

Common Side Effects and Drug-Drug Interactions of Antiretroviral Therapy

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AETC Program National Centers and HIV Curriculum

- **National Coordinating Resource Center** – serves as the central web –based repository for AETC Program training and capacity building resources; its website includes a free virtual library with training and technical assistance materials, a program directory, and a calendar of trainings and other events. Learn more: <https://aidsetc.org/>
- **National Clinical Consultation Center** – provides free, peer-to-peer, expert advice for health professionals on HIV prevention, care, and treatment and related topics. Learn more: <https://nccc/ucsf.edu>
- **National HIV Curriculum** – provides ongoing, up –to-date HIV training and information for health professionals through a free, web –based curriculum; also provides free CME credits, CNE contact hours, CE contact hours, and maintenance of certification credits. Learn more: www.hiv.uw.edu

Learning Objectives

By the end of this presentation, learners will be able to:

1. Describe common and notable adverse effects associated with antiretroviral therapy
2. Recommend strategies for managing adverse effects
3. Identify common drug-drug interactions between ART and over-the-counter medications as well as prescription medications
4. Utilize an online tool to assess drug-drug interactions with ART

Notes

- Discussing antiretroviral therapy (ART) related adverse effects, HIV disease itself can also cause long term effects and complications
- Focusing on modern antiretrovirals (ARVs) most used today
- Generalities of common adverse effects and notable interactions
- Every patient is different. What works for most, may not work for all.

ADVERSE EFFECTS

Definitions

- Adverse effect and side effect predominantly used interchangeably
- Adverse Effects – unintended pharmacologic effects
- Side Effect – secondary, unwanted effect
- Can occur when taking medication as prescribed

- Allergy – immune response
 - Patients often confuse side effects with allergy. Educate and document accordingly

Modern antiretrovirals are generally well tolerated

- Discontinuation rates of common ARVs (due to adverse effects)
 - Bictegravir/emtricitabine/tenofovir ~1.6% over 5 years, 3.4% (age 65+)
 - Darunavir/cobicistat/emtricitabine/tenofovir ~4%
 - Dolutegravir/lamivudine 2-8%

Assessing potential adverse effects

- Temporal relationship
 - Onset of potential adverse effect in relationship to initiation of ART
- Severity
- Relieving or aggravating factors
- Known adverse effect/side effect?
 - Check drug information database, prescribing information, literature
- Validate patient concerns
- Patient preference
 - interfering with daily life? Want to keep same regimen vs. switch?

Common ART related adverse effects

Gastrointestinal

Central
Nervous
System

Cardiovascular/
Metabolic

Renal/Hepatic

Pregnancy

ART Adverse Effects - Gastrointestinal

- Gastrointestinal
 - Nausea, vomiting, diarrhea
 - General side effect of most ART, at least initially, usually self-limiting
 - Vomiting – can also be associated with pill aversion vs. actual side effect
 - Consider taking with food

protease
inhibitors

cobicistat

ritonavir

ART Adverse Effects – Central Nervous System

- Headache
 - Common, self-limiting initial adverse effect
- Dizziness
- Abnormal dreams
 - Efavirenz! (~6%)
- Insomnia
- INSTI class in particular

INSTI

NNRTI

ART Adverse Effects – Central Nervous System

- INSTIs and neuropsychiatric adverse effects
 - Study of ~21,000
 - Overall discontinuations (12.5-50%)
 - Dolutegravir < elvitegravir < raltegravir
 - Discontinuations due to CNS adverse effects:
 - Dolutegravir 2.7%
 - elvitegravir 1.3%
 - Raltegravir 1.7%
 - (prior to widespread bictegravir use)



ART Adverse Effects - Cardiovascular

- Lipodystrophy / Weight Gain
- Multifactorial – diet, lifestyle, genetics, drug
- Real World data, not captured in initial studies
- Mechanism unknown
 - “return to health” phenomenon – doesn’t explain it all

INSTI > NNRTI, PI

bictegravir,
dolutegravir >
elvitegravir, raltegravir

NNRTI: rilpivirine >
efavirenz

Tenofovir alafenamide
(TAF)

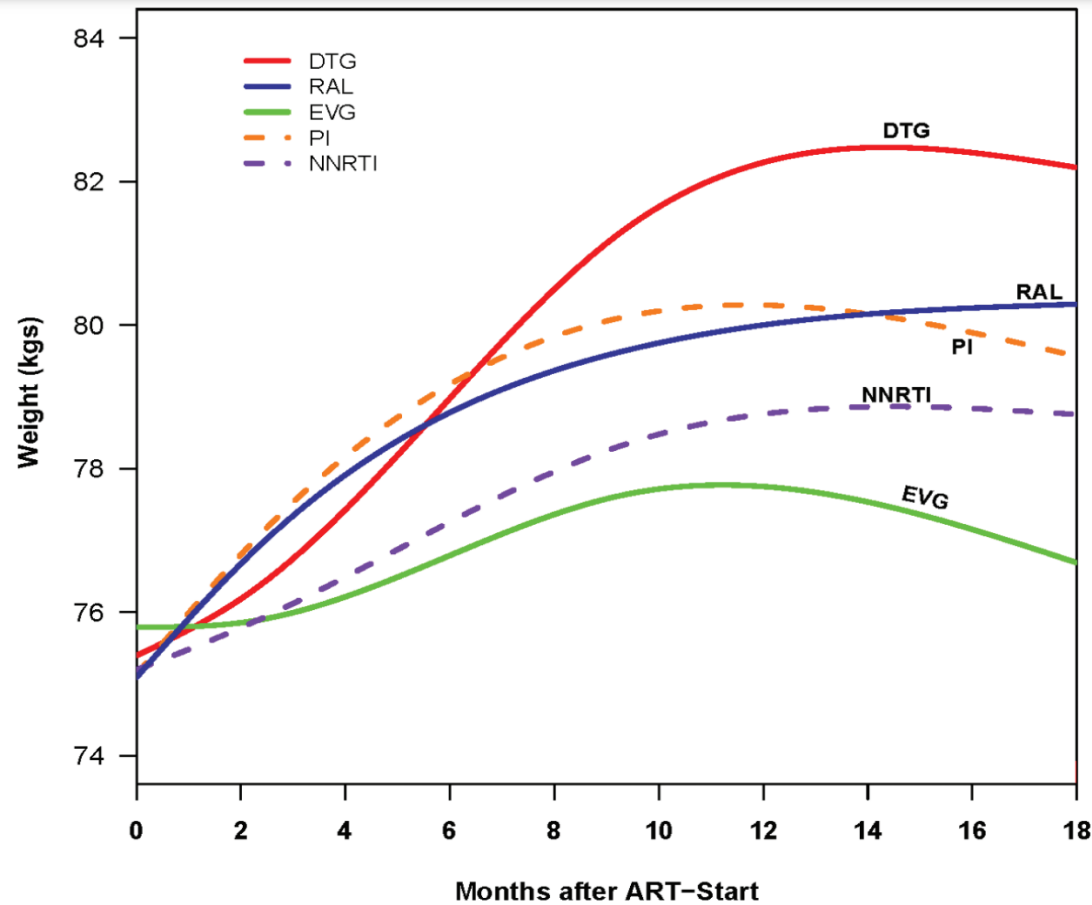
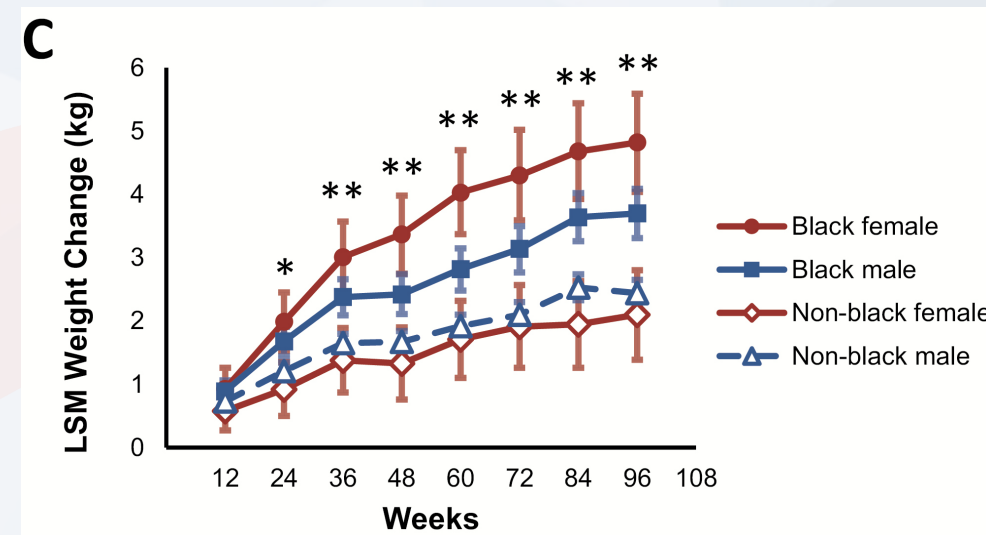
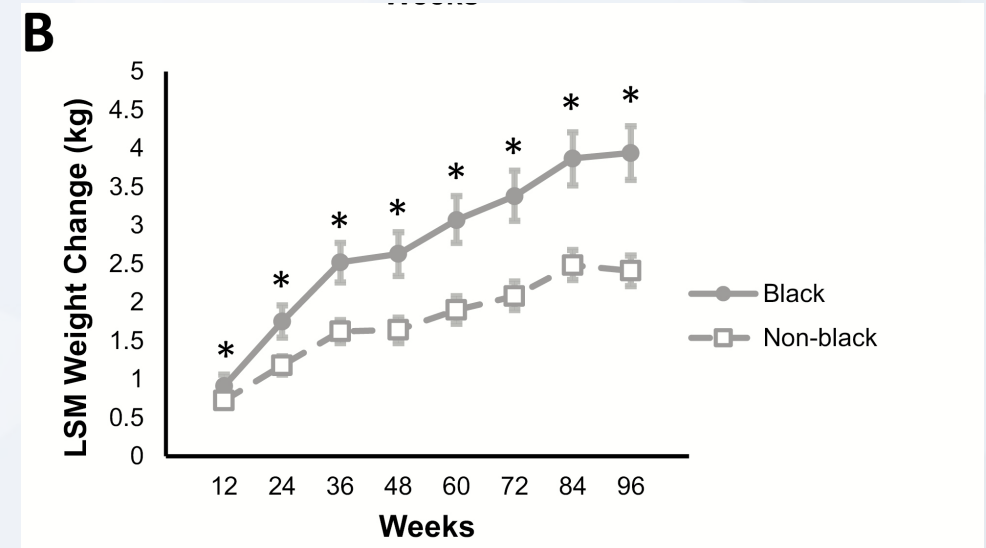
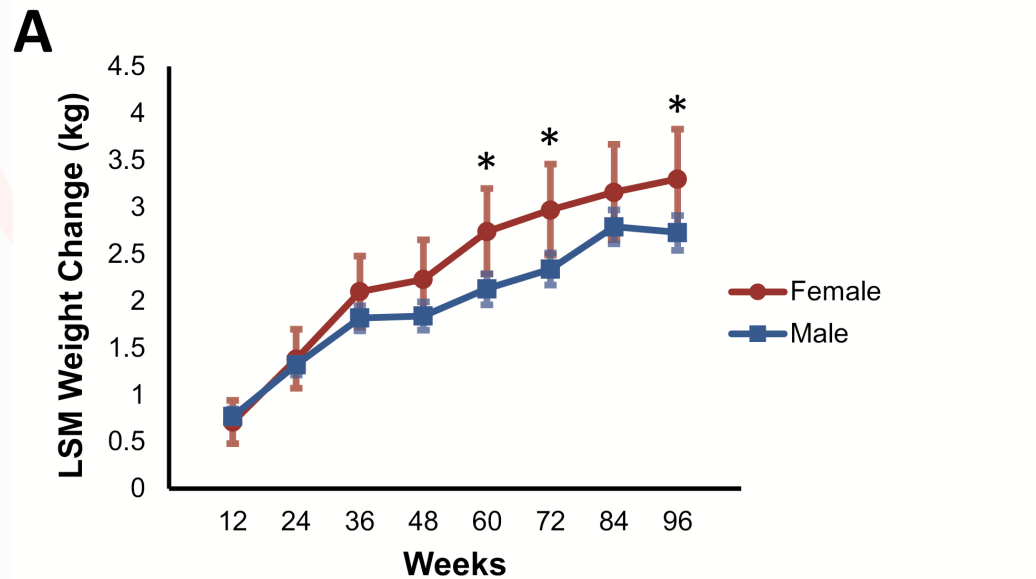


Figure 1. Changes in weight within 18 months of treatment initiation among persons living with human immunodeficiency virus, by antiretroviral regimen. Abbreviations: ART, antiretroviral therapy; DTG, dolutegravir; EVG, elvitegravir; NNRTI, nonnucleoside reverse transcriptase inhibitor; PI, protease inhibitor; RAL, raltegravir.

ART Adverse Effects - Cardiovascular

- Risk Factors for Weight Gain
 - Female
 - Black race



ART Adverse Effects - Cardiovascular

- Sequelae
 - Increased weight
 - Change in BMI / obesity status
 - Diabetes?
 - Increased cardiovascular risk

Strategies to manage adverse effects

Time (adjustment period)

Food

Schedule change

Supportive Care

Switch

Counseling regarding side effects

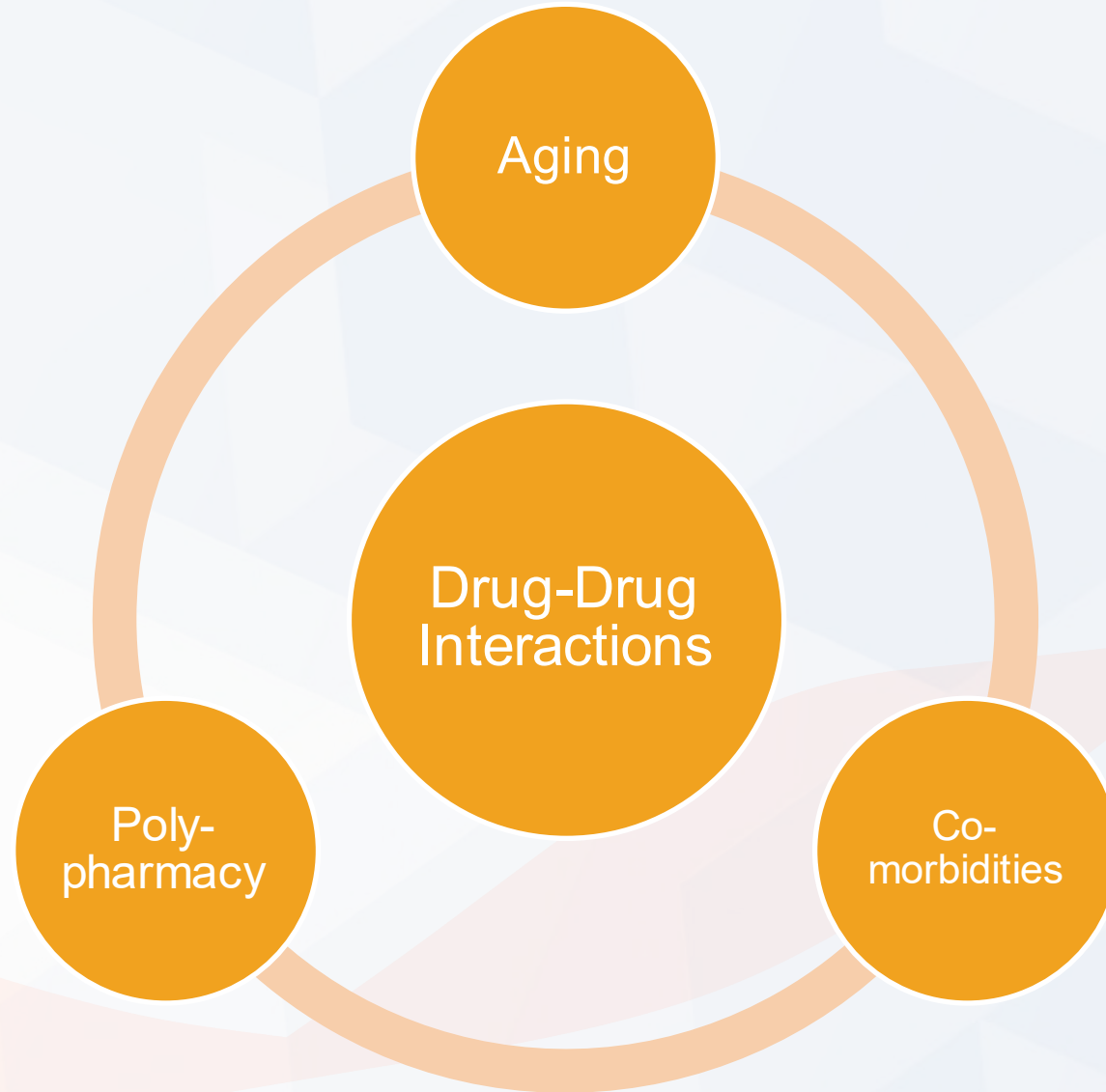
- Focus on common, expected side effects
- Length of time to expect side effects
- Management of side effects
- When to call provider
- Stopping medication (no stretching doses!)
- Validating patient concerns
- Educate regarding why you think their symptoms are/aren't related to ART

