Principles of Conservative Prescribing

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DISCLOSURES

Original FLIP Project *Work Funded by*

Attorney Generals' Consumer & Prescriber Education Program (Neurontin Settlement)
Cook County Hospital- UIC College of Pharmacy
Formulary **L**everaged **I**mproved **P**rescribing Project

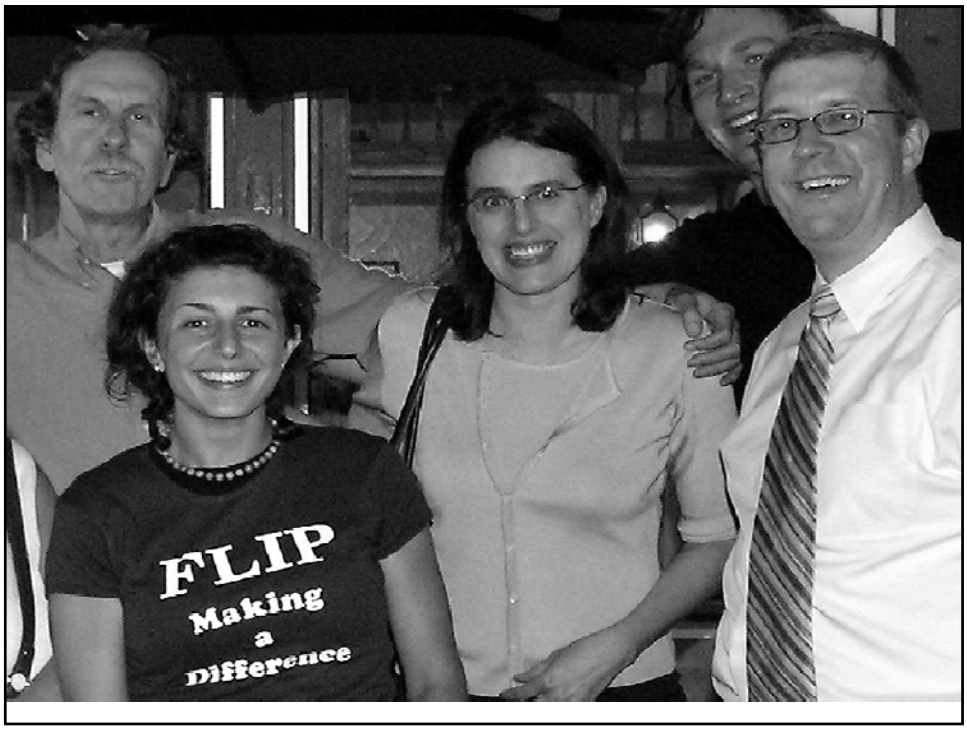
Speaker conflicts resolved through peer review.

Illinois Council of Health-System Pharmacists 2013 Annual Meeting

The Formulary Leveraged Improved Prescribing (FLIP) Team

From left to right: Laura Frankel, Dr. Bill Galanter, Dr. Bruce Lambert (PI), Dr. Marcia Edison, Dr. Gordy Schiff (PI), Sayeh Nikpay, Dr. Amy Lodolce, Jay Duhig, Dr. Mike Koronkowski

the FLIP side of drug claims



CURRENT CONFLICTS/DISCLOSURES

- Commercial -NONE
- Grant Funding:
  - AHRQ -*PROMISES Ambulatory Safety & Malpractice*
  - AHRQ *CERT HIT–CEDAR (Adverse Drug Reaction detection); UIC Patient Safety CERT*
  - FDA - *CPOE Evaluation CPOEMS*
  - Harvard Risk Management Fndn – *Diagnosis Errors*
  - Commonwealth Fund –*Medical Home Evaluation*
  - ONC –RAND- *Clinical Decision Support*
  - NSPF- *USP MedMarx CPOE Errors*

Outline

- What is conservative prescribing
  - 24 Principles for more judicious, careful rational drug use

Outline

- What is conservative prescribing
  ….and dispensing, …and counseling
  – 24 Principles for more judicious, careful rational drug use

Outline

- What is conservative prescribing
  ….and dispensing, …and counseling
  – 24 Principles for more judicious, careful rational drug use
- Role for pharmacist, pharmacy in this new paradigm
  – Benefits for patients and pharmacist
  – New thinking and roles

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MAYO CLINIC

A Decade of Reversal: An Analysis of 146 Contradicted Medical Practices

Vinay Prasad, MD; Andrae Vandross, MD; Caitlin Toomey, MD; Michael Cheung, MD; Jason Rho, MD; Steven Quinn, MD; Satish Jacob Chacko, MD; Durga Borkar, MD; Victor Gall, MD; Senthil Selvaraj, MD; Nancy Ho, MD; and Adam Cifu, MD

Abstract

Objective: To identify medical practices that offer no net benefits.

Methods: We reviewed all original articles published in 10 years (2001-2010) in one high-impact journal. Articles were classified on the basis of whether they addressed a medical practice, whether they tested a new or existing therapy, and whether results were positive or negative. Articles were then classified as 1 of 4 types: replacement, when a new practice surpasses standard of care; back to the drawing board, when a new practice is no better than current practice; reaffirmation, when an existing practice is found to be better than a lesser standard; and reversal, when an existing practice is found to be no better than a lesser therapy. This study was conducted from August 1, 2011, through October 31, 2012.

Results: We reviewed 2044 original articles, 1344 of which concerned a medical practice. Of these, 981 articles (73.0%) examined a new medical practice, whereas 363 (27.0%) tested an established practice. A total of 947 studies (70.5%) had positive findings, whereas 397 (29.5%) reached a negative conclusion. A total of 756 articles addressing a medical practice constituted replacement, 165 were back to the drawing board, 146 were medical reversals, 138 were reaffirmations, and 139 were inconclusive. Of the 363 articles testing standard of care, 146 (40.2%) reversed that practice, whereas 138 (38.0%) reaffirmed it.

Conclusion: The reversal of established medical practice is common and occurs across all classes of medical practice. This investigation sheds light on low-value practices and patterns of medical research.

Published by Elsevier Inc on behalf of Mayo Foundation for Medical Education and Research ■ Mayo Clin Proc. 2013;88(8):790-798

