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Medication Reconciliation

Disclosure

- Dr. Saffel has no vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity, or any affiliation with an organization whose philosophy could potentially bias my presentation.

2

Objectives

- After attending this presentation, you should be able to:
  - Understand the process of Medication Reconciliation
  - Design a Medication Reconciliation process that fits your practice setting
  - Develop and implement measurable outcomes to determine success of a Medication Reconciliation process

3

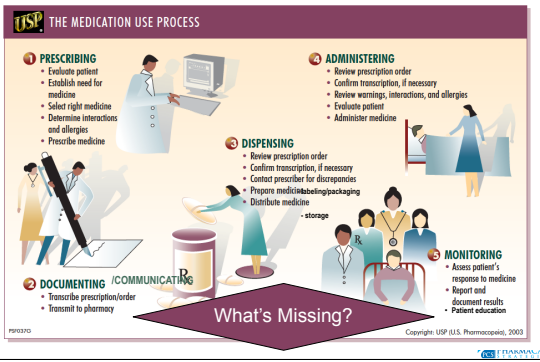
Medication Error

- Preventable event that may cause or lead to:
  - Inappropriate medication use
  - Patient harm

- Related to:
  - Procedures & systems
    - Prescribing
    - Order communication
    - Labeling
    - Packaging
    - Nomenclature
    - Compounding
    - Dispensing
    - Distribution
    - Administration
    - Education
    - Monitoring
    - Use

4

Medication Use Process



5

The Medication Reconciliation Problem

Question 1

- Medication reconciliation is the process of:
  a. Checking the stock bottle against the prescription three time during the dispensing process to verify accuracy.
  b. Obtaining and documenting a **complete** and **accurate** list of a patient's **current medicines** upon admission and **comparing** this list to the prescriber's **admission, transfer and/or discharge orders** to **identify** and **resolve** discrepancies.
  c. Checking through the medication cart to verify that all of the medications in the cart are active, in date, and recorded appropriately on the medication administration record (MAR).
  d. Checking the medications in the tote against the delivery manifest to verify receipt.

7

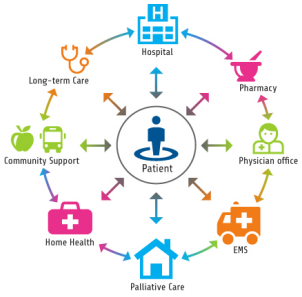
Medication Reconciliation

- A process for obtaining and documenting a **complete** and **accurate** list of a patient's **current medicines** upon admission and **comparing** this list to the prescriber's **admission, transfer and/or discharge orders** to **identify** and **resolve** discrepancies.
  - This is done to avoid medication errors such as omissions, duplications, dosing errors, or drug interactions.
- Conducted at every **transition of care** in which new medications are ordered or existing orders rewritten.

Joint Commission Sentinel Event Alert Issue 35, January 25, 2006

Transitions in Care

"The movement of patient between healthcare locations, providers, or different levels of care within the same location as their needs change…"



National Transitions in Care Coalition. www.ntocc.org. Accessed June 8, 2015

10

Scope of the Problem

- Between 10%-67% of medication histories have at least one error.[1]
- Up to one third of these errors have the potential to cause patient harm.[2]
- More than 50% of medication errors occur at transitions of care.[3]
- Patients with one or more medicines missing from their discharge information are 2.3 times more likely to be readmitted to hospital than those with correct information on discharge.[4]
- 85% of discrepancies in medication treatment originate from poor medication history taking.[5]

References: 1. Tam VC, Knowles SR *et al. CMAJ* 2005;173(5): 510-5. 2. Cornish PL, Knowles SR *et al. Arch Intern Med* 2005;165:424-9. 3. Sullivan C, Gleason KM *et al. J Nurs Care Qual* 2005; 20:95-98. 4. Stowasser DA, Stowasser M, Collins DM. *Journal of Pharmacy Practice and Research* 2002;32:133- 40. 5. Gleason KM, McDaniel MR *et al. J Gen Intern Med*; DOI:10.1007/s11606-010-1256-6.

11

Where Errors Occur in Reconciling Medications

- Admission 22 %
- Transfer 66 %
- Discharge 12 %
- For admission and transition discrepancies about 50 % were intercepted prior to reaching the patient.
- For discharges only 28 % were intercepted prior to reaching the patient.

Santell J. Journal of Qual and Patient Saf. 2006;32:225-9

Scope of the Problem - Long Term Care

- Findings:
  - Medication discrepancies occurred in nearly 75% of SNF admissions from hospitals
  - 20% incidence of ADEs caused by medication changes upon transfer between facilities.
  - ADEs due to medication changes occurred most often upon transfer from the hospital back to the nursing home
- Conclusion:
  - Incomplete or inaccurate communication between facilities was identified as a potential factor in these occurrences.
- Recommendation:
  - Implement medication reconciliation at admission back to the long-term care facility.

Boockvar K, et al. Arch Intern Med. 2004;164;545-50

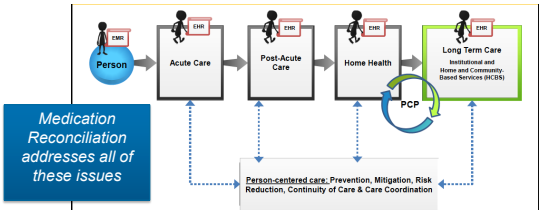
Scope of the Problem - Long Term Care

- Benefit of Medication Reconciliation:
  - A discrepancy related adverse event was less likely in the group of residents who had **medication reconciliation performed by a pharmacist with physician communication** upon transfer from acute care to long-term care
  - Most common discrepancies:
    - Omissions
    - Additions to therapy
    - Dosage changes

Boockvar K, et al. Arch Intern Med. 2004;164;545-50

Why is Medication Reconciliation Important?

- The most frequent occurring medical error is a **medication error**.
- The most frequent cited category of root causes for serious adverse events is **ineffective communication**.
- The most vulnerable part of a process is the **handoffs.**



Question 2

- When should medication reconciliation take place?
  a. When transferring from one care setting to another (during transitions of care).
  b. Monthly or whenever there is a significant change in condition.
  c. Quarterly or whenever a high-risk medication is ordered.
  d. Annually.

16

Regulations and Standards Regarding Medication Reconciliation

18

Question 3

- Which of the following organizations have published guidance on performing mediation reconciliation?
  a. FDA – Good Manufacturing Processes
  b. Joint Commission – National Patient Safety Goals
  c. Congress – IMPACT Act of 2014
  d. b and c
  e. All of the above

19

The Joint Commission (TJC) National Patient Safety Goal (NPSG) Requirements

- Requirement 8.a. To implement a process for obtaining and documenting a complete list of the patient's current medications upon the patient's admission to the organization and with the involvement of the patient.
  - This process includes a comparison of the medications that the organization provides to those on the list.
- Requirement 8.b. A complete list of the patient's medications is communicated to the next provider of service when it refers or transfers a patient to another setting, service, practitioner, or level of care within or outside the organization. The complete list of medications is also provided to the patient when discharged from the facility.

IMPACT Act of 2014 Requires Medication Reconciliation

- Impacts all Post-Acute Care (PAC) providers: SNF, HHC, LTCH, IFR
- Medication Reconciliation reporting required for SNFs as of 10/1/18
- Medication Reconciliation differs from Drug Regiment Review (DRR)
  - **Medication Reconciliation** – the process of comparing the medications a patient is taking (and should be taking) with newly ordered medications in order to identify and resolve discrepancies (Reference: The Joint Commission, National Patient Safety Goals)
  - **Drug Regimen Review (DRR)** – a review of all medications the patient is currently using in order to identify any potential adverse effects and drug reactions, including ineffective drug therapy, significant side effects, significant drug interactions, duplicate drug therapy, and noncompliance with drug therapy. (Reference: Home Health Conditions of Participation §484.55c)

CMS states "*using Drug Regimen Review (DRR) supports a systematic approach to Medication Reconciliation that improve quality and patient safety, especially around transitions of care.*"

Impact Act of 2014 Cross Setting Quality Measure: Drug Regimen Review. https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/MMS/Downloads/Drug-Regimen-Review-Comment-Summary.pdf. Accessed May 24, 2017.

22

CMS Proposes Incorporating Medication Reconciliation as Part of Drug Regimen Review

- QRP Measure Title: Drug Regimen Review Conducted with Follow-Up for Identified Issues
- *Proposed* Description:
  - Percentage of stays in which a drug regimen review was conducted at the Admission each tine **potentially significant medication issues were identified** throughout the stay there was:
    - **Timely follow-up** with a physician, and
    - **Completed prescribed/recommended actions** in response to the identified issue
  - Follow up and action must take place within **1 calendar day** from identification
- Potential clinically significant medication issues are those that, in the clinician's professional judgment, warrant outreach to a physician and timely completion of any recommended actions to avoid adverse outcomes

Impact Act of 2014 Cross Setting Quality Measure: Drug Regimen Review. https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/MMS/Downloads/Drug-Regimen-Review-Comment-Summary.pdf. Accessed May 24, 2017.

23

Importance of MR and DRR

- Medication review in PAC is generally considered to include:
  - Medication Reconciliation (MR) for all medications, and
  - Drug Regiment Review (DRR) for high risk medications.
- As a process measure, MR and DRR are expected to:
  - Reduce re-hospitalizations,
  - Reduce adverse events related to medications, and
  - Improve health outcomes.

Impact Act of 2014 Cross Setting Quality Measure: Drug Regimen Review. https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/MMS/Downloads/Drug-Regimen-Review-Comment-Summary.pdf. Accessed May 24, 2017.

24

Additional Proposed Guidance – Decrease Polypharmacy

- Assessment & Action
  - Prescribers will review and record the total number of routine and as needed medications at each periodic visit.
  - The **creatinine clearance level** will be calculated on admission, with changes in condition, and at least annually
    - The Cockcroft Gault score and laboratory results will be used to determine dosing based on major drug guides and prescribing references
- Expected Outcome:
  - Number of scheduled and PRN medications will not increase and medications will be congruent with diagnoses with no duplications present.
    - Goal: **9 or fewer scheduled medications** with number of administrations no more than 3 different times daily.
    - Medication doses will be appropriate for age/renal/hepatic status of older adults.

Impact Act of 2014 Cross Setting Quality Measure: Drug Regimen Review. https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/MMS/Downloads/Drug-Regimen-Review-Comment-Summary.pdf. Accessed May 24, 2017.

25

Additional Proposed Guidance – Reduce Adverse Drug Reactions (ADR)

- Assessment & Action
  - The resident's record and physical exam will be used to verify adverse drug reactions occurring in the time from the last periodic exam.
    - Medications identified as resulting in ADRs including reactions or ER/ hospitalizations will be adjusted or discontinued based on overall plan of care.
    - Monitoring guidelines will be individualized and in place for high risk medications: i.e., insulin, digoxin, warfarin, anti-psychotics.
- Expected Outcome
  - No adverse drug reactions
  - No drugs ordered to treat side effects or adverse reactions, and
  - No hospitalizations or ED visits resulting from adverse drug reactions.

Impact Act of 2014 Cross Setting Quality Measure: Drug Regimen Review. https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/MMS/Downloads/Drug-Regimen-Review-Comment-Summary.pdf. Accessed May 24, 2017.

26

Additional Proposed Guidance – Decrease Inappropriate Prescribing

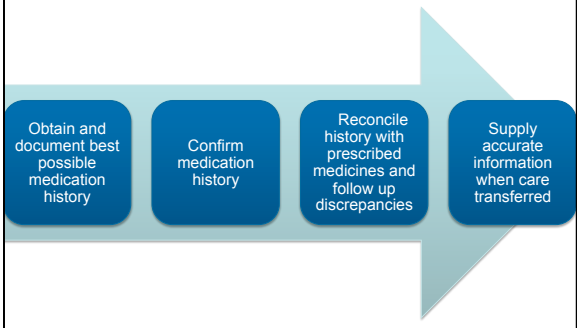
- Assessment & Action:
  - The current MAR will be compared to the Beers list, CMS guidelines, and the facility pharmacist's recommendations to ascertain appropriateness of current medication regimen
    - Medications found to be in conflict with the Beers list, CMS guidelines, and/or facility pharmacist's recommendations should be discontinued or adjusted unless compelling evidence exists for continuance.
    - The Beers list, CMS guidelines, and/or facility pharmacist's recommendations should be used when planning medication initiation, reviewing established medication regimens, or making changes in the medication regimen.
- Expected Outcome:
  - No inappropriate prescribing as evidenced by the medication regimen which contains no drugs in conflict with the Beers lists, CMS guidelines, and/or pharmacist recommendations.

Impact Act of 2014 Cross Setting Quality Measure: Drug Regimen Review. https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/MMS/Downloads/Drug-Regimen-Review-Comment-Summary.pdf. Accessed May 24, 2017.