Counseling regarding side effects

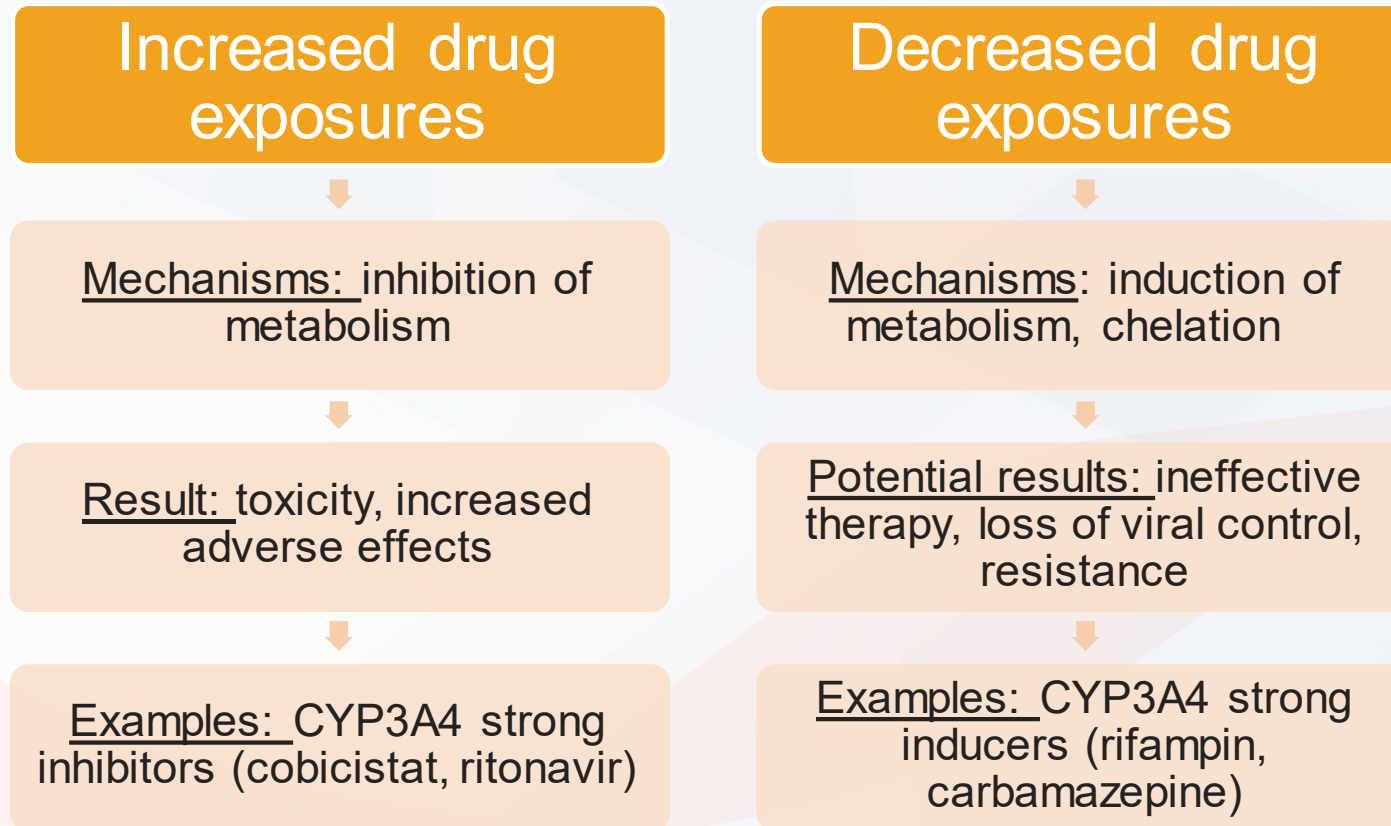
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QUESTION PAUSE

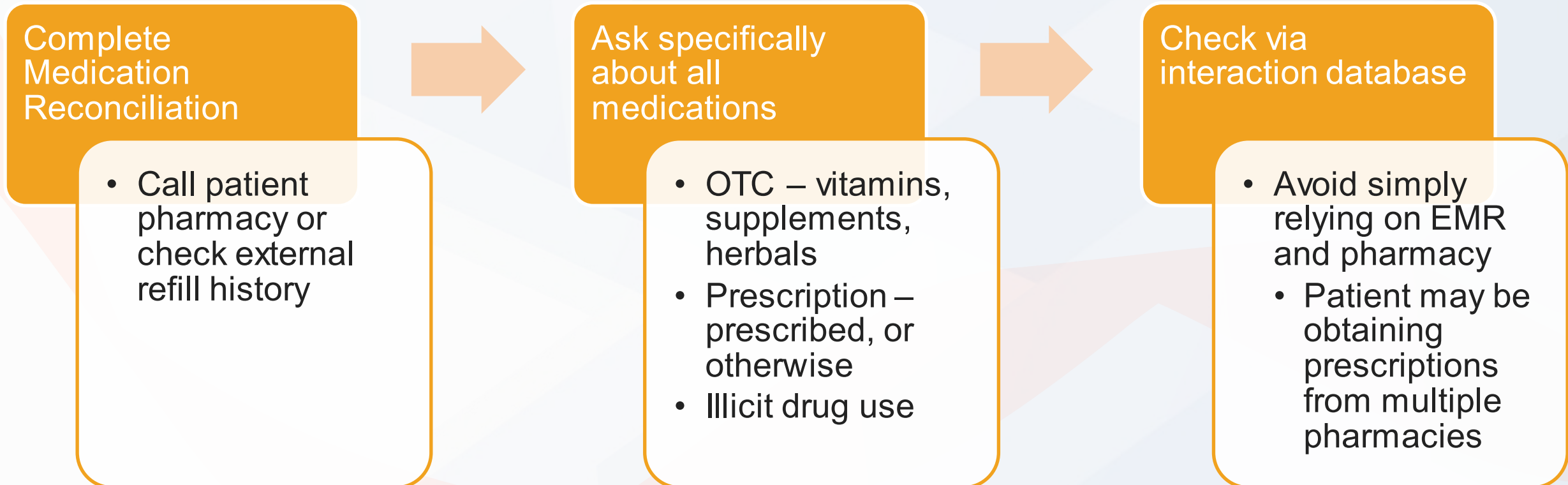
DRUG-DRUG INTERACTIONS



Significance of Drug-Drug Interactions with ART



Drug-Drug Interactions - Assessment



Good rule of thumb: assume there is at least one interaction with ART – check if can be managed, or requires therapy adjustment

Drug-Drug Interactions – Over the Counter





- Cations

- Aluminum
- Calcium (OTC antacids!)
- Iron
- Magnesium
- Zinc

- Management

- Administer separately 2-4 hours (depending on drug)
- Bictegravir/dolutegravir have data to support taking these supplements at the same time under fed conditions

- Monitor!

 Bictegravir	 Dolutegravir
 Elvitegravir	 Raltegravir
 Rilpivirine	 Atazanavir

Drug-Drug Interactions – Over the Counter

- Acid reducing agents
 - Proton-pump inhibitor (PPI)
 - Histamine 2 blocker (H2 blocker)
 - Cations (OTC antacids!)
- Management
 - PPIs are contraindicated with rilpivirine
 - Caution with: H2 blockers and rilpivirine, atazanavir
 - Administer separately
- Monitor!

Rilpivirine

Atazanavir

Drug-Drug Interactions – Over the Counter

- OTC nasal steroids
 - Fluticasone Case Study
 - Significantly increased fluticasone levels due to inhibition of metabolism (by strong CYP3A4 inhibitors)
 - Results in reduced serum cortisol concentrations
 - Cushing’s syndrome
 - Adrenal suppression
- Management
 - Consider infrequent use vs. chronic use
 - Counsel patients, offer alternatives
- Monitor!

✓ Drug-Drug Interactions

✗ Flonase Allergy Relief [OTC] (Fluticasone (Nasal)) – Ritonavir (CYP3A4 Inhibitors (Strong))

Cobicistat

Ritonavir

Drug-Drug Interactions – Prescription

- Statins
 - Atorvastatin Case Study
 - Significantly increased atorvastatin levels due to inhibition of metabolism (by strong CYP3A4 inhibitors)
 - Cobicistat + atazanavir
 - A single 10mg dose of atorvastatin
 - AUC increased 9.2 fold
 - Maximum concentration increased 18.9 fold
- Management
 - Avoid: lovastatin, simvastatin
 - Start lowest dose, then titrate: atorvastatin, rosuvastatin
 - Max doses with strong CYP3A4 inhibitors
 - Counsel patients
- Monitor!

Cobicistat

Ritonavir

And the list
goes on..

Anticoagulants/
Antiplatelets

Oral
contraceptives

Opioids

Antiepileptics

Steroids

Herbals – St.
John's Wort

Join us live or online for The Liverpool Course 2023 on Wednesday 13th September. For more details, [click here](#)

Looking for interactions with COVID-19 therapies, including Paxlovid? [Click here for covid19-druginteractions.org](https://www.covid19-druginteractions.org)

If a drug is not listed below it cannot automatically be assumed it is safe to coadminister

HIV Drugs	Co-medications	Drug Interactions
<input type="text" value="Search HIV drugs..."/>	<input type="text" value="Search co-medications..."/>	<input type="checkbox"/> Check HIV/ HIV drug interactions
<input checked="" type="radio"/> A-Z <input type="radio"/> Class <input type="radio"/> Trade	<input checked="" type="radio"/> A-Z <input type="radio"/> Class <input type="radio"/> Trade	Drug Interactions will be displayed here
Selected HIV Drugs will be displayed here.	Selected Co-medications will be displayed here.	
<input type="checkbox"/> Abacavir (ABC)	<input type="checkbox"/> Abacavir (ABC)	
<input type="checkbox"/> Albuvirtide (ABT)	<input type="checkbox"/> Abatacept	
<input type="checkbox"/> Atazanavir alone (ATV)	<input type="checkbox"/> Abemaciclib	
<input type="checkbox"/> Atazanavir/cobicistat (ATV/c)	<input type="checkbox"/> Abiraterone	
<input type="checkbox"/> Atazanavir + ritonavir (A	<input type="checkbox"/> Abrocitinib	

University of Liverpool HIV Drug Interaction Checker

<https://www.hiv-druginteractions.org/checker>

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QUESTION PAUSE

THANK YOU!