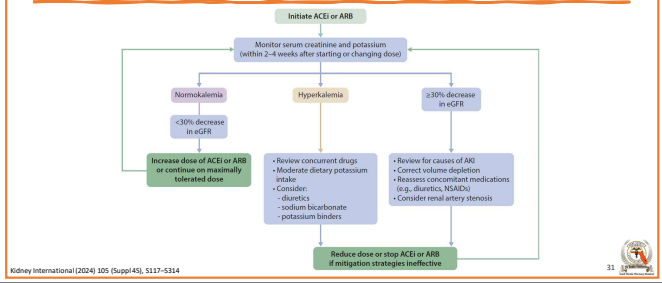
CKD Management – Blood Pressure



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Knowledge Check:

True or False: ACE inhibitors or ARBs should be discontinued in CKD patients if serum creatinine increases by > 30% from baseline.

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Knowledge Check:

True or ~~False~~**:** ACE inhibitors or ARBs should be discontinued in CKD patients if serum creatinine increases by > 30% from baseline.

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CKD Management – Glycemic Control

- Diabetes is the **leading cause** of CKD worldwide, accounting for **about 40%** of CKD cases.
- Individuals with diabetes and CKD are at an increased risk for:
  - Progression to kidney failure
  - CV events
  - Acute and long-term diabetes-related complications
- Early diagnosis and management of diabetes-related CKD can significantly slow its progression and reduce the risk of CV events.
- **Goal:** HbA1c < 7%

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CKD Management – Glycemic Control

- **SGLT2 Inhibitors**
- **ns-MRA**
- **GLP-1 RA**
- **Biguanides**

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CKD Management – Glycemic Control

SGLT2 Inhibitors

- **First line therapy:** Sodium-glucose cotransporter-2 inhibitors
- Reduce glucose and sodium reabsorption in the proximal tubules of the kidneys, which decrease glomerular hyperfiltration and reduce glomerular hypertension
- SGLT2i:
  - Reduce hyperglycemia
  - Slow CKD progression
  - Lower CV risk

Empagliflozin
Canagliflozin
Dapagliflozin

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CKD Management – Glycemic Control

SGLT2 Inhibitors

- Recommended in patients with:
  - Type 2 diabetes, CKD, and an eGFR ≥ 20 mL/min per 1.73 m^2
  - CKD:
    - eGFR ≥ 20 mL/min per 1.73 m^2 with urine ACR ≥ 200 mg/g
    - Heart failure (irrespective of level of albuminuria)
  - eGFR 20 to 45 mL/min per 1.73 m^2 with urine ACR < 200 mg/g
- **Monitor:** Genital mycotic infections and UTI, serum creatinine, blood glucose, blood pressure

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CKD Management – Glycemic Control

ns-MRA

- Inhibits the effects of aldosterone in the body.
- Most appropriate for adults with T2D at high risk of CKD progression and CV events.
- Start in patients with:
  - T2D, eGFR > 25 mL/min per 1.73 m^2, normal potassium levels, and albuminuria > 30 mg/g despite maximum tolerated dose of RASi
  - May be added to RASi and SGLT2i for treatment of CKD and T2D

Finerenone

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CKD Management – Glycemic Control

ns-MRA

- **Monitor:**
  - Potassium
  - eGFR

K^+ ≤4.8 mmol/l	K^+ 4.9–5.5 mmol/l	K^+ >5.5 mmol/l
• Initiate finerenone - 10 mg daily if eGFR 25–59 ml/min/1.73 m^2 - 20 mg daily if eGFR ≥60 ml/min/1.73 m^2 • Monitor K^+ at 1 month after initiation and then every 4 months • Increase dose to 20 mg daily, if on 10 mg daily • Restart 10 mg daily if previously held for hyperkalemia and K^+ now ≤5.0 mmol/l	• Continue finerenone 10 mg or 20 mg • Monitor K^+ every 4 months	• Hold finerenone • Consider adjustments to diet or concomitant medications to mitigate hyperkalemia • Recheck K^+ • Consider reinitiation if/when K^+ ≤5.0 mmol/l

Kidney International (2024) 105 (Suppl 4S), S117–S314

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CKD Management – Glycemic Control

GLP-1 RA

- Enhances insulin secretion, inhibits glucagon release, slows gastric emptying and promotes weight loss, which **improves glycemic control and reduces albuminuria.**
- Start GLP-1 RA for patients with:
  - T2D and CKD who have not achieved individualized glycemic targets.
- **Monitor:**
  - Blood glucose
  - Body weight
  - Serum creatinine

Liraglutide
Semaglutide (injectable)
Dulaglutide

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CKD Management – Glycemic Control

Biguanides

- **First line therapy**
- Improves insulin sensitivity and enhances peripheral glucose uptake.
- Delays the progression of CKD and reduces the risk of CV events.
  - Do **NOT** initiate if eGFR 30-45 mL/min per 1.73 m^2
  - Discontinue if eGFR < 30 mL/min per 1.73 m^2
- **Monitor**
  - Blood glucose
  - eGFR
  - Vitamin B12

Metformin

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Knowledge Check:

Which of the following statements about SGLT2 inhibitors in CKD patients is correct?

a) They are only effective in patients with type 2 diabetes.

b) They have been shown to reduce the risk of heart failure and progression of kidney disease in both diabetic and non-diabetic patients.

c) They are contraindicated in patients with an eGFR below 60 mL/min/1.73m^2.

d) They should be started at the highest dose to achieve maximal renal protection.

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Knowledge Check:

Which of the following statements about SGLT2 inhibitors in CKD patients is correct?

a) They are only effective in patients with type 2 diabetes.

b) They have been shown to reduce the risk of heart failure and progression of kidney disease in both diabetic and non-diabetic patients.

c) They are contraindicated in patients with an eGFR below 60 mL/min/1.73m^2.

d) They should be started at the highest dose to achieve maximal renal protection.

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Delaying CKD Progression and Managing its Complications

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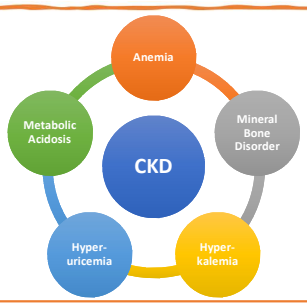
CKD Complications



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CKD Management – Anemia

BACKGROUND	DIAGNOSIS	MANAGEMENT

What it is:
• Reduced production of erythropoietin (EPO) by the kidneys, resulting in low RBCs.
• Defined as Hgb < 11 g/dL in men and < 10 g/dL in women.
Prevalence:
• Increases with CKD progression.
• Mean hemoglobin is lower in both men and women with an eGFR < 60.
	Signs and Symptoms:
	• Fatigue
	• Weakness
	• SOB
	• Pale skin and cold extremities
	Diagnostic Workup:
	• Blood tests:
	  • CBC
	  • Iron panel
	  • Vitamin B12
	  • Folate levels
	• Exclude nonrenal causes
		Goals:
		• Increase Hgb levels
		• Improve symptoms, quality of life, and prevent CV complications
		Treatment:
		• Iron therapy
		• Erythropoiesis-stimulating agents (ESAs)

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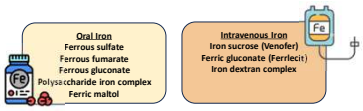
CKD Management – Anemia

IRON

- Iron deficiency is common among patients with CKD.
- Indicated in patients with CKD who have a TSAT ≤ 20 percent and/or a serum ferritin concentration ≤ 500 ng/mL.
- Not recommended in patients with CKD who have a TSAT > 30 percent.



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CKD Management – Anemia

IRON

- Dose:
  - **Oral:** 65 – 200 mg/day
  - **IV:** cumulative dose of approximately 1000 mg
- IV iron administration is restricted to:
  - Patients with CKD on hemodialysis and/or receiving ESAs
  - Unable to tolerate oral iron or failure of oral therapy
  - Severe anemia (Hgb < 7 g/dL)
- **Adverse effects**: oral - constipation, dark and tarry stools; IV – hypersensitivity
- **Monitor:** Hgb, Hct, vitamin B12, TSAT, serum ferritin

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CKD Management – Anemia

ESAs

- ESAs stimulate the production of RBCs and can prevent the need for blood transfusions.
- **Indicated in patients with:**
  - Hgb < 10 g/dL
  - TSAT > 20% and ferritin > 200 ng/mL
- **Contraindication:**
  - Uncontrolled hypertension
  - Pure red cell aplasia
  - Pregnant/breastfeeding women, neonates, and infants

Epoetin alfa
Darbepoetin alfa
Methoxy polyethylene glycol-epoetin beta

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CKD Management – Anemia

ESAs

- **Epoetin alfa**
  - Dose: 50 to 100 units/kg every 1-2 weeks
- **Darbepoetin**
  - Dose: 0.45 mcg/kg every 2 to 4 weeks
- **Methoxy polyethylene glycol-epoetin beta**
  - Dose: 0.6 mcg/kg every 2 weeks or 1.2 mcg/kg once monthly
- Dose should be held or discontinued if hemoglobin exceeds 11 g/dL.
- **Adverse effects:** Hypertension, arthralgia/bone pain, injection site pain
- **Monitor:** Hgb, Hct, TSAT, serum ferritin, BP

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CKD Management – Anemia

Hemoglobin Monitoring

In patients who do not have anemia	• **Stage 3**: When it is clinically indicated and at least yearly • **Stage 4-5**: Every 6 months
In patients who have anemia and are not treated with ESAs	• When it is clinically indicated and at least every 3 months for patients on hemodialysis
In patients who have anemia and are treated with ESAs	• Every 2 weeks to 3 months

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Knowledge Check:

True or False: All CKD patients, regardless of stage, should be started on a high-dose erythropoiesis-stimulating agent (ESA) to correct anemia.

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Knowledge Check:

~~True~~ or **False:** All CKD patients, regardless of stage, should be started on a high-dose erythropoiesis-stimulating agent (ESA) to correct anemia.