27

The Medication Reconciliation Process

Four Key Steps to Medication Reconciliation



29

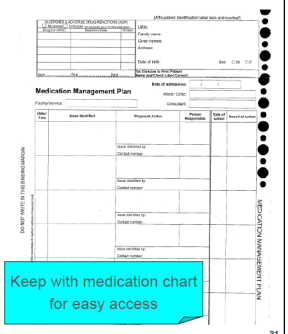
Step 1 Obtain Medication History

- Obtain best possible medication history (BPMH)
  - Use information from patient and caregiver interviews, discharge history, physician referrals, and other sources
  - Compile a comprehensive list of current medications including:
    - Prescription medications
    - Sample medications
    - Vitamins
    - Nutraceuticals
    - Over-the-counter (OTC) drugs

Example: Medication Reconciliation Form

Supports key steps of Medrec

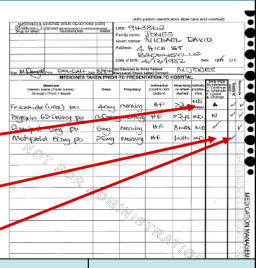
1. Obtain and document best possible medication history
2. Confirm medication history
3. Reconcile history with prescribed medicines
4. Document issues/discrepancies and actions
5. Supply accurate information when care transferred



31

Example: Completed Mediation Reconciliation

- Capture of complete and accurate medication history on admission
- Allows for shared accountability
- Doctors plan column helps with reconciliation
- Identifies is supply required at discharge



Include:
- Drug name
- Dose
- Route
- Strength
- Frequency

- Indication (reason)
- Last dose
- Who is providing the information
- Who is collecting the information

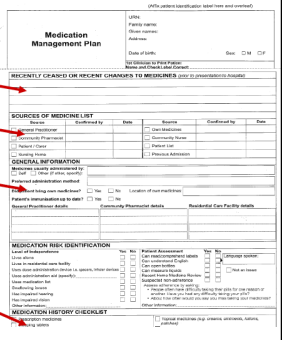
Step 2 Confirm Accuracy

- Use a second source to confirm the information obtained
  - Review the patient's medication list
    - Provided by discharging facility
    - Corroborated by family
  - Inspect medication containers when available
  - Contact community pharmacists and physicians (with patient's consent)
  - Review previous patient health records

Example: Changes and Confirmation

Prompts for and consolidates information

- Recently ceased or changed medicines
- Confirmation of history
  - Several sources may be needed
- General information
  - Who administers
  - Immunisation status (children)
  - Community contacts
- Checklist to assist in completing history



34

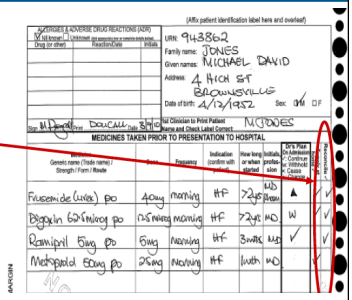
Step 3 Reconcile with Current Prescribed Medications

- Compare the patient's medication history with their current prescribed treatment.
- If there are discrepancies:
  - Discuss with prescriber
  - Ensure reasons for changes to therapy are documented

Example: Reconciliation

To ensure patient receives all intended medications

Column to reconcile each medicine



36

Step 4 Supply Accurate and Complete List

- When patients are transferred between facilities or the community, ensure that the person taking over their care is provided with an **accurate and complete list** of the patient's medications.
- Ensure that the care provider, patient, and/or caregiver are also provided with information about any **changes** that have been made to medications.

Question 4

- All of the following activities are steps to complete a medication reconciliation *except*:
  a. Obtain and document best possible medication history.
  b. Confirm medication history.
  c. Reconcile history with prescribed medicines and follow up discrepancies.
  d. Provide the patient with report in three formats; printed, video, and audio recording.
  e. Supply accurate information when care transferred.

38

Effective Medication Reconciliation

- To be successful needs to be built into the process of care – not added to it:
  – e.g. replace multiple histories with one that is used throughout episode of care
- **Integrate** steps into existing processes: – Patient flow, medication management system
- Best conducted in environment of shared accountability
- Multiple approaches
  – Models will differ from hospital to nursing facility to community

40

Medication Reconciliation – Safe Practice Recommendations

1. Develop a formal and **systematic** approach to reconciling patient medicines across the continuum
   - Multidisciplinary, reps from key depts (ED, ICU, pre-admission, med/surg units, pharmacy, Q&S unit)
2. Create **P&Ps** that outline roles,tasks in each step in the process
3. Adopt a **standardized form** for collecting pre-admission medication list and reconciling medications
   - Place in consistent, highly visible location with patient's chart - easily accessible when medicines are ordered
   - Electronic and paper

Massachusetts Coalition for prevention of medical errors http://www.maccoalition.org/initiatives.shtml

41

Medication Reconciliation – Safe Practice Recommendations (con't)

4. Assign **responsibility** for obtaining **BPMH** to someone with sufficient expertise
   - Shared accountability (prescriber, nurse and pharmacist work together)
5. Assign **responsibility** for resolving **variances** to someone with sufficient expertise
6. Establish **specific time frames** within which medicines should be reconciled
   < 24 hours

Massachusetts Coalition for prevention of medical errors http://www.maccoalition.org/initiatives.shtml

42

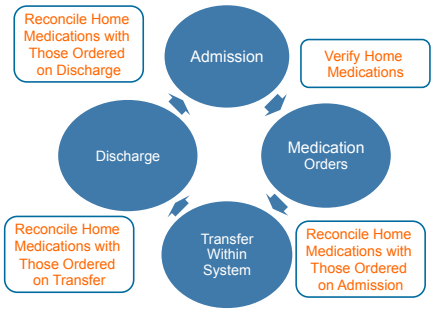
Medication Reconciliation – Safe Practice Recommendations (con't)

7. Provide clinicians ready **access** to **drug information** and a **pharmacist consult** when needed
8. **Improve access** to complete medication list at admission
9. Provide **orientation** and ongoing **training** to all health professionals
10. **Monitor** performance and provide **feedback**

Massachusetts Coalition for prevention of medical errors http://www.maccoalition.org/initiatives.shtml

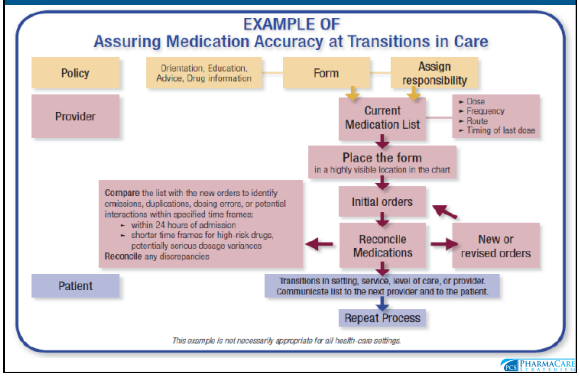
43

Medication Reconciliation



44

Medication Reconciliation Process



Goals with Admission

- Obtain as accurate as possible a list of medications (name, dose, frequency..) that the patient is receiving at home or other care setting
- Ensure that a conscious decision is made to continue, discontinue, or modify current medications the patient is receiving when writing admission orders
- Document discrepancies and resolve if needed

Sources of Information

- Patient or caregiver
- Prior provider of care (hospital, nursing home, home care)
- Primary Care Physician
- Insurer (claims data)
- Pharmacy (inpatient/outpatient)

Goals with Transitions

- Ensure that a conscious decision is made to continue, discontinue, or modify current medications the patient is receiving from last transition point
- Ideally compare to admission list of medications
- Document discrepancies and resolve if needed
- Share with patient and other providers as necessary

Sources of Information

- Medication Administration Record
- Pharmacy profile (inpatient/outpatient)
- Prior provider of care (hospital, nursing home, home care)
- Primary Care Physician
- Insurer (claims data)
- Patient or caregiver
- Original medication list

Goals on Discharge

- Ensure that a conscious decision is made to continue, discontinue, or modify current medications the patient is receiving from last transition point
- Compare to original list of medications obtained at admission to 'facility'
- Document discrepancies and resolve if needed
- Share with patient and other providers

Challenges

- Engaging everyone in the process
  - Patient, caregivers
    - Making it an expectation of the patient that they receive a current list at discharge
    - Making it a patient responsibility to bring the list to the next provider of care
    - With time the quality of data will improve if we follow the above
  - Physicians, all providers of care
  - Financial incentives expected by some

Thank You!

Getting to Goal: Taking A Patient-Centered Approach to Diabetes Management
Self-Assessment Questions

1. A 59-year-old female patient presents to clinic today with newly-diagnosed type 2 diabetes mellitus and an A1c of 7.6%. PMH is significant for HTN, HL, stage IV CKD and osteoporosis. Labs are WNL, except Scr, which is 2.1 mg/dL, and an eGFR of 27 ml/min/1.73m^2. Which of the following medications should be initiated in addition to lifestyle modifications?

    a. Metformin
    b. Pioglitazone
    c. Linagliptin
    d. Canagliflozin

2. A 55-year-old female patient with newly-diagnosed type 2 diabetes mellitus, heart failure reduced ejection fraction (EF 30%) and hypertension, presents to your clinic today for diabetes management. She states she cannot tolerate her metformin 500 mg ER prescription and would like a new medication to manage her diabetes. Her most recent A1c was 7.4% and her medication regimen includes atorvastatin 80 mg daily, lisinopril 20 mg daily, furosemide 80 mg twice daily, spironolactone 25 mg daily and carvedilol 25 mg twice daily. She adamantly refuses to use an injectable medication. Her labs are WNL, except for Scr, which is 1.7 mg/dL, and eGFR 40 mL/min/1.73m^2. Which of the following medications would be most appropriate to initiate?

    a. Liraglutide 0.6 mg daily
    b. Saxagliptin 2.5 mg daily
    c. Sitagliptin 50 mg daily
    d. Canagliflozin 100 mg daily

3. A patient presents to your clinic for a diabetes management visit. He is currently taking insulin degludec 25 units subcutaneously once daily and metformin 1000 mg twice daily for management of his type 2 diabetes mellitus. His physician would like to start him on Xultophy® 100/3.6 mg (insulin degludec and liraglutide). Which of the following would be the most appropriate starting dose of Xultophy® 100/3.6 mg (insulin degludec and liraglutide)?

    a. 10 units
    b. 15 units
    c. 16 units
    d. 30 units

4. Which of the following medications has been shown to reduce cardiovascular risk in patients with type 2 diabetes mellitus?

    a. Lixisenatide
    b. Sitagliptin
    c. Liraglutide
    d. Canagliflozin

Getting to Goal: Taking A Patient-Centered Approach to Diabetes Management
Self-Assessment Questions

5. A 57-year-old woman presents to clinic for diabetes management. She states she has lost her job and insurance; therefore, she is unable to pay for some of her medications now. Her current medication regimen includes metformin 1000 mg twice daily, empagliflozin 25 mg daily, aspirin 81 mg daily, atorvastatin 40 mg daily and liraglutide 1.8 mg daily. Her most recent A1c was 7.1% and her labs are WNL. Which of the following recommendations would be most appropriate?

    a. Discontinue liraglutide and empagliflozin and initiate glipizide 5 mg twice daily
    b. Continue empagliflozin, discontinue liraglutide and initiate dulaglutide 1.5 mg once weekly
    c. Continue liraglutide, discontinue empagliflozin and initiate glipizide 5 mg twice daily
    d. Discontinue empagliflozin and liraglutide and initiate dulaglutide 1.5 mg once weekly

6. Which of the following would be the most appropriate counseling point regarding the use of the Victoza® pen?

    a. Must be injected 15 minutes before breakfast
    b. Eat smaller more frequent meals to reduce nausea
    c. Prime pen before each use
    d. Each pen is stable at room temperature for 42 days after the first use

7. A 45-year-old female patient with a 3-year history of type 2 diabetes mellitus and a past medical history significant for heart failure reduced ejection fraction (HFrEF), hypertension and dyslipidemia presents to your clinic today for diabetes management. Her most recent A1c was 8.1% (6/23/17) and her medication regimen includes metformin 1000 mg twice daily, lisinopril 40 mg daily, metoprolol succinate 100 mg daily, atorvastatin 40 mg daily and furosemide 80 mg twice daily. She refuses to use an injectable medication at this time. Her most recent EF was 25% (5/18/17). Which of the following medications would be most appropriate to initiate to better control this patient's type 2 diabetes mellitus?

    a. Empagliflozin
    b. Albiglutide
    c. Saxagliptin
    d. Pioglitazone

8. A 53-year-old male patient presents to your clinic for a diabetes management visit. His past medical history is significant for diabetes, hypertension, hyperlipidemia, and morbid obesity. His current medications include glipizide 10 mg twice daily, metformin 1000 mg twice daily, atorvastatin 40 mg daily, aspirin 81 mg daily, and lisinopril 40 mg daily. He states he has been trying to lose weight by limiting his carbohydrate intake; however, has only lost 5 lbs. His fasting plasma glucose readings range from 146-178 mg/dL and his 2-hour post-prandial glucose readings are all over 200 mg/dL. His current weight is 305 lbs, his A1c is 8.7% and his Scr is 1.2 mg/dL. Which of the following recommendations is most appropriate at this time?

    a. Increase glipizide to 20 mg twice daily
    b. Initiate liraglutide 0.6 mg daily
    c. Initiate insulin glargine 10 units daily
    d. Initiate sitagliptin 100 mg daily

Getting to Goal: Taking A Patient-Centered Approach to Diabetes Management
Self-Assessment Questions

9. Which of the following medications should be tapered or discontinued upon initiating rapid-acting (mealtime) insulin therapy?

    a. Glipizide
    b. Metformin
    c. Victoza
    d. Sitagliptin

10. A 67-year-old female patient presents today for a diabetes management visit. She is currently taking metformin 1000 mg twice daily, glipizide 10 mg twice daily and sitagliptin 25 mg daily for management of her type 2 diabetes mellitus. Her past medical history is significant for stage 4 chronic kidney disease and stage 3 breast cancer. Today her laboratory values show an eGFR of 25 ml/min/1.73m^2 and a Scr of 2.3 mg/dL. Her most recent A1c 2 months ago was 10.2%. Which of the following is the most appropriate treatment option for this patient?

    a. Discontinue glipizide and initiate insulin aspart 4 units three times daily before meals
    b. Initiate exenatide 5 mcg twice daily before meals
    c. Discontinue metformin and initiate insulin glargine 10 units daily
    d. Discontinue metformin and initiate insulin aspart 4 units three times daily before meals

Getting To Goal: Taking A Patient-Centered Approach To Diabetes Management

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Disclosures

Dr. Christie Schumacher has no conflicts of interest to disclose.

