

Disclosure

- I have the following financial relationship to disclose:
 - Speaker's Bureau for Sanofi Pharmaceuticals



J. R. Stan

Educational Objectives

- At the conclusion of this session, the participant should be able to:
 - Describe the mechanism of action and the therapeutic application of several recently introduced drugs.
 - Identify essential information to more effectively counsel patients on changes in the therapeutic application(s) of existing drugs, such as the recent recommendations for the treatment of hypertension, lipids and mental health disorders.
 - Compare and contrast changes in the current therapeutic approach to various disease processes, including drugs used in mental health, pain management, cardiovascular health, diabetes, women's health and miscellaneous conditions.
 - Evaluate evidence-based studies to appropriately respond to questions and concerns from prescribers and patients on recent reports in the health professions literature.



References and Additional Information

- I have provided a separate handout with additional information not detailed in the following slides.
- In addition, to provide you with additional information on the materials included in these slides, please refer to the reference source included on each slide.

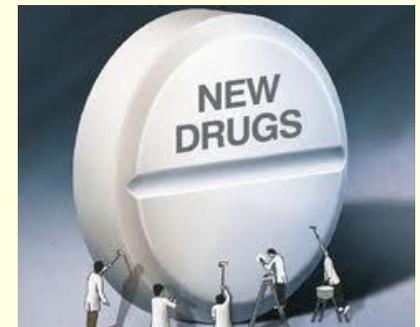


FDA Approvals Decline in 2013

- The FDA approved 27 first-of-a-kind drugs in 2013, down from 39 new medications in 2012, which was a 15-year high.
 - Despite the decline, FDA officials say the tally of innovative medications approved last year is in line with the historical trend. On average, the FDA has approved 28 first-of-a-kind drugs annually over the past five years.

Additional materials in handout

FDA.com, December 31, 2013



Reference for Drugs Introduced in 2013

- The January, 2014 issue of *Pharmacist's Letter* contains a list of the new drugs approved by the FDA in 2013.
 - The first section lists new molecular entities approved in 2013, the second and third sections list significant new biologicals and significant new dosage forms of previously approved drugs.



3 “Breakthrough” Drugs Approved in 2013

- Three of the 26 drugs approved in 2013 were approved with the ***Breakthrough Therapy*** designation:
 - **Sofosbuvir** (Solvadi®) for hepatitis C. Cost is \$1000/tablet and it is usually used for 12 weeks (\$84,000).
 - **Ibrutinib** (Imbruvica®) for mantle cell lymphoma (MCL)
 - **Obinutuzumab** (Gazyva®) for chronic lymphocytic leukemia

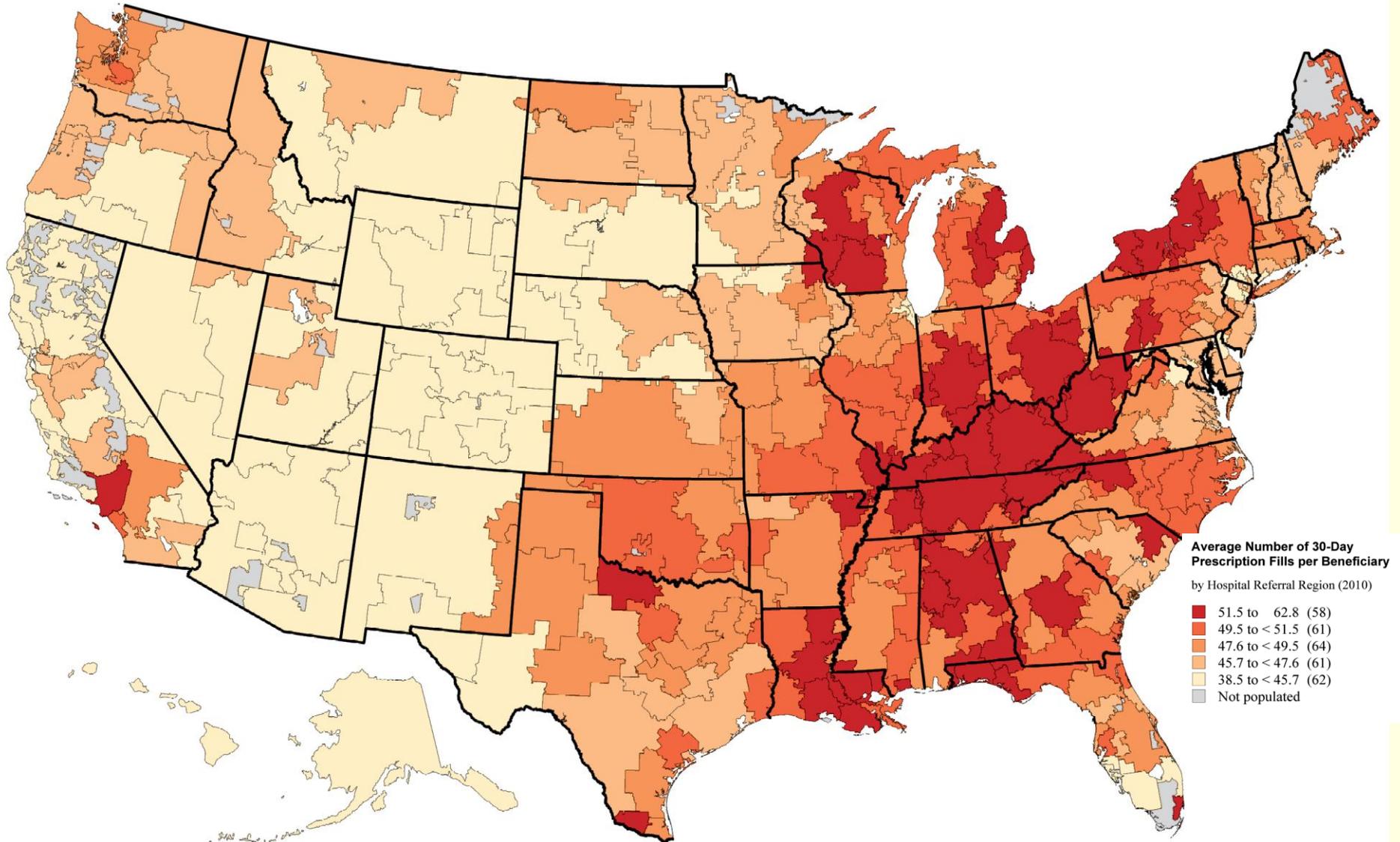
Nearly 7 in 10 Americans are on prescription drugs

- Nearly 70% of Americans are on at least one prescription drug, and more than half take two, Mayo Clinic researchers say.
 - Antibiotics, antidepressants and painkilling opioids are most commonly prescribed.
- 20% of patients are on five or more prescription medications.