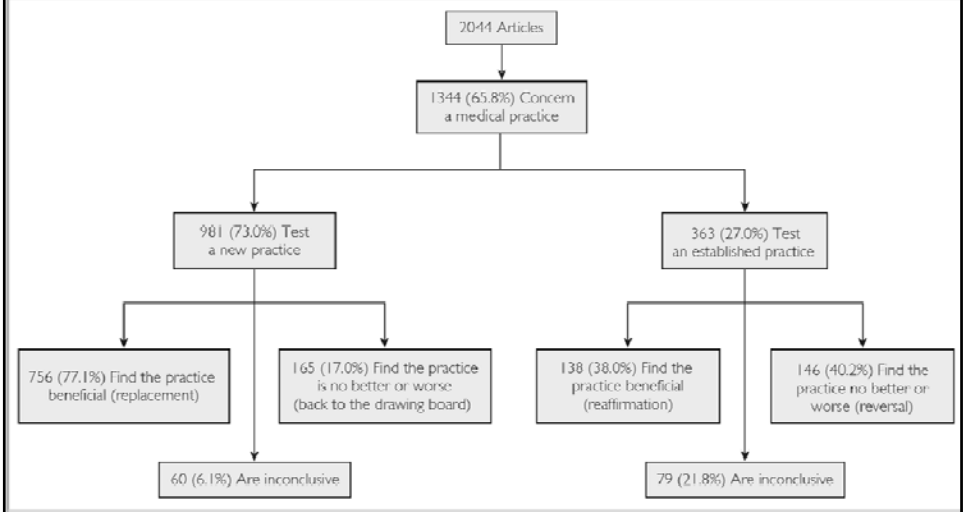


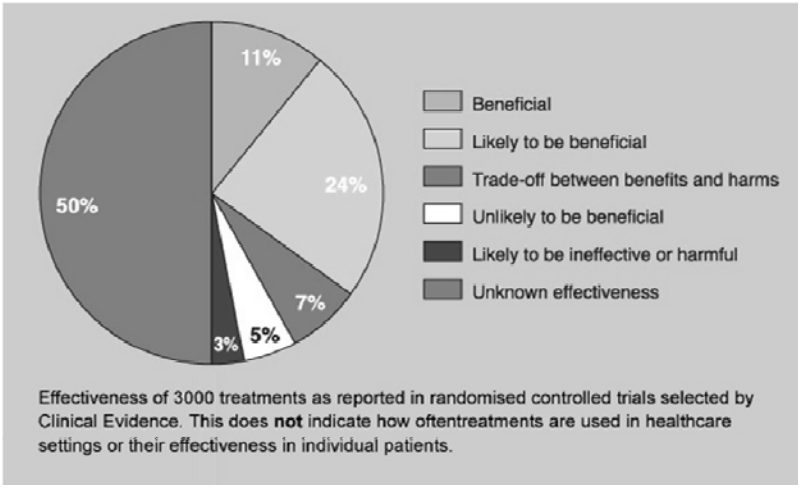
FIGURE 1. A breakdown of articles concerning a medical practice.

Mayo Clin Proc 2013

TABLE 1. Number (Percentage) of Reversal, Reaffirmation, and Inconclusive Articles by Year

Year	Reversal	Reaffirmation	Inconclusive
2001 (n=48)	14 (29.2)	20	14
2002 (n=26)	12 (46.2)	9	5
2003 (n=31)	12 (38.7)	12	7
2004 (n=33)	12 (36.4)	15	6
2005 (n=41)	19 (46.3)	14	8
2006 (n=20)	12 (60.0)	5	3
2007 (n=54)	18 (33.3)	17	19
2008 (n=32)	15 (46.9)	13	4
2009 (n=35)	16 (45.7)	16	3
2010 (n=43)	16 (37.2)	17	10
Total (N=363)	146 (40.2)	138 (38.0)	79 (21.7)

UK NHS Health Technology Assessment Programme
BMJ Publisher



"The usefulness of any source of information is equal to its relevance, multiplied by its validity, divided by the work required to extract the information

"Clinical Evidence presents the dark as well as the light side of the moon."

U.S. Deaths from Vioxx
More than Vietnam War

- 1/1999--9/2004: 106.7 million rofecoxib prescriptions in US
  - 17·6% were high-dose, mostly to older patients
- In 2 Merck-sponsored randomized trials: 2.25 relative risks for AMI
  - 5x for high-dose rofecoxib and 2x for the standard dose
  - Background rate AMI control NSAID users varied from 7·9 per 1000 person-years in CLASS1 to 12·4 per 1000 person-years in TennCare.
- Using Merck studies relative risks w/ these background rates 88,000– 140,000 excess cases serious coronary disease in US
- Using US national case-fatality rate-44%,suggests thousands of deaths attributable to rofecoxib use (~38,000-61,000)

Graham Lancet 2005

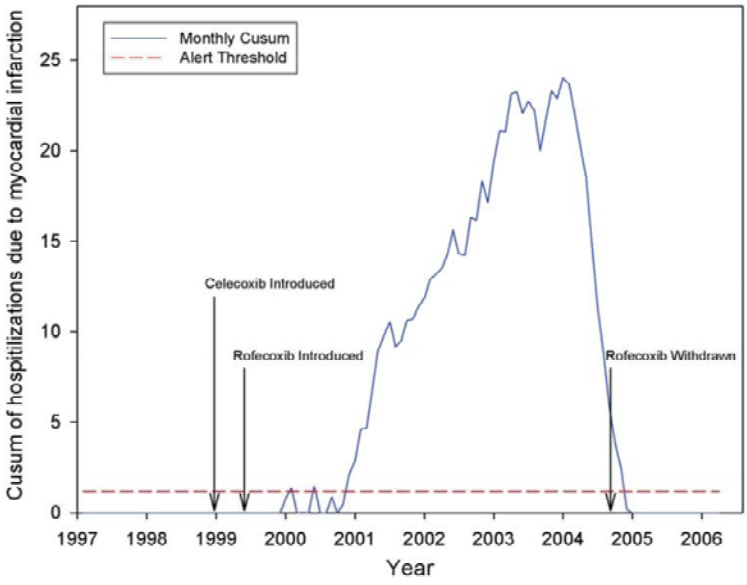
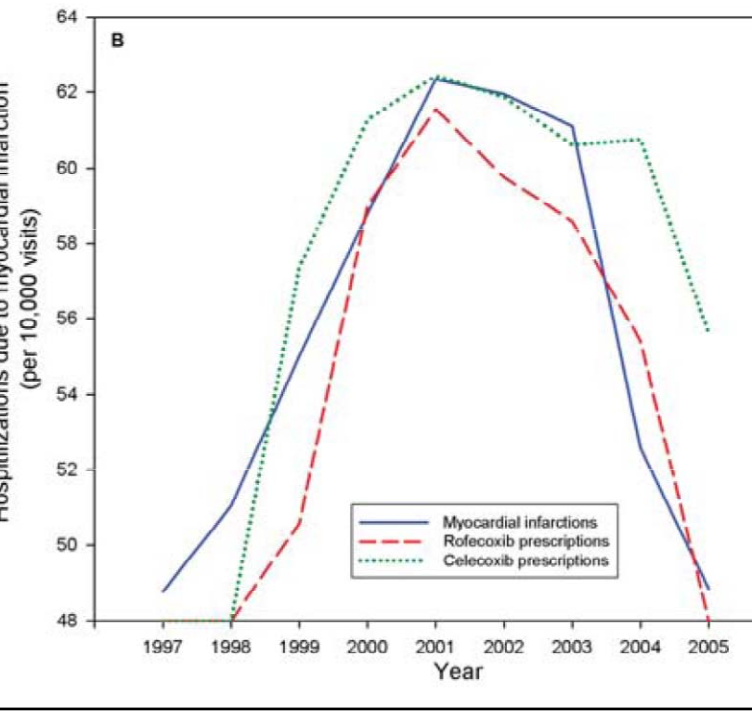


Figure 1. Cumulative sum (CUSUM) chart of monthly incidence of hospitalizations due to myocardial infarction from January 1, 1 30, 2006. Assigning 1997 and 1998 as a baseline period, a target mean of 47.1 hospitalizations due to myocardial infarctions pe a standard deviation of 2.8 per 100,000.The threshold for CUSUM was calculated as 1.18, yielding an average-run-length of 50 (dashe aberration, two standard deviations from baseline, was initially detected in January of 2000, with a CUSUM value of 1.37 and 5

PARTNERS' DATA

Brownstein PLOS 2007



Womens Health Initiative (WHI) Estrogen Rx

Adverse event	Relative risk (95% CI)	Change in number of events per 10,000 women in one year
Breast cancer	1.26 (1.00-1.59)	8 more
Heart disease	1.29 (1.02-1.63)	7 more
Stroke	1.41 (1.07-1.85)	8 more
Pulmonary embolism	2.13 (1.39-3.25)	8 more
Colorectal cancer	0.63 (0.43-0.92)	6 fewer
Hip fracture	0.66 (0.45-0.98)	5 fewer

NEJM 2007

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL REPORT

The Decrease in Breast-Cancer Incidence in 2003 in the United States

Peter M. Ravdin, Ph.D., M.D., Kathleen A. Cronin, Ph.D., Nadia Howlader, M.S., Christine D. Berg, M.D., Rowan T. Chlebowski, M.D., Ph.D., Eric J. Feuer, Ph.D., Brenda K. Edwards, Ph.D., and Donald A. Berry, Ph.D.

