

AVOIDING ADVERSE EVENTS IN OLDER PERSONS

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Faculty/Presenter Disclosure

- **Faculty:** Luis Viana
- **Relationships with commercial interests:**
 - none

Disclosure of Commercial Support

- This program has received no financial or in kind support from any organization.
- Potential for conflict(s) of interest:
 - None

Mitigating Potential Bias

- **No input from outside commercial organizations occurred in the preparation of this presentation**
- **Any recommendations for therapy are based on evidence based medicine**

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

The Problem

- 1 in 6 hospital admissions of older adults is a result of an adverse drug event
 - rate is 4 times higher than that seen in younger persons
- if > 75 years old, 1 in 3 hospital admissions is a result of an adverse drug event

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Adverse Drug Events (ADE)

- adverse drug reaction – most common
 - accounts for $\frac{3}{4}$ of hospital admissions from ADE's
 - any response to a drug that is noxious or unintended
 - occurs at doses for prophylaxis, diagnosis, or therapy
- medication error
- therapeutic failure
- adverse drug withdrawal event
- overdose

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Adverse Drug Reaction (ADR)

- common examples seen in nursing homes
 - medication induced hypoglycemia
 - elevated INR when taking warfarin
 - medication related falls
 - antipsychotics
 - antidepressants
 - benzodiazepines

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

**Why are older persons more likely to
experience an ADR/ADE?**



AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Older Persons – a unique population

- Key differences compared to younger adults
 - underrepresented in clinical trials
 - comorbidity, multimorbidity
 - polypharmacy
 - pharmacokinetics
 - greater vulnerability to ADR's



Herrera AP, Snipes SA, King DW, et al. Am J Public Health 2010;100S105-12
Davies, EA, O'Mahoney MS. Br J Clin Pharmacol 2015;80;796-807.

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Underrepresented in clinical trials

- persons >65 yrs old make up $\frac{2}{3}$ of the cancer population, but represent about 25% of those persons enrolled in clinical trials
- “fit” older persons are more likely to participate in clinical trials compared to a frail older person

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Underrepresented in clinical trials

**“The drugs we are using in older people have
not been properly evaluated”**

(European Medicines Agency)

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

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Why more ADR/ADE in older persons?

Multimorbidity

- two or more concurrent chronic medical conditions
- prevalence in Canada
 - 74% of persons >65 y.o. have at least one of **11** chronic conditions
 - increased from **17.4% (2003)** to **24.3% (2009)**

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Multimorbidity

- multiple prescribers working in isolation on different comorbid conditions in the same older frail individual
- individual conditions can be managed effectively

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Multimorbidity

- health as the absence of disease is difficult to achieve in the person with multiple comorbidities
- need to consider the patient's other medical conditions, on lifestyle or quality of life

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Multimorbidity



Complex polypharmacy & care regimen



Potentially inappropriate prescribing



ADR & ADE

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Why more ADR/ADE in older persons?

Polypharmacy

- lack of consensus on a definition
- not just the use of increasing numbers of medications to manage multiple comorbidities – **polymedicine**
- 5 medications has often been used as the number to denote polypharmacy – what do you think?

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Polypharmacy

- denotes the inappropriate use of multiple medications
- use of medications which are not clinically indicated
- includes use of over the counter (OTC) medications
- increased risk of drug interactions and ADE's

Davies, EA, O'Mahoney MS. Br J Clin Pharmacol 2015;80;796-807.
Fulton MM, Allen ER. J Am Acad Nurs Pract 2007;17:123-32.

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Polypharmacy

- from a numbers standpoint

# of regularly scheduled medications	Odds ratio (95% confidence ratio) of experiencing an ADE
<5	1.0
5-6	2.0
7-8	2.8
≥9	3.3

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AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Pharmacokinetics and pharmacodynamics