Overall Use of Rx Medications: Medicare Part D

www.dartmouthatlas.org/downloads/reports/Prescription_Drug_Atlas, 10-15-13



Generic Drugs Continue to Grow

- Generics now account for 84% of the total US pharmaceutical market volume, reaching an all-time high in 2012.
 - However, brand name drugs made up about 75% of dollars spent on prescription drugs.



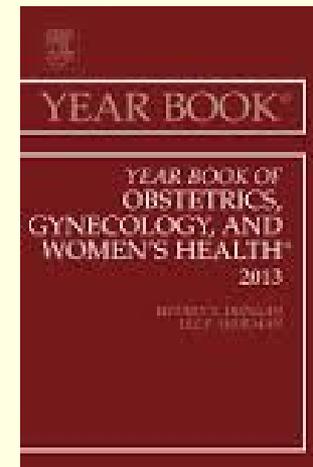
New York Times, March 18, 2013

Just 3 Generics Save \$28.9 Billion in 2012

- In 2012, just three new generic products contributed \$28.9 billion to reduction in medicine spending.
 - These three drugs are:
 - Lipitor® (atorvastatin)
 - Plavix® (clopidogrel)
 - Seroquel® (quetiapine)

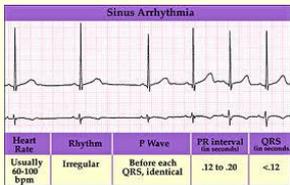


“Big” Drug-Related Stories in 2013



The Biggest Medical News of 2013

- **Major Drug Alerts with Antibiotics and Cardiac Arrhythmias**
 - Azithromycin poses the risk for torsades de pointes.
 - The fluoroquinolones increase the risk for permanent peripheral neuropathy and cardiac arrhythmias.
 - Clarithromycin + calcium-channel blockers is associated with increases in acute kidney injury, hypotension, and death. And can cause cardiac arrhythmias.



Azithromycin (Zithromax®), Z-Pak®) and Sudden Cardiac Death

- In 2012 a study conducted at Vanderbilt on a TennCare cohort showed that patients taking azithromycin had a small increased risk for sudden cardiac death compared with patients taking amoxicillin, ciprofloxacin, or no antibiotic at all.



Azithromycin (Zithromax[®], Z-Pak[®]) and Sudden Cardiac Death

- As a follow-up to this *NEJM* study, in March 2013, FDA officially warned of this risk.
 - The FDA stated that patients at risk for this azithromycin-induced arrhythmia include those who already have a prolonged QT interval, low blood levels of potassium or magnesium, and an abnormally slow heart rate, or who take drugs to treat arrhythmias.
 - Elderly patients and patients with cardiac disease also may be more susceptible to the arrhythmogenic effects of the antibiotic.

Another Link with Azithromycin and Levofloxacin to Arrhythmias

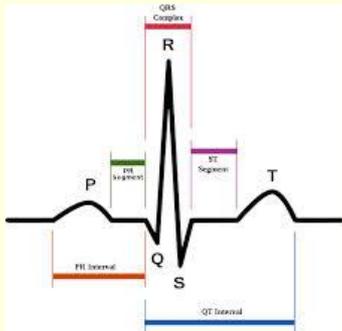
- A cohort study among US veterans showed that compared with amoxicillin, azithromycin resulted in a statistically significant increase in mortality and arrhythmia risks on days 1 to 5, but not 6 to 10.
 - Levofloxacin, which was predominantly dispensed for a minimum of 10 days, resulted in an increased risk throughout the 10-day period.

Azithromycin and Sudden Cardiac Death: Conflicting Data

- A study out of Denmark in the *NEJM*, May 2, 2013 **shows no excess heart deaths for azithromycin** in a general population of young and middle-aged adults. (The previous study was in a high-risk population.)
 - This study looked at data for adults aged 18-64 years and compared more than a million users of azithromycin vs more than a million users of penicillin VK and found that current, past, or recent use of azithromycin was **not** more likely to increase risk for cardiovascular death when compared with penicillin VK.

Azithromycin and Sudden Cardiac Death

- The FDA advised clinicians to put the cardiac risk of azithromycin in an "appropriate context," because other antibiotics in the macrolide class, as well as non-macrolides such as fluoroquinolones, can prolong the QT interval.
 - “Heart rhythm problems” is a precaution in the PI.
 - **Question: Does this impose legal implications on the pharmacist?**



FDA.gov, March 12, 2013

Cardiovascular Events After Clarithromycin Use in Lower Respiratory Tract Infections

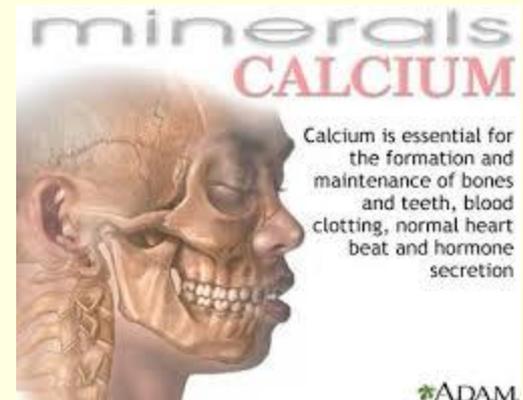
- According to a study in the *British Medical Journal*, the use of clarithromycin (Biaxin®) in the setting of acute exacerbations of chronic obstructive pulmonary disease or community acquired pneumonia may be associated with increased cardiovascular events.
 - These findings require confirmation in other datasets.



The Biggest Medical News of 2013

■ Major Alerts with Supplements

- Calcium supplement are associated with higher all-cause and cardiovascular death rates but not with deaths from stroke.
- Antioxidative nutritional supplements are more likely to cause than prevent cancer.



Taking Vitamins & Supplements to Improve Health: “A Waste of Money”

- More than half of all adults in the U. S. take some sort of multivitamin in hopes of preventing heart disease and cancer or even to aid with memory.
 - But an editorial published in the December 17, 2013 issue of *Annals of Internal Medicine* says that using supplements and multivitamins to prevent chronic conditions is a waste of money.



Supplements and Vitamins: “A Waste of Money”

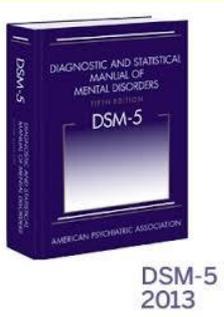
- In an editorial, Dr. Edgar Miller, professor at Johns Hopkins University School of Medicine, said:
 - "The (vitamin and supplement) industry is based on anecdote, people saying 'I take this, and it makes me feel better.' It's perpetuated. But when you put it to the test, there's no evidence of benefit in the long term. It can't prevent mortality, stroke or heart attack."



The Biggest Medical News of 2013

■ **DSM-5 Released**

- After more than a decade of development and more than 2 years of frequently searing controversy, the fifth edition of the ***Diagnostic and Statistical Manual of Mental Disorders (DSM-5)*** was finally released.
- Some are concerned that the DSM-5 will result in the mislabeling of potentially millions of people who are basically normal.