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CKD Management – Mineral Bone Disorder

BACKGROUND	DIAGNOSIS	MANAGEMENT
What it is: • Systemic disorder of mineral and bone metabolism leading to bone and CV complications. • It is associated with fractures, CVD, and increased mortality. **How it happens:** • Phosphorus retention • Calcium and vitamin D abnormalities • Secondary hyperparathyroidism • Vascular calcification	**Signs and Symptoms** (*Often asymptomatic in early stages) • Bone pain • Fractures • Muscle weakness **Diagnostic Workup:** • Laboratory tests (phosphorus, calcium, PTH, vitamin D) • Imaging • Bone biopsy 	**Goals:** • Normalize phosphorus and calcium levels • Control PTH levels to prevent SHPT and bone disease • Minimize vascular calcification and CV risks **Treatment:** • Phosphate binders • Vitamin D analogs • Calcimimetics • Dietary restrictions

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CKD Management – Mineral Bone Disorder

Phosphate Binders

- Blocks the absorption of dietary PO_4 by binding to it in the intestine.
  - Must take with meals
- Start when the serum phosphorus level is persistently elevated **> 5.5 mg/dL**.
- Non-calcium-containing phosphate binders are preferred.
- Monitor levels at least annually.

Drug	Dose	Safety/Side effects
Aluminum-based Phosphate Binders		
Aluminum hydroxide	300-600 mg PO TID	**SE:** aluminum intoxication, osteomalacia, constipation, nausea Treatment duration limited to 4 weeks
Calcium Based Phosphate Binders		
Calcium acetate	1,334 mg PO TID	**SE:** hypercalcemia, constipation, nausea
Calcium carbonate	500 mg PO TID	
Non-calcium, Non-aluminum Phosphate Binders		
Sevelamer carbonate	800 – 1,600 mg PO TID	**CI:** bowel obstruction
Sevelamer hydrochloride		**SE:** n/v/d, dyspepsia, constipation, abdominal pain, flatulence
Lanthanum carbonate	500 mg PO TID	**SE:** n/v/d, constipation
Ferric citrate*	420 mg PO TID	**SE:** diarrhea, constipation, discolored feces
Sucroferric oxyhydroxide	500 mg PO TID	Iron absorption occurs with ferric citrate

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CKD Management – Mineral Bone Disorder

Secondary Hyperparathyroidism:

- Develops because of vitamin D deficiency and disordered calcium.
- PTH levels generally start to increase when eGFR is <60 mL/min/1.73 m^2.

Vitamin D Analogs

- **Calcitriol**
- Increases calcium concentrations and inhibits PTH secretions.
- **Dose:** 0.25 – 0.5 mcg PO daily
- **Adverse effects:** Hypercalcemia

Calcimimetics

- **Cinacalcet (Sensipar)**
- Mimics calcium and increases the sensitivity of receptors on PTH gland.
- **Dose:** 30 – 180 mg PO daily
- **Adverse effects:** Hypocalcemia

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CKD Management – Mineral Bone Disorder

Monitoring

Stage 3	• **Calcium and phosphate:** every 6-12 months • **PTH:** based on baseline level and CKD progression
Stage 4	• **Calcium and phosphate:** every 3 -6 months • **PTH:** every 6-12 months
Stage 5	• **Calcium and phosphate:** every 1-3 months • **PTH:** every 3-6 months

Initiate monitoring at CKD stage 3

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CKD Management – Hyperkalemia

BACKGROUND	DIAGNOSIS	MANAGEMENT

What it is:
• Serum potassium levels > 5.5 mmoL/L.
• Results from impaired renal potassium excretion as kidney function declines.
Prevalence
• Increases with CKD progression:
  • CKD stage 3 to 4: 10-15%
  • CKD stage 5 or dialysis: 40-50%
• Most common in patients on RAS inhibitors.
	Signs and Symptoms (*Often asymptomatic in mild cases)
	• Cardiac arrhythmias
	• Muscle weakness
	• Fatigue
	• Nausea
	Diagnostic Workup:
	• Laboratory test
	• EKG
	• Potential contributing factors (medications, diet, etc.)
		Goals:
		• Prevent life-threatening cardiac complications
		• Correct potassium levels
		Treatment:
		• Potassium exchange agents
		• Diuretics
		• Dietary restriction

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CKD Management – Hyperkalemia

Address Correctable Factors:
- Review potential medications, other than RAS inhibitors
- Assess dietary potassium intake

Medications:
- Potassium exchanging agents
- Diuretics

Last Resort:
- Reduce dose or discontinue RASi/MRA

Medications associated with increased risk of hyperkalemia:
RAS inhibitors (ACEi/ARBs)
Potassium-sparing diuretics
Digoxin
NSAIDs
Sulfamethoxazole/Trimethoprim
Cyclosporine and tacrolimus

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CKD Management – Hyperkalemia

K^+ EXCHANGE AGENTS

	Sodium Zirconium Cyclosilicate (SZC)	Patiromer	Polystyrene Sulfonates (SPS or CPS)
Mechanism of action	Traps K^+ in exchange for hydrogen and sodium cations	Calcium-potassium exchange polymer	Sodium or calcium - potassium exchange resin
Formulation	Oral: powder for reconstitution	Oral: powder for reconstitution	Oral: powder for reconstitution, suspension Rectal: enema
Dose	10 g 3 times daily for up to 48 hours, followed by 10 g once daily	8.4 – 25.2 g PO daily	15-60 g daily
Onset of effect	1 hour	4-7 hours	Hours to days (variable)
Duration of effect	N/A	24 hours	6 – 24 hours (variable)
Administration pearls	Separate administration by at least 2 hours before or 2 hours after	Both bind to many oral drugs; separate administration by at least 3 hours before or3 hours after	
Adverse effects	Peripheral edema	Constipation, nausea, diarrhea	Nausea/vomiting, diarrhea, constipation

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CKD Management – Metabolic Acidosis

BACKGROUND	DIAGNOSIS	MANAGEMENT
What it is: • Decrease in bicarbonate levels (< 22 mEq/L) • It is associated with increased risk of protein catabolism, muscle wasting, and inflammation. **Prevalence** • Increases with CKD progression	**Signs and Symptoms** (*Often asymptomatic in mild cases) • Muscle weakness • Fatigue • Bone pain or fractures • Nausea/vomiting **Diagnostic Workup:** • Laboratory test ▪ BMP ▪ Arterial blood gas ▪ Anion gap (uremic acidosis vs. bicarbonate loss)	**Goals:** • Normalize serum bicarbonate levels (target 22-26 mEq/L) • Prevent complications **Treatment:** • Sodium bicarbonate ▪ **Dose:** 15.4 – 23.1 mEq/day • Sodium citrate/citric acid* • Dietary restrictions **Sodium citrate should be avoided in patients also taking aluminum-containing antacids*

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CKD Management – Hyperuricemia

BACKGROUND	DIAGNOSIS	MANAGEMENT
What it is: • Elevated serum uric acid levels due to impaired renal excretion of uric acid as kidney function declines. • Defined as a serum uric acid concentration of ≥ 6.8 mg /dL. **Prevalence** • eGFR consistent with CKD stage 3 was associated with about twice the prevalence of gout	**Signs and Symptoms** (*Often asymptomatic in mild cases) • Gout (joint pain, swelling, redness, tenderness) • Reduced appetite • Fatigue or malaise **Diagnostic Workup:** • Laboratory test (serum uric acid levels) • Imaging	**Goals:** • Reduce uric acid levels to prevent complications. **Treatment - for patients who are symptomatic** • Xanthine oxidase inhibitors • Uricosuric agents • Low-dose colchicine • Glucocorticoids (intra-articular/oral) • NSAIDs • Dietary restriction

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CKD Management – Hyperuricemia

XANTHINE OXIDASE INHIBITORS

- Reduces serum uric acid production.
- **Allopurinol:** 100 – 800 mg daily
- **Febuxostat:** 40 – 90 mg daily
- Preferred agent in individuals with CKD after 1st episode of gout.
- **Monitor:**
  - CBC
  - LFTs
  - Renal function

XOIs

Allopurinol
Febuxostat

Uricosuric

Probenecid

URICOSURIC AGENTS

- Inhibits reabsorption of uric acid in the kidneys.
- **Probenecid:** 250 mg twice daily
- **Monitor:**
  - CBC
  - eGFR

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CKD Management – Hyperuricemia

OTHER AGENTS

Symptomatic treatment of acute gout in CKD:.

- **Colchicine:**
  - Dose: 1.2 mg followed by 0.6 mg 1 hour later (Max: 2.4 mg/day)
  - Monitor: CBC, CrCl, LFTs, colchicine toxicity
- **Glucocorticoids**
- **NSAIDs**

Prophylaxis:

- Anti-inflammatory treatment may also be used as prophylaxis to reduce the risk of gout attacks.

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CKD Management – CVD

- Individuals with CKD are at an **increased risk of CVD and atherosclerosis.**
- Atherosclerotic risk management in individuals with CKD should be the same treatment as for those without CKD.
- Prevention of ASCVD should include:
  - Pharmacological therapy
  - Dietary and lifestyle intervention
  - CKD-MBD management

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CKD Management – CVD

LIPID MANAGEMENT

- **Adults aged ≥ 50 years with eGFR < 60 mL/min per 1.73 m² (Stage 3 to 5, non-dialysis/non-transplant):**
  - Treat with statin or statin/ezetimibe
- **Adults aged ≥ 50 years with CKD and eGFR ≥ 60 mL/min per 1.73 m² (Stage 1 to 2):**
  - Treat with a statin
- **Adults aged 18-49 years with CKD (non-dialysis/non-transplant), consider statin therapy if have:**
  - Known coronary disease, diabetes mellitus, prior ischemic stroke, or estimated 10-year incidence of coronary death or nonfatal MI > 10%

Atorvastatin
Rosuvastatin
Simvastatin
Pravastatin
Lovastatin
Pitavastatin
Fluvastatin

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CKD Management – CVD

ANTIPLATELET THERAPY

- **Oral low-dose aspirin:**
  - Recommended for secondary prevention of recurrent ischemic CV events
- No definitive recommendation on when to use aspirin for primary prevention in individuals at high risk – further research required.
- May consider adding PPI when prescribing antiplatelet/antithrombotic therapy to reduce GI bleeding risk.
- If there is an aspirin intolerance, consider other antiplatelet therapy, such as a $P2Y_{12}$ inhibitors.

Clopidogrel
Ticagrelor
Prasugrel

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CKD Management – Atrial Fibrillation

DIAGNOSIS	PROPHYLAXIS	RATE/RHYTHM CONTROL
• BP and pulse-based screening. • Followed up with an ECG if detected irregular pulse. • Wearable device should be initiated if reported symptoms suggest atrial fibrillation, but ECG is nondiagnostic.	• Oral anticoagulation – DOACs • Bleeding risk score should be considered to identify modifiable risk factors.	• Consider reversible causes of atrial fibrillation. • Medical therapy to control ventricular rate to less than 90 bpm at rest. • Consider rhythm control with cardioversion, antiarrhythmic therapy, and/or catheter ablation.