Learning Objectives

- Discuss recent updates in national guidelines in regard to the care of patients with type 2 diabetes mellitus
- Explain the mechanism of action, efficacy and place in therapy for each of the medications used in the treatment of type 2 diabetes mellitus
- Design a treatment plan to improve blood glucose control and lower A1c levels in patients with type 2 diabetes mellitus, taking into account co-morbid conditions and patient specific factors
- Apply evidence from the cardiovascular outcomes trials (CVOTs) to support therapeutic recommendations for patients with type 2 diabetes mellitus

ADA Hyperglycemia Recommendations

A1c <7%
- General recommendation by the ADA

Less stringent goal of A1c <7.5–8%
- Severe hypoglycemia
- Limited life expectancy
- Advance complications
  - e.g. moderate to severe renal dysfunction
- Extensive comorbid conditions

More stringent goal of A1c <6–6.5%
- Short disease duration
- Long life expectancy
- No significant cardiovascular disease (CVD)

Diabetes Care. 2017;39:S1-S135.

Oral Medications and Non-insulin Injectable Agents

Oral Medications and Non-insulin Injectable Agents

Oral Medications

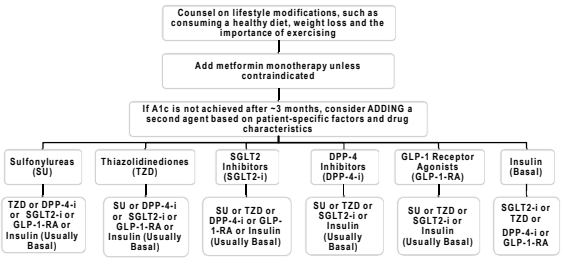
- Biguanides
- Sulfonylureas (SU)
- Meglitinides
- Thiazolidinediones (TZDs)
- Sodium-glucose cotransporter-2 inhibitors (SGLT2-i)
- Dipeptidyl peptidase-4 inhibitors (DPP-4-i)
- α-Glucosidase inhibitors
- Dopamine agonists
- Bile acid sequestrants

11 Classes

Non-insulin Injectable Agents

- Glucagon-like peptide-1 receptor agonists (GLP-1-RA)
- Amylinomimetics

ADA Hyperglycemia Algorithm



Adapted From: Diabetes Care. 2017;39:S1-S135

Pathophysiologic Changes

Pancreas
- ↓ β-cell function
  - ↓ Insulin and amylin secretion
- ↑ α-cell stimulation
  - ↑ hepatic gluconeogenesis

Brain
- Impaired satiety
- ↓ Dopamine

Peripheral Tissue
- ↓ GLUT-4

Kidney
- ↑ Glucose reabsorption

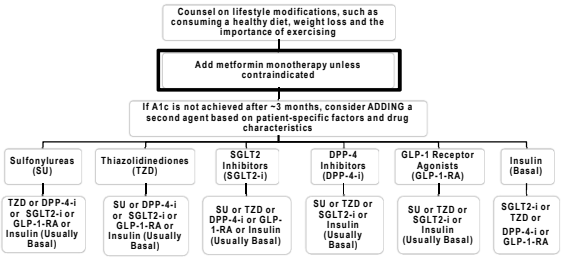
GI Tract
- Incretin deficiency and/or resistance

Adipose Tissue (fat)
- ↑ Cytokines
- ↑ Inflammatory mediators
- ↑ Free fatty acids
- ↓ Adiponectin

Inflammation
Insulin resistance
Impaired thrombolysis
↑ BP
Dyslipidemia
↑ Body weight

Diabetes Care. 2009;58:773-95

ADA Hyperglycemia Algorithm



Adapted From: Diabetes Care. 2017;39:S1-S135

Biguanides (Metformin)

MOA

- ↓ Hepatic glucose production
- ↑ Insulin sensitivity
- ↓ Intestinal absorption of glucose

Efficacy

- 1–1.5% ↓ A1c
- Greater effect on FPG
  - Also effective on PPG

Diabetes Care. 2017;39:S1-S135.
Endocr Pract. 2016;22:84-113.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

Biguanides (Metformin)

Initial Metformin Dosing

- IR: 500 mg once or twice daily, or 850 mg once daily
  - ER: 500 mg once daily
- Max effective dose: 2000 mg for both dosage forms

Diabetes Care. 2017;39:S1-S135.
Endocr Pract. 2016;22:84-113.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

Biguanides (Metformin)

Renal Insufficiency	eGFR (mL/min/1.73m^2)	Maximum Daily Dose	Recommended Monitoring
None or Mild	≥60	2550 mg (2000 mg)	Renal function annually
Moderate	45–59	2000 mg	Renal function every 3–6 months
	30–44	1000 mg	Renal function every 3 months Lower dose by 50% or use half of the maximum dose Do not start new patients on metformin, can be continued if renal function drops to this level
Severe	<30	Do not use	

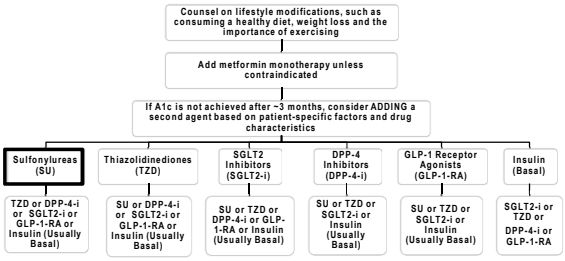
Diabetes Care. 2011;34:1431-37.

Biguanides (Metformin)

Advantages	Disadvantages
• Weight neutral • Inexpensive • Low risk of hypoglycemia • ↓ CVD risk	• GI side effects • Vitamin B_{12} deficiency • Avoid in renal impairment • eGFR <30 mL/min/1.73m^2

Diabetes Care. 2017;39:S1-S135.
Endocr Pract. 2016;22:84-113.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

ADA Hyperglycemia Algorithm



Adapted From: Diabetes Care. 2017;39:S1-S135.

Sulfonylureas

MOA

- Closes K_{ATP} channels on β-cell membrane
- Stimulates insulin secretion

Classes

- First generation agents rarely used
  - Not recommended in current guidelines
  - Chlorpropamide, tolbutamide
- Second generation agents
  - Glyburide, glipizide, glimepiride

Diabetes Care. 2017;39:S1-S135.
Diabetes Care. 2012;35:1364-79.
Endocr Pract. 2016;22:84-113.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

Sulfonylureas

Efficacy

- 1–2% ↓ A1c
- ↓ PPG

Renal Function Dosing

- Avoid in poor renal function
  - Glipizide: CrCl <10 mL/min
  - Glimepiride: CrCl <30 mL/min
  - Glyburide: CrCl <50 mL/min

Diabetes Care. 2017;39:S1-S135.
Diabetes Care. 2012;35:1364-79.
Endocr Pract. 2016;22:84-113.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

Sulfonylureas

Drug	Initial Dose	Maximum Daily Dose
Glyburide (DiaBeta®)	2.5–5 mg once or twice daily	20 mg
Glipizide (Glucotrol®)	2.5–5 mg once or twice daily (once daily with extended-release)	40 mg (maximum effective daily dose = 20 mg)
Glimepiride (Amaryl®)	1–2 mg daily	8 mg

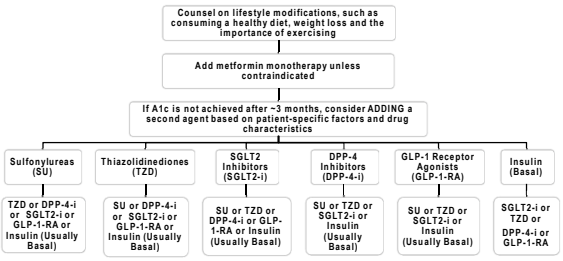
Diabetes Care. 2012;35:1364-79.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

Sulfonylureas

Advantages	Disadvantages
• Inexpensive • Extensive experience • ↓ Microvascular risk	• Hypoglycemia • Weight gain • Reduced efficacy over time

Diabetes Care. 2017;39:S1-S135.
Diabetes Care. 2012;35:1364-79.
Endocr Pract. 2016;22:84-113.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

ADA Hyperglycemia Algorithm



Adapted From: Diabetes Care. 2017;39:S1-S135.

Meglitinides

MOA

- Similar to sulfonylureas → stimulate insulin secretion from the pancreas
  - Glucose-dependent
  - More rapid onset (peak after 1 hour) and shorter duration of action than SU

Efficacy

- 0.5–1.5% ↓ A1c
  - Repaglinide shown to ↓ A1c more than nateglinide
- Most effective on PPG

Diabetes Care. 2017;39:S1-S135.
Diabetes Care. 2012;35:1364-79.
Endocr Pract. 2016;22:84-113.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

Meglitinides

Drug	Initial Dose	Maximum Daily Dose	Notes
Repaglinide (Prandin®)	0.5–1 mg with each meal (Increase in weekly intervals as needed)	16 mg	Take 15 minutes before meals; skip if skipping meal
Nateglinide (Starlix®)	120 mg with each meal (Initiate at 60 mg if A1c is near goal)	360 mg	Take 1 – 30 minutes before meals; skip dose if skipping meal

Diabetes Care. 2012;35:1364-79.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

Meglitinides

Advantages	Disadvantages
• Can be used in patients that are unable to take a SU due to sulfa allergy • Dosing flexibility	• More expensive than SU • Hypoglycemia • Weight gain • Frequent dosing schedule

Diabetes Care. 2017;39:S1-S135.
Diabetes Care. 2012;35:1364-79.
Endocr Pract. 2016;22:84-113.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

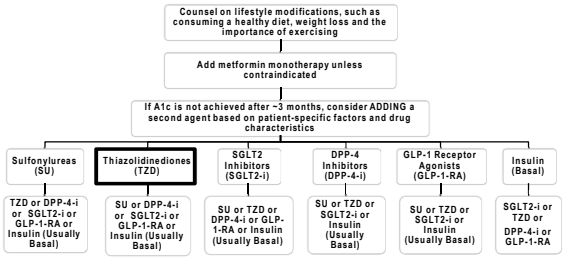
Meglitinides

Place in Therapy

- Consider instead of a SU in patients with
  - Irregular eating schedules
  - Late post-prandial hypoglycemia from SUs

Diabetes Care. 2017;39:S1-S135.

ADA Hyperglycemia Algorithm



Adapted From: Diabetes Care. 2017;39:S1-S135.

Thiazolidinediones (TZDs)

MOA

- Peroxisome proliferator-activated receptor-γ (PPAR-γ) agonist
- Increases expression of genes responsible for glucose metabolism
  - ↑ Insulin sensitivity

Efficacy

- 0.5 – 1.4% ↓ A1c
- ↓ FPG

Diabetes Care. 2017;39:S1-S135.
Diabetes Care. 2012;35:1364-79.
Endocr Pract. 2016;22:84-113.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

Thiazolidinediones (TZDs)

Rosiglitazone (Avandia®)

- No longer frequently used
  - REMS prescribing recently removed
  - Risk of MI and CV death

Diabetes Care. 2012;35:1364-79.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

Thiazolidinediones (TZDs)

Pioglitazone (Actos®) dosing

- Initial: 15 mg once daily
- Maximum: 45 mg once daily
- Dose titration is slower
- Maximum effect after initiation or dose change may not be observed for 8–12 weeks
  - Counsel to prevent nonadherence!
- Now available as a generic medication

Diabetes Care. 2012;35:1364-79.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

Thiazolidinediones (TZDs)

Advantages	Disadvantages

• No hypoglycemia
• Durability
• ↑ HDL, ↓ LDL and TGs (pioglitazone)
	• Weight gain
	• Fluid retention
	  • Peripheral edema
	  • Worse with insulin use
	• ↑ Risk of fractures
	  • Caution in patients with osteoporosis
	• ↑ Risk of heart failure
	• ↑ Risk of bladder cancer (pioglitazone)

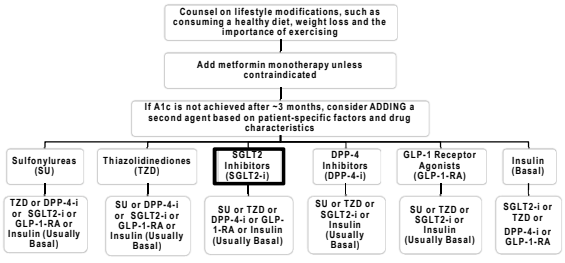
Diabetes Care. 2017;39:S1-S135.
Diabetes Care. 2012;35:1364-79.
Endocr Pract. 2016;22:84-113.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

Clinical Question

A 47-year-old woman presents to clinic for diabetes management. She states she has lost her job and insurance; therefore, she is unable to pay for some of her medications at this time. Her current medication regimen includes metformin 1000 mg twice daily, canagliflozin 300 mg daily and sitagliptin 100 mg daily. Her most recent A1c was 7.1% and her labs are WNL. Which of the following recommendations would be most appropriate at this time?

a. Discontinue sitagliptin and canagliflozin and initiate glipizide 5 mg twice daily
b. Continue canagliflozin, discontinue sitagliptin and initiate liraglutide 0.6 mg daily
c. Continue sitagliptin, discontinue canagliflozin and initiate glipizide 5 mg twice daily
d. Discontinue canagliflozin and sitagliptin and initiate liraglutide 0.6 mg daily

ADA Hyperglycemia Algorithm



Adapted From: Diabetes Care. 2017;39:S1-S135.