DSM-5 Questioned

■ Examples:

- Normal grief may be misdiagnosed as *Major Depressive Disorder*.
- Forgetfulness of old age may now be interpreted as *Mild Neurocognitive Disorder*.
- Premenstrual Dysphoric Disorder (PMDD) is classified as a “mental illness.”
- A child with temper tantrums has *Disruptive Mood Dysregulation Disorder*.



DSM-5 Questioned

- "Drug companies take marketing advantage of the loose *DSM* definitions by promoting the misleading idea that everyday life problems are actually undiagnosed psychiatric illness caused by a chemical imbalance and requiring a solution in pill form," Dr. Frances writes.



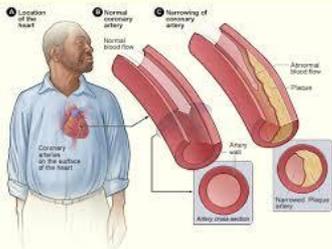
The Biggest Medical News of 2013

Additional materials in handout

■ New Cholesterol Guidelines Abandon LDL Targets

- New guidelines released in November caused an immediate stir with the assertion that there is simply no evidence from randomized controlled trials to support treatment to a specific cholesterol target level.

- Gone are the recommended LDL- and non-HDL-cholesterol targets, specifically those that ask providers to treat patients with cardiovascular disease to less than 100 mg/dL or the optional goal of less than 70 mg/dL.



Half of U.S. Population Age 40-75 on a Statin?

- According to the *NEJM*, March 19, 2014, the new recommendations suggesting that instead of working to lower a patient's "bad" LDL cholesterol to specific numeric targets, practitioners should embrace a new online calculator that factors in characteristics such as smoking and obesity to predict an individual's risk of heart disease.



- This is projected to increase statin usage to up to half of the U.S. population age 40–75.

Not Everyone Agrees: AAACE Rejects Guidelines

- The American Association of Clinical Endocrinologists (AAACE) does not endorse the guidelines from the AHA and ACC.
 - In a letter to its members, AAACE questioned the scientific basis of the guidelines and said certain at-risk populations of patients will be underserved by them.
 - They recommend that practitioners refer to their 2012 Guidelines: *AAACE Lipid and Atherosclerosis Guidelines, Endocr Pract 2012; 18 (Suppl, 11:1-78)*



American Association of Clinical Endocrinology (AACE) Guidelines for Lipids

Lipid Goals for Patients at Risk for Coronary Artery Disease

Lipid Parameter	Goal (mg/dL)	Evidence Level
Total cholesterol	<200	1
LDL-C	<100; <70 in <i>all</i> very high risk patients)	1
HDL-C	As high as possible, but at least >40 in men and women	1
Non-HDL-C	30 above LDL-C goal	1
Triglycerides	<150	1
Apolipoprotein B	<90 in patients at risk of CAD, including those with diabetes <80 in patients with established CAD or diabetes plus one or more additional risk factors	4

Note: Adapted from the AACE Lipid and Atherosclerosis Guidelines.
Source: Endocr. Pract. 2012;18(Suppl.1):1-78

The Biggest Medical News of 2013

Additional materials in handout

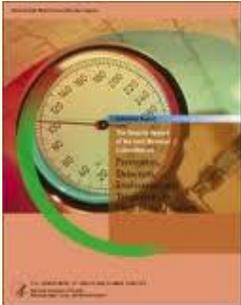
■ New hypertension guidelines

- After almost 2 years of waiting, in December 2013, the U.S. National Heart, Lung and Blood Institute released the 8th Annual JNC 2013 recommendations.



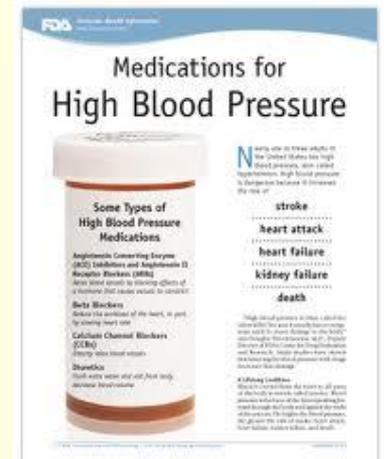
JNC 8 Recommendations

- The gist of the recommendations is that people 60 and older don't need to be treated as aggressively as was previously thought.
- Specific recommendations:
 - Treatment goals for older people should be set at 150/90 mm Hg.
 - The goal for other groups is 140/90, including diabetics and those with chronic kidney disease (CKD) who were previously recommended to be treated to the goal of 130/90.



JNC 8 Recommendations

- Four classes of medicines were *equally* recommended as appropriate initial therapy in non-black hypertensive population:
 - ACE inhibitors
 - angiotensin receptor blockers
 - calcium channel blockers
 - thiazide-type diuretics
- Note that β -blockers are no longer recommended for initial treatment of uncomplicated hypertension.



The Biggest Medical News of 2013

■ Obesity Declared a Disease

- After much impassioned debate, the AMA in June 2013 voted overwhelmingly to label obesity a disease that requires a range of interventions to advance treatment and prevention.
 - The decision could have implications for provider reimbursement, public policy, patient stigma, and International Classification of Diseases coding.



The Biggest Medical News of 2013

- **Diet to Prevent Alzheimer's, Fecal Transplant Pills**
 - New dietary guidelines for the prevention of Alzheimer's disease have been developed.
 - Pills containing a concentrate of fecal bacteria can stop recurrent *Clostridium difficile* infections by rebalancing the bacteria in the gut.



Recent Developments with Drugs Used in Endocrinology with focus on Diabetes



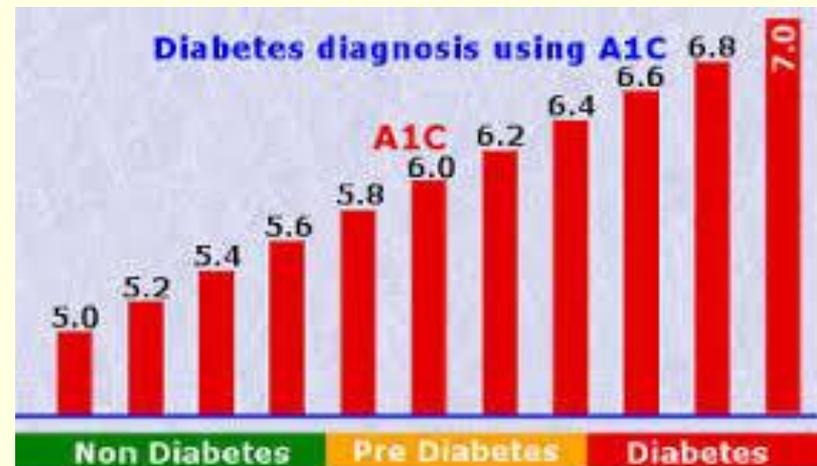
Changing Treatment Goals for Type 2 Diabetes

- Historically, sugar was the defining feature of *diabetes mellitus* (means “excess urination of honey.”)
 - Thus treatment focused on lowering blood glucose levels.
- However, based on high-quality evidence from meta-analyses, glucose control should no longer be the main focus of treatment.
 - A new approach to the care emphasizes proven interventions that improve duration and quality of life.