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CKD Progression Monitoring

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Monitoring for Progression of CKD

- Albuminuria and GFR should be assessed **annually** in individuals with CKD.
- Individuals at higher risk for CKD progression should undergo more frequent monitoring of albuminuria and eGFR.
- Triggers for further evaluation:
  - A change in eGFR of > 20% in individuals with CKD.
  - A change in eGFR of > 30% in individuals with CKD receiving hemodynamically active therapies
  - Doubling of ACR

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Medication Management in CKD

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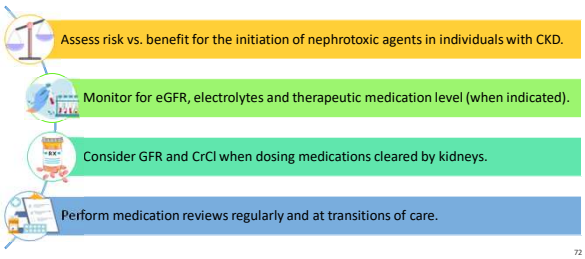
Pharmacists' Role in CKD



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Takeaway Points:

- Encourage dietary sodium restriction, weight management, smoking cessation, and increased physical activity to reduce risk factors.
- Aim for optimal blood pressure (SBP < 120 mmHg) using RASi to delay CKD progression.
- Utilize agents like SGLT2 inhibitors and GLP-1 RAs in individuals with CKD and diabetes for renal and cardiovascular protection.
- Manage complications associated with CKD utilizing pharmacological and non-pharmacological approach.
- Monitor eGFR and ACR annually for CKD progression.

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Thank you!

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A New Look for Chronic Obstructive Pulmonary Disease (COPD) – Guideline Management and New Treatments

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Disclosure

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Abbreviations

AAT: Alpha-1 Antitrypsin
ACh: Acetylcholine
ADEs: Adverse Drug Effects
BRFSS: Behavioral Risk Factor Surveillance System
cAMP: Cyclic Adenosine Monophosphate
CAT: COPD Assessment Test
CDC: Centers for Disease Control
COPD: Chronic Obstructive Pulmonary Disease
DDI: Drug-drug Interactions
EOS: Eosinophils
FEV: Forced Expiratory Volume
FVC: Forced Vital Capacity
ICS: Inhaled Corticosteroids
LABA: Long-acting Beta Agonists
LAMA: Long-acting Muscarinic Agonists
LDCT: Low-dose computed tomography
mMRC: Modified Medical Research Council
MOA: Mechanism of Action
PDE-3 Inh: Phosphodiesterase-3 Inhibitor
PDE-4 Inh: Phosphodiesterase-4 Inhibitor
SABA: Short-acting Beta Agonists
SAMA: Short-acting Muscarinic Agonists
SR: Sustained Release
USPSTF: United States Preventive Services Taskforce
VHC: Valved-holding Chamber
WHO: World Health Organization

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Objectives

- Provide an overview of Chronic Obstructive Pulmonary Disease (COPD) as a disease state
- Review the diagnosis and management strategies of COPD
- Summarize the key changes reported in the 2024 GOLD Guidelines

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Overview of COPD

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COPD as a Disease State

Chronic Obstructive Pulmonary Disease (COPD):
Heterogeneous lung condition characterized by chronic respiratory symptoms due to abnormalities of the airways and/or alveoli that cause persistent, often progressive, airflow obstruction

2024, 2025 Global Initiative for Chronic Obstructive Lung Disease

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Epidemiology

- COPD is the **4th leading cause of death worldwide**, responsible for 3.5 million deaths in 2021 (5% of global deaths)
- Nearly 90% of COPD deaths in individuals under 70 occur in low- and middle-income countries (LMICs)
- COPD ranks 8th as a leading cause of poor health globally

2024 World Health Organization (Nov 2024)

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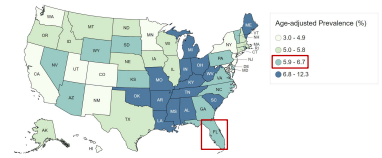
Epidemiology

- COPD prevalence ranged from 3%-12%, based on the Behavioral Risk Factor Surveillance System (BRFSS).



Data Source: CDC Behavioral Risk Factor Surveillance System (BRFSS), 2022. Age-adjusted COPD prevalence based on affirmative response to the question: "Has a doctor, nurse, or other health professional ever told you that you have COPD, emphysema, or chronic bronchitis?"

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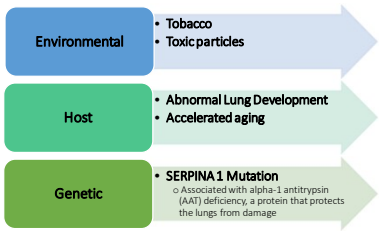
Risk Factors Leading to COPD



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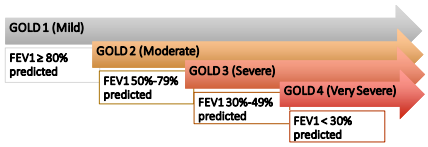
Diagnosis and Initial Assessment

- Diagnosis should be **considered** in any patient presenting with symptoms and a post bronchodilator **FEV1/FVC < 0.7**
- Forced Expiratory Volume (FEV): how much air you can blow out of your lungs in one second during a big, forceful exhale
- Forced Vital Capacity (FVC): total amount of air you can blow out after taking a deep breath
- FEV/FVC: how much of your total air you can exhale quickly (impaired when obstruction exists)



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Assessment Tool – mMRC

- Assesses the degree of breathlessness
- Helps categorize symptom burden

Modified MRC (mMRC) Dyspnea Scale				
mMRC Grade 0	**mMRC Grade 1**	**mMRC Grade 2**	**mMRC Grade 3**	**mMRC Grade 4**
Breathless with strenuous activity	Breathless when hurrying or walking up a slight hill	I walk slower than people of the same age or I have to stop for breath when walking on my own pace	Stop for breath after 100 meters or after a few minutes	Too breathless to leave the house or breathless when dressing/undressing

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Assessment Tools - CAT

- More comprehensive tool
- Consists of 8 questions scored 0-5
- The higher the score, the greater the impact of the disease on the patient

COPD Assessment Tool (CAT)		
Category	**Scale**	**Score**
Cough	0, 1, 2, 3, 4, 5	
Phlegm	0, 1, 2, 3, 4, 5	
Chest tightness	0, 1, 2, 3, 4, 5	
Breathlessness (e.g. walking up stairs)	0, 1, 2, 3, 4, 5	
Limitation while performing activities at home	0, 1, 2, 3, 4, 5	
Confidence leaving home despite condition	0, 1, 2, 3, 4, 5	
Soundly sleep	0, 1, 2, 3, 4, 5	
Amount of energy	0, 1, 2, 3, 4, 5	
	Total Score =	

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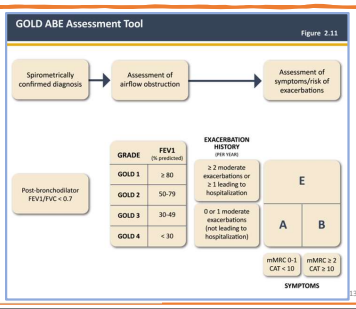
Assessment of COPD

Determine the severity of airflow obstruction, the impact of disease on the patient's health status and the risk of future events



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Knowledge Check

1. COPD is a pulmonary condition characterized by acute respiratory symptoms (shortness of breath, sputum production and cough) that are often non-progressive
   a) True
   b) False

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Knowledge Check

1. COPD is a pulmonary condition characterized by acute respiratory symptoms (shortness of breath, sputum production and cough) that are often non-progressive
   a) True
   b) False

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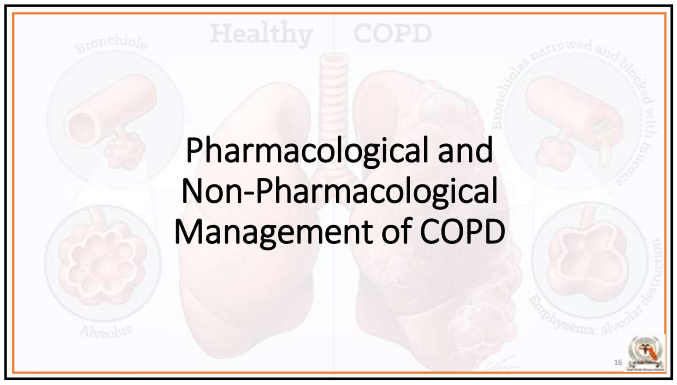

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Goals of Treatment

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Pharmacotherapy – Beta Agonists

- **MOA:** Bind to the beta-2-adrenergic receptors in the airways leading to relaxation of smooth muscle
- **Duration:**
  - SABA: ~ 4-6 hrs
  - LABA: ~ 12 hrs
- **ADEs:**
  - Tachycardia
  - Tremors
  - Hypokalemia

SABA	LABA
• Albuterol	• Arformoterol
• Fenoterol	• Formoterol
• Levalbuterol	• Indacaterol
• Terbutaline	• Olodaterol
	• Salmeterol

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Pharmacotherapy – Anticholinergics

- **MOA:** Relax airway smooth muscle by blocking the bronchoconstriction effects produced by ACh
- **Duration:**
  - SAMA: ~ 6-9 hrs
  - LAMA: ~ 12-24 hrs
- **ADEs:**
  - Dry mouth
  - Metallic taste

SAMA	LAMA
• Ipratropium bromide • Oxitropium bromide	• Aclidinium bromide • Glycopyrronium bromide • Glycopyrrolate • Tiotropium • Umeclidinium • Revefenacin

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Pharmacotherapy – ICS

- **MOA:** Reduce inflammation in the airways, consequently improving symptom severity and lung function
- **Duration:**
  - Combination treatment: ~12-24 hrs
- **ADEs:**
  - Oral thrush
  - Voice changes
  - Sore throat / Irritation
  - Pneumonia

Used in combination with LABA/LAMA or both
• Beclomethasone • Budesonide • Mometasone • Fluticasone furoate • Fluticasone propionate

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Pharmacotherapy – Methylxanthines

- **MOA:** Non-selective phosphodiesterase inhibitor that relaxes smooth muscle and reduces airway response to stimuli
- **Duration:** ~24 hrs
- **ADEs:**
  - Atrial/Ventricular Arrhythmia
  - Grand Mal Convulsion
  - Nausea
  - Headache
  - Insomnia
  - Heartburn

Monitor DDI ⚠
• Aminophylline • Theophylline (SR)