SGLT2 Inhibitors (SGLT2-i)

MOA

- Blocks glucose reabsorption in the proximal renal tubule
  - Increases urinary glucose excretion

Efficacy

- 0.5–1% ↓ A1c

Farxoga [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2014.
Invokana [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; 2013.
Jardiance [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; 2014.

SGLT2 Inhibitors (SGLT2-i)

Drug	Initial Dose	Dosing Considerations
Canagliflozin (Invokana®)	100 mg daily before first meal	May ↑ to 300 mg daily if eGFR >60 mL/min/1.73m^2 Maximum 100 mg daily if eGFR 45–60 mL/min/1.73m^2 Not recommended: eGFR <45 mL/min/1.73m^2
Dapagliflozin (Farxiga®)	5 mg daily in the morning with or without food	May ↑ to 10 mg daily Not recommended: eGFR <60 mL/min/1.73m^2
Empagliflozin (Jardiance®)	10 mg daily with or without food	May ↑ to 25 mg daily if eGFR >60 mL/min/1.73m^2 Maximum 10 mg daily if eGFR 45–60 mL/min/1.73m^2 Not recommended: eGFR <45 mL/min/1.73m^2

Farxoga [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2014.
Invokana [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; 2013.
Jardiance [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; 2014.

SGLT2 Inhibitors (SGLT2-i)

Advantages

- Possible weight loss
  - ~ 2 kg
    - Stabilizes over 6–12 months
- ↓ Blood pressure
- ↓ Risk of hypoglycemia
- ↓ CV risk (EMPA-REG)

Disadvantages

- Expensive
- Genital mycotic infections/ Genitourinary infections
- Polyuria
- Hypotension/volume depletion/ dizziness
- Diuretic effect – use with caution in patients on diuretics
  - Consider ↓ in diuretic dose
- ↑ Scr (transient)
- Euglycemic ketoacidosis
- ↓ BMD and possible ↑ risk of foot amputations with canagliflozin

Farxoga [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2014.
Invokana [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; 2013.
Jardiance [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; 2014.
FDA Safety Communication. http://www.fda.gov/Drugs/DrugSafety/ucm475463.htm.

EMPA-REG (Empagliflozin) Cardiovascular Outcomes Trials (CVOTs)

Primary Outcome (MACE)

- HR 0.86 (0.74–0.99)

Cardiovascular Death

- HR 0.62 (0.49–0.77)

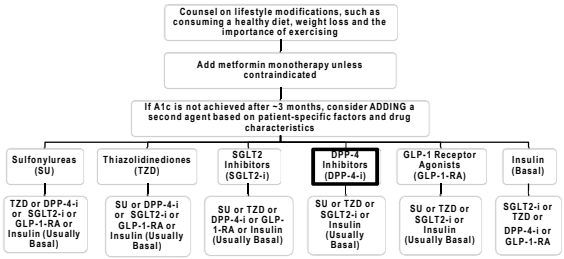
Hospitalization for Heart Failure

- HR 0.65 (0.50–0.85)

MACE = Major adverse cardiovascular events

N Engl J Med 2015;373(22):2117-2128.

ADA Hyperglycemia Algorithm



Adapted From: Diabetes Care. 2017;39:S1-S135.

Dipeptidyl Peptidase-4 Inhibitors (DPP-4-i)

MOA

- Inhibits the breakdown of glucagon-like peptide-1 (GLP-1) secreted during meals
- Prolongs action of endogenous GLP-1
  - ↑ Glucose-dependent pancreatic insulin secretion
  - ↓ Glucagon secretion
    - ↓ Hepatic glucose production

Efficacy

- 0.5–0.8% ↓ A1c
- ↓ FPG and PPG

Diabetes Care. 2017;39:S1-S135.
Diabetes Care. 2012;35:1364-79.
Endocr Pract. 2016;22:84-113.
Diabetes Care. 2012;35:1364-79.
Pharmacotherapy: A Pathophysiologic Approach, 10th ed. New York: McGraw-Hill; 2017.

Dipeptidyl Peptidase-4 Inhibitors (DPP-4-i)

Drug	Normal Dose	Renal Dose Adjustments	
		CrCl 30–50 mL/min	CrCl <30 mL/min
Sitagliptin (Januvia®)	100 mg once daily	50 mg once daily	25 mg once daily
Saxagliptin (Onglyza®)	5 mg once daily	2.5 mg once daily	
Linagliptin (Tradjenta®)	5 mg once daily	None	
Alogliptin (Nesina®)	25 mg once daily	12.5 mg once daily†	6.25 mg once daily

†Dose adjust if CrCl 30–59 mL/min

Diabetes Care. 2012;35:1364-79.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.
Diabetes Care. 2012;35:1364-79.

Dipeptidyl Peptidase-4 Inhibitors (DPP-4-i)

Advantages	Disadvantages
• Low risk of hypoglycemia • Weight neutral • Well-tolerated	• Expensive • Avoid in patients with a history of or those at risk for pancreatitis • Severe joint pain • Reversible upon discontinuation • Saxagliptin and alogliptin may ↑ the risk of heart failure or worsen heart failure in patients who have heart or kidney disease (FDA warning)

Diabetes Care. 2017;39:S1-S135.
Diabetes Care. 2012;35:1364-79.
Endocr Pract. 2016;22:84-113.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.
FDA Med Watch. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm494252.htm (accessed May 6, 2016).

Dipeptidyl Peptidase-4 Inhibitors (DPP-4-i) Cardiovascular Outcomes Trials (CVOTs)

	Primary Outcome (MACE)	Hospitalization for Heart Failure
TECOS (Sitagliptin)	0.98 (0.88–1.09)	1.00 (0.83–1.20)
SAVOR-TIMI 53 (Saxagliptin)	1.00 (0.89–1.12)*	1.27 (1.07–1.51)
EXAMINE (Alogliptin)	0.96 (≤1.16)	----------

*MACE + unstable angina

N Engl J Med. 2015;373(3):232-42.
N Engl J Med. 2013;369(14):1317-1325.
N Engl J Med. 2013;369(14):1327-1335.

Dipeptidyl Peptidase-4 Inhibitors (DPP-4-i) Cardiovascular Outcomes Trials (CVOTs)

EXAMINE Post-Hoc Analysis – Hospital Admission for Heart Failure			
Patients	Alogliptin	Placebo	HR (95% CI)
All patients	106 (3.9%)	89 (3.3%)	1.19 (0.90–1.58)
History of HF	63 (8.2%)	65 (8.5%)	1.00 (0.71–1.42)
No History of HF	43 (2.2%)	24 (1.3%)	1.76 (1.07–2.90)

2016 FDA Warning – Risk of HF

The Lancet 2015;85(9982)2067-2076

Dipeptidyl Peptidase-4 Inhibitors (DPP-4-i) Cardiovascular Outcomes Trials (CVOTs)

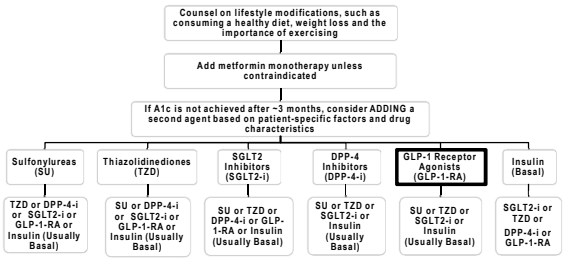
Sitagliptin	• May be safe to use in patients with HF
Saxagliptin	• Avoid use in patients with HF
Alogliptin	• Avoid use in patients with HF

Clinical Question

A 30-year-old male patient with a 1-year history of type 2 diabetes mellitus and a past medical history significant for heart failure reduced ejection fraction (HFrEF), hypertension and dyslipidemia presents to your clinic today for diabetes management. His most recent A1c was 8.1% (4/23/17) and his medication regimen includes metformin 1000 mg twice daily, lisinopril 40 mg daily, carvedilol 25 mg twice daily, atorvastatin 40 mg daily and furosemide 40 mg daily. He refuses to use an injectable medication at this time. His most recent EF was 35% (1/18/17). Which of the following medications would be most appropriate to initiate to better control this patient's type 2 diabetes mellitus?

a. Empagliflozin
b. Glyburide
c. Saxagliptin
d. Pioglitazone

ADA Hyperglycemia Algorithm



Adapted From: Diabetes Care. 2017;39:S1-S135.

Incretin Analogs (GLP-1-RA)

MOA

- Synthetic analog of human GLP-1 that binds to GLP-1 receptors
  - Glucose-dependent insulin secretion
  - ↓ Glucagon secretion
    - ↓ Hepatic glucose production
  - Slows gastric emptying
  - ↑ Satiety
  - ↓ Food intake and promote weight loss

Efficacy

- 0.5 – 1% ↓ A1c
- ↓ FPG and PPG

Diabetes Care. 2017;39:S1-S135.
Diabetes Care. 2012;35:1364-79.
Endocr Pract. 2016;22:84-113.
Diabetes Care. 2012;35:1364-79.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

Incretin Analogs (GLP-1-RA)

Drug	Initial Dose	Dosing Considerations
Exenatide (Byetta®)	5 mcg SQ twice daily 60 minutes before meals	↑ to 10 mcg twice daily after 1 month if tolerated Do not use if CrCl <30 mL/min
Exenatide ER (Bydureon®)	2 mg SQ once every seven days (weekly)	Take without regard to meals Do not use if CrCl <30 mL/min
Liraglutide (Victoza®)	0.6 mg SQ once daily independent of meals	↑ dose weekly by 0.6 mg based on glycemic control and tolerance (maximum: 1.8 mg once daily)
Lixisenatide (Adlyxin®)	10 mcg SQ once daily x 14 days; then 20 mcg once daily	Administer within one hour prior to the first meal Missed dose → administer as soon as possible
Albiglutide (Tanzeum®)	30 mg SQ once weekly	↑ to 50 mg once weekly as tolerated Missed dose → administer within 3 days
Dulaglutide (Trulicity®)	0.75 mg SQ once weekly	↑ to 1.5 mg once weekly as tolerated Missed dose → administer within 3 days

Diabetes Care. 2012;35:1364-79.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.
Diabetes Care. 2012;35:1364-79.

Incretin Analogs (GLP-1-RA)

Advantages	Disadvantages
• Preserved β-cell function and increase β-cell mass in animals • Minimal risk of hypoglycemia • Modest weight loss ~3–5 kg • ↓ CV risk (LEADER)	• Cost • Injectable • Nausea, vomiting and GI side effects • C-cell hyperplasia/medullary thyroid tumors in animals • Avoid in patients with a history of or those at risk for pancreatitis

Diabetes Care. 2017;39:S1-S135.
Diabetes Care. 2012;35:1364-79.
Endocr Pract. 2016;22:84-113.
Diabetes Care. 2012;35:1364-79.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

LEADER (Liraglutide) Cardiovascular Outcomes Trials (CVOTs)

Primary Outcome (MACE)
HR 0.87 (0.78–0.97)

CV Death
HR 0.78 (0.66–0.93)

N Engl J Med. 2016; 375(4):311-22

SUSTAIN-6 (Semaglutide) Cardiovascular Outcomes Trials (CVOTs)

Primary Outcome (MACE)
HR 0.74 (0.58–0.95)

Non-Fatal Stroke
HR 0.61 (0.38–0.99)

N Engl J Med. 2016;375:1834-1844.

ELIXA (Lixisenatide)
Cardiovascular Outcomes Trials (CVOTs)

Primary Outcome (MACE + unstable angina)
HR 1.02 (0.89–1.17)

Noninferior compared to placebo

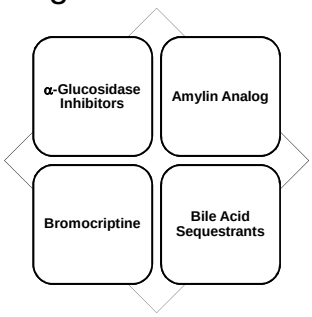
N Engl J Med. 2015;373:2247-2257

Clinical Question

A 48-year-old female (height 64 inches; weight 256 lbs.) with a 3-month history of type 2 diabetes mellitus presents to your clinic today for diabetes management. Her past medical history is significant for hypothyroidism, hypertension and dyslipidemia. Her most recent A1c is 7.8% (6/1/17) and her labs are within normal limits (WNL). Her current medication regimen includes aspirin 81 mg daily, amlodipine 10 mg daily, metformin 1000 mg twice daily, lisinopril 40 mg daily, levothyroxine 75 mcg daily and atorvastatin 40 mg daily. She states she has been unsuccessful implementing lifestyle modifications and is trying to lose weight; however, has a hard time controlling her food intake. Which of the following medications would be the most appropriate to initiate?

a. Liraglutide
b. Glipizide
c. Dapagliflozin
d. Sitagliptin

3rd Line Agents



α-Glucosidase Inhibitors

MOA

- Slows absorption of glucose from intestine into the bloodstream
- Slows breakdown of large carbohydrates into smaller absorbable sugars

2 Agents Available

- Acarbose (Precose®)
- Miglitol (Glyset®)

Efficacy

- 0.5–0.8% ↓ A1c
- Targets postprandial glucose
  - Monitor PPG

Diabetes Care. 2017;39:S1-S135.
Diabetes Care. 2012;35:1364-79.
Endocr Pract. 2016;22:84-113.
Diabetes Care. 2012;35:1364-79.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

α-Glucosidase Inhibitors

Advantages	Disadvantages
• Low risk of hypoglycemia • Weight neutral	• May not be as effective in patients using low carb diets • GI side effects • Flatulence, diarrhea, abdominal pain • Frequent dosing schedule

Diabetes Care. 2017;39:S1-S135.
Diabetes Care. 2012;35:1364-79.
Endocr Pract. 2016;22:84-113.
Diabetes Care. 2012;35:1364-79.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

Amylin Analog

Pramlintide (Symlin®)

- Used in type 1 and type 2 DM as adjunct therapy in patients using bolus insulin

MOA

- Synthetic analog of human amylin
  - Amylin is co-secreted with insulin and has similar effects as GLP-1
    - ↓ PPG levels
    - ↓ Glucagon secretion
    - ↓ Gastric emptying
    - ↑ Satiety

Efficacy

- 0.5–1% ↓ A1c
- Very effective at controlling PPG

Symlin® [package insert]. San Diego (CA): Amylin Pharmaceuticals, Inc.; 2008.