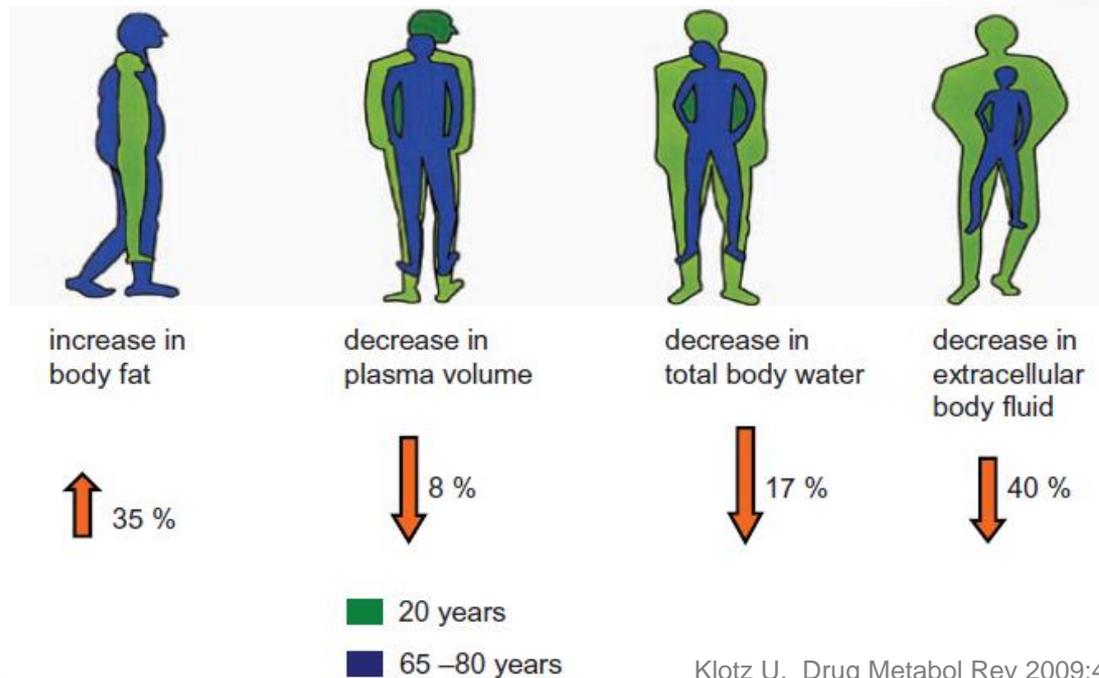
- altered drug distribution
 - less water, less muscle mass, relative increase in fat mass
 - affects where the drug goes in the body and drug concentration
- decreased ability to break down (metabolize) and clear drugs

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Pharmacokinetics and pharmacodynamics

- altered drug distribution



Klotz U. Drug Metabol Rev 2009;41:67-76.

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Pharmacokinetics and pharmacodynamics

- **altered drug distribution**
 - smaller volume of distribution in older persons
 - drug concentrations likely higher with the same dose of medication compared to a younger person

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Pharmacokinetics and pharmacodynamics

- **altered drug distribution**
 - will require smaller doses of water soluble drugs to achieve a desired therapeutic effect and avoid potential toxicity or adverse drug reactions

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Pharmacokinetics and pharmacodynamics

- **decreased drug clearance**
 - liver size and hepatic blood flow decrease resulting in decreased drug clearance
 - result more drug available (bioavailability) and decreased drug clearance leading to higher drug levels

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Pharmacokinetics and pharmacodynamics

- **decreased drug clearance** (renal)
 - kidney function decreases with age
 - instead of being eliminated from the body, medications can accumulate resulting in a higher than expected drug concentration
 - antibiotics, antivirals, anticoagulants, diuretics, digoxin

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Pharmacokinetics and pharmacodynamics

- **decreased drug clearance** (from the brain)
 - medications can enter the brain from the blood stream by passive diffusion (ie. from an area of high concentration to an area of low concentration)

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Pharmacokinetics and pharmacodynamics

- **decreased drug clearance** (from the brain)
 - one mechanism (P-gp efflux transporter activity) is responsible for the transport of some drugs from the brain back to the bloodstream
 - this mechanism restricts brain uptake of some substances by transporting them immediately out of the brain

Toornvliet R, van Berckel BNM, Luurtsema G, et al. Clin Pharmacol Ther 2006;79:540-8.
Klotz U. Drug Metab Rev 2009;41:67-76.

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Pharmacokinetics and pharmacodynamics

- **decreased drug clearance** (from the brain)
 - this clearance activity is decreased in older persons
 - as a result, for some medications, the brain may be exposed to higher drug and toxin levels in older compared to younger persons

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Pharmacokinetics and pharmacodynamics

- **decreased drug clearance** (from the brain)
 - amitriptyline, citalopram, doxepin, olanzapine, paroxetine, quetiapine, risperidone, sertraline, venlafaxine, fluoxetine, haloperidol, trazodone

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AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Why more ADR/ADE in older persons?