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Pharmacotherapy – PDE-4 Inhibitor

- **MOA:** Inhibit the breakdown of cAMP reducing inflammation
- **Duration:** ~24 hrs
- **ADEs:**
  - Nausea
  - Diarrhea
  - Abdominal Pain
  - Reduced Appetite
  - Weight Loss
  - Headache
  - Sleep Disturbances

Add-on therapy
• Roflumilast

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Pharmacotherapy – Mucolytic Agents

- **MOA:** Increase the production of a thinner mucus promoting an easier clearance
- **Duration:** ~12 hrs
- **ADEs:**
  - Nausea
  - Vomiting
  - Diarrhea

Add-on therapy
• N-acetylcysteine • Carbocysteine • Erdosteine

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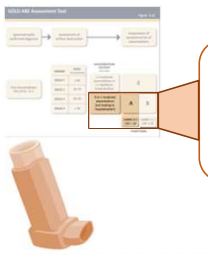
Initial Pharmacological Treatment



≤ 1 moderate exacerbations per year
mMRC 0-1 / CAT < 10

Group A
- A short- or long-acting bronchodilator

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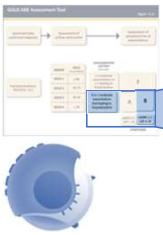
Initial Pharmacological Treatment



≤ 1 moderate exacerbations per year
mMRC ≥ 2 / CAT ≥ 10

Group B
- LABA + LAMA

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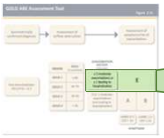
Initial Pharmacological Treatment



≥ 2 moderate exacerbations per year or ≥ 1 leading to hospitalization per year

Group E
- LABA + LAMA

LABA + LAMA + ICS if eosinophil (eos) ≥ 300

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Follow-up Pharmacological Treatment

- **Review:**
  - Stable patients: Every 6-12 months
  - Non-stable patients: Every 3-6 months
  - Post-exacerbation: Every 4 weeks
- **Assess:**
  - Response to treatment
  - Recent hospitalizations, symptom burden, quality of life
  - Comorbidities
- **Adjust:**
  - If responsive, maintain initial therapy
  - If non-responsive, assess treatable trait (dyspnea vs exacerbation)

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De Miguel Díez et al. - Journal of Clinical Medicine - 2024

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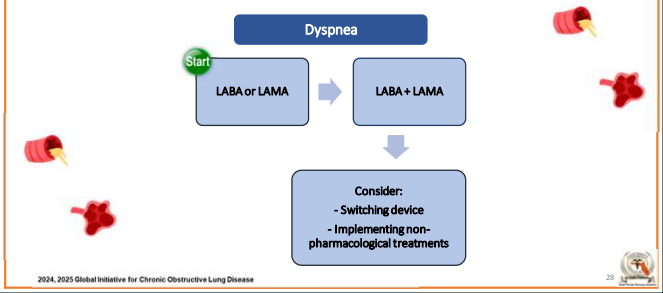
Follow-up Treatment – Dyspnea



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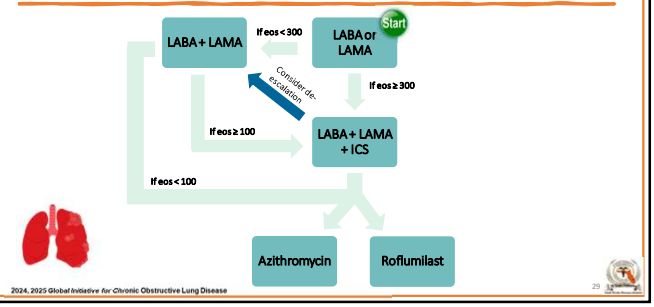
Follow-up Treatment – Exacerbations



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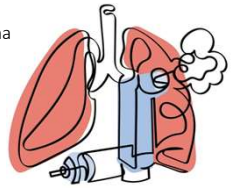
Follow-up Pharmacological Treatment

- Factors to consider when initiating an Inhaled Corticosteroid (ICS) treatment:
  - History of hospitalizations
  - Blood eosinophil count
  - History of, or concomitant asthma



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Severe but not Life-threatening Exacerbations

- **Administer supplemental oxygen**
- **Bronchodilators**
  - Increase dose or frequency of short-acting bronchodilators
  - Combine SABA + SAMA
  - Consider the use of spacers and nebulizers
  - Consider the use of long-acting bronchodilators once the patient is stable
- **Oral corticosteroids**
  - A dose of 40 mg prednisone-equivalent daily for 5 days
  - Oral prednisolone and intravenous steroids are equally effective
  - Nebulized budesonide provides similar benefits to IV methylprednisolone and may be sufficient
- **Oral antibiotics**
  - Consider when signs of bacterial infection are present (e.g. increase in dyspnea, sputum purulence, and sputum volume)
  - Duration should not exceed 5 days

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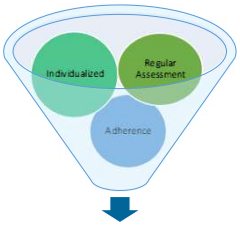
COPD Management – Key Points

- Management should be determined based on:
  - Symptom severity
  - Exacerbation risk
  - Side effects
  - Comorbidities
  - Availability
  - Cost
  - Patient's preference
  - Response
  - Ability to use the inhaler



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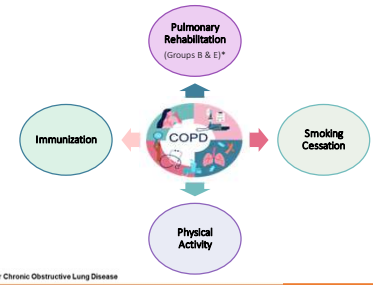
Non-pharmacological treatment



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Follow-up Non-pharmacological Treatment

Dyspnea
- Stress management
- Pulmonary rehabilitation (PR)
- Exercise program post PR

Exacerbations
- Avoidance of aggravating factors
- Ways to monitor/manage worsening symptoms
- Pulmonary rehabilitation (PR)
- Exercise program post PR

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Knowledge Check

2. In which of the following scenarios should an inhaled corticosteroid, such as budesonide, be added to a patient's therapy?
   a) A patient with one exacerbation that didn't lead to hospitalization
   b) A patient with two exacerbations that didn't lead to hospitalization and an eosinophil count of 320 cells/microliters
   c) A patient with one exacerbation that led to hospitalization and an eosinophil count of 50 cells/microliters

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Knowledge Check

2. In which of the following scenarios should an inhaled corticosteroid, such as budesonide, be added to a patient's therapy?
   a) A patient with one exacerbation that didn't lead to hospitalization
   b) A patient with two exacerbations that didn't lead to hospitalization and an eosinophil count of 320 cells/microliters
   c) A patient with one exacerbation that led to hospitalization and an eosinophil count of 50 cells/microliters

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Key Changes 2024

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Key Changes 2024

Update

- **Hyperinflation**
  - Contributes to disease burden and progression
  - Hyperinflation can be addressed with bronchodilators, supplemental oxygen, heliox, pulmonary rehabilitation, inspiratory muscle training, or surgery
- **Pre-bronchodilator spirometry**
  - Can be used as an initial test to investigate whether symptomatic patients have obstruction
- **Screening in targeted population**
  - A low-dose computed tomography (LDCT) is recommended in patients 50-80 y/o with a ≥ 20 pack-year smoking
- **Blood eosinophil count in the initial Assessment**
  - A higher eosinophil count is associated with increased inflammation
  - Repeated elevated eosinophils can help clinicians estimate the likelihood of a beneficial preventive response to an ICS in addition to a bronchodilator
- **Patients with Interstitial Lung abnormalities**
  - Clinical Evaluations and follow-up monitoring should be performed on patients with lung fibrosis as they are more likely to progress and have poor outcomes

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Key Changes 2024

Update

- **Smoking Cessation**
  - All individuals who smoke should be strongly encouraged and supported to quit
- **Managing inhaled therapy**
  - Expanded to include information regarding the patient's ability to use the delivery system correctly and choice of inhaler
- **Immunization**
  - Updated to be in alignment with current guidance from CDC

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Smoking Cessation Treatment

Update

Ask ⇨ Advice ⇨ Assess ⇨ Assist ⇨ Arrange

- **Clinical treatment guideline for tobacco cessation in adults**
  - Behavioral support
  - Pharmacological therapy
    - Varenicline, Nicotine Replacement Therapy (NRT), Bupropion – first line
    - Combination NRT
  - Bupropion + NRT/Varenicline – Alternative
- The effect of vaping/e-cigarettes remains controversial
- Consider patient preference, polypharmacy, comorbidities, and level of nicotine dependency prior to choosing a pharmacological therapy

(Leone et al., *Initiating pharmacologic treatment in tobacco-dependent adults. an official American Thoracic Society Clinical Practice guideline 2020*)

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Adherence / Proper Inhaler Use

Update

- **Factors that impact the patient's ability to use an inhaler:**
  - Cognitive ability
  - Manual dexterity
  - Coordination
  - Previous education regarding inhaler technique

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Adherence / Proper Inhaler Use

Update

Dry Powder Inhalers (DPIs)

Breathe out fully	Place the mouthpiece between your lips and create a seal
Breathe in quickly and deeply	Hold your breath for 10 seconds
Remove the mouthpiece from your mouth and breathe out slowly	Rinse your mouth and spit out

2022 American Lung Association (Sep 2022)

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Adherence / Proper Inhaler Use

Update

Metered Dose Inhalers (MDIs)

- Shake inhaler and prime medication
- Breathe out fully
- Place the mouthpiece between your lips and seal it
- Breathe in deep and steady as you press the canister
- Hold your breath for ~10 seconds
- Remove the mouthpiece from your mouth and breathe out slowly
- Rinse your mouth and spit out

2022 American Lung Association (Sep 2022)

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Adherence / Proper Inhaler Use

Update

MDI + Valved-holding Chamber (VHC)

- Shake inhaler and prime medication
- Put the inhaler into the VHC
- Breathe out fully
- Put chamber mouthpiece in the mouth
- Press inhaler and breathe in deep and steadily
- Hold your breath for ~10 seconds
- Remove the mouthpiece from your mouth and breathe out slowly
- Rinse your mouth and spit out

2022 American Lung Association (Sep 2022)

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Immunization

Update

- **Vaccination recommendations** are updated in line with current guidance from CDC