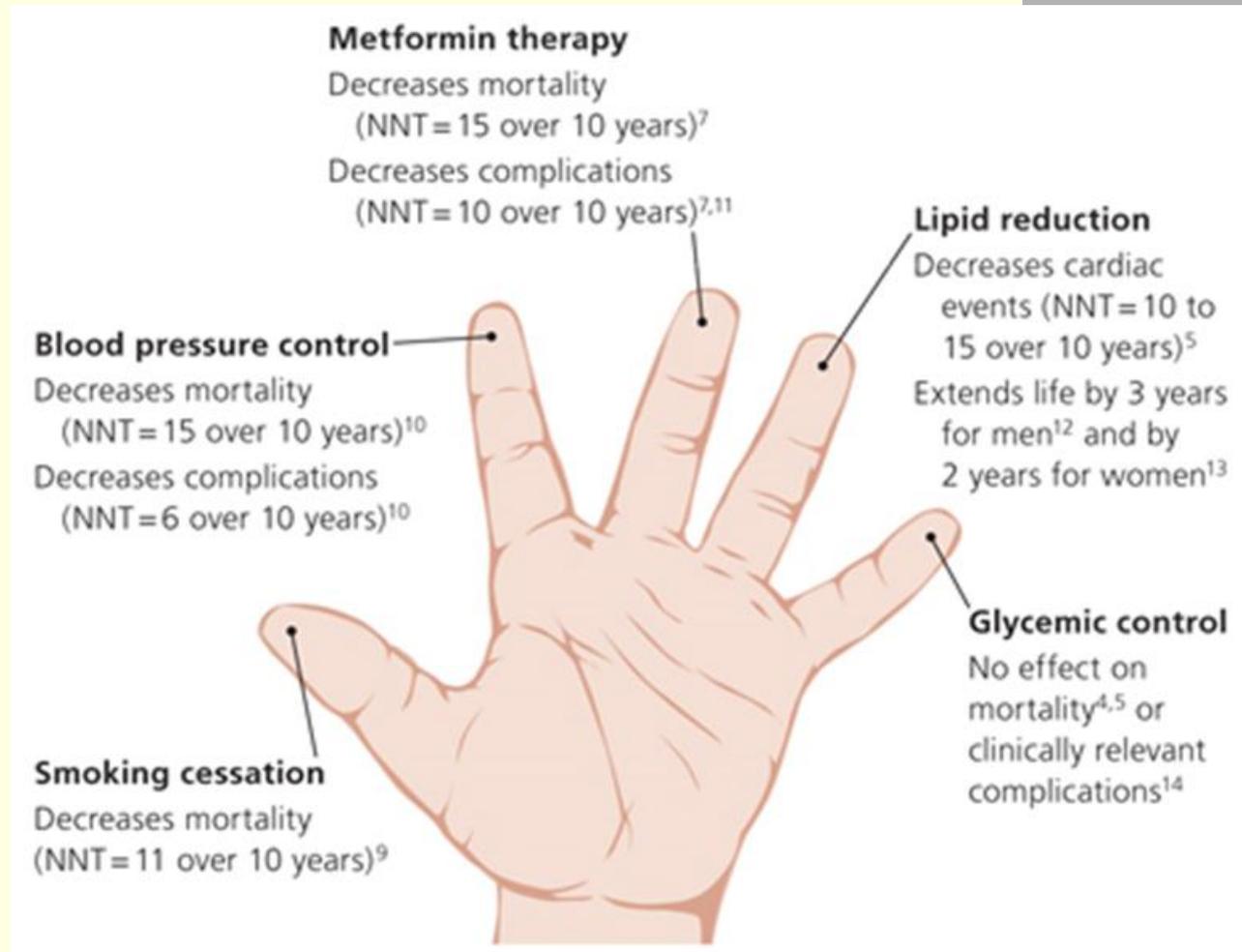


Changing Treatment Goals for Type 2 Diabetes

- 2014 revised guidelines from the ADA and the European Association for the Study of Diabetes propose less stringent goals, e.g., A1c <8%, for most patients with diabetes who have a history of severe hypoglycemia, short life expectancy or several comorbidities.

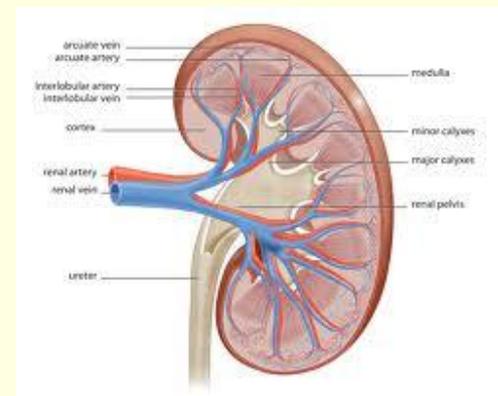


Changing Approach for Management of Type 2 Diabetes: “Lending a Hand”



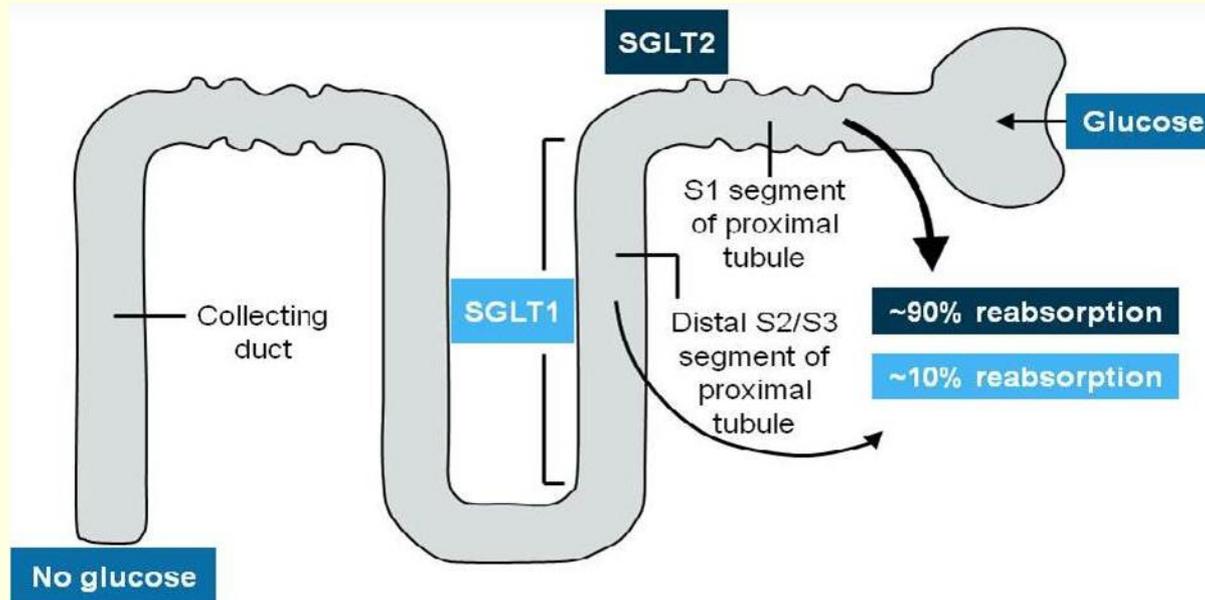
Sodium Glucose Cotransporter 2 (SGLT2) Inhibitors: New Class of Diabetes Drugs