Greater vulnerability to ADR's and ADE's

- reduction of compensatory mechanisms
 - sympathetic response to postural hypotension
 - heat/thirst, fluid balance
 - hypoglycemia/hyperglycemia

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS



AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

**ALWAYS THINK OF
MEDICATIONS AS THE
MEDICAL DIAGNOSIS OF A
NEW SYMPTOM**

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Identify a clinical symptom as an ADE

- falls – orthostatic hypotension, hypoglycemia
 - antipsychotics, antidepressants, benzodiazepines, sedatives hypnotics
 - blood sugar lowering medications
- heart failure
 - calcium channel blockers, NSAID's

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Identify a clinical symptom as an ADE

- delirium
 - opioids
 - medications with anticholinergic effects
- bleeding
 - ASA, clopidogrel, anticoagulants
 - SSRI's

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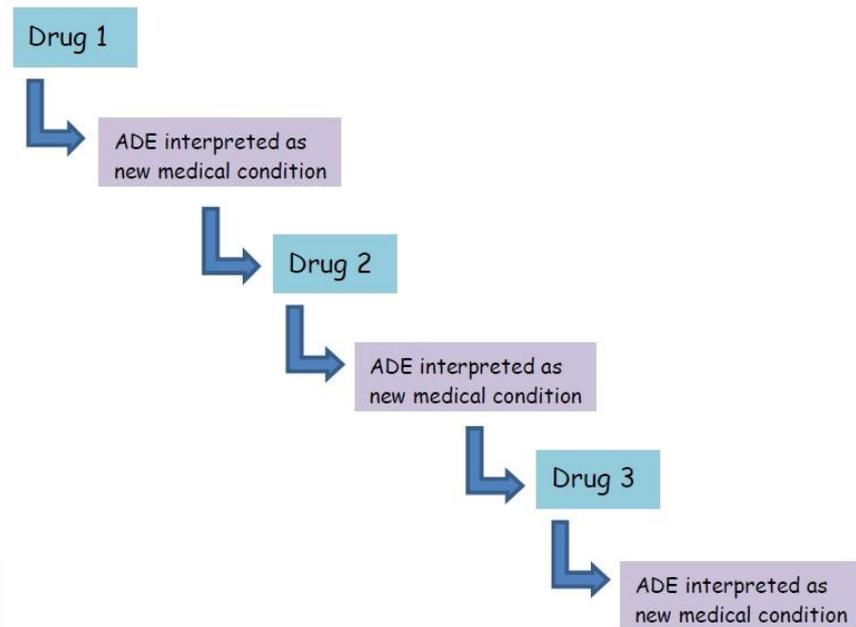
Identify a clinical symptom as an ADE

- especially if there might be a temporal relationship with starting and stopping a medication

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Identify a clinical symptom as an ADE

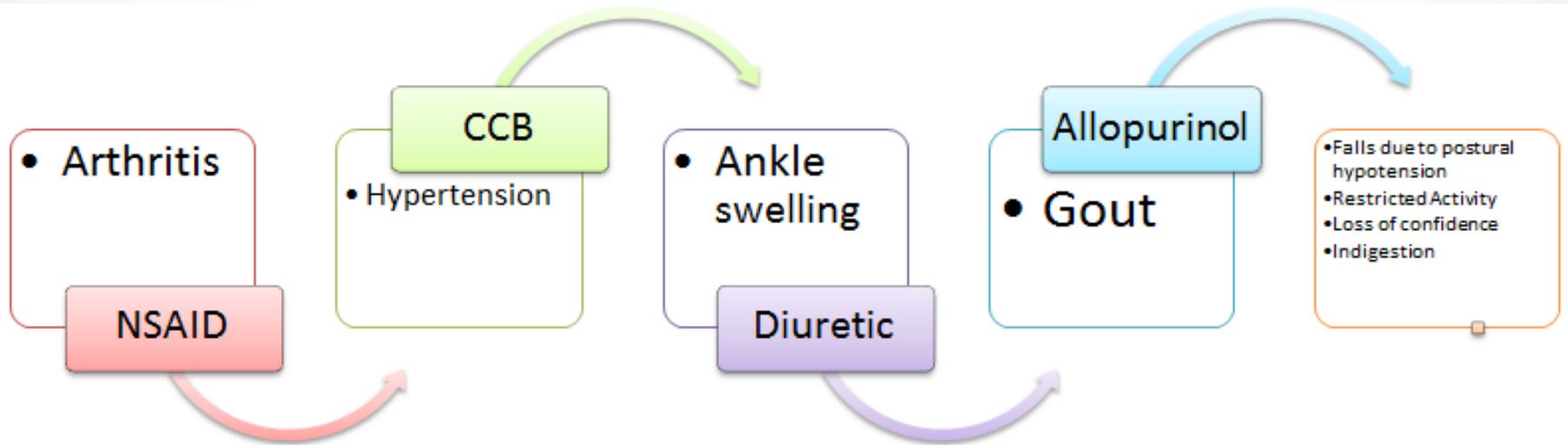
- avoid the prescribing cascade



AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Identify a clinical symptom as an ADE

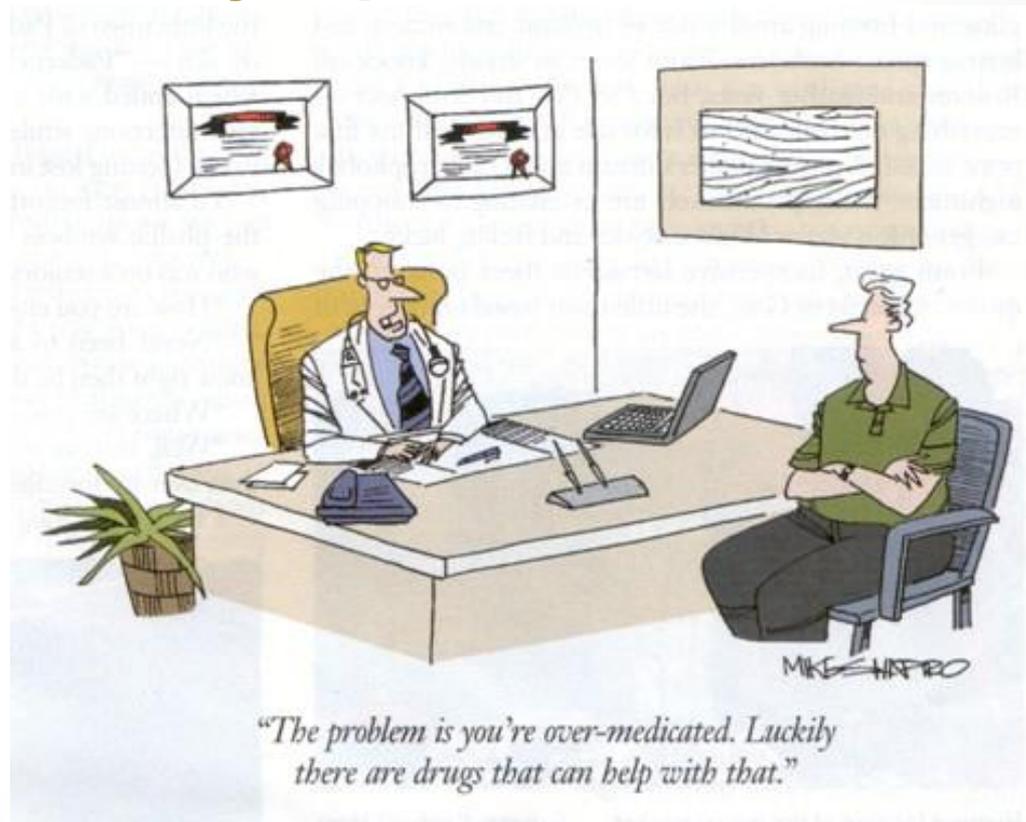
- avoid the prescribing cascade



AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Identify a clinical symptom as an ADE

- avoid the prescribing cascade



AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

GO LOW & GO SLOW

Use lower doses or don't give the drug as often

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Go low & go slow (but go)

- because of altered drug distribution, metabolism and clearance, older persons require lower medication doses as compared to younger persons to achieve a given therapeutic effect while avoiding an adverse drug event

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Go low & go slow (but go)

- but don't be afraid to use a medication – especially when it may improve the quality of life for the older person
 - use medications as per the patient's priorities

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Follow up when initiating or modifying a medication

- schedule a 2-4 week follow up
- encourage patient to self monitor if possible
- pharmacists should be encouraged to help
- educate patient on possible ADR's and time frame

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Follow up when initiating or modifying a medication

- have a specific target to assess the success of a new medication

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

**Primary Care Physician should review all
medication recommendations**

- each additional prescriber increases the risk of an ADE by 30%

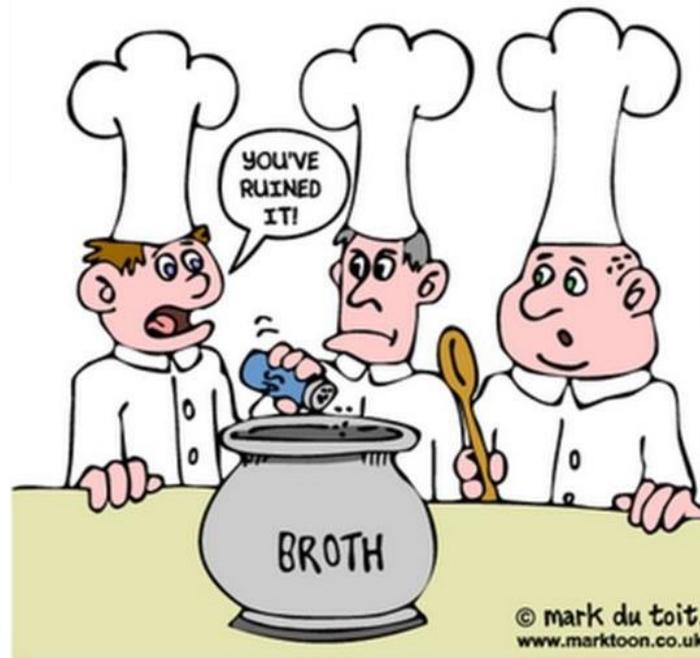
AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Primary Care Physician should review all medication recommendations

- impact of multimorbidity
- must balance risks vs benefit of the many recommended treatment strategies for multiple medical conditions
- patient centred approach
 - must know the patient's priorities

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

**Primary Care Physician should review all
medication recommendations**



AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Medication reconciliation

- a medication list from the dispensing pharmacy is not necessarily what the patient is actually taking
- what the patient says they're taking and what they're actually taking can be very different
- pharmacist's role in medication reconciliation

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Clinical tools and education

- **Beers + STOPP/START criteria**
 - evidence based clinical tools to identify potentially inappropriate medications for older persons
 - using these clinical tools has been proven to reduce ADE's in older persons

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Clinical tools and education

- Pretorius, RW, Gataric G, Swedlund SK, Miller JR. Reducing the Risk of Adverse Drug Events in Older Adults. *Am Fam Phys* 2013;87:331-6.
- Poudel A, Balloková A, Hubbard RE, et al. Algorithm of medication review in frail older people: Focus on minimizing the use of high-risk medications. *Geriatr Gerontol Int* 2016;16:1002-13.

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Clinical tools and education

- geriatric curriculum – what's your experience?
 - mandatory or elective courses
- focused prescriber education in geriatric pharmacotherapy has been shown to prevent prescribing errors in multimorbid older persons



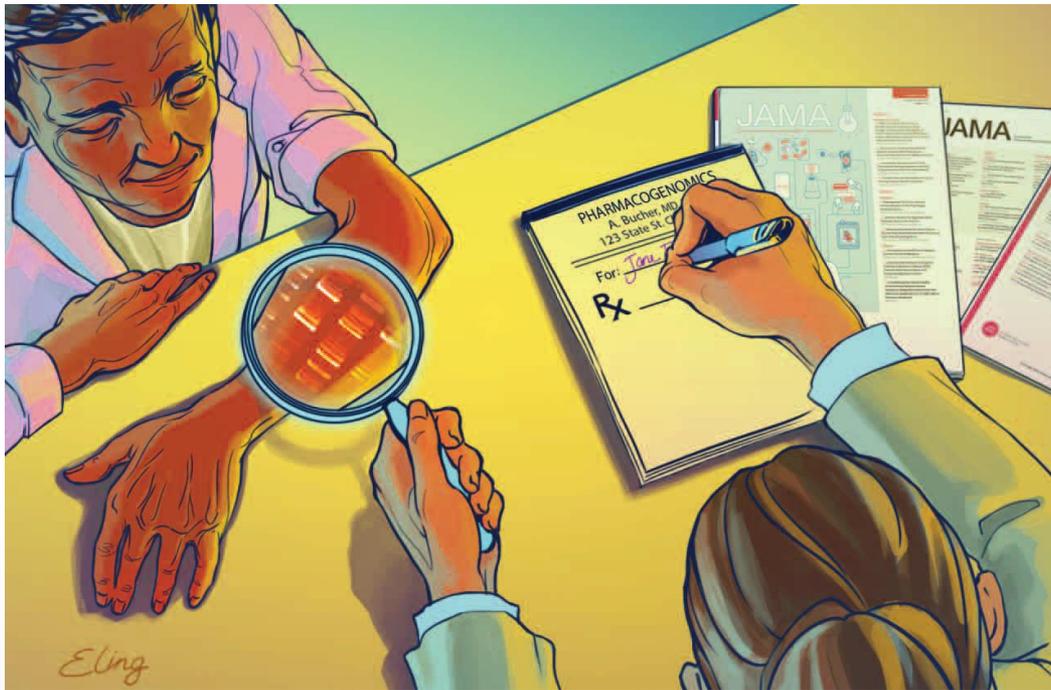
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Concerns with deprescribing

- adverse drug withdrawal events (ADWE's)
- return of the medical condition
- reversal of drug drug interactions
- damage to the doctor-patient relationship

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Individualized medication therapy
Pharmacogenomics



AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Individualized medication therapy Pharmacogenomics

- personalized medicine
 - humans are 99.9% genetically identical
 - some of the 0.1% genetic variation among people affects their capacity to respond to medications
 - these variations can lead to the medicine causing unintended adverse effects or result in therapeutic failure
 - genotype guided drug selection and dosing

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Individualized medication therapy Pharmacogenomics

METABOLISM

Ultrarapid metabolizers¹

- Too rapid drug metabolism
- No drug response at ordinary dosage (nonresponders)



Extensive metabolizers² (normal)

- Expected response to standard dose



Intermediate metabolizers²

- May experience some or a lesser degree of the consequences of the poor metabolizers



Poor metabolizers¹

- Too slow or no drug metabolism
- Too high drug levels at ordinary dosage
- High risk for ADRs

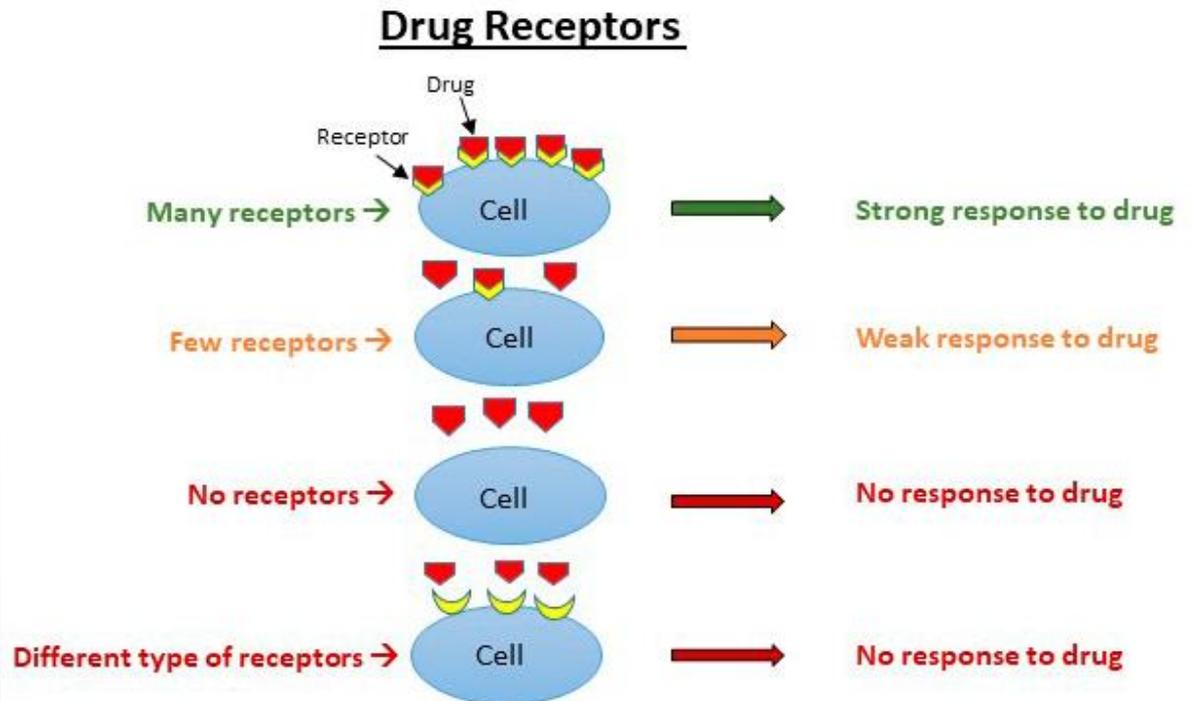


AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Individualized medication therapy

Pharmacogenomics

BIOMARKER STATUS



AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Individualized medication therapy

- pharmacogenomics/personalized medicine
 - avoid trial and error
 - increase chance for clinical efficacy
 - decrease chance for adverse effects



AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Individualized medication therapy

- personalized medicine
- IGNITE through the University of Florida, see
 - <https://ignite-genomics.org/spark-toolbox/clinicians/>



AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Close relationship between prescriber and pharmacist

- detailed medication reviews
 - MedsCheck (??) review must address IESC
 - indication, efficacy, safety, compliance
- medication reconciliation
 - pharmacist led medication reconciliation
- independent pharmacist practitioners who are hired by the long term care home

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS

Vanessa's Law

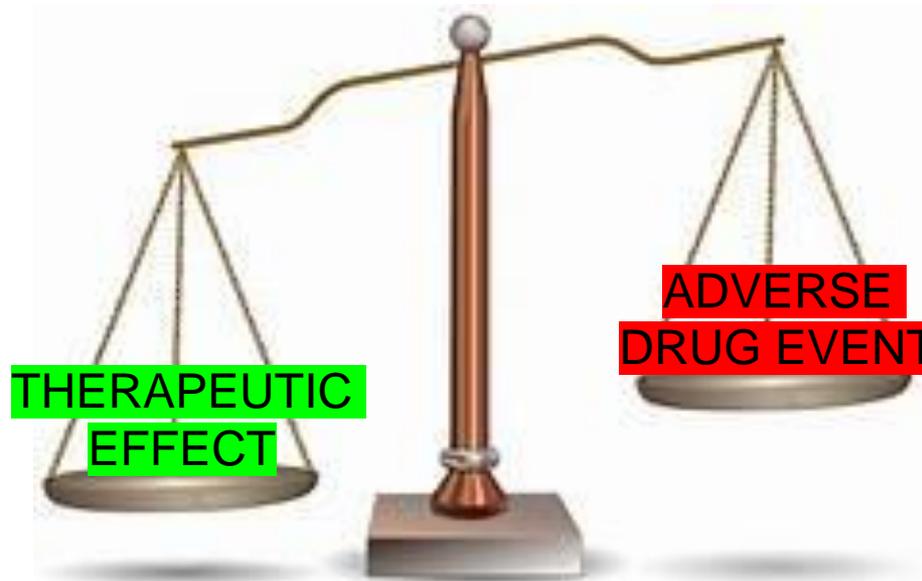
Protecting Canadians from Unsafe Drugs Act

- mandatory reporting of serious adverse drug reactions and medical device incidents to Health Canada, effective December 2019

A **serious adverse drug reaction (serious ADR)** is a noxious and unintended response to a drug that occurs at any dose and that

- requires in-patient hospitalization or prolongation of existing hospitalization,
- causes congenital malformation,
- results in persistent or significant disability or incapacity,
- is life-threatening, or
- results in death.^{3,4,5}

AVOIDING ADVERSE DRUG EVENTS IN OLDER PERSONS





Conference 2019
Practical Pearls
in Long Term Care



**Please remember to complete your
evaluations.**

Evaluations can be found on the Mobile App.

Thank you.