Influenza	Recommended in all people aged ≥ 6 months
COVID-19	Two doses of the 2024-2025 vaccine are recommended in all adults ≥ 65 y/o and people 6 months-64 y/o who are immunocompromised, 6 months apart
Pneumococcal	One dose of PCV20 or one dose of PCV15 followed by one dose of PPSV23 is recommended in adults ≥ 50 y/o or adults 19-49 y/o with risk conditions
Respiratory syncytial virus (RSV)	A single dose is recommended in all adults aged ≥ 75 y/o or adults aged 60-74 y/o at increased risk for RSV
Tdap (dTaP/dTPa)	Recommended in people ≥ 10 y/o ; either tetanus and diphtheria (Td) or tetanus, diphtheria and pertussis (Tdap) toxoids can be used for the decennial booster
Zoster (Shingles)	Two doses recommended in adults ≥ 50 y/o or adults ≥ 19 y/o who are immunocompromised

2025 Centers for Disease Control (Nov 2024)

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Knowledge Check

3. What are the major updates in the 2024 GOLD report regarding vaccination in patients with COPD?
   a) Only vaccination against Influenza & COVID-19 are recommended in patients with COPD
   b) Vaccination against Influenza, COVID-19, Pneumococcal infections, Tdap and, in patients ≥ 50 y/o, Varicella Zoster and Respiratory Syncytial virus are recommended
   c) Vaccination against Influenza, COVID-19, Pneumococcal infections, Tdap, Varicella Zoster in patients ≥ 50 y/o and Respiratory Syncytial virus in patients ≥ 60 y/o are recommended

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Key Changes 2025

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Pharmacotherapy – PDE-3/4 Inhibitor

Update

- **MOA:** Dual PDE-3/4 inhibitor, with anti-inflammatory properties and relaxes the airway smooth muscle was well.
- **Duration:** ~12 hrs
- **ADEs:**
  - Back pain
  - Diarrhea
  - Hypertension
  - Urinary Tract Infections
- **Place in therapy:** additional studies needed

Add-on therapy
- **Ensifentrine**

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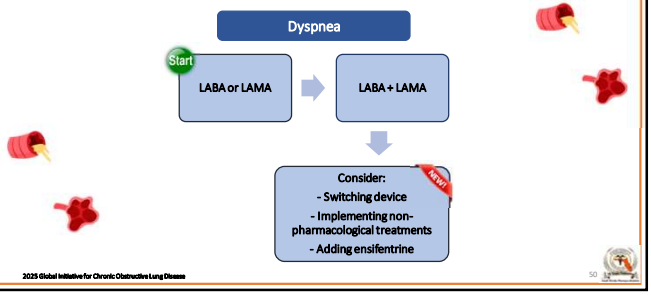
Follow-up Treatment – Dyspnea

Update



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Pharmacotherapy – Biologic

Update

- **MOA:** Monoclonal antibody that exerts its anti-inflammatory effects by inhibiting the interleukin-4 (IL-4) and interleukin-13 (IL-13)
- **Duration:** 2 weeks
- **ADEs:**
  - Viral infection
  - Headache
  - Nasopharyngitis / Rhinitis
  - Back pain / Toothache
  - Gastritis / Diarrhea
  - Injection site reactions
  - Urinary tract infection
  - Eosinophilia
- **Place in therapy:** reserved for patients with chronic bronchitis, eos ≥ 300 and unresponsive or that have failed treatment

Add-on therapy
- **Dupilumab**

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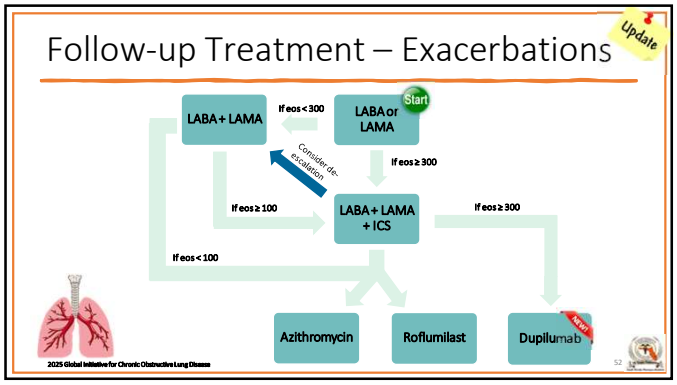

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What's Love Got to Do with It: HF Guideline Updates

Mayte Lezcano, PharmD
Jackson Memorial Hospital
Miami, FL
January 25th, 2025

29 Years Featuring
South Florida Pharmacy Residents

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Objectives

- Discuss the pathophysiology of HF and its impact on cardiac output and systemic circulation
- Review current pharmacological treatment guidelines for HF and the evidence supporting their use
- Explore how common comorbidities (such as hypertension, diabetes, and renal impairment) influence heart failure treatment decisions and medication adjustments
- Analyze the best practices for implementing GDMT to minimize CHF exacerbations and hospital readmission rates
- Review the role of pharmacists in optimizing heart failure care through medication management, patient education, and interdisciplinary collaboration to improve clinical outcomes

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Abbreviations

ACA: Affordable Care Act
ACC: American College of Cardiology
ACE-I: angiotensin-converting enzyme inhibitors
AFib: atrial fibrillation
AHA: American Heart Association
AKI: acute kidney injury
ARB: angiotensin receptor blocker
ARNI: angiotensin receptor/neprilysin inhibitor
AT: angioneuro
AV: atrioventricular
BB: beta-blocker
BBW: black box warning
BID: twice daily
BP: blood pressure
BSA: body surface area
C/I: contraindicated
CHF: congestive/chronic heart failure
CI: cardiac index
CMS: Centers for Medicare & Medicaid Services
CO: cardiac output
CPAP: continuous positive airway pressure
CrCl: creatinine clearance
CRT: cardiac resynchronization therapy
DHP: dihydropyridines
DILE: drug-induced lupus erythematosus
EF: ejection fraction
eGFR: estimated glomerular filtration rate
EPI: epinephrine
gtt: given
GDMT: guideline-directed medical therapy
h/o: history of
H2O: water
HF: heart failure
HFimpEF: heart failure with improved EF
HFmrEF: heart failure with mildly reduced ejection fraction
HFpEF: heart failure with preserved ejection fraction
HFrEF: heart failure with reduced ejection fraction
HR: heart rate
ICD: implantable defibrillator
IV: intravenous
K+: potassium
mg: mg
MRA: mineralocorticoid receptor antagonist
N/V: nausea/vomiting
Na+: sodium
NE: norepinephrine
NSAID: non-steroidal anti-inflammatory drug
NSR: normal sinus rhythm
NYHA: New York Heart Association
O2: oxygen
PO: by mouth
RAAS: renin-angiotensin-aldosterone system
s/s: signs/symptoms
SCr: serum creatinine
SGLT2-I: sodium/glucose cotransporter 2 inhibitors
SNS: sympathetic nervous system
SV: stroke volume
TID: three times daily
TNFi: tumor necrosis factor inhibitors
UTI: urinary tract infection

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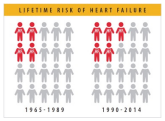
Epidemiology

- ~6.7 million Americans >20 years of age are diagnosed with HF
- The lifetime risk of HF has increased to 24%
- Approximately 33% of the United States (US) adult population is at-risk for HF (Stage A HF) and 24-34% of the US population have pre-HF (Stage B HF)
- African American, American Indian, and Alaska Native individuals have the highest all-cause HF mortality rates



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J Card Fail. 2023;29(10):1412-1451.
J Am Coll Cardiol. 2022;79:250–63.

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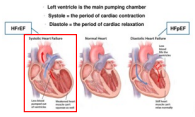
Pathophysiology

- HF occurs when the heart **cannot supply O_2-rich blood** to the body due to the **ventricles impaired ability to fill or eject blood**
  - **CO** (volume of blood pumped by heart in 1 minute) **= HR x SV**
    - A **normal cardiac output** ~4 to 8 L/min
    - A **normal SV** (the amount of blood pumped by the left ventricle with each beat) is ~70 mL/beat

HFrEF	HFpEF
•**Systolic HF w/ EF ≤ 40%** = **pumping problem**	•**Diastolic HF w/ EF ≥50%** = **filling problem**
•Structural ventricular *hypokinetic* abnormalities •Poor contractility + dilated ventricle •**Increase in end-diastolic** volume due to cardiomegaly → decrease ventricular muscle mass	•Diagnosis of exclusion •Muscle stiffness + muscle thickness •Decrease in end-diastolic volume due to stiff ventricle



J Card Fail. 2022;28(5):e1-e167.

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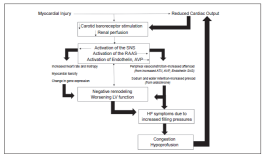
Compensatory Mechanisms

- **HFrEF is a ⇩ CO state** → inadequate tissue perfusion → body compensates by activating SNS and RAAS → ⇧ volume or force/speed of contractions → temporarily ⇧ CO but **causes myocyte damage & cardiac remodeling**



PSAP Book 2021, Chronic Heart Failure

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Left Ventricular Ejection Fraction

Classification	LVEF
HFrEF	≤ 40%
HFmrEF	41 – 49%
HFpEF	≥50%
HFimpEF	≤ 40% at baseline, a ≥ 10-point increase from baseline, and a second measurement of > 40%

J Card Fail. 2022;28(5):e1-e167.

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Classification Systems

	ACC/AHA Stages		NYHA Functional Classes
A	High risk of HF **WITHOUT** structural heart disease or s/s		No corresponding category
B	Structural heart disease **WITHOUT** HF s/s	I	No limitations of physical activity; Ordinary physical activity does not cause s/s
Clinical Diagnosis of HF			
C	Structural heart disease **WITH** prior or current s/s of HF	I	No limitations of physical activity; Ordinary physical activity does not cause s/s
		II	Slight limitations of physical activity; Comfortable at rest, but **minimal** activity **causes** s/s of HF
		III	Marked limitations of physical activity; Comfortable at rest, less than **minimal** exertion **causes** HF s/s
D	Advanced HF **WITH** s/s at rest or recurrent hospitalizations	IV	Unable to carry on **ANY** physical activity w/o HF symptoms **OR** HF s/s **at rest**

J Card Fail. 2022;28(5):e1-e167.