- In March 2013, the FDA approved a novel glucose-lowering agent, **canagliflozin (Invokana®)** for the treatment of adults with type 2 diabetes.
- Canagliflozin is the first in a new class of drugs, an oral inhibitor of sodium glucose cotransporter 2 (SGLT2). It cost ~\$9/day.
 - Others in the SGLT2 inhibitors class include empagliflozin, dapagliflozin and ipragliflozin.



Mechanism of Action of SGLT2 Inhibitors

- SGLT2 is a protein in humans that facilitates glucose reabsorption in the kidney. SGLT2 inhibitors block the reabsorption of glucose in the kidney, increase glucose excretion, lower blood glucose levels, and also results in weight loss.



2nd SGLT Inhibitor Approved: Dapagliflozin (Farxiga®)

- In 2014, the FDA approved the second SGLT Inhibitor, dapagliflozin (Farxiga®), from BMS.
 - In clinical trials the most common side effects were genital fungal infections and urinary-tract infections.
 - Because a numeric increase in bladder cancer was seen with dapagliflozin in one of these trials, dapagliflozin is not recommended for patients with active bladder cancer or moderate to severe renal impairment.



Albiglutide (Tanzeum®)

The 3rd Injectable Incretin Mimetic for Type 2 Diabetes

- In April 2014, the FDA approved albiglutide (Tanzeum®) as a **once-a-week** injection for treating adults with type 2 diabetes.
 - It has the same warning as the other incretin mimetics that tumors of the thyroid gland were observed in rodent studies.
 - The biggest difference with albiglutide is that it is given once-a-week rather than once daily as is liraglutide (Victoza®).
 - But exenatide (Bydureon®) is a once-weekly incretin mimetic, too.

“Low T” Treatments in Older Men May Increase Cardiovascular Risk

- Among a cohort of men in the VA system who underwent coronary angiography and had a low serum testosterone level were 30% more likely to have a heart attack or stroke or to die during a 3-year period than men with low hormone levels who didn't take the supplements.
 - Hormone users and nonusers were in their early 60s on average, and most had other health problems including high blood pressure, unhealthy cholesterol and diabetes.

Endocrine Society Blows Whistle on “Low-T” Drive

- Professional society guidelines recommend testosterone therapy for patients with symptomatic testosterone deficiency.
- However, some feel that the dramatic increase in testosterone use among older men with normal testosterone levels do not meet the clinical guidelines for treatment.

Journal of Clinical Endocrinology & Metabolism, January, 2014



Recent Developments in Women's Health



Plan B One-Step® OTC for All Ages

- Plan B One-Step® is the first emergency contraceptive that retailers can sell on regular store shelves, even in stores without a pharmacy.
- Other brands will follow after exclusivity runs out for Plan B One-Step®, in April 2016.
- The new versions can be bought by men and women of ALL ages.
- ella® (ulipristal acetate) will remain prescription-only.



Plan B One-Step® OTC for All Ages

- Emergency contraception is similarly safe in both adolescents and adults, and safer than pregnancy. Even repeated use is NOT riskier, but it may not be smart.
- Emergency contraceptives are LESS effective, cause MORE menstrual irregularities, and can cost MORE than regular use of the pill or other hormonal contraceptives.

Pharmacist's Letter, August 2013



Plan B One-Step® OTC for All Ages

- Encourage women to use a regular contraceptive first, but don't discourage using an emergency contraceptive if that's all they will use.
- Women on the pill CAN use emergency contraception if they miss doses of their OC.



Can Health Care Practitioner Have a “Conscientious Objection” to Contraceptives?

- Medical and Pharmacy organizations supports an individual’s ability to choose not to prescribe, administer or dispense a medication for personal, religious and moral reasons and also supports the establishment of systems to ensure patient’s access to legally prescribed therapy.
- In February 2014, a Tennessee Pharmacist sued Walgreens after being fired for refusing to sell Plan B One-Step®.



Pharmacies Often Misinform Young Females About Plan B®

- Female adolescents requesting emergency contraception (EC) at pharmacies are often given incorrect information, partly due to confusion about changing regulations.
 - Female callers posing as 17-year-old adolescents call 943 pharmacies in five U.S. cities (**Nashville**, Philadelphia, Cleveland, Austin, and Portland) using a standard script.



Pharmacies Often Misinform Young Females About Plan B®

- Incorrect information included incorrectly telling adolescents that their parents had to be informed.
 - The report concluded that “Adolescents requesting EC from pharmacies are often given pharmacy policies in ethics-laden and confusing terms. They are told of false barriers to EC access, and there is confusion concerning the evolving policies regarding EC dispensing.”

Journal of adolescent Health, January, 2014



Emergency Contraception Less Effective in Large Women

- In 2013, new research on Europe's version of Plan B® (called NorLevo®) has found that the pill doesn't work in women who weigh >176 lbs and loses effectiveness at 166 lbs.
 - According to CDC, the average American women weighs 166.2 pounds
- HRA Pharma states that a dose increase of levonorgestrel is not proven to be a solution for this problem. They advise heavier women to discuss IUD insertion with their providers.



2014 American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin For Treating Vasomotor Symptoms of Menopause and Vaginal Atrophy

- The *2014 Practice Bulletin* introduces new drug information, but there are no new risks or dangers.
 - While the hormone therapy recommendations are similar to prior recommendations, there is more evidence to support nonhormonal alternatives such as SSRIs and SNRIs for management of vasomotor symptoms.



2014 American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin For Treating Vasomotor Symptoms of Menopause and Vaginal Atrophy

- Hot flashes affect from 50% to 82% of US women who experience natural menopause, and 10% to 40% report vaginal atrophy.
- Of those who have hot flashes, 87% suffer daily and 33% have 10 or more episodes daily.
- Median duration of vasomotor symptoms is from 4 to 10.2 years.



2014 American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin For Treating Vasomotor Symptoms of Menopause and Vaginal Atrophy

- The new *Practice Bulletin* states that HT should **not** be discontinued at age 65 years, because some women have hot flashes longer.



2014 American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin For Treating Vasomotor Symptoms of Menopause and Vaginal Atrophy

- The Bulletin also points out what to **avoid**:
 - Testosterone poses no benefit (except improved sexual satisfaction), but comes with multiple risks.
 - Too little evidence supports benefit of compounded bioidentical hormones, phytoestrogens, herbal remedies, or exercise.
 - Clonidine and gabapentin have shown some efficacy but are not FDA-approved for treating menopausal symptoms.



More Controversy From the WHI: Hormone Therapy for Menopausal Women Should Be Restricted by Dose, Time

- Hormone therapy should only be used for a short period of time near the time of menopause for women experiencing hot flashes and not as therapy for chronic disease prevention.
 - These findings are the latest results to emerge from follow-up analysis of the WHI study.

JAMA, October 2, 2013, Vol 310, No. 13



Non-hormonal Agent Approved for Hot Flashes

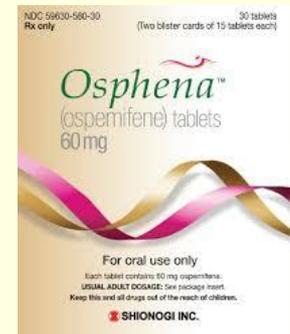
- Paroxetine (Paxil®) has been used off-label for many years for menopausal symptoms.
- **Paroxetine mesylate (Brisdelle®)** was approved in 2013 as the first non-hormonal treatment for hot flashes.
 - It contains a lesser amount of paroxetine than is used for depression.



Ospemifene (Osphena®) Approved for Dyspareunia

- In February 2013, the FDA approved **ospemifene (Osphena®)** for treating moderate to severe dyspareunia in postmenopausal women.
 - Ospemifene is a novel selective estrogen receptor modulator (**SERM**) that makes vaginal tissue thicker and less fragile, resulting in a reduction in the amount of pain women experience with sexual intercourse.

FDA.gov, February 27, 2013



Ospemifene (Osphena®)

Approved for Dyspareunia

- Osphena® has estrogenic effects on vaginal tissue, but raloxifene and tamoxifen don't.
- It seems as effective as vaginal estrogen for dyspareunia, but Osphena® costs \$160/month, compared to \$75/month for Vagifem®.
- Osphena® can cause or worsen hot flashes and increase the risk of blood clots. similar to other SERMs.
 - Low-dose vaginal estrogens don't increase the risk of thrombosis.

Duavee®: Combination of Conjugated Estrogens + Bazedoxifene

- In October 2013, the FDA approved **Duavee®**, a combination of conjugated estrogens with **bazedoxifene**, an estrogen agonist/antagonist that substitutes for a progestin.
 - Bazedoxifene reduces the risk for endometrial hyperplasia.
 - The combination of conjugated estrogens and bazedoxifene is indicated only for postmenopausal women who still have a uterus.



FDA.gov, October 8, 2013

New PI Labeling: Use Bisphosphonates 3-5 Years for Low Risk Patients

- In June 2013, the FDA changed the labeling in the PI for the bisphosphonates to suggest stopping the bisphosphonate 3 to 5 years in patients with low fracture risk.
 - They may need to continue if they have a high fracture risk.

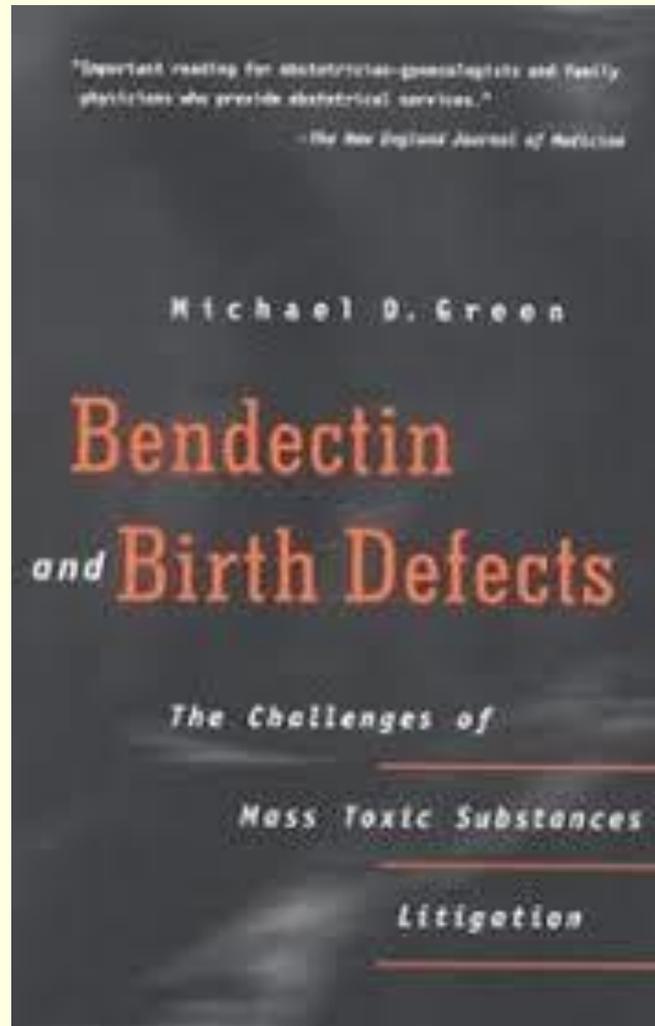


Osteoporosis and Fracture Risk with SSRIs

- SSRIs inhibit a protein that transports serotonin. The protein has been discovered in bone as well, raising the possibility these drugs may affect bone strength.
 - According to a report at the American Society for Bone and Mineral Research (ASBMR) 2013 Annual Meeting, the use of SSRIs was associated with a higher risk of fracture than use of glucocorticoids and proton-pump inhibitors (PPIs), which are well-known for their link to fractures.



Do you remember or have heard of Bendectin®?



New “Old” Drug for “Morning Sickness”

- Anybody remember Bendectin®?
- In April 2013, the FDA approved the combination of doxylamine and pyridoxine (**Diclegis®**) to treat pregnant women with nausea and vomiting who have not adequately responded to dietary and lifestyle changes for the management of hyperemesis gravidarum.

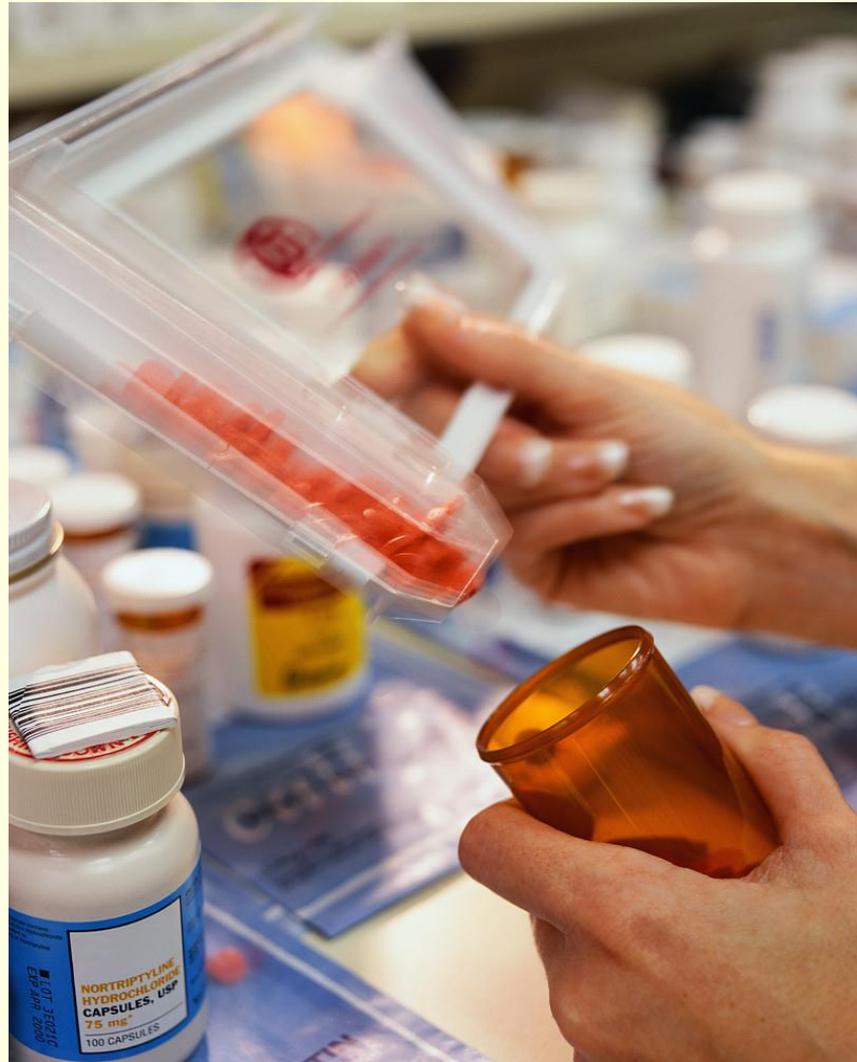


Body Builders and Breast Cancer Drugs

- To off-set some of the side effects of testosterone and anabolic steroids, many body-builders and “week-end warriors” are turning to anti-estrogens such as anastrozole (Arimidex®), tamoxifen (Nolvadex®) and exemestane (Aromasin®).
 - Side effects such as gynecomastia and low sex drive is a result of having too much estrogen, which results from too much testosterone.



Recent Developments with Miscellaneous Drugs



Acetaminophen Linked to Rare Skin Reactions

- In August 2013, the FDA warned that acetaminophen is associated with a risk of the rare, and potentially fatal skin reactions **Stevens-Johnson Syndrome (SJS)**, **toxic epidermal necrolysis (TEN)**, and **acute generalized exanthematous pustulosis (AGEP)**.

FDA.gov, August 1, 2013



Does This Have Acetaminophen in It?

- Acetaminophen is in more than 600 products. Do you know all of them?
- Help your patients use acetaminophen as directed to avoid unintentional overdose by referring them to the following website:



Naproxen Has Less Cardiovascular Risk than other NSAIDs

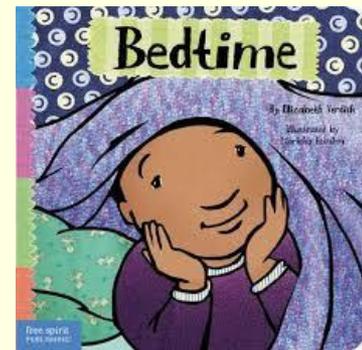
- Researchers undertook meta-analyses of NSAIDs versus placebo found that the vascular risks of high-dose diclofenac, and possibly ibuprofen, are comparable to coxibs, whereas **high-dose naproxen is associated with less vascular risk than other NSAIDs.**
 - Although NSAIDs increase vascular and gastrointestinal risks, the size of these risks can be predicted, which could help guide clinical decision making.

FDA Advisory Committee Says Naproxen is Not Safer

- In February 2014, when the FDA Arthritis Advisory Committee (AAC) and Drug Safety and Risk Management (DSARM) Advisory Committee considering changing the labeling of naproxen, just 9 of the 25 panel members said they believed naproxen has a lower risk of cardiovascular thrombotic events than other available NSAIDs.
- They recommended no change in the labeling of NSAIDs regarding cardiovascular toxicity.

Chronotherapeutics: Take ASA at Bedtime for Optimum Effects

- Taking aspirin at bedtime instead of in the morning might reduce acute cardiac events.
 - This study showed that intake of aspirin compared with intake on awakening reduced morning platelet reactivity, which might reduce excess cardiovascular events during the high risk morning hours.



AAOS: Don't Use Intraarticular Hyaluronic Acid (Viscosupplementation)

- The June 2013 American Academy of Orthopaedic Surgeons (AAOS) clinical practice guideline for knee osteoarthritis (OA) offers a strong recommendation *against* the use of intraarticular hyaluronic acid (HA viscosupplementation) for symptomatic knee OA.

Medscape.com, June 19, 2013



AAOS: Don't Use Glucosamine and Chondroitin Sulfate

- The revised guideline also recommends against the use of acupuncture, *the use of glucosamine and chondroitin sulfate*, and arthroscopy with lavage for primary knee OA.



AAOS: Don't Use More Than 3000 mg/day of Acetaminophen

- The guideline also reduced the maximum dosage for acetaminophen from 4000 to 3000 mg/day, with a note that it does not recommend for or against the use of acetaminophen, opioids, or pain patches because evidence of efficacy is inconclusive.



Another Dosage Form of Diclofenac

- In October 2013, the FDA approved Zorvolex®, a “low-dose” (20% lower than the normal dose) capsule of diclofenac.
- Zorvolex® contains diclofenac as submicron particles that are approximately 20 times smaller than their original size.
 - The reduction in particle size provides an increased surface area, leading to faster dissolution.

Other Dosage Forms of Diclofenac

- Cataflam®—immediate-release
- Voltaren®—delayed-release
- Arthrotec®—combined with misoprostol
- Voltaren Topical Gel®
- Flector®—transdermal patch
- Cambia®—powder mixed with potassium bicarbonate, for the treatment of acute migraine
- Zipsor®—liquid-filled soft gelatin capsule
- Pennsaid®—a topical solution in a DMSO vehicle. Has DMSO “taste” after applying.
- Zorvolex®—a “low-dose” capsule

FDA Approves First Single-Entity Hydrocodone Extended-Release

- In October 2013, the FDA approved a single-entity hydrocodone bitartrate extended-release called Zohydro ER®.
 - It is a Schedule II Controlled Substance indicated for the management of pain severe enough to require daily around-the-clock long-term treatment and for which alternative options are inadequate.
 - It is dosed every 12 hours and is available in 10, 15, 20, 30, 40 and 50 mg.

FDA.gov, October 25, 2013



IR & ER Oxycodone Approved: Xartemis XR®

- In March 2014, the FDA approved an **extended-release** combination of oxycodone and acetaminophen (Xartemis XR®) for the management of **acute pain**.
 - The drug has both immediate- and extended-release components to allow pain relief within an hour, with twice-daily dosing.



FDA Approves Naloxone Self-Injector

- In April 2014, the FDA approved a prescription treatment that can be used by family members or caregivers to treat a person known or suspected to have had an opioid overdose.
- Evzio® is a form of naloxone (Narcan®) that delivers a single dose via a hand-held auto-injector that can be carried in a pocket or stored in a medicine cabinet.

FDA.gov, April 3, 2014



WHO Warns of a Post-Antibiotic Era Where Common Infections Kill

- On April 30, 2014, the World Health Organization (WHO) warned that a post-antibiotic era in which common infections and minor injuries lead to death is a real possibility this century.
 - Very high rates of resistance to treatments have been observed in all regions, in bacteria that cause common infections such as those related to wounds, pneumonia, and urinary-tract and bloodstream conditions.



WHO Warns of a Post-Antibiotic Era Where Common Infections Kill

- Resistance to antibiotics is particularly acute with tuberculosis, affecting about 630,000 people globally, and drug effectiveness is declining among patients with malaria, HIV and influenza.
- In the case of gonorrhoea, 10 countries have reported that the disease is untreatable by any antibiotic.



CDC Warns that Gonorrhea is on the Verge of Being Untreatable

- Data analyzed from the Gonococcal Isolate Surveillance Project and city-level gonorrhea incidence rates from surveillance data for 17 cities during 1991–2006 found a strong likelihood of future increases in gonorrhea incidence caused by emerging cephalosporin resistance.



Resistance to Azithromycin (Zithromax® , Z-Pak®)

- More experts now recommend NOT using azithromycin or other macrolides for most acute respiratory infections.
- Pneumococcal infections are becoming more resistant to macrolides than to penicillin.
 - And strains that are resistant to penicillin are usually also resistant to macrolides.



Restrict Use Ketoconazole (Nizoral®) Oral Tablets

- On July 26, 2013, the FDA announced that clinicians should no longer prescribe ketoconazole (Nizoral®) tablets as a first-line therapy for *any* fungal infection because of the risk for severe liver injury, adrenal insufficiency, and adverse drug interactions.



FDA.gov, July 26, 2013

Restrict Use Ketoconazole (Nizoral®) Oral Tablets

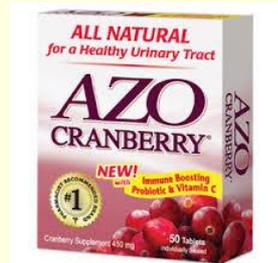
- The restriction does not apply to topical formulations of ketoconazole in creams, shampoos, foams, and gels.
 - The FDA's action coincides with the European Union (EU) drug regulators to *withdraw* ketoconazole tablets from EU national markets.
 - The European Medicines Agency (EMA) stated in a news release that "the risk of liver injury is greater than the benefits in treating fungal infections."



Cranberry Products for UTI?

- Several years ago, reports in the *NEJM* and *JAMA* added credence to claims for cranberry juice.
 - They postulated that it prevents *Escherichia coli* from attaching to bladder cells.
- However, a recent Cochran review concluded that the most current evidence fails to demonstrate sufficient effectiveness for cranberry products in preventing UTIs.

American Family Physician, December 1, 2013



OTC Nasacort® (Triamcinolone) Approved - 1st OTC Nasal Steroid

- In October, 2013, the FDA approved Nasacort® Allergy 24HR OTC treatment of seasonal and year-round nasal allergies in adults and children 2 years of age and older.
 - Nasacort® is the first and only nasal steroid to be available without a prescription and will be marketed by Sanofi's consumer healthcare division, Chattem.



New Combination Drug for COPD: Breo Ellipta®

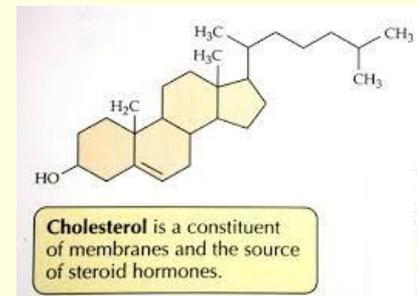
- A combination of fluticasone furoate + the long-acting β -agonist vilanterol was approved in May 2013 as a once-daily inhaled therapy for the treatment of COPD.
 - It is being called the “son of Advair®” since it is marketed by GSK, makers of Advair®.
 - In contrast to Advair Diskus®, which is dosed twice daily, the new once-daily inhaler contains a different, reputedly more stable side-chain variant of fluticasone, with vilanterol in place of salmeterol.



New Combo Product Approved for Hyperlipidemia

- 2013 approval of atorvastatin (Lipitor®) and ezetimibe (Zetia®) as **Liptruzet®**.
- Liptruzet® is available from Merck as a once-daily tablet containing 10 mg of ezetimibe combined with 10, 20, 40, or 80 mg of atorvastatin.
 - This is similar to Vytorin except it contains atorvastatin rather than simvastatin.

FDA.gov, May 3, 2013



Enalapril Approved in Liquid Form: Epaned®

- The ACE inhibitor enalapril (Vasotec®) was approved in 2013 in a liquid form called Epaned®.
 - It is approved for high blood pressure in adults and children 1 month and older.



FDA Advisory Panel: Calcitonin (Miacalcin®, Fortical®) Should Be Removed

- March, 2013 and FDA advisory panel recommended removal of calcitonin (Miacalcin®, Fortical®) due to a lack of efficacy in the prevention/treatment of osteoporosis and an association with cancer.



“Atypical Antidepressant”: Vortioxetine (Brintellix®)

- **Vortioxetine (Brintellix®)** was approved October 2013, it is similar to the SSRIs, but is being called an “atypical antidepressant” and a “serotonin modulator and stimulator” since it works by inhibiting the reuptake of serotonin and as a partial agonist of serotonin.
 - It may cause more nausea than some of the others.



Penis Amputated After Priapism with Sildenafil (Viagra®)

- According to Colombia's *La Nacion* newspaper, 66-year-old Gentil Ramirez Polania reportedly overdosed deliberately in order to impress his new girlfriend, but wound up with an inflamed and fractured penis that was showing signs of gangrene after experiencing an erection for several days.
- As a result, he underwent amputation so the gangrene would not spread.





Questions?