Amylin Analog

Advantages	Disadvantages
• ↓ PPG • ↓ Weight	• GI side effects • Nausea, vomiting, diarrhea • Hypoglycemia • Injectable • Frequent dosing schedule

Symlin® [package insert]. San Diego (CA): Amylin Pharmaceuticals, Inc.; 2008.

Dopamine Agonist

Bromocriptine (Cycloset®)

- Initial: 0.8 mg once daily
- Usual dose: 1.6–4.8 mg daily
- Administration within 2 hours of awakening

MOA

- Unknown
- Thought to reset hypothalamic circadian activities altered by obesity
  - ↓ Insulin resistance and glucose production

Efficacy

- 0.6–0.7% ↓ A1c

Diabetes Care. 2017;39:S1-S135.
Endocr Pract. 2016;22:84-113.
Diabetes Care. 2011;34(4):789-794.
Diabetes Care. 2012;35:1364-79.
Diabetes Care. 2012;35:1364-79.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

Dopamine Agonist

Advantages	Disadvantages
• No hypoglycemia • Weight neutral • No renal dosing adjustments • 52-week safety study showed bromocriptine ↓ CV composite end point by 40%	• Cost • Dizziness, syncope, nausea, fatigue

Diabetes Care. 2017;39:S1-S135.
Endocr Pract. 2016;22:84-113.
Diabetes Care. 2011;34(4):789-794.
Diabetes Care. 2012;35:1364-79.
Diabetes Care. 2012;35:1364-79.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

Bile Acid Sequestrants

Colesevelam (Welchol®)

- 3.75 g per day
  - Taken as 6 tablets once daily or 3 tablets twice daily with meals
  - Packets have unfavorable taste

MOA

- ↓ Hepatic insulin resistance
- ↓ Hepatic glucose production
- ↓ Intestinal glucose absorption

Efficacy

- 0.5% ↓ A1c

Diabetes Care. 2017;39:S1-S135.
Diabetes Care. 2012;35:1364-79.
Endocr Pract. 2016;22:84-113.
Diabetes Care. 2012;35:1364-79.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

Bile Acid Sequestrants

Advantages	Disadvantages

• ↓ LDL 20%
• Weight neutral
• Low risk of hypoglycemia
	• Expensive
	• GI side effects
	  • Nausea
	  • Bloating
	  • Constipation
	• ↑ Triglycerides
	• May ↓ absorption of other drugs
	• Taste of powder
	• Pill burden

Diabetes Care. 2017;39:S1-S135.
Diabetes Care. 2012;35:1364-79.
Endocr Pract. 2016;22:84-113.
Diabetes Care. 2012;35:1364-79.
Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York: McGraw-Hill; 2017.

Patient Considerations When Choosing the Most Appropriate Agent

Patient Considerations

- How much will the medication lower the patient's A1c?
- Will it affect FPG or PPG or both?
- What is the patient's preferred route of administration?
- Is the patient at risk for hypoglycemia?
- How much will the therapy cost my patient?
- What is the side effect profile and tolerability?
- What is the patient's PMH and comorbidity profile?

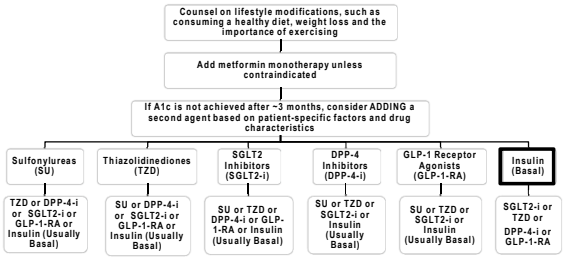
Clinical Question

A 77-year-old female patient presents today for a diabetes management visit. She was recently diagnosed with type 2 diabetes mellitus 2 months ago and her primary care physician recommended lifestyle modifications and started her on metformin 500 mg twice daily. Her past medical history is significant for stage 4 chronic kidney disease and stage 3 breast cancer. Today her laboratory values show an eGFR of 25 ml/min/1.73m^2 and a Scr of 2.3 mg/dL. Her most recent A1c 2 months ago was 8.2%. Which of the following is the most appropriate treatment option for this patient?

a. Continue current therapy
b. Continue metformin and add dapagliflozin 5 mg once daily
c. Discontinue metformin and add linagliptin 25 mg once daily
d. Discontinue metformin and add exenatide extended release 2 mg once weekly

Insulin Therapy

ADA Hyperglycemia Algorithm



Adapted From: Diabetes Care. 2017;39:S1-S135

Basal Insulins

Generic Name	Manufacturer	Administration Options	Maximum Dose Per Pen Injection	Room Temperature Expiration
Intermediate-acting Insulins				
Humulin N®	Lilly	10 mL vial, 3 mL prefilled pen	60 units	Vial: 28 days; Pen: 14 days
Novolin N®	Novo Nordisk	10 mL vial, 3 mL prefilled pen	60 units	30 days
Long-acting Insulins				
Glargine (Lantus®, Toujeo®)	Sanofi-Aventis	U-100: 10 mL vial, 3 mL prefilled pen U-300: 1.5 mL prefilled pen	80 units	28 days
Glargine (Basaglar®)	Lilly	3 mL prefilled pen	80 units	28 days
Degludec (Tresiba U-100®, Tresiba U-200®)	Novo Nordisk	U-100: 3 mL prefilled pen U-200: 3 mL prefilled pen	U-100 pen: 80 units U-200 pen: 160 units	56 days
Detemir (Levemir®)	Novo Nordisk	10 mL vial, 3 mL prefilled pen	60 units	42 days

Bolus Insulins

Generic Name	Manufacturer	Administration Options	Maximum Dose Per Pen Injection	Room Temperature Expiration
Rapid-acting Insulins				
Lispro (Humalog®, Humalog U-200®)	Lilly	Insulin pen 3 mL, 3 mL or 10 mL vial	60 units	28 days
Aspart (Novolog®)	Novo Nordisk	Insulin pen 3 mL, 10 mL vial	60 units	28 days
Glulisine (Apidra®)	Sanofi-Aventis	Insulin pen 3 mL, 10 mL vial	80 units	28 days
Short-acting Insulins				
Regular (Humulin R®)	Lilly	U-100: 3 mL or 10 mL vial U-500: 20 mL vial	-	28 days
Regular (Novolin R®)	Novo Nordisk	10 mL vial	-	30 days

Initiating Insulin Therapy

- **Start with basal insulin only**
  - Usually in addition to oral medications
    - Do not discontinue non-insulin medications when starting basal insulin
  - Begin at 10 units once daily or 0.1–0.2 units/kg once daily
  - Utilize scale on next slide for faster titration after initiation
  - Adjust by 10–20% as needed
- **Once FPG is controlled, if PPG is still elevated, consider adding rapid-acting insulin with meals**
  - Start with largest meal or all meals
    - Usually start with 4 units
  - Dose adjustment: increase/decrease by ~2 units

T2DM patients have higher insulin requirements than T1DM

Titrating Basal Insulin

Fasting Plasma Glucose (3-day average)	Amount of Basal Insulin to Add
100–120	2 units
121–140	4 units
141–180	6 units
181–200	8 units
>200	10 units

Initiating Insulin Therapy

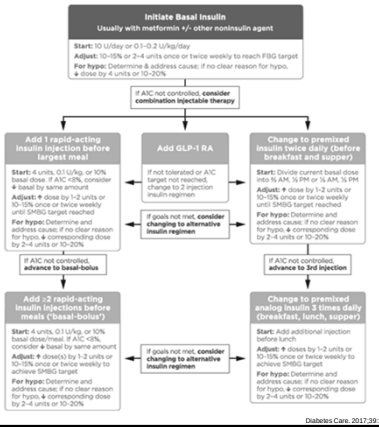
If patient is on a sulfonylurea, taper off after bolus (mealtime) insulin is added

Patient may continue metformin, GLP-1-RA, DPP-4-i and SGLT2-i therapy with basal/bolus regimen

May decrease insulin requirements

All other non-insulin agents should be discontinued

Initiating Insulin Therapy



Diabetes Care. 2017;39:S1-S135.

Basal Insulin and GLP-1-RA Combination Products

Xultophy® 100/3.6 (insulin degludec/liraglutide)
Soliquia™ 100/33 (insulin glargine/lixisenatide)

Xultophy® 100/3.6 and Soliquia™ 100/33

Basal insulin/GLP-1-RA fixed combination

- Work together to cover both FPG and PPG
- Once daily injection

GLP-1-RA	Long-acting basal insulin
• ↑ glucose-dependent insulin secretion • ↓ inappropriate glucagon secretion • ↓ gastric emptying • ↑ satiety	• Provides steady concentration of insulin throughout the day

Xultophy [package insert]. Bagsvaerd, Denmark: Novo Nordisk A/S; 2016.
Soliqua [package insert]. Bridgewater, NJ: Sanofi-Aventis US LLC; 2016.

Xultophy® 100/3.6 and Soliquia™ 100/33

Drug	Initial Dose	Maximum Dose
Xultophy® 100/3.6 mg (insulin degludec and liraglutide)	16 units (16 units of insulin degludec and 0.58 mg of liraglutide) once daily at same time each day with or without food	Maximum daily dosage is 50 units (50 units of insulin degludec and 1.8 mg of liraglutide)
Soliqua™ 100/33 (insulin glargine/ lixisenatide)	Patients inadequately controlled on <30 units of basal insulin • Initiate 15 units (15 units insulin glargine/5 mcg lixisenatide) subcutaneously once daily within one hour prior to the first meal	Maximum daily dosage is 60 units (60 units of insulin glargine and 20 mg of lixisenatide)
	Patients inadequately controlled on 30–60 units of basal insulin • Initiate 30 units (30 units insulin glargine/10 mcg lixisenatide) subcutaneously once daily within one hour prior to the first meal	

Xultophy [package insert]. Bagsvaerd, Denmark: Novo Nordisk A/S; 2016.
Soliqua [package insert]. Bridgewater, NJ: Sanofi-Aventis US LLC; 2016.

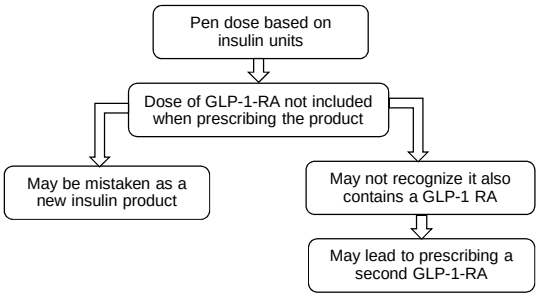
Xultophy® 100/3.6 and Soliquia™ 100/33 Clinical Considerations

May be mistaken as insulin products

- Ratio indicates product contains 2 separate ingredients
  - Sum of ratios ≠ 100
- When using generic names, both ingredients should be displayed and not truncated
  - Use brand names to reduce risk

Xultophy [package insert]. Bagsvaerd, Denmark: Novo Nordisk A/S; 2016. Soliqua [package insert]. Bridgewater, NJ: Sanofi-Aventis US LLC; 2016.

Xultophy® 100/3.6 and Soliquia™ 100/33 Clinical Considerations



Xultophy [package insert]. Bagsvaerd, Denmark: Novo Nordisk A/S; 2016. Soliqua [package insert]. Bridgewater, NJ: Sanofi-Aventis US LLC; 2016.

Xultophy® 100/3.6 and Soliquia™ 100/33 Clinical Considerations

Fixed ratio dosing complicates converting from the GLP-1-RA product to the combination product

→

May be used at doses which contain less than the currently approved doses of the single GLP-1-RA components

Xultophy [package insert]. Bagsvaerd, Denmark: Novo Nordisk A/S; 2016. Soliqua [package insert]. Bridgewater, NJ: Sanofi-Aventis US LLC; 2016.

Xultophy® 100/3.6 and Soliquia™ 100/33 Clinical Considerations

Example

- Patient previously taking 1.8 mg of liraglutide
- To receive the same amount of liraglutide in Xultophy® 100/3.6 mg they would need to administer a 50 unit dose.