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National Readmission Rates

2018 30-Day All-Cause Adult Readmissions by Expected Payer			
Payer	Rank	30-Day Readmissions	Rate
Medicare	2	178,000	22.9%
Medicaid	4	30,800	28.0%
Private Insurance	2	15,800	17.6%
Self-pay	5	5,100	18.2%

Based off the 2024 CMS condition-specific readmission measures updates and specifications report, the national observed readmission rate in the combined three-year dataset was 19.8%. For the individual years, the observed rates were as follows:

- July 1, 2020 – June 30, 2021: 20.2%
- July 1, 2021 – June 30, 2022: 19.3%
- July 1, 2022 – June 30, 2023: 19.8%

CMS. 2024 Condition-Specific Readmission Measure Updates and Specifications Report

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Trends in 30- and 90-Day Readmission Rates for HF (2010 – 2017)

Objective
- To investigate temporal trends of 30- and 90-day HF readmissions rates from 2010 to 2017 in patients from all-payer sources using The National Readmission Database

Population
- A total of 6 669 313 index HF hospitalizations for 30-day, and 5 077 949 index HF hospitalizations for 90-day readmission, were included
- 77% Medicaid insured

Results
- 1,213,402 (18.2%) encounters had a readmission within 30 days
- 30-day adjusted HF-specific increased from 8.1% to 8.7% and all-cause readmissions increased from 14.8% to 16.0%
- 1,585,445 (31.2%) encounters had a readmission within 90 days
- 90-dayadjusted HF-specific increased from 18.3% to 19.9% and all-cause readmissions increased from 30.9 % to 34.6%

Conclusion
- The rates of adjusted HF-specific and all-cause 30- and 90-day readmissions have increased from 2010 to 2017
- 90-day higher proportion of readmissions indicate gap in long-term strategies for management
- HRRP can disproportionately penalize hospitals that serve patients with lower socioeconomic status and income → CMS instituted the risk adjustment to make it more lenient towards hospitals taking care of patients with lower socioeconomic status

J Am Coll Cardiol. 2019;73(2):351-346.

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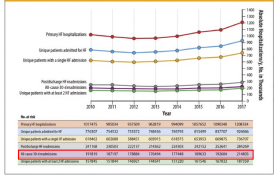
US Trends for HF Hospitalizations

US TRENDS FOR OVERALL HEART FAILURE (HF) HOSPITALIZATIONS, UNIQUE PATIENT VISITS, AND POSTDISCHARGE HF READMISSIONS



J Am Coll Cardiol. 2022;79:150–62.

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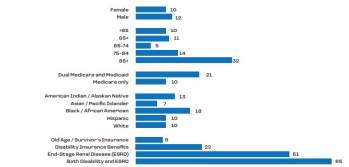
CMS 2022 Hospitalization Rate of HF among Medicare Enrollees (per 1000)



CMS. 2024. Heart Failure Disparities in Medicare Fee-For-Service Beneficiaries.

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Factors Associated With HF Hospital Readmissions

Patient	• Poor health literacy • Physical/cognitive impairment • Perceived lack of effect
Therapy	• Polypharmacy • Regimen complexity → non-compliance • Side effects
Socioeconomic Factors	• Out-of-pocket expenses • Difficult access to pharmacy • Homelessness
Health System	• Poor communication • No automatic refills • Difficulty navigating financial assistance programs

Front Pharmacol. 2021;12:732760.

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Drug-Induced HF Exacerbations

Mechanism	Drug Class	Examples	Contribution
Volume Overload	NSAIDs	Ibuprofen (Advil®) Naproxen (Aleve®)	Cause sodium and water retention, increasing preload
	Corticosteroids	Prednisone (Deltasone®) Methylprednisolone (Medrol®)	Promote fluid retention and weight gain
	Thiazolidinediones	Pioglitazone (Actos®) Rosiglitazone (Avandia®)	Increase fluid retention, worsening HF
	Calcium channel blockers	Amlodipine (Norvasc®) Nifedipine (Adalat®, Procardia®)	Vasodilation can cause reflex fluid retention
	Sodium-containing drugs	Sodium bicarbonate	High sodium content leads to fluid overload
Decreased Cardiac Function	Beta-Blockers (if not titrated)	Metoprolol (Toprol XL®) Carvedilol (Coreg®)	Can reduce cardiac output if started too quickly
	Antiarrhythmics	Flecainide Dronedarone (Multaq®)	Negative inotropic effects can worsen heart function
	Chemotherapy agents	Doxorubicin (Adriamycin®) Trastuzumab (Herceptin®)	Direct cardiotoxic effects impair heart contractility
	Anesthetics	Propofol (Diprivan®)	Depress myocardial contractility and blood flow
	Sedatives	Benzodiazepines, barbiturates	Lower heart rate and cardiac output

Circulation. 2016;134(6):e32-e69.

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Hospital Readmissions Reduction Program (HRRP): Heart Failure

Purpose

- **HRRP** is part of the **ACA** and is managed by the **CMS**
- It seeks to **penalize hospitals with higher-than-expected readmission rates** for specific conditions
- HRRP is designed to **enhance patient outcomes and reduce unnecessary readmissions**, holding hospitals accountable for post-discharge care and encouraging better overall management of chronic conditions

Measurement

- Hospitals are **evaluated based on their 30-day readmission rates** (defined as a patient being readmitted to any hospital within 30 days of discharge from an initial hospitalization for the same condition)

Penalties

- **Hospitals with readmission rates higher than the national average for these conditions face financial penalties**
- These penalties are applied as a reduction in Medicare payments, **up to 3% of the hospital's reimbursement**

Impact on Acute Care

- Encourages hospitals to improve **discharge planning** and post-discharge care coordination
- **Focus on preventive care** → Hospitals are incentivized to implement strategies to prevent readmissions, such as improving patient education, follow-up care, and disease management programs
- **Financial strain** → Hospitals with high readmission rates may face significant financial penalties, which can lead to reduced operating margins
- **Collaboration with outpatient services** → Acute care hospitals often partner with outpatient services, rehabilitation centers, and home health providers to ensure continuous patient care and minimize the risk of readmission

CMS. Hospital Readmissions Reduction Program (HRRP).

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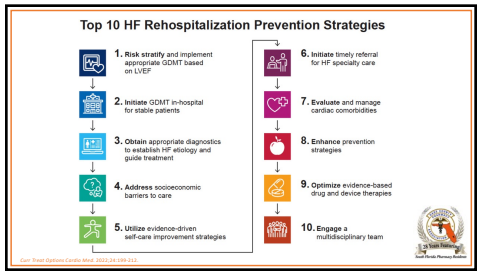
Top 10 HF Rehospitalization Prevention Strategies
1. Risk stratify and implement appropriate GDMT based on LVEF
2. Initiate GDMT in-hospital for stable patients
3. Obtain appropriate diagnostics to establish HF etiology and guide treatment
4. Address socioeconomic barriers to care
5. Utilize evidence-driven self-care improvement strategies
6. Initiate timely referral for HF specialty care
7. Evaluate and manage cardiac comorbidities
8. Enhance prevention strategies
9. Optimize evidence-based drug and device therapies
10. Engage a multidisciplinary team

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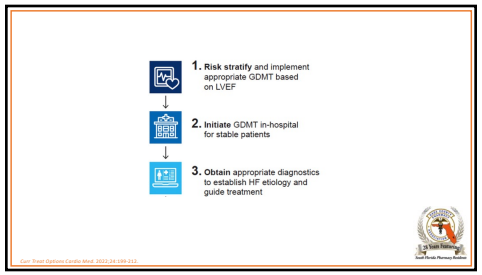
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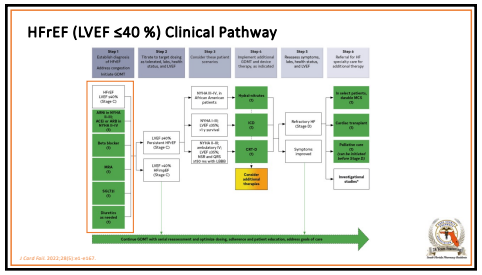
HFrEF (LVEF ≤40 %) Clinical Pathway

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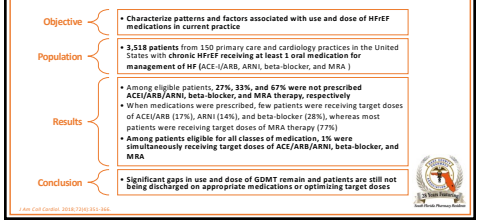
The CHAMP-HF Registry Study



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Knowledge Check #1

Which of the following therapies incorporated into GDMT provides *only* symptomatic relief?

A. Sacubitril/Valsartan (Entresto®)
B. Hydralazine/Isosorbide Dinitrate (BiDil®)
C. Furosemide (Lasix®)
D. Carvedilol (Coreg®)

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D. Carvedilol (Coreg®)

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Pharmacologic Agents with Morbidity and Mortality Benefits
(Class I, Strong Recommendation)

22

	ACE-Inhibitor	ARB	ARNI	Direct Vasodilator
Examples	Lisinopril (Zestril®)	Losartan (Cozaar®)	Sacubitril/Valsartan (Entresto®)	Hydralazine/Isosorbide Dinitrate (BIDil®)
Cost	$	$$	$$$	$
Target Doses	**40 mg daily**	**150 mg daily**	**97/103 mg twice daily**	**75/40 mg mg TID** = 2 tablets
MOA	• **Inhibits the conversion of ATI to ATII** → ⇩ vasoconstriction & ⇩ aldosterone secretion • Breakdown of bradykinin → induces dry cough	• Competitively bind **& blocks ATI receptor** → RAAS activation → ⇩ preload/afterload	• **Inhibits neprilysin angiotensin II type-I receptor** (RAAS) • **Inhibits the degradation of vasodilatory peptides**, including natriuretic peptides, substance p, bradykinin	• **Nitrates:** ⇧ availability of NO → venous vasodilation & **⇩ preload** • **Hydralazine: arterial vasodilator→ ⇩ afterload**

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	ACE-Inhibitor	ARB	ARNI	Direct Vasodilator
ADRs	• **HYPER**kalemia (caution w/ K^+ sparing diuretics, aldosterone antagonists, K^+ supplements) • Transient ⇧ SCr • **ACE-I > ARB:** Cough/angioedema			• Headache, flushing • Hydralazine: DILE, ⇧ HR • Concomitant use of PDE-5i
Clinical Pearls	• Do **NOT** combine ACE-I ± ARB/ARNI • **Monitor:** BP, K^+, SCr • **Washout period of 36 hours** when switching from **ACE-I → ARNI** • Contraindicated in bilateral renal artery stenosis, h/o **angioedema**			• African Americans with NYHA class III to IV HFrEF who are receiving optimal medical therapy with ACE-I/ARB, beta blockers, and MRA • Alt for ACEI/ARB-intolerant pts

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Discharge on Sacubitril/Valsartan vs. ACEi/ARB in Older Patients with HFrEF

Objective
- Compare **5-year clinical outcomes** of **Sacubitril/Valsartan versus ACEi/ARB** in older patients with HFrEF post-hospital discharge using a decision analysis model

Mortality Reduction
- **Absolute Survival Gain: 6.3% improvement with Sacubitril/valsartan**
- NNT among patients 66 to 74-year-old patients: 84
- NNT among patients 85+ years-old: 67

Readmission Rates
- **Sacubitril/Valsartan reduced 30-day readmission rates by approximately 8%-10% compared to ACEi/ARB**

QALYs
- Sacubitril/Valsartan led to a gain of 0.32 QALYs (about 3.8 months) over 5 years

Am Heart J. 2022;250:23-28.