SUMMARY

An initial analysis of data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) registries shows that the age-adjusted incidence rate of breast cancer in women in the United States fell sharply (by 6.7%) in 2003, as age-adjusted incidence of breast cancer by an average of about 0.5% per year, a rise that was particularly evident among women who were 50 years of age or older[3] (Fig. 1). Changes in reproductive factors, in the use of menopausal hormone-replacement therapy, in mammographic screening, in environmental exposures, and in diet have all

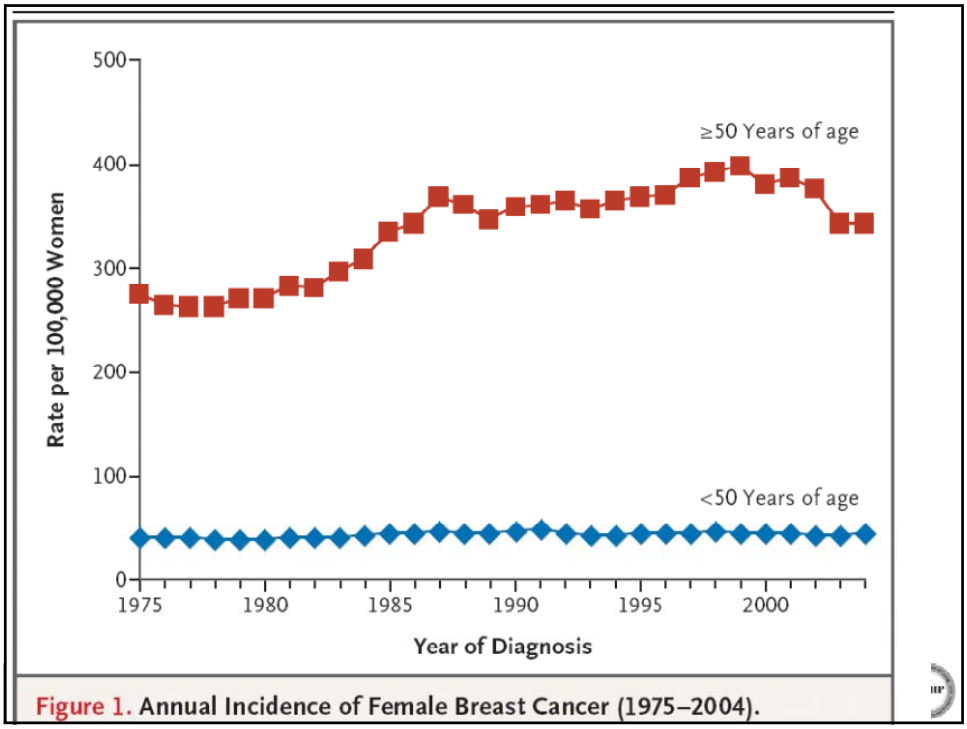


Figure 1. Annual Incidence of Female Breast Cancer (1975–2004).

National Cancer Institute
U.S. National Institutes of Health | www.cancer.gov

In English | En español

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News

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Posted: 04/18/2007

Decrease in Breast Cancer Rates Related to Reduction in Use of Hormone Replacement Therapy

The sharp decline in the rate of new breast cancer cases in 2003 may be related to a national decline in the use of hormone replacement therapy (HRT), according to a new report in the April 19, 2007, issue of the *New England Journal of Medicine*. The report used data from the Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute (NCI), part of the National Institutes of Health.

Age-adjusted breast cancer incidence rates in women in the United States fell 0.7 percent in 2003. During this same period, prescriptions for HRT declined rapidly, following highly-publicized reports from the Women's Health Initiative (WHI) study that showed an increased risk of breast cancer, heart disease, stroke, blood clots, and urinary incontinence among postmenopausal women who were using hormone replacement therapy that included both estrogen and progestin. The two most commonly prescribed forms of HRT in the United States, Premarin® and PremproTM, had their steepest declines starting in 2002-2003 — from 61 million prescriptions written in 2001 to 21 million in 2004.

Led by senior investigator Donald Berry, PhD., of the University of Texas M.D. Anderson Cancer Center, Houston, Texas, the research team showed that the decrease in breast cancer incidence began in mid-2002 and leveled off after 2003. Comparing rates from 2001 and 2004 showed a decrease in annual age-adjusted incidence of 8.8 percent. The decrease occurred only in women over the age of 50 and was more evident in women with cancers that were estrogen receptor (ER) positive -- tumors that need estrogen in order to grow and multiply. The speed at which breast cancer rates declined after the WHI announcements may indicate that extremely small ER positive breast cancers may have stopped

The NEW ENGLAND JOURNAL of MEDICINE

Chlebowski NEJM 2009

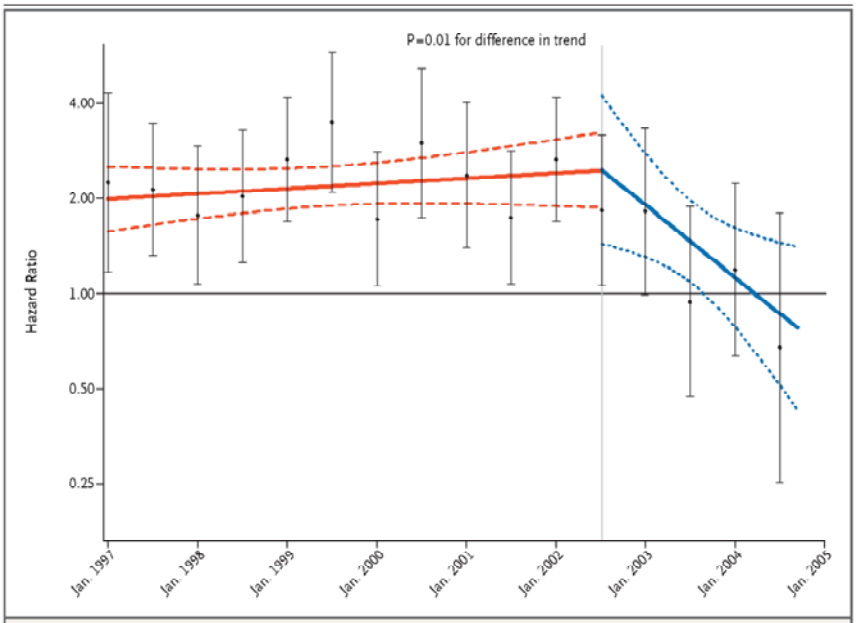

Figure 3. Adherence-Adjusted Effects over Time of Estrogen plus Progestin on the Risk of Breast Cancer in the WHI

REVIEW ARTICLE

ONLINE FIRST | LESS IS MORE

Principles of Conservative Prescribing

Gordon D. Schiff, MD; William L. Galanter, MD, PhD; Jay Duhig, MA; Amy E. Lodolce, PharmD, BCPS; Michael J. Kvoronkowski, PharmD; Bruce L. Lambert, PhD

Judicious prescribing is a prerequisite for safe and appropriate medication use. Based on evidence and lessons from recent studies demonstrating problems with widely prescribed medications, we offer a series of principles as a prescription for more cautious and conservative prescribing. These principles urge clinicians to (1) think beyond drugs (consider nondrug therapy, treatable underlying causes, and prevention); (2) practice more strategic prescribing (defer nonurgent drug treatment; avoid unwarranted drug switching; be circumspect about unproven drug uses; and start treatment with only 1 new drug at a time); (3) maintain heightened vigilance regarding adverse effects (suspect drug reactions; be aware of withdrawal syndromes; and educate patients to anticipate reactions); (4) exercise caution and skepticism regarding new drugs (seek out unbiased information; wait until drugs have sufficient time on the market; be skeptical about surrogate rather than true clinical outcomes; avoid stretching indications; avoid seduction by elegant molecular pharmacology; beware of selective drug trial reporting); (5) work with patients for a shared agenda (do not automatically accede to drug requests; consider nonadherence before adding drugs to regimen; avoid restarting previously unsuccessful drug treatment; discontinue treatment with unneeded medications; and respect patients' reservations about drugs); and (6) consider long-term, broader impacts (weigh long-term outcomes, and recognize that improved systems may outweigh marginal benefits of new drugs).

Arch Intern Med. 2011;171(16):1433-1440.
Published online June 13, 2011.
doi:10.1001/archinternmed.2011.256

In striving to relieve suffering and prolong life, we often turn to medications. Drugs are the therapy physicians most frequently deploy, with more than 60% of people younger than 65 years receiving a prescription drug each year.[1,2] It is often impossible for patients and physicians alike

messages and interests of the pharmaceutical industry, but there is an alternate paradigm that represents a radical shift in prescribing attitudes and behaviors. Ironically, the term we believe best describes this paradigm is *conservative prescribing*. Although

A. Think beyond drugs

- Consider, learn prescribe nondrug rx such as diet, exercise or physical therapy
- Look for and treat underlying causes rather than just masking symptoms with drugs
- Prevention rather than just treatment of advanced disease.

Thinking beyond drugs

- 1. Seek non-drug alternatives as a first rather than as a last resort.

Drugs: What else can you do

- *Hypertension*
- *Pain*
- *Insomnia*
- *Anxiety*
- *Worry*
- *Arthritis*
- *Overweight*
- *Lipids*
- *CHF*
- *Asthma*
- *Headaches*
- *Fatigue*
- *Neuropathy*
- *Infections*

Drugs: What else can you do?

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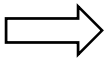
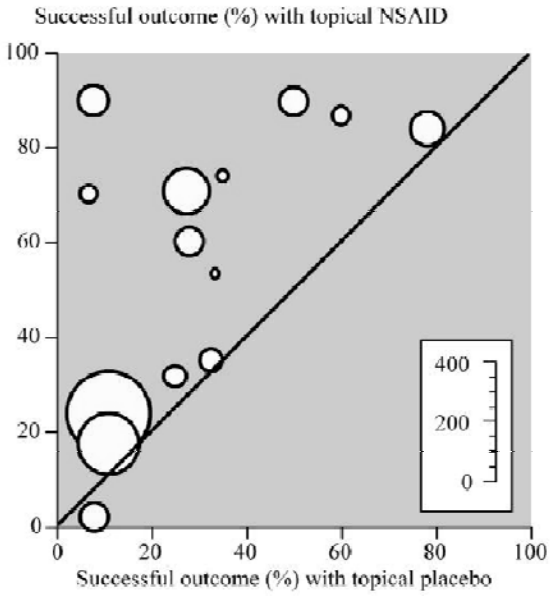


- Diet modification
- Exercise
- Lifestyle changes
- Supportive counseling
- Smoking cessation
- Meditation
- Orthotics
- Physical therapy
- Accupuncture
- Relationships
- Allergen removal
- Surgery
- Topical Rx



Topical NSAIDs in chronic musculoskeletal pain

Randomised double-blind studies of topical NSAID compared to topical placebo for two-week outcome of successful treatment. Inset scale shows size of individual trials

4 trials (1,502 patients)
Mean placebo response rate 26% (7%-78%)
Mean treatment response 48% (2%-90%)

Mason *et al. BMC Musculoskeletal Disorders* 2004

Thinking beyond drugs

- 2. Consider potentially treatable underlying causes of problems rather than just treating the symptoms with a drug.

Diagnose rather than mask sx

- "Arthritis" pain --?→ statin related
  --?→ celiac sprue
  --?→ work-related trauma
- Impotence --?→ pituitary tumor
  --?→ drug related
  --?→ marital discord
- Allergies --?→ environmental causes (plant, pet, shampoo)

Thinking beyond drugs

- 3. Look for opportunities for prevention rather than focusing on treating symptoms or advanced disease.

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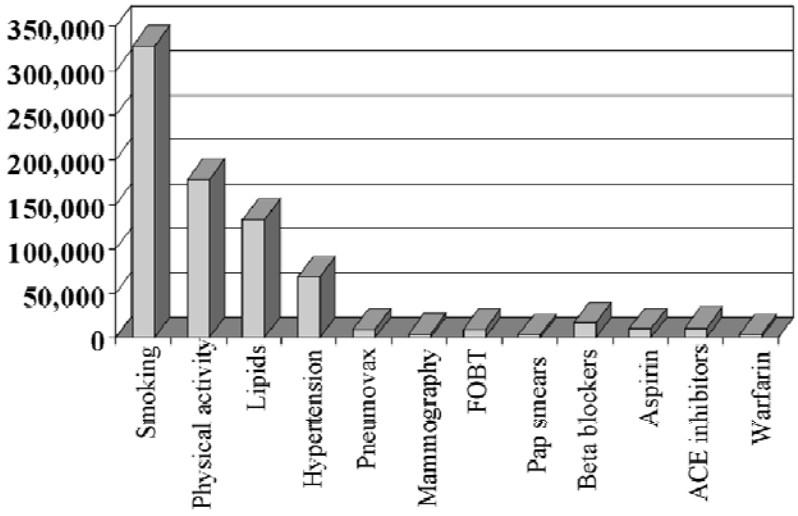
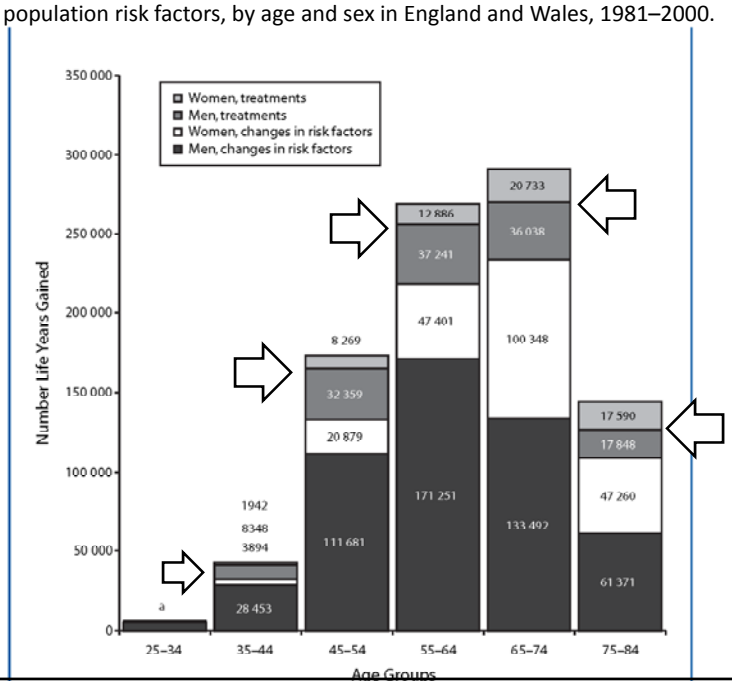


Potential Number of Lives Saved by Success in Primary Prevention

Adapted from: Woolf SH. The need for perspective in evidence-based medicine. JAMA 1999;282:2358-65.

Life-years gained from coronary heart disease treatments and changes in population risk factors, by age and sex in England and Wales, 1981–2000.



Unal Am J Public Health 2005

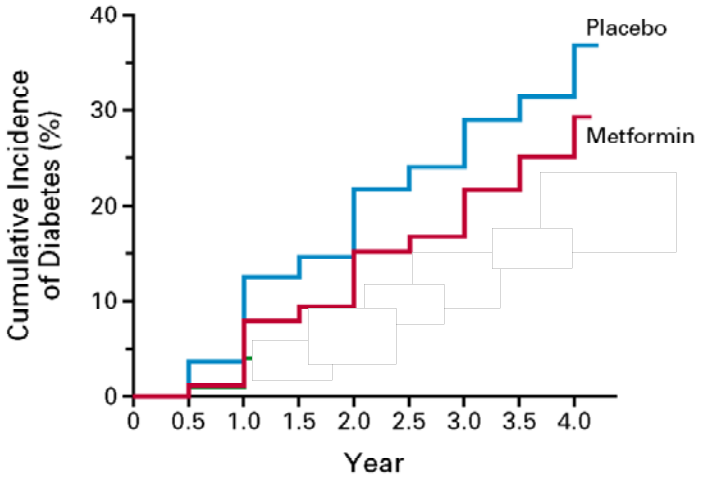
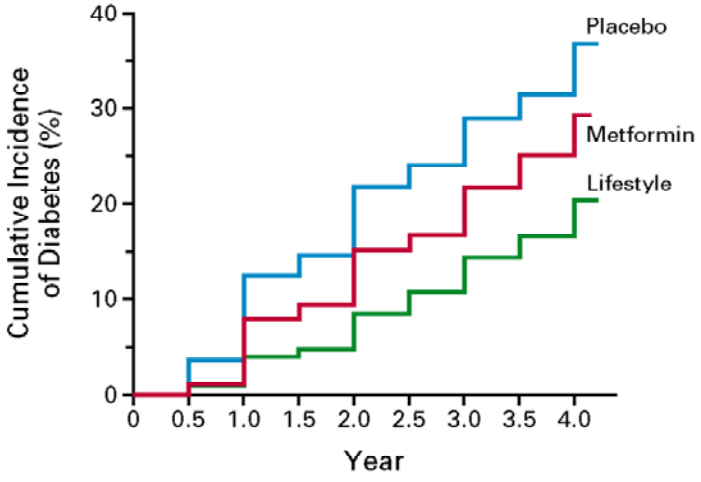


Figure 2. Cumulative Incidence of Diabetes According to Study Group.

The diagnosis of diabetes was based on the criteria of the American Diabetes Association.[11] The incidence of diabetes differed significantly among the three groups ($P<0.001$ for each comparison).

Diabetes Prevention Program Research Group. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *NEJM*, 346 (6), 393-403.



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B. More strategic prescribing

- Learn just a few drugs, learn well
- Defer drug treatment if drugs can be safely started after a trial of non-drug therapy
- Avoid frequent/unwarranted drug switching
- Be circumspect about unproven drug uses
- Whenever possible, start only 1 new drug

Practicing more strategic prescribing

- 4. Use the "test of time" as a diagnostic and therapeutic trial whenever possible

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Deferring to later time

- Reassurance and open door w/ option to start rx later
- When is this just as efficacious?
  - Otitis media w/ effusion
  - Sinusitis-even bacterial
  - Back-pain
  - Selected cancers
  - Need for research

IDSA GUIDEL

IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults

Anthony W. Chow,[1] Michael S. Benninger,[2] Itzhak Brook,[3] Jan L. Brozek,[4,5] Ellie J. C. Goldstein,[6,7] Lauri A. Hicks,[8] George A. Pankey,[9] Mitchel Seleznick,[10] Gregory Volturo,[11] Ellen R. Wald,[12] and Thomas M. File Jr[13,14]

[1]Division of Infectious Diseases, Department of Medicine, University of British Columbia, Vancouver, Canada; [2]Otolaryngology, The Head and Neck Institute, Cleveland Clinic, Ohio; [3]Department of Pediatrics, Georgetown University School of Medicine, Washington, D.C.; [4]Department of Clinical Epidemiology and Biostatistics and [5]Department of Medicine, McMaster University, Hamilton, Ontario, Canada; [6]Department of Medicine, David Geffen School of Medicine at the University of California, Los Angeles, [7]R. M. Alden Research Laboratory, Santa Monica, California; [8]National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; [9]Department of Infectious Disease Research, Ochsner Clinic Foundation, New Orleans, Louisiana; [10]Division of General Internal Medicine, University of South Florida College of Medicine, Tampa; [11]Department of Emergency Medicine, University of Massachusetts, Worcester; [12]Department of Pediatrics, University of Wisconsin School of Medicine and Public Health, Madison; [13]Department of Infectious Diseases, Northeast Ohio Medical University, Rootstown; and [14]Summa Health System, Akron, Ohio

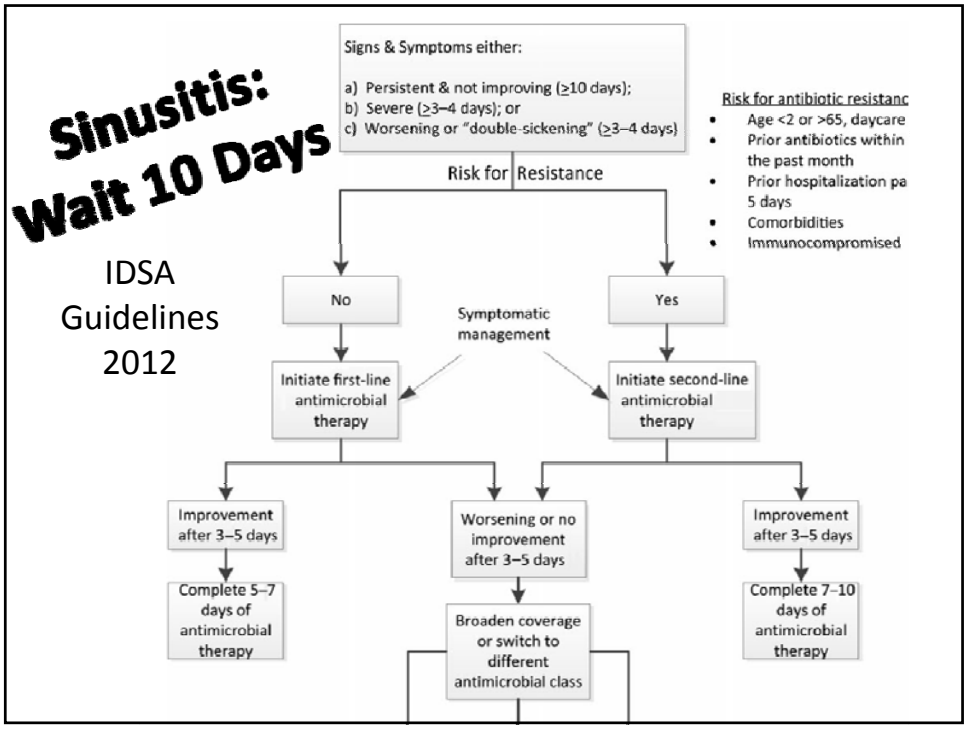
Evidence-based guidelines for the diagnosis and initial management of suspected acute bacterial rhinosinusitis in adults and children were prepared by a multidisciplinary expert panel of the Infectious Diseases Society of America comprising clinicians and investigators representing internal medicine, pediatrics, emergency medicine, otolaryngology, public health, epidemiology, and adult and pediatric infectious disease specialties. Recommendations for diagnosis, laboratory investigation, and empiric antimicrobial and adjunctive therapy were developed.

EXECUTIVE SUMMARY

management based on risk assessment for antimicrobial

Sinusitis: Wait 10 Days

IDSA Guidelines 2012



Practicing more strategic prescribing

- 5. Use only a few drugs and learn to use them well.

Learn a few drugs well

- Master dosing, adverse effects, interactions, even pill appearance prevents errors

Practicing more strategic prescribing

- 6. Avoid frequent or "impulse" switching of drugs without clear, compelling evidence-based reasons.

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Practicing more strategic prescribing

- 7. Be skeptical about "individualizing" therapy

"Individualized" therapy?

- Claim that results only apply to "average" patient, not yours
- Industry way to dismiss disappointing trials
- Ad hoc empiric unscientific trials fraught with error and hazards
- Yes, when drives precaution
  - Geriatric, liver disease, low literacy

Practicing more strategic prescribing

- 8. Whenever possible, start only one drug at a time.

Treat Everything at Once?

- HBP
- Headaches
- UTI
- Trichomonas
- Dyspepsia
- Onychomycosis

.....all on 1st visit

- How can you interpret adverse event?
- Even if improves: which drug to attribute
- Ignorance of drug-drug interactions (DDI)

- Fixed drug combinations a problem here?

C. Heightened vigilance for adverse effects:

- Suspect drug reactions when patients report problems
- Educate patients about side effects so they can anticipate and report reactions
- Be aware of dug withdrawal syndromes

Vigilance w/ adverse effects

- 9. Have high index of suspicion for adverse drug effects

Suspect new & old drug reactions

- No matter how weird or unlikely

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Suspect new & old drug reactions

- No matter how weird or unlikely
- Consider possibility that unreported
  - Heroes –discovery of ADRs not just of new drugs

Table 3. **Rates of Adverse Drug Events.***

Variable	Adverse Events	Event Rate
	no. (%)	*no./100 patients*
Total adverse drug events	181	27.4
Severity		
Fatal or life-threatening	0	—
Serious	24 (13)	3.6
Significant	157 (87)	23.8
Preventability		
Ameliorable	51 (28)	7.7
Preventable	20 (11)	3.0
Not preventable	110 (61)	16.6
Serious and preventable or ameliorable	11 (6)	1.7

Gandhi NEJM 2003

CEDR

Calling for Earlier Detection of Adverse Reactions

BRIGHAM AND WOMEN'S HOSPITAL

HARVARD MEDICAL SCHOOL

CERTs Centers for Education & Research on Therapeutics

AHRQ Agency for Healthcare Research and Quality
Advancing Excellence in Health Care • www.ahrq.gov

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Jose Figueroa MD, MPH (Resident)

Administrative/Support
Elissa Klinger, MS (Project Manager)

Generic Questions – All Medications

SINCE STARTING THE MEDICATION HAVE YOU HAD ANY NEW OR WORSENING PROBLEMS WITH:

- Stomach or intestinal problems?
  - *Nausea/vomiting*
  - *Diarrhea*
  - *Constipation*
  - *Stomach pain*
  - *Heartburn*
- Problems with memory or confusion?
  - *Memory problems*
  - *Confusion*
- Muscle aches?
- Skin rash?
- Dizziness or problems with balance?
- Frequent headaches?
- Problems with sexual function?
- Have you gained or lost more than 10 pounds?

54

Vigilance w/ adverse effects

- 10. Educate patients about possible adverse drug reactions to ensure they are recognized as early as possible.

Worry about drugs, not about warning patients

- MDs fail to discuss risks 65-91% of time
- Fears that would “scare off compliance” misguided and unfounded.
- Early recognition far outweighs risk of suggestion

Can MDS Warn of Potential Side Effects w/out Fear of Causing them?

- RCT discharge education for pts receiving scripts for ACE-I, NSAID, TMP/SMX
  - 2 intervention, 2 control firms U Wisc
- Interviewed by phone 14 days later
- No difference incidence targeted side effects between 2 groups (38% vs. 37%)

Lamb Arch Intern Med 1994

Vigilance w/ adverse effects

- 11. Be alert to clues that you may be treating withdrawal symptoms.

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Gastroenterology
OFFICIAL JOURNAL OF THE AGA INSTITUTE
GASTROENTEROLOGY 2009;137:80–87

CLINICAL—ALIMENTARY TRACT

Proton-Pump Inhibitor Therapy Induces Acid-Related Symptoms in Healthy Volunteers After Withdrawal of Therapy

CHRISTINA REIMER,* BO SØNDERGAARD,* LINDA HILSTED,‡ and PETER BYTZER*

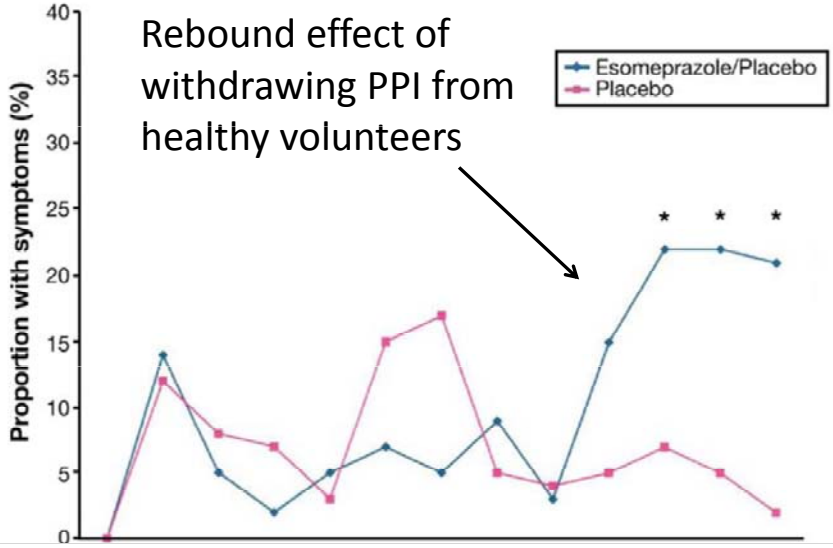
*Department of Medical Gastroenterology, Køge University Hospital, Copenhagen University; and the ‡Department of Clinical Biochemistry, Rigshospitalet, Copenhagen, Denmark

See related article, Arora G et al, on page 725 in *CGH*; see editorial on page 20.

BACKGROUND & AIMS: Rebound acid hypersecretion (RAHS) has been demonstrated after 8 weeks of treatment with a proton-pump inhibitor (PPI). If RAHS induces acid-related symptoms, this might lead to PPI dependency and thus have important implications. **METHODS:** A randomized, double-blind, placebo-controlled trial with 120 healthy

20 to 33 defined daily doses per 1,000 persons per day. In 2006, approximately 7% of the Danish population was treated with a PPI.[1] Although the incidence of new treatments with PPIs remains stable, the prevalence of long-term treatment is rising.[2] The reasons for the increasing long-term use are not fully understood.

Treatment with PPIs is initiated mainly by primary care physicians, usually as empirical therapy for dyspeptic symptoms. Empirical PPI therapy for ≥4 weeks in patients with uninvestigated dyspepsia is supported by dys-



REIMER, GASTROENTEROLOGY 2009

Table 3. Comparison of Proportion With Heartburn, Acid Regurgita

Week	PPI (n = 59)	Placebo (n = 59)
0	0% (0/59)	0% (0/60)
8	3.4% (2/59)	3.5% (2/57)
9	15.3% (9/59)	5.1% (3/59)
10	22.0% (13/59)	6.8% (4/59)
11	22.0% (13/59)	5.1% (3/59)
12	20.7% (12/58)	1.7% (1/59)

NOTE. Score >2 corresponding to symptoms causing at least mild discon

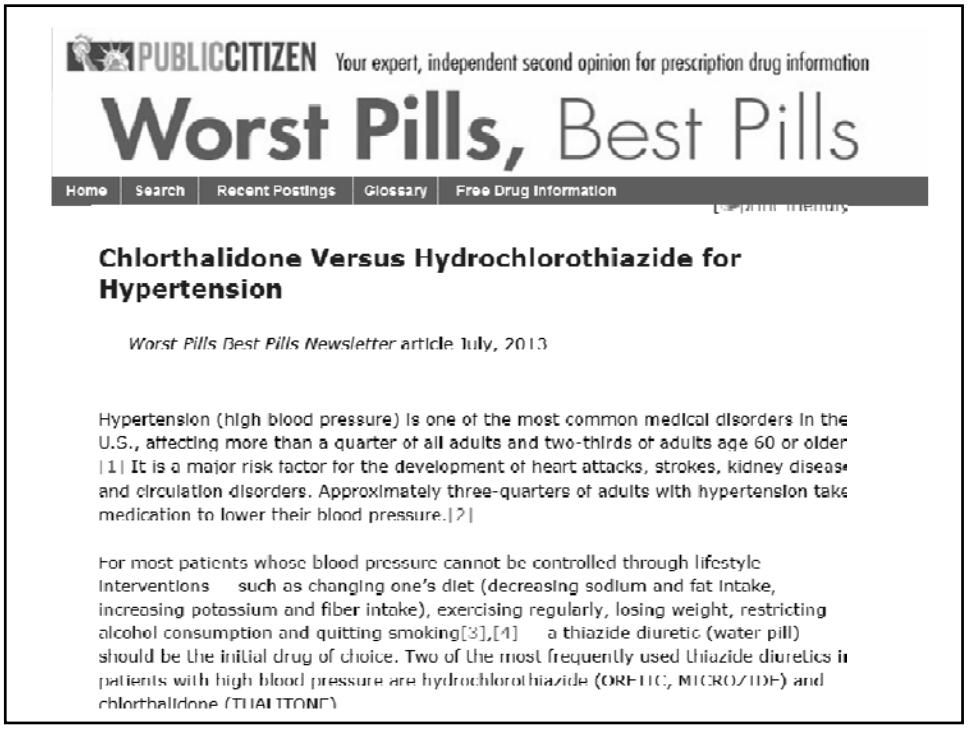
REIMER, GASTROENTEROLOGY 2009

D. Caution/skepticism new drugs:

- Seek out, use unbiased info sources
- Wait until drugs have sufficient time on market to be proven to be safe
- Be skeptical about surrogate markers of benefit (such as improving a lab test)
- Avoid stretching indications to pt or diseases different than those in trials
- Avoid seduction by elegant molecular pharmacology w/out proven benefits
- Beware of trial selective reporting.

Skepticism towards new drugs

- 12. Learn about new drugs and new indications from trustworthy, unbiased sources, independent drug bulletins, and colleagues with reputations for integrity and conservative prescribing.



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Worst Pills, Best Pills

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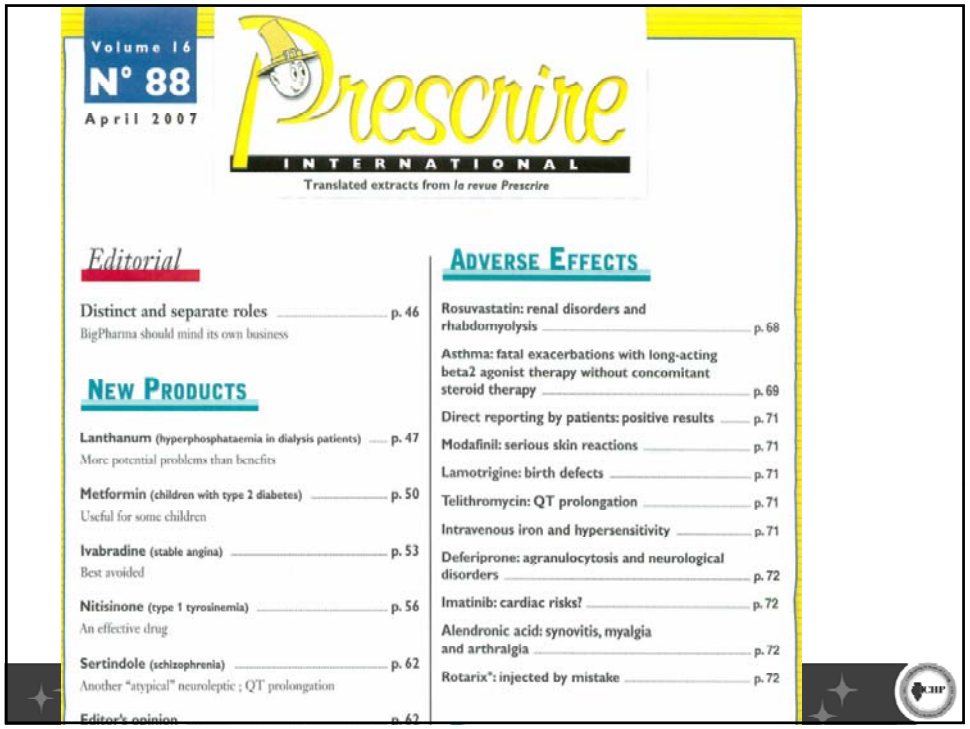
Chlorthalidone Versus Hydrochlorothiazide for Hypertension

Worst Pills Best Pills Newsletter article July, 2013

Hypertension (high blood pressure) is one of the most common medical disorders in the U.S., affecting more than a quarter of all adults and two-thirds of adults age 60 or older [1] It is a major risk factor for the development of heart attacks, strokes, kidney disease and circulation disorders. Approximately three-quarters of adults with hypertension take medication to lower their blood pressure.[2]

For most patients whose blood pressure cannot be controlled through lifestyle interventions such as changing one's diet (decreasing sodium and fat intake, increasing potassium and fiber intake), exercising regularly, losing weight, restricting alcohol consumption and quitting smoking[3],[4] a thiazide diuretic (water pill) should be the initial drug of choice. Two of the most frequently used thiazide diuretics in patients with high blood pressure are hydrochlorothiazide (ORETIC, MICROZIDE) and chlorthalidone (THALITONE)



Volume 16
N° 88
April 2007

Prescrire
INTERNATIONAL
Translated extracts from *la revue Prescrire*

Editorial

NEW PRODUCTS

ADVERSE EFFECTS

23 Years Ratings New Drug "Advances"

by Prescrire (1981-2003)

Rating	#	%
Bravo	7	0.2%
A real advance	77	2.7%
Offers an advantage	217	7.6%
Possibly helpful	455	15.8%
Nothing new	1,913	66.6%
Not acceptable	80	2.8%
Judgment reserved	122	4.2%
Total	2,871	100

Prescrire's ratings of new products and indications over the last 10 years

Prescrire's ratings of new products and indications over the last 10 years (a)										
PRESCRIRE'S RATING	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Bravo	0	0	0	1	1	0	0	0	0	0
A real advance	4	0	1	1	2	0	0	1	0	1 (b)
Offers an advantage	5	6	4	8	14	6	3	3	3	3 (c)
Possibly helpful	23	12	20	31	27	25	14	22	13	14
Nothing new	34	41	38	69	79	57	62	49	53	42
Not acceptable	7 (d)	7	19	17	15	23	19	19	16	15 (e)
Judgement reserved	6	4	2	8	3	9	6	3	7	7 (f)
Total	79	70	84	135	141	120	104	97	92	82

Skepticism towards new drugs

- 13. Even if seemingly safer or more effective for a particular indication, don't be in a rush to use new drugs.

ORIGINAL CONTRIBUTION

Timing of New Black Box Warnings and Withdrawals for Prescription Medications

Karen E. Lasser, MD, MPH
Paul D. Allen, MD, MPH
Steffie J. Woolhandler, MD, MPH
David U. Himmelstein, MD
Sidney M. Wolfe, MD
David H. Bor, MD

Context Recently approved drugs may be more likely to have unrecognized adverse drug reactions (ADRs) than established drugs, but no recent studies have examined how frequently postmarketing surveillance identifies important ADRs.

Objective To determine the frequency and timing of discovery of new ADRs described in black box warnings or necessitating withdrawal of the drug from the market.

Design and Setting Examination of the *Physicians' Desk Reference* for all new chemical entities approved by the US Food and Drug Administration between 1975 and 1999, and all drugs withdrawn from the market between 1975 and 2000 (with or without a prior black box warning).

Main Outcome Measures Frequency of and time to a new black box warning or drug withdrawal.

Results A total of 548 new chemical entities were approved in 1975-1999; 56 (10.2%) acquired a new black box warning or were withdrawn. Forty-five drugs (8.2%) acquired 1 or more black box warnings and 16 (2.9%) were withdrawn from the market. In Kaplan-Meier analyses, the estimated probability of acquiring a new black box warning or being withdrawn from the market over 25 years was 20%. Eighty-one major changes to drug labeling in the *Physicians' Desk Reference* occurred including the addition of 1 or more black box warnings per drug, or drug withdrawal. In Kaplan-Meier analyses, half of these changes occurred within 7 years of drug introduction; half of the withdrawals occurred within 2 years.

Conclusions Serious ADRs commonly emerge after Food and Drug Administration approval. The safety of new agents cannot be known with certainty until a drug has been on the market for many years.

ADVERSE DRUG REACTIONS (ADRs) are believed to be a leading cause of death in the United States.[1] Prior to approval, drugs are studied in selected populations[2,3] for limited periods, possibly contributing to an increased risk of ADRs after approval. Pharmaceutical companies frequently market new drugs heavily to both patients and clinicians before the full range of ADRs is ascertained. Inadequate clinician reporting may delay detection of postmarketing ADRs; less than 10% of all

Skepticism towards new drugs

- 14. Be certain the drug actually improves patient-centered clinical outcomes, rather than just treating or masking a "surrogate marker."

Surrogate Endpoints

- Blood pressure
- HbA1C
- Serum Glucose
- Serum cholesterol
- HDL
- Hemoglobin
- PVC's
- Cardiac output
- Serum Sodium
- CD4 count
- HIV Viral Load
- FEV1
- Albuminuria
- Tumor markers
- Tumor size
- Composites

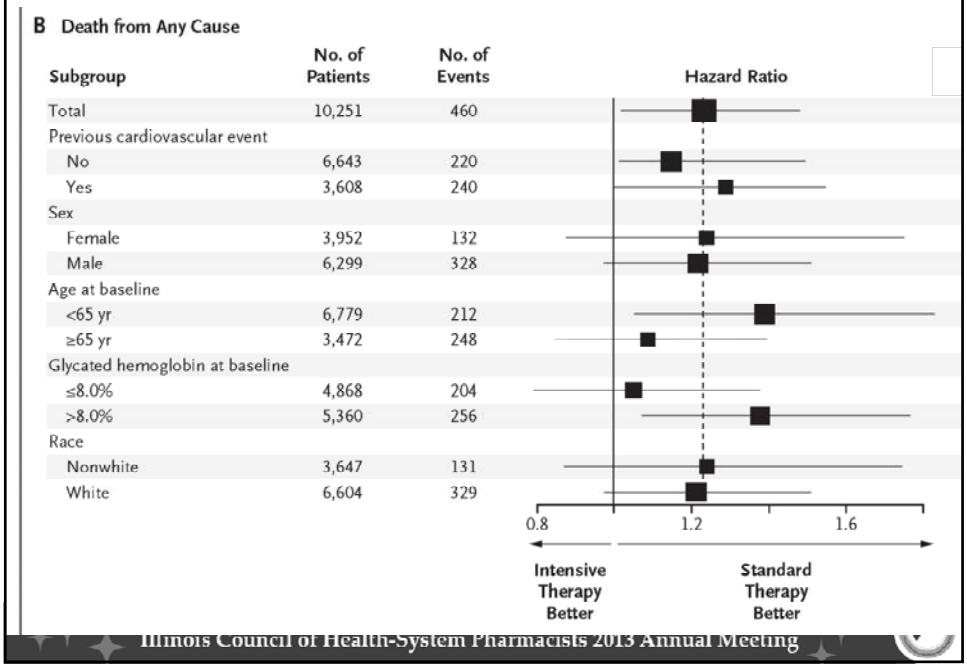
Clinically Relevant Endpoints