The Issue

- Not feasible for an insulin-naïve patient to continue to receive 1.8 mg of liraglutide → would receive 50 units of insulin degludec in the combination product.
- Requires decreasing the dose of the GLP-1-RA when starting these agents
  - ↓ some of the beneficial weight loss and satiety effects

Clinical Question

A patient presents to your clinic for a diabetes management visit. He is currently taking insulin glargine 55 units subcutaneously once daily and metformin 1000 mg twice daily for management of his type 2 diabetes mellitus. His physician would like to start him on Soliqua™ 100/33 (insulin glargine/lixisenatide). Which of the following would be the most appropriate starting dose of Soliqua™ 100/33 (insulin glargine/lixisenatide)?

a. 10 units
b. 15 units
c. 16 units
d. 30 units

Getting To Goal: Taking A Patient-Centered Approach To Diabetes Management

Christie Schumacher, PharmD, BCPS, BCACP, BC-ADM, CDE
Associate Professor, Pharmacy Practice
Midwestern University Chicago College of Pharmacy
Clinical Pharmacist, Advocate Medical Group

Choosing Medications Wisely by Actively Deprescribing: The How's and the Why's

Manju T Beier, Pharm D, BCGP, FASCP
Senior Partner, Geriatric Consultant Resources LLC
Adjunct Clinical Associate Professor of Pharmacy,
The University of Michigan, Ann Arbor, MI

1

Learning Objectives

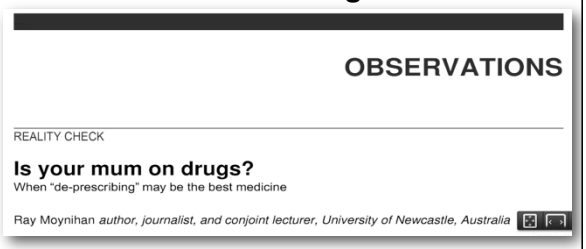
At the end of the session, the participants will be able to:

- Define Deprescribing and what it includes during medication regimen review.
- Briefly describe clinical evidence and outcomes of stopping some long standing medications.
- Develop strategies for evaluating and successfully stopping selected medications.
- Discuss *Choosing Wisely* initiative embraced by multiple professional societies and how it matches the De-prescribing approach in older adults.

Disclosures

- Dr. Beier has received speaker honoraria from Sunovion Pharmaceuticals on topics other than this presentation.

A New Paradigm?



BMJ 2011;343:d518

5

And the beat goes on……..

LESS IS MORE
Polypharmacy—Time to Get Beyond Numbers
Michael A. Steinman

"Numbers are not the enemy. Unnecessary, ineffective, and harmful prescribing is. Keeping our eye on the ball and addressing the systems of care that lead to these problems will help us meet this challenge".

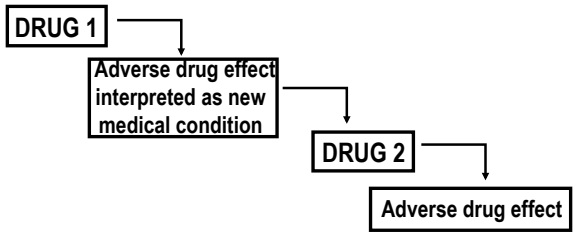
JAMA Intern Med. 2016;176(4):482-483.

6

Risk Factors in Older Adults

- Polypharmacy is pervasive!
  - Multiple Prescribers
  - Multiple Pharmacies
  - More therapeutic options
- Special populations
  - Critically ill, older, complex patients
  - Patients on psychiatric and/or pain medications
  - Advanced dementia in NHs
  - During transitions of care

The Prescribing Cascade



Rochon PA, Gurwitz JH. *BMJ* 315: 1096-99, 1997

Deprescribing

"Systematic process of identifying and **discontinuing drugs** in instances in which existing or potential harms outweigh existing or potential benefits."

- patient's care goals, functioning, life expectancy, values, and preferences

JAMA Intern Med. 2015;175(5):827-834

10

When To Consider?

- **Course Complete**
  - No indication
  - Resolution of problem
- **Not Safe**
  - Prescribing cascade
  - Beers criteria meds/high risk
- **Not effective**
  - Persistent symptoms
  - Unknown benefit
  - Polypharmacy for single condition?
- **Not aligned with goals**
  - Palliative care
  - End of Life care
  - Personal preferences

BMJ 2016;353:i2893 doi: 10.1136/bmj.i2893

When to Consider? (cont'd)

- New syndrome or prescribing cascade (toxicity)?
- Advanced disease, terminal illness, extreme frailty
- High-risk drugs or **combinations**
- Preventive drugs for scenarios associated with no increased risk despite stopping drug:
  - Stopping statins for primary prevention in older adults
- Patient/family willing to participate in shared decision
- Cost considerations

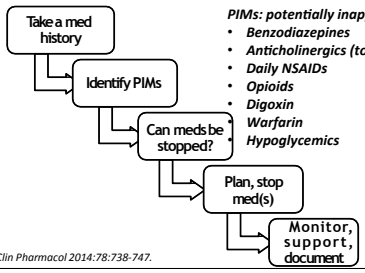
JAMA Intern Med. 2015;175(5):827-834
JAMA. 2016;316(19):1971-1972. doi:10.1001/jama.2016.15212

Deprescribing: The How?

- Bring all medications to visit (prescription and non-prescription)
- Ascertain current indications for each drug:
  - Look at patient and drug factors
  - Do benefit-risk analysis
  - High-risk medications (Beers Criteria)
- Consider patient expectations and preferences
- Prioritize drugs for discontinuation (D/C)
- Implement and monitor D/C

JAMA Intern Med. 2015;175(5):827-834

Strategies for Deprescribing



PIMs: potentially inappropriate medications
- ***Benzodiazepines***
- ***Anticholinergics (total burden)***
- ***Daily NSAIDs***
- ***Opioids***
- ***Digoxin***
- ***Warfarin***
- ***Hypoglycemics***

Reeve E, et al. Br J Clin Pharmacol 2014:78:738-747.

Barriers to Deprescribing

- Don't want to stop meds started by someone else
- Perception of inadequate care
- Provider-patient relationship
- Perception of "giving up"
- Concern about adverse "withdrawal" events

Gnjidic D, et al. Clin Geriatr Med 2012;28:237-253.

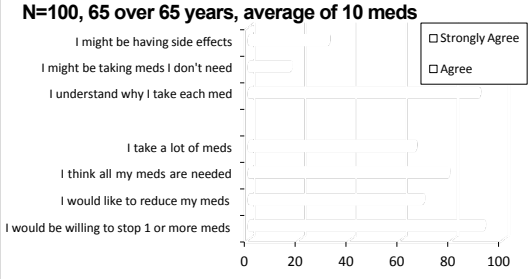
16

Question

Most older adults are convinced that their prescribed medications are necessary and are not willing to stop any medication.

A. True
B. False

What Do Patients Think?
N=100, 65 over 65 years, average of 10 meds



Reeve E, et al. JAGS 2013;61:1508-1514.

Deprescribing Benefits

- ***MOBILITY***- potential improvement
- ***COGNITION***- potential improvement, less delirium
- ***FALLS***- less falls
- ***QUALITY OF LIFE***- improvement
- ***HARMS?***- little or none if done with mindfulness, one at a time

Deprescribing Benefits on QOL

- Mean age 82.8 years
- 61% > 3 co-morbidities
- Mean 7.7 meds
- Mean 4.9 drugs withdrawn
- 2% restarted
- Successful withdrawal in 81%
- 14% died, at mean age 89 years
- No attributable deaths/ events
- **88% reported global improvement in health**
- Antihypertensives, nitrates, diuretics, statins, oral hypoglycemics, PPIs…

Garfinkel D, Mangin D. Arch Intern Med 2010 Oct 11;170(18):1648-54.

GLOBAL ASSESSMENT OF GENERAL HEALTH

88% improved

(67% significant improvement)

Garfinkel D, Mangin D. Arch Intern Med 2010 Oct 11;170(18):1648-54.

Which Medications Can Be Stopped?

Pharmacotherapy. 2016 Jul;36(7):774-80. doi: 10.1002/phar.1776.

Not needed
- Some dietary supplements
- Limited duration of treatment
  - Proton pump inhibitors
  - Sedatives/Opioids
  - Bisphosphonates
  - antipsychotics

Not effective
- , sulfonylureas

Not safe
- Beers STOPP meds

Not aligned
- Cholinesterase (end of life)
- Statins (primary prevention), antidiabetic agents

23

Proton Pump Inhibitors:
Health Canada / FDA drug safety communications

Overarching recommendation:
PPIs should be prescribed at the lowest dose and shortest duration of therapy appropriate to the condition being treated

Why Limit Use of PPI?

Fractures
- FDA: possible increased risk of hip, wrist and spine fractures

C. difficile diarrhea
- Reduced gastric acidity promotes bacterial colonization with pathogenic bacteria

Community Acquired Pneumonia: Conflicting data
- GI bacterial translocation

Hypomagnesemia
- FDA: use > 1 year is associated with hypomagnesemia
- 25% of cases not resolved through supplementation, PPI had to be DC'd

- Chronic Kidney Disease
- Dementia

Drugs Aging (2017) 34:265–287

Fractures: FDA Drug Safety Communication. May 25, 2010.
Magnesium :FDA Drug Safety Communication. March 2, 2011
CDAD: FDA Drug Safety Communication. February 8, 2012.

Appropriate Use of PPIs

PL Detail-Document, Proton Pump Inhibitors: Appropriate Use and Safety Concerns. Pharmacist's Letter/Prescriber's Letter. April 2016.

Indication	Recommended Duration
Intermittent, mild heartburn	● 2 weeks (once daily), ● no more than 3 treatments/year
GERD • **Non-erosive** • **Erosive** • **Severe**	 ● 4 - 8 weeks (once daily) ● 4 - 8 weeks or indefinitely (once daily) ● Indefinitely (once or twice daily)
Barrett's esophagus	● Indefinitely
Peptic ulcers	● 4 - 8 weeks (once or twice daily)
NSAID induced ulcers	● Long-term therapy with risk factors, as long as NSAID

Strategies for Deprescribing PPIs

- Stop or… **STOP**
- Consider tapering by reducing dose then frequency

- Return of significant symptoms **MONITOR**
- Return of milder or intermittent symptoms
- No symptoms

H2RA: Histamine 2 receptor antagonists

- Restart PPI or… **ALTERNATIVES**
  - PRN antacids, H2RA or even PPI
  - Intermittent course of H2RA or PPI
  - Nonpharmacologic measures

http://www.open-pharmacy-research.ca/wordpress/wp-content/uploads/ppi-deprescribing-algorithm-cc.pdf

27

Question

Deprescribing is <u>best defined</u> by which of the following?

A. Stopping one medication per week until they are all discontinued
B. Discontinuing medications for whom burden exceeds benefit
C. Discontinuing all medications on admission to hospice
D. Discontinuing medications the patient cannot afford

28

Other Medication Classes to Consider

- Cholinesterase Inhibitors
  - Advanced dementia
  - End of life care
- Statins for primary prevention
  - Recent evidence to consider deprescribe
  - Risk exceeds benefit for age >75 years
    - Myopathy, myalgias, muscle weakness, cognitive dysfunction

Gurwitz JH, Statins for Primary Prevention in Older Adults. *JAMA*. 2016;316(19):1971-1972. doi:10.1001/jama.2016.15212
Curfman G. Risks of Statin Therapy in Older Adults. *JAMA Intern Med*. Published online May 22, 2017. doi:10.1001/jamainternmed.2017.1457
Sachs GA. Improving Prescribing Practices Late in Life. A Task for all Clinicians, Not Just Nursing Home Physicians. *JAMA Intern Med*. 2014;174(11):1771-1772. doi:10.1001/jamainternmed.2014.3277

Problems with Clinical Practice Guidelines

- CPGs typically focus on a single disease but elderly usually have multiple co-existing medical conditions
- The evidence supporting guidelines may not have been obtained from older patient populations with their multiple co-morbidities
- Adverse events are evaluated with less rigor and precision than are benefits in most trials
- CPGs focus on biomedical outcomes than QOL

Arch Intern Med. 2011 Mar 28;171(6):550-6. doi: 10.1001/archinternmed.2011.31.

31

Question

The *Choosing Wisely* campaign aims to promote conversations between clinicians and patients by helping patients choose care that is:

A. Supported by evidence
B. Not duplicative of other tests or procedures already received
C. Truly necessary and free from harm
D. All of the above

What is the *Choosing Wisely* Campaign?

- Developed to raise professional and public awareness and to question and discuss tests and treatments
- These treatments and tests may lack efficacy or cause potential harm
- Started by ABIM Foundation and partnered with Consumer Reports.
- Goal is a national dialogue on avoiding wasteful or unnecessary medical tests, treatments and procedures.
- Over 70 medical specialty societies are participating in the campaign.
- http://www.choosingwisely.org/
- http://consumerhealthchoices.org/

Developing the Campaign

- **Medical literature:**
  - An ethicist in NEJM 2010, called on specialty societies to identify five tests and procedures as a way for physicians to constructively address the cost and waste issue during the health care reform debate
  - In 2010 "Less is More" section of the *Archives of Internal Medicine* addressed the issue to overtesting and overtreating
- **Lay Literature** highlighted the issue of treatment and testing.
  - Writers such as Shannon Brownlee, in her book *Overtreated*
  - Rosemary Gibson and Janardan Prasad Singh in *The Treatment Trap*
  - John Abramson, MD in Overdosed America

Launching the *Choosing Wisely* campaign

- In April 2012 the ABIM Foundation, along with Consumer Reports, formally launched the *Choosing Wisely* campaign with the release of "Top Five" lists from nine specialty societies.
- More than 70 societies comprising over one million clinicians are now partners of the *Choosing Wisely* campaign.

37

AMDA developed a list of five practices or tests that are common in the post-acute/long-term care setting, but lack the scientific evidence to support their use.
September, 2013

38

AMDA Recommendations: 2013

- Don't insert percutaneous feeding tubes in individuals with advanced dementia. Instead, offer oral assisted feedings.
- Don't use Sliding Scale Insulin for long-term diabetes management for individuals residing in the nursing home.
- Don't obtain a urine culture unless there are clear signs and symptoms that localize to the urinary tract.
- Don't prescribe antipsychotic medications for behavioral psychological symptoms of dementia (BPSD) in individuals with dementia without an assessment for an underlying cause of the behavior.
- Don't routinely prescribe lipid-lowering medications in individuals with a limited life expectancy.

39

AMDA has developed a list of five additional practices or tests that are common in the post-acute/long-term care setting, but lack the scientific evidence to support their use.
March, 2015

AMDA Recommendations: New in 2015

- Don't place an indwelling urinary catheter to manage urinary incontinence.
- Don't recommend screening for breast, colorectal or prostate cancer if life expectancy is estimated to be less than 10 years.
- Don't obtain a *C. difficile* toxin test to confirm "cure" if symptoms have resolved.
- Don't recommend aggressive or hospital-level care for a frail elder without a clear understanding of the individual's goals of care and the possible benefits and burdens.
- Don't initiate antihypertensive treatment in individuals ≥60 years of age for systolic blood pressure (SBP) <150 mm Hg or diastolic blood pressure (DBP) <90 mm Hg.

41

American Geriatrics Society Select Recommendations:

- **Don't prescribe a medication without conducting a drug regimen review.**
- Don't prescribe cholinesterase inhibitors for dementia without periodic assessment for perceived cognitive benefits and adverse gastrointestinal effects.
- Avoid using prescription appetite stimulants or high-calorie supplements for treatment of anorexia or cachexia in older adults; instead, optimize social supports, provide feeding assistance and clarify patient goals and expectations.

42

American Geriatrics Society Select Recommendations:

- Avoid physical restraints to manage behavioral symptoms of hospitalized older adults with delirium.
- Avoid using medications other than metformin to achieve hemoglobin A1c<7.5% in most older adults; moderate control is generally better.
- Don't use benzodiazepines or other sedative-hypnotics in older adults as first choice for insomnia, agitation or delirium.

43

ASHP: First Pharmacy Society: May 2016 Possible Topics

- Anticoagulants
- Medication reconciliation
- Antimicrobials
- Prescribing Cascade
- Herbal Medications

Choosing Wisely: Pharmacy's role in effective use of medications.
American Journal of Health-System Pharmacy Sep 2015, 72 (18) 1529-1530; **DOI:** 10.2146/ajhp150324

The Future of Deprescribing Research

1. Use patient-centered outcomes like physical or cognitive function, or QOL
2. Ensure there is scientific rationale to support medication discontinuation
3. Enroll under-represented patient populations (cognitively impaired, functionally impaired)
4. Build in safety measures to detect and protect from harm

JAMA Intern Med. 2015;175(10):1630-1632. doi:10.1001/jamainternmed.2015.4309.

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Editorial

Going Home on the Right Medications

Prescription Errors and Transitions of Care

Jeremy M. Kahn, MD, MS; Derek C. Angus, MD, MPH

46

The Dangers of 'Polypharmacy,' the Ever-Mounting Pile of Pills, NY Times April 2016

47

How Are We Doing?

- Which of the following statements **do not** pertain to AMDA's "Choosing Wisely" campaign?
  - Don't obtain a C. difficile toxin test to confirm "cure" if symptoms have resolved.
  - Don't initate anthypertensive treatment in individuals ≥60 years of age for systolic blood pressure (SBP) <150 mm Hg or diastolic blood pressure (DBP) <90 mm Hg.
  - Don't continue any NSAIDs therapy on admission to the nursing home
  - Don't routinely prescribe lipid-lowering medications individuals with a limited life expectancy

Summary

- Periodically, conduct medication review to identify medicines that are no longer needed
- Periodically, ensure drug regimen is compatible with patient/family preferences regarding care
- Stopping medications can be done!
- Monitor for adverse events after drug discontinuation
  - Withdrawal reaction
  - Intolerable symptoms of disease

Other Clinical Pearls

- Reconcile Medications
- Substitute or Eliminate High Cost Drugs
- Consolidate/Streamline
- Identify Additive Adverse Drug Effects
- Identify Possible Prescribing Cascade
- Recognize Potential Drug Interactions

50

Online Resources

- Deprescribing.org
  - Founded by a Canadian pharmacist and physician,
- Medstopper.com
  - This website allows you to enter a list of patient medications and it will then prioritize them in order of when to stop
- http://www.polypharmacy.scot.nhs.uk
  - This website from the National Health Service (NHS) Scotland includes a seven-step process for review of the patient with polypharmacy and other resources

The American Psychiatric Association Practice Guideline on the Use of Antipsychotics to Treat Agitation or Psychosis in Patients With Dementia

Victor I. Reus, M.D., Laura J. Fochtmann, M.D., M.B.I., A. Evan Eyler, M.D., M.P.H., Donald M. Hilty, M.D., Marcela Horvitz-Lennon, M.D., M.P.H., Michael D. Jibson, Ph.D., M.D., Oscar L. Lopez, M.D., Jane Mahoney, Ph.D., R.N., PMHCNS-BC, Jagoda Pasic, M.D., Ph.D., Zaldy S. Tan, M.D., M.P.H., Cheryl D. Wills, M.D., Richard Rhoads, M.D., Joel Yager, M.D.

At its December 2015 meeting, The APA Board of Trustees approved the APA Practice Guideline Writing Group's "Practice Guideline on the Use of Antipsychotics to Treat Agitation or Psychosis in Patients With Dementia." [The full guideline is available at http://psychiatryonline.org/doi/book/10.1176/appi.books.9780890426807]

INTRODUCTION

The goal of this guideline is to improve the care of patients with dementia who are exhibiting agitation or psychosis. More specifically, this guideline focuses on the judicious use of antipsychotic medications when agitation or psychosis occurs in association with dementia and does not review evidence for or focus on other pharmacological interventions. The guideline is intended to apply to individuals with dementia in all settings of care as well as to care delivered by generalist and specialist clinicians. Recommendations regarding treatment with antipsychotic medications are not intended to apply to individuals who are receiving antipsychotic medication for another indication (e.g., chronic psychotic illness) or individuals who are receiving an antipsychotic medication in an urgent context.

Expert consensus suggests that use of an antipsychotic medication in individuals with dementia can be appropriate, particularly in individuals with dangerous agitation or psychosis, and can minimize the risk of violence, reduce patient distress, improve patient's quality of life, and reduce caregiver burden. However, in clinical trials, the benefits of antipsychotic medications are at best small (Corbett et al., 2014; Kales et al., 2015) whether assessed through placebo-controlled trials, head-to-head comparison trials, or discontinuation trials. There is also consistent evidence that antipsychotics are associated with clinically significant adverse effects, including mortality. Consequently, decisions about the treatment of psychosis or agitation in an individual with dementia will be an outgrowth of the initial assessment and an understanding of the goals and preferences of the patient (if clinically feasible) and the patient's surrogate decision maker (if relevant) with input from family or others involved with the patient. Such decisions will also need to balance the potential benefits and harms of a particular intervention as compared to other therapeutic options for the individual patient. The full text of the practice guideline includes a detailed description of expert consensus findings and research evidence related to effects of antipsychotic medication in individuals with dementia. It also describes aspects of guideline implementation that are relevant to individual patients' circumstances and clinical presentation.

Overview of the Development Process

Since the 2011 publication of the Institute of Medicine report, *Clinical Practice Guidelines We Can Trust*, there has been an increasing focus on using clearly defined, transparent processes for rating the quality of evidence and the strength of the overall body of evidence in systematic reviews of the scientific literature. This guideline was developed using a process intended to be consistent with the recommendations of the Institute of Medicine (2011), the Principles for the Development of Specialty Society Clinical Guidelines of the Council of Medical Specialty Societies (2012) and the requirements of the Agency for Healthcare Research and Quality (AHRQ) for inclusion of a guideline in the National Guidelines Clearinghouse. Parameters used for the guidelines' systematic review are included with the full text of the guideline; the development process is fully described in the following document available on the American Psychiatric Association (APA) website: http://www.psychiatry.org/File%20Library/Psychiatrists/Practice/Clinical%20Practice%20Guidelines/Guideline-Development-Process.pdf. To supplement the expertise of members of the guideline work group, we used a "snowball" survey methodology (Yager 2014) to identify experts on the treatment of agitation or psychosis in individuals with dementia. Results of this expert survey are included in the Appendix of the full practice guideline.

Rating the Strength of Research Evidence and Recommendations

The guideline recommendations are rated using GRADE (Grading of Recommendations Assessment, Development and Evaluation), which is used by multiple professional organizations around the world to develop practice guideline recommendations

(Guyatt et al., 2013). With the GRADE approach, the strength of a guideline statement reflects the level of confidence that potential benefits of an intervention outweigh the potential harms (Andrews et al., 2013). This level of confidence is informed by available evidence, which includes evidence from clinical trials as well as expert opinion and patient values and preferences. Evidence for the benefit of a particular intervention within a specific clinical context is identified through systematic review and is then balanced against the evidence for harms. In this regard, harms are broadly defined and might include direct and indirect costs of the intervention (including opportunity costs) as well as potential for adverse effects from the intervention. Whenever possible, we have followed the admonition to current guideline development groups to avoid using words such as "might" or "consider" in drafting these recommendations as they can be difficult for clinicians to interpret (Shiffman et al., 2005).

As described under Guideline Development Process, each final rating is a consensus judgment of the authors of the guideline and is endorsed by the APA Board of Trustees. A "recommendation" (denoted by the numeral 1 after the guideline statement) indicates confidence that the benefits of the intervention clearly outweigh harms. A "suggestion" (denoted by the numeral 2 after the guideline statement) indicates uncertainty (i.e., the balance of benefits and harms is difficult to judge, or either the benefits or the harms are unclear). Each guideline statement also has an associated rating for the "strength of supporting research evidence." Three ratings are used–high, moderate, and low (denoted by the letters A, B, and C, respectively)–and reflect the level of confidence that the evidence for a guideline statement reflects a true effect based on consistency of findings across studies, directness of the effect on a specific health outcome, and precision of the estimate of effect and risk of bias in available studies (Agency for Healthcare Research and Quality 2014; Balshem et al., 2011; Guyatt et al., 2006).

It is well recognized that there are guideline topics and clinical circumstances for which high quality evidence from clinical trials is not possible or is unethical to obtain (Council of Medical Specialty Societies, 2012). For example, many questions need to be asked as part of an assessment and inquiring about a particular symptom or element of the history cannot be separated out for study as a discrete intervention. It would also be impossible to separate changes in outcome due to assessment from changes in outcomes due to ensuing treatment. Research on psychiatric assessments and some psychiatric interventions can also be complicated by multiple confounding factors such as the interaction between the clinician and the patient or the patient's unique circumstances and experiences. For these and other reasons, many topics covered in this guideline have relied on forms of evidence such as consensus opinions of experienced clinicians or indirect findings from observational studies rather than being based on research from randomized trials. The GRADE working group and guidelines developed by other professional organizations have noted that a strong recommendation may be appropriate even in the absence of research evidence when sensible alternatives do not exist (Andrews et al., 2013; Brito et al, 2013; Djulbegovic et al., 2009; Hazlehurst et al., 2013).

Proper Use of Guidelines

The APA Practice Guidelines are assessments of current scientific and clinical information provided as an educational service. The guidelines 1) should not be considered as a statement of the standard of care or inclusive of all proper treatments or methods of care; 2) are not continually updated and may not reflect the most recent evidence, as new evidence may emerge between the time information is developed and when the guidelines are published or read; 3) address only the question(s) or issue(s) specifically identified; 4) do not mandate any particular course of medical care; 5) are not intended to substitute for the independent professional judgment of the treating provider; and 6) do not account for individual variation among patients. As such, it is not possible to draw conclusions about the effects of omitting a particular recommendation, either in general or for a specific patient. Furthermore, adherence to these guidelines will not ensure a successful outcome for every individual, nor should these guidelines be interpreted as including all proper methods of evaluation and care or excluding other acceptable methods of evaluation and care aimed at the same results. The ultimate recommendation regarding a particular assessment, clinical procedure, or treatment plan must be made by the clinician in light of the psychiatric evaluation, other clinical data, and the diagnostic and treatment options available. Such recommendations should be made in collaboration with the patient, whenever possible, and incorporate the patient's personal and sociocultural preferences and values in order to enhance the therapeutic alliance, adherence to treatment, and treatment outcomes. For all of these reasons, APA cautions against the use of guidelines in litigation. Use of these guidelines is voluntary. APA provides the guidelines on an "as is" basis, and makes no warranty, expressed or implied, regarding them. APA assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of the guidelines or for any errors or omissions.

GUIDELINE STATEMENTS

Assessment of Behavioral/Psychological Symptoms of Dementia

Statement 1. APA recommends that patients with dementia[1] be assessed for the type, frequency, severity, pattern, and timing of symptoms. (1C)

Statement 2. APA recommends that patients with dementia be assessed for pain and other potentially modifiable contributors to symptoms as well as for factors, such as the subtype of dementia, that may influence choices of treatment. (1C)

[1]Throughout this guideline, we use the term *dementia*, which was used in the evidence that was considered in developing these recommendations. These recommendations are also meant to apply to individuals with major neurocognitive disorder, as defined in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, 5th ed.* (DSM–5).

Statement 3. APA recommends that in patients with dementia with agitation or psychosis, response to treatment be assessed with a quantitative measure. (1C)

Development of a Comprehensive Treatment Plan

Statement 4. APA recommends that patients with dementia have a documented comprehensive treatment plan that includes appropriate person-centered nonpharmacological and pharmacological interventions, as indicated. (1C)

Assessment of Benefits and Risks of Antipsychotic Treatment for the Patient

Statement 5. APA recommends that nonemergency antipsychotic medication should only be used for the treatment of agitation or psychosis in patients with dementia when symptoms are severe, are dangerous, and/or cause significant distress to the patient. (1B)

Statement 6. APA recommends reviewing the clinical response to nonpharmacological interventions prior to nonemergency use of an antipsychotic medication to treat agitation or psychosis in patients with dementia. (1C)

Statement 7. APA recommends that before nonemergency treatment with an antipsychotic is initiated in patients with dementia, the potential risks and benefits from antipsychotic medication be assessed by the clinician and discussed with the patient (if clinically feasible) as well as with the patient's surrogate decision maker (if relevant) with input from family or others involved with the patient. (1C)

Dosing, Duration and Monitoring of Antipsychotic Treatment

Statement 8. APA recommends that if a risk/benefit assessment favors the use of an antipsychotic for behavioral/psychological symptoms in patients with dementia, treatment should be initiated at a low dose to be titrated up to the minimum effective dose as tolerated. (1B)

Statement 9. APA recommends that if a patient with dementia experiences a clinically significant side effect of antipsychotic treatment, the potential risks and benefits of antipsychotic medication should be reviewed by the clinician to determine if tapering and discontinuing of the medication is indicated. (1C)

Statement 10. APA recommends that in patients with dementia with agitation or psychosis, if there is no clinically significant response after a 4-week trial of an adequate dose of an antipsychotic drug, the medication should be tapered and withdrawn. (1B)

Statement 11. APA recommends that in a patient who has shown a positive response to treatment, decision making about possible tapering of antipsychotic medication should be accompanied by a discussion with the patient (if clinically feasible) as well as with the patient's surrogate decision maker (if relevant) with input from family or others involved with the patient. The aim of such a discussion is to elicit their preferences and concerns and to review the initial goals, observed benefits and side effects of antipsychotic treatment, and potential risks of continued exposure to antipsychotics, as well as past experience with antipsychotic medication trials and tapering attempts. (1C)

Statement 12. APA recommends that in patients with dementia who show adequate response of behavioral/psychological symptoms to treatment with an antipsychotic drug, an attempt to taper and withdraw the drug should be made within 4 months of initiation, unless the patient experienced a recurrence of symptoms with prior attempts at tapering of antipsychotic medication. (1C)

Statement 13. APA recommends that in patients with dementia whose antipsychotic medication is being tapered, assessment of symptoms should occur at least monthly during the taper and for at least 4 months after medication discontinuation to identify signs of recurrence and trigger a reassessment of the benefits and risks of antipsychotic treatment. (1C)

Use of Specific Antipsychotic Medications, Depending on Clinical Context

Statement 14. APA recommends that in the absence of delirium, if nonemergency antipsychotic medication treatment is indicated, haloperidol should not be used as a first-line agent. (1B)

Statement 15. APA recommends that in patients with dementia with agitation or psychosis, a long-acting injectable antipsychotic medication should not be utilized unless it is otherwise indicated for a co-occurring chronic psychotic disorder. (1B)

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Interactive Antipsychotics

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July 15, 2017

Disclosure

- No relevant financial disclosures.
- All antipsychotics are considered "off-label" use in patients with dementia.

Objectives

- 1. List the assessments recommended by the APA prior to starting an antipsychotic for BPSD.
- 2. Describe the risks associated with the use of antipsychotics in patients with dementia.
- 3. Identify 3 reasons to consider a GDR of an antipsychotic in a pt w/ dementia.
- 4. Name 3 reasons to postpone a GDR of an antipsychotic in a pt w/ dementia.

AMERICAN PSYCHIATRIC ASSOCIATION

- AMERICAN PSYCHIATRIC ASSOCIATION PRACTICE GUIDELINE on the use of Antipsychotics to Treat Agitation or Psychosis in Patients with Dementia
- May 2016

Background

- Overwhelming majority of older adults with dementia will develop psychosis or agitation during the course of their illness.
- Symptoms are often persistent, occur with increasing frequency as cognition worsens, and are more prevalent among NH residents or inpatient facilities compared to community settings

Caveats

- Applies to individuals with dementia in *all settings of care* as well as to care delivered by generalist and specialist clinicians
- Not intended to apply to individuals who are receiving antipsychotic medication for another indication (e.g., chronic psychotic illness) or individuals who are receiving an antipsychotic medication in an urgent context.

More Caveats

- For most behavioral interventions there have not been a sufficient number of large-scale, well-controlled studies from which to draw conclusions about efficacy or safety in treating agitation or psychosis
- None of the available studies have reported direct harm to patients from behavioral interventions
- Placebo-controlled trials of non-antipsychotic medications have not been reviewed in this practice guideline, and, thus, no recommendations are made about the appropriateness or sequence of their use based on their benefits and harms.
- No conclusions can be drawn from head-to-head comparisons *between non-antipsychotic drugs* (e.g., antidepressants, cholinesterase inhibitors, memantine*) and antipsychotic drugs* because of insufficient evidence

Positive™ Approach to Care

Caveats, cont.

- Patients with dementia who are enrolled in clinical trials are not likely to be representative of the full range of individuals for whom clinical use of an antipsychotic medication might be considered.
- Significant physical illness (e.g., cardiopulmonary or renal impairments, cancer), use of certain medications (e.g., anticoagulants), or severe aggression requiring emergent intervention are typical exclusions.
- Other psychiatric disorders, including substance use disorders, are also common exclusion criteria.

Recommendation Evidence

- A "recommendation" (denoted by the numeral 1 after the guideline statement) indicates confidence that the benefits of the intervention clearly outweigh the harms.
- "Strength of supporting research evidence." Three ratings are used:
  - A - high
  - B - moderate
  - C - and low
- (Agency for Healthcare Research and Quality 2014; Balshem et al. 2011; Guyatt et al. 2006)

Assessment of Behavioral/Psychological Symptoms of Dementia

- **Statement 1.** Patients should be assessed for the type, frequency, severity, pattern, and timing of symptoms. **(1C)**
- **Statement 2.** Patients should be assessed for pain and other potentially modifiable contributors to symptoms as well as for factors, such as the subtype of dementia, that may influence choices of treatment. **(1C)**
- **Statement 3.** In patients with dementia with agitation or psychosis, response to treatment be assessed with a quantitative measure. **(1C)**
  - Neuropsychiatric Inventory Questionnaire (NPI-Q)
  - Cohen-Mansfield Agitation Inventory (CMAI)

Development of a Comprehensive Treatment Plan

- **Statement 4.** Patients should have a documented comprehensive treatment plan that includes appropriate person-centered nonpharmacological and pharmacological interventions, as indicated. **(1C)**
  - Must be reassessed over time, with modifications made to address changes in the patient's cognitive status, symptom evolution, and treatment response

Assessment of Benefits and Risks of Antipsychotic Treatment for the Patient

- **Statement 5.** Non-emergency antipsychotic medication should only be used in patients with dementia when agitation and psychosis symptoms are severe, are dangerous and/or cause significant distress to the patient. **(1B)**
- **Statement 6.** Response to non-drug interventions should be reviewed prior to use of antipsychotic medication.**(1C)**
- **Statement 7.** Before non-emergency treatment with an antipsychotic, the potential risks and benefits should be assessed by the physician and discussed with the patient and the patient's surrogate decision maker, with input from the family. **(1C)**

Dosing, Duration, and Monitoring of Antipsychotic Treatment

- **Statement 8.** Treatment should be initiated at a low dose and titrated to the minimum effective dose.**(1B)**
- **Statement 9.** If the patient experiences significant side effects, the risks and benefits should be reviewed to determine if the antipsychotic should be discontinued.**(1C)**
- **Statement 10.** If there is no significant response after a 4-week time period, the medication should be tapered and withdrawn. **(1B)**

Dosing, Duration, Monitoring, cont.

- **Statement 11.** In a patient who has shown a positive response to treatment, decision making about possible tapering of antipsychotic medication should be accompanied by a discussion with the patient (if clinically feasible), surrogate decision maker/family (if relevant) and caregivers. **(1C)**
- **Statement 12.** In patients who show adequate response to the medication, an attempt to taper and withdraw the antipsychotic should be made within four months of starting. **(1C)**
- **Statement 13.** In patients whose antipsychotic medications are being tapered, symptoms should be assessed at least every month during tapering and for at least four months after the medication is discontinued.**(1C)**

Use of Specific Antipsychotic Medications, Depending on Clinical Context

- **Statement 14**. If non-emergency antipsychotic medication treatment is to be used, haloperidol should not be used first.(1B)
- **Statement 15**. A long-acting injectable antipsychotic should NOT be used unless it is administered for a co-occurring chronic psychotic disorder.(1B)

Long-acting injectables

- No studies have examined the use of long-acting injectable antipsychotic medications in individuals with dementia.
- Longer duration of action of these medications suggests that they would be associated with an increased risk of harm relative to oral formulations or short-acting parenteral formulations of antipsychotic medications, particularly in frail elders.

Risks

- In addition to mortality, other serious adverse events of antipsychotic medications in individuals with dementia have been reported, including stroke, acute cardiovascular events, metabolic effects, and pulmonary effects

Cost

- No known studies on the cost-effectiveness of antipsychotic treatment for individuals with dementia in inpatient or nursing facilities or for severely agitated or aggressive individuals who require constant supervision.

Limitations

- Small number of head-to-head trials *comparing different pharmacological and nonpharmacological treatments* for agitation or psychosis in dementia and an even fewer number of trials with parallel placebo or sham treatment arms.
- Trials often fail to examine *quality of life* or other outcomes that patients and families view as most important.
- Studies also have not assessed the *optimal time at which an attempted tapering* of antipsychotic medication is indicated.
- There is insufficient evidence to determine whether individuals with *more severe* dementia, psychosis, or agitation will have a greater *risk of relapse* with antipsychotic discontinuation.
- Studies have not examined optimal timing of assessment *during* antipsychotic treatment *or after* an attempt at tapering antipsychotic treatment

Limitations, cont.

- The optimal frequency of laboratory and physical assessments to detect metabolic or other side effects of treatment is unknown.
- Unclear whether laboratory data or other findings could predict which patients are at the highest risk of stroke or mortality or whether other interventions could reduce such risks.

Quality Measures

Choosing Wisely

- Choosing Wisely recommendations from APA
  - "Don't prescribe antipsychotic medications to patients for any indication without appropriate initial evaluation and appropriate ongoing monitoring"
  - "Don't routinely use antipsychotics as first choice to treat behavioral and psychological symptoms of dementia."

SIMULATED IDT MTG

Instructions

- 5 members per group
- Each member plays one role:
  - Social work
  - Nursing
  - CNA/Activity Staff
  - Psychiatrist/Psychologist
  - Provider/Medical Director

Instructions – Step 1

- 1. SW – give name of resident, diagnosis, behavior, name of medication w/ dose, strength, frequency, date med started, last GDR, and outcome
- 2. Nursing – summarize behavior tracking sheet
- 3. CNA/Activity staff – summarize ADLs, activity participation
- 4. Psychiatrist/psychologist – any med side effects or concerns, AIMS, EKG
- 5. Provider/Medical Director – make list of potential candidates for GDR

20 minutes

Instructions – Step 2

- Using building layout, suggest no more than 2 residents per unit to trial a GDR
- having side effects to medications/large functional decline/no appropriate dx
- OR
- starting with highest likelihood of success (no behaviors, h/o successful GDR)

10 minutes

Discussion: Patients to Consider a GDR

- Group A
- Group B
- Group C

15 min

Helpful information

- When & why was medication started?
  - Hospitalization for delirium vs UTI vs refusing insulin
- What is triggering the behaviors?
  - Certain staff, time of day, activity
- Are behavior interventions working?
- If delusion/visual hallucination, is the patient bothered by them?
- Do the care plans match the behaviors the medication is intended to treat?
- Do the behaviors match the diagnosis?

Reasons to GDR

- Medication not working for behavior
- Inadequate indication (wandering, etc.)
- Prolonged QTC
- Family unwilling to accept risk (black box warning)
- Side effects (tardive dyskinesia, dysphagia)

Reasons to postpone GDR

- Recent inpatient psych stay
- Recent failed GDR
- Recent GDR of another psychotropic medication (benzo, VPA, SSRI, etc.)
- Family request (must document very well)

Unit	Name	Behavior Tracking	Reasons to GDR	Reasons NOT
A	Michael	nights	no recent GDR	
A	Martha	random (few)		recent failed GDR
A *	Muhammad	random	not working, no GDR attempted, TD	
A *	Janet	days	Prolonged QTC, lack of indication, TD	
B *	Linda	wkend days	Lack of indication	
B *	Pat	eves consistently	prolonged QTC	
B	Estelle	none	no behaviors	Recent inpatient psych
B	Salvador	random days	no recent GDR	
C *	Lizzie	wkend nights	dysphagia, no recent GDR	
C *	Margaret	1 episode	prolonged QTC, rare behaviors	
C	Deborah	random eves (few)	no GDR attempted	same room as Margaret
C	Billy	1 episode	no GDR attempted, rare behaviors	