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	Beta-Blockers		MRAs		SGLT2-I
Examples	Metoprolol Succinate (Toprol XL®)	Carvedilol (Coreg®)	Spironolactone (Aldactone®)	Eplerenone (Inspra®)	Dapagliflozin (Farxiga®) Empagliflozin (Jardiance®)
Cost	$	$	$	$$	$$$
Target Doses	**200 mg daily**	**<85 kg: 25 mg BID** **>85 kg: 50 mg BID (CR: 60 mg daily)**	**25 mg daily**	**50 mg daily**	**10 mg daily**
MOA	• **Blocks catecholamines** from binding to β receptors → ⇩ vasoconstriction		• **Competitively binds aldosterone receptors in the distal tubule** & collecting duct of the nephron		• **Inhibits SGLT2 in the proximal renal tubules** → ⇩ reabsorption of glucose

J Card Fail. 2022;28(5):e1-e167.

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	Beta-Blockers	MRAs	SGLT2-I
ADRs	• BBW: do NOT d/c abruptly, **taper over 1-2 W** • Caution in: DM (worsen ⇧ BG & mask ⇩ BG), bronchospastic diseases (asthma, COPD), Reynaud's • ⇩ HR, fatigue, ⇩ BP, dizziness, depression, impotence	• Spironolactone: Gynecomastia, breast tenderness, impotence • Eplerenone: ⇧ TG • ⇧ K, SCr	• Ketoacidosis • ⇩ BP • AKI • **UTIs** • Weight loss • ⇧ urination • ⇧ thirst
Clinical Pearls	• Monitor: HR • **Metoprolol IV:PO = 1:2.5** • Toprol XL can be split	• Do NOT initiate for HF if: ➢ **K⁺ >5 mEq/L** (>5.5 mEq/L for eplerenone) ➢ **CrCl or eGFR <30 mL/min/1.73²** ➢ **SCr >2 mg/dL** (females) or >2.5mg/dL (males)	• **Cr: dialysis, eGFR <30 (D) or <20 (E)**

J Card Fail. 2022;28(5):e1-e167.

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SGLT-2 Inhibitor	Mortality Reduction	Morbidity Reduction	Decreased Hospitalizations	Key Trials
Dapagliflozin (Farxiga®)	Yes	Yes	Yes	DAPA-HF, DECLARE-TIMI 58
Empagliflozin (Jardiance®)	Yes	Yes	Yes	EMPEROR-Reduced, EMPA-REG OUTCOME
Canagliflozin (Invokana®)	Yes (CV mortality)	Yes	Yes	CANVAS, CREDENCE
Ertugliflozin (Steglatro®)	Unclear	Limited evidence	Yes	VERTIS-CV

J Card Fail. 2022;28(5):e1-e167.

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Pharmacologic Agents that Provide Symptomatic Relief
(Class I, Strong Recommendation)

29

Loop Diuretics		
Examples	Furosemide (Lasix®)	Bumetanide (Bumex®)
Cost	$	$
Target Doses	Titrate as needed to an effective dose	Titrate as needed to an effective dose
MOA	• Inhibits reabsorption of electrolytes in the thick ascending loop of Henle in the nephron	

J Card Fail. 2022;28(5):e1-e167.

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Loop Diuretics	
ADRs	• HYPO: Ca^{2+}, K^+, Mg^+, Na^+, Cl^- • HYPER: Uric acid, glucose, triglycerides, HCO_3, total cholesterol • **Ototoxicity** • Hypersensitivities in sulfa allergies
Clinical Pearls	• Available as continuous infusion • If Loop alone not enough to meet clinical requirements, add on thiazides or thiazide-like diuretic • **Bumetanide dose works equally well whether given as a pill (PO) or injection (IV)** • **Furosemide oral dose is only 50% as effective as the IV dose**

J Card Fail. 2022;28(5):e1-e167.

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Pharmacologic Agents that Decrease Hospitalizations
(Class IIb, Weak Recommendation)

32

Cardiac Glycoside	
Example	Digoxin (Lanoxin®)
Cost	$
Doses	0.125 - 0.25mg QD (Loading dose NOT necessary)
MOA	Inhibits Na+/K+ATPase (repolarizes) → **(+) inotropic effect** → PSNS effect → **(-) chronotropic effect**

J Card Fail. 2022;28(5):e1-e167.

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	Cardiac Glycoside
ADRs	• ↑toxicity risk: ↓K+ & Mg & ↑Ca+ • Dehydration
Clinical Pearls	• Add-on to improve symptoms, exercise intolerance, & quality of life • ↓ dose if female, small, old, or renal impaired • **Requires renal dosing adjustments (not recommended in CrCl <30 mL/min or dialysis)** • IV:PO **≈** dose 20-50% • **Goal level in HF: 0.5 – 0.9 ng/mL** • Monitor: Electrolytes, CrCl, HR • Initial toxic s/s: N/V, ↓ appetite, ↓ HR • **Severe toxic s/s: vision changes (blurry/greenish halos)**

J Card Fail. 2022;28(5):e1-e167.

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Drugs That Increase Digoxin Levels (Risk of Toxicity)

- **Amiodarone**
- **Verapamil**
- **Diltiazem**
- **Quinidine**
- **Macrolides** (e.g., erythromycin, clarithromycin)
- **Antifungals** (e.g., itraconazole, ketoconazole)
- **Spironolactone**
- **Cyclosporine**
- **Propafenone**

Drugs That Decrease Digoxin Levels (Reduced Effectiveness)

- **Rifampin**
- **St. John's Wort**
- **Cholestyramine**
- **Antacids** (e.g., aluminum hydroxide)
- **Sucralfate**

J Card Fail. 2022;28(5):e1-e167.

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Digoxin and Mortality Risk

Study	Population	Findings	Conclusion
DIG Trial (Digitalis Investigation Group)	HFrEF	No significant effect on overall mortality, but **increased mortality** in patients with higher digoxin levels (>1.2 ng/mL).	**Increased mortality** risk with **toxic digoxin levels**, highlighting the importance of monitoring.
Post-Hoc Analysis of DIG Trial (2013)	HFrEF with NSR	**Higher mortality** risk in women on digoxin compared to men. Elevated levels associated with adverse outcomes.	Mortality risk higher in **women** and with **elevated levels** of digoxin.
OPTIMIZE-HF Registry (2006)	Hospitalized patients with decompensated HF	**Higher mortality** with digoxin use post-discharge, especially in patients with normal sinus rhythm.	Digoxin use post-discharge linked to **increased mortality** in **normal sinus rhythm** patients.
PROPENSITY-MATCHED Analysis (2015 - Kaiser Permanente)	Newly diagnosed HF	**72% increased risk of death** in patients using digoxin compared to non-users. Higher risk in **normal sinus rhythm** patients.	Digoxin associated with **higher mortality** risk, particularly in **normal sinus rhythm**.
AFFIRM Trial (Atrial Fibrillation Follow-up Investigation of Rhythm Management)	Afib	Higher all-cause mortality associated with digoxin use, even after adjusting for confounders.	**Increased mortality** with digoxin, especially in **atrial fibrillation** patients.

Am Heart J. 2022;250:10-28.

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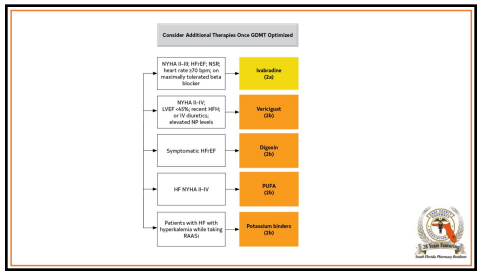

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	Soluble guanylate cyclase
Examples	Vericiguat (Verquvo®)
Recommendation	Class IIb, Weak
Cost	$$$$
Doses	Initial: 2.5mg once daily with food; double the dose every ≥ 2 weeks to a target maintenance dose of 10 mg once daily as tolerated based on BP and clinical symptoms

J Card Fail. 2022;28(5):e1-e167.

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	Soluble guanylate cyclase
MOA	Increases cyclic GMP levels by stimulating soluble guanylate cyclase, which leads to vasodilation and reduced cardiac workload
ADRs	• **Hypotension** • Dizziness, lightheadedness • GI upset • Anemia, fatigue
Clinical Pearls	• **Avoid during pregnancy** • **Not recommended** for patients taking **nitrates or PDE-5 inhibitors** due to **risk of severe hypotension** • Formulation may contain **lactose**

J Card Fail. 2022;28(5):e1-e167.

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	Hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blockers
Examples	Ivabradine (Corlanor®)
Recommendation	Class IIa, Moderate
Cost	$$
Doses	Initial: 2.5 to 5mg po BID in patients with a history of conduction defects or who may experience hemodynamic compromise due to bradycardia. Adjust dose every ≥ 2 weeks as needed.

J Card Fail. 2022;28(5):e1-e167.

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	Hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blockers
MOA	Selectively inhibits the If ("funny") channel in the sinoatrial node, slowing the heart rate without affecting blood pressure or myocardial contractility. → Reduces cardiac workload and improves symptoms
ADRs	Hypotension, anemia, pregnancy, nitrate therapy
Clinical Pearls	• Ivabradine is recommended for patients with heart failure with reduced ejection fraction (HFrEF) who meet the following criteria: o NYHA Class II-III heart failure symptoms o Sinus rhythm with a resting heart rate of ≥70 bpm o Already receiving maximum tolerated doses of beta-blockers or have a contraindication to beta-blocker use • The SHIFT trial showed a 26% reduction in heart failure hospitalizations in patients treated with ivabradine compared to placebo

J Card Fail. 2022;28(5):e1-e167.

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7. Evaluate and manage cardiac comorbidities

Curr Treat Options Cardio Med. 2022;24:199-212.

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Role of PUFAs and Potassium Binders in HFrEF

Polyunsaturated Fatty Acids (PUFAs)

Role

- **Omega-3 PUFAs** (e.g., EPA/DHA) are used as an **adjunct therapy** in patients with **heart failure with reduced ejection fraction (HFrEF)** to reduce cardiovascular mortality and hospitalizations (GISSI-HF Trial)

Recommendation

- **Class IIa** (Moderate benefit)

Mechanism

- In the setting of ischemia-induced ventricular fibrillation, which includes stabilization of ischemic-induced myocyte membrane resting depolarization

Potassium Binders (Patiromer and sodium zirconium cyclosilicate)

Role

- Used to manage **hyperkalemia** in heart failure patients, especially those on **renin-angiotensin-aldosterone system inhibitors (RAASi)** like ACE inhibitors, ARBs, or MRAs

Recommendation

- **Class II** (Weak benefit)

J Card Fail. 2022;28(5):e1-e167.

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Intravenous Iron in HFrEF (Class IIa, Moderate benefit)

Trial	Reference	Sample Size	Intervention	Primary Outcome	Results
CONFIRM-HF	Ponikowski P, van Veldhuisen DJ, Comin-Colet J, et al. Beneficial effects of long-term intravenous iron therapy with ferric carboxymaltose in patients with symptomatic heart failure and iron deficiency*. *Eur Heart J*. 2015;36(11):657-668.	304 symptomatic HF patients with left ventricular ejection fraction ≤45%, elevated BNP, and iron deficiency (ferritin <100 ng/mL)	1:1 ratio, ferric carboxymaltose (FCM, n=152) or placebo (saline, n=152) for 12 weeks	Change in 6-min-walk-test (AWT) distance from baseline to Week 24	• Treatment with FCM significantly prolonged 6MWT distance at Week 24 • FCM was associated with a significant reduction in the risk of hospitalizations for worsening HF
AFFIRM-HF	Ponikowski P, Kirwan BA, Anker SD, et al. Ferric carboxymaltose for iron deficiency at discharge after acute heart failure: a multicentre, double-blind, randomised, controlled trial. *Lancet*. 2020;396(10266):1895-1904.	1125 patients with hospitalized for acute heart failure with concomitant iron deficiency (ID) defined as ferritin <100 µg/L, or 100-299 µg/L with transferrin saturation <20%), and had a left ventricular ejection fraction of less than 50%	1:1 to receive intravenous ferric carboxymaltose or placebo for up to 24 weeks, dosed according to the extent of iron deficiency	Composite of total hospitalizations for heart failure and cardiovascular death up to 52 weeks after randomization	• 293 primary events occurred in the FCM group and 372 occurred in the placebo group • 370 total cardiovascular hospitalizations and cardiovascular deaths occurred in the FCM group and 461 occurred in the placebo group

Conclusion: Treatment with intravenous ferric carboxymaltose in patients with chronic heart failure and iron deficiency, with or without anemia, improves symptoms, functional capacity, and quality of life; the side-effect profile is acceptable.

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Pharmacological Management: Summary

- Decrease in mortality:
- ACE-I, ARBs, or ARNI
- Beta-Blockers
- MRAs
- SGLT2-Inhibitors

- Symptomatic relief:
- Loop Diuretics

J Card Fail. 2022;28(5):e1-e167.

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9. Optimize evidence-based drug and device therapies

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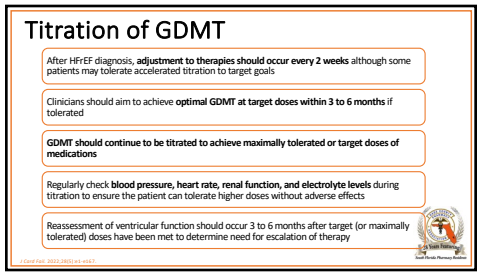
Titration of GDMT
After HFrEF diagnosis, adjustment to therapies should occur every 2 weeks although some patients may tolerate accelerated titration to target goals
Clinicians should aim to achieve optimal GDMT at target doses within 3 to 6 months if tolerated
GDMT should continue to be titrated to achieve maximally tolerated or target doses of medications
Regularly check blood pressure, heart rate, renal function, and electrolyte levels during titration to ensure the patient can tolerate higher doses without adverse effects
Reassessment of ventricular function should occur 3 to 6 months after target (or maximally tolerated) doses have been met to determine need for escalation of therapy

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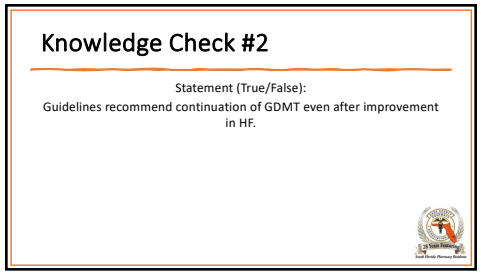
Knowledge Check #2
Statement (True/False):
Guidelines recommend continuation of GDMT even after improvement in HF.

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Knowledge Check #2

Statement (True/False):
Guidelines recommend continuation of GDMT even after improvement in HF.

Answer: TRUE! The TRED-HF (Withdrawal of Pharmacologic Treatment for Heart Failure in Patients with Recovered Dilated Cardiomyopathy) demonstrated that 50% of subjects withdrawn from GDMT had a recurrent HF event within 6 months of admission.

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5. Utilize evidence-driven self-care improvement strategies

J Curr Treat Options Cardio Med. 2022;24:199-212.

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Non-Pharmacological Management

Lifestyle Modifications
- Smoking cessation → Reduces further damage to the heart and lungs
- Alcohol reduction/avoidance → Excessive alcohol can weaken the heart muscle
- Stress management → Techniques like meditation, counseling, or yoga to reduce the negative effects of stress on heart health

Dietary Modifications
- Low sodium diet → Helps reduce fluid retention and decrease the workload on the heart
- Fluid restriction → May be necessary in cases of severe fluid overload
- Heart-healthy diet → Emphasizes fruits, vegetables, whole grains, and lean proteins to improve overall cardiovascular health

Weight Management
- Regular exercise → Aerobic exercise tailored to patient capacity, can improve heart function and endurance
- Cardiac rehabilitation → Supervised programs designed to improve heart health and physical fitness

Monitoring and Patient Education
- Daily weight checks → To detect early signs of fluid retention
- Symptom tracking → Monitoring for shortness of breath, swelling, or fatigue to report early signs of worsening HF
- Control of hypertension, diabetes, and sleep apnea → Proper management of these conditions can improve HF outcomes

J Card Fail. 2022;28(5):e1-e167.

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4. Address socioeconomic barriers to care

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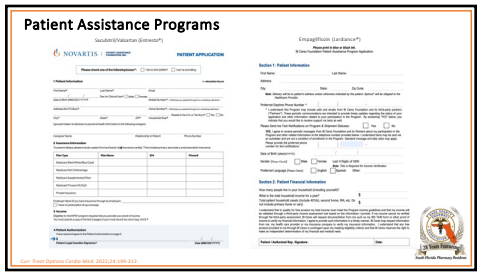
Patient Assistance Programs

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Discount Redemptions
Next best thing to free.
A 90-day supply of select meds for $750
PROTECT FLORIDA PATIENTS
Defend 340B!
$4 30-day | $10 90-day
GoodRx
ScriptCYCLE

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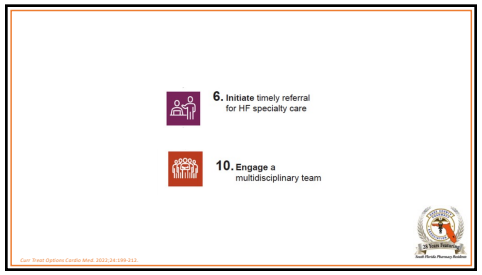
6. Initiate timely referral for HF specialty care
10. Engage a multidisciplinary team

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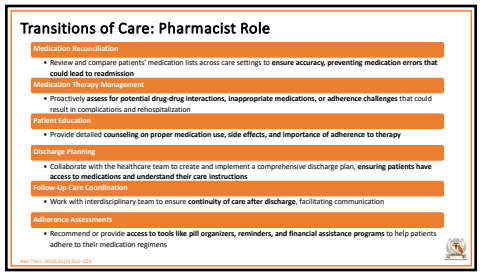
Transitions of Care: Pharmacist Role
Medication Reconciliation
• Review and compare patients' medication lists across care settings to ensure accuracy, preventing medication errors that could lead to readmission
Medication Therapy Management
• Proactively assess for potential drug-drug interactions, inappropriate medications, or adherence challenges that could result in complications and rehospitalization
Patient Education
• Provide detailed counseling on proper medication use, side effects, and importance of adherence to therapy
Discharge Planning
• Collaborate with the healthcare team to create and implement a comprehensive discharge plan, ensuring patients have access to medications and understand their care instructions
Follow-Up Care Coordination
• Work with interdisciplinary team to ensure continuity of care after discharge, facilitating communication
Adherence Assessments
• Recommend or provide access to tools like pill organizers, reminders, and financial assistance programs to help patients adhere to their medication regimens

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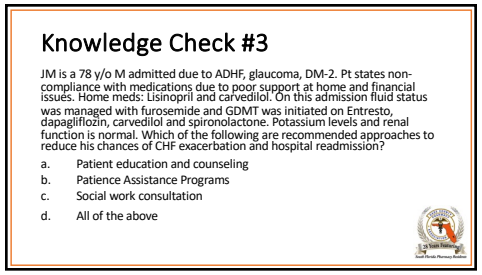
Knowledge Check #3
JM is a 78 y/o M admitted due to ADHF, glaucoma, DM-2. Pt states non-compliance with medications due to poor support at home and financial issues. Home meds: Lisinopril and carvedilol. On this admission fluid status was managed with furosemide and GDMT was initiated on Entresto, dapagliflozin, carvedilol and spironolactone. Potassium levels and renal function is normal. Which of the following are recommended approaches to reduce his chances of CHF exacerbation and hospital readmission?
a. Patient education and counseling
b. Patience Assistance Programs
c. Social work consultation
d. All of the above

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Knowledge Check #3

JM is a 78 y/o M admitted due to ADHF, glaucoma, DM-2. Pt states non-compliance with medications due to poor support at home and financial issues. Home meds: Lisinopril and carvedilol. On this admission fluid status was managed with furosemide and GDMT was initiated on Entresto, dapagliflozin, carvedilol and spironolactone. Potassium levels and renal function is normal. Which of the following are recommended approaches to reduce his chances of CHF exacerbation and hospital readmission?

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c. Social work consultation
d. **All of the above**

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References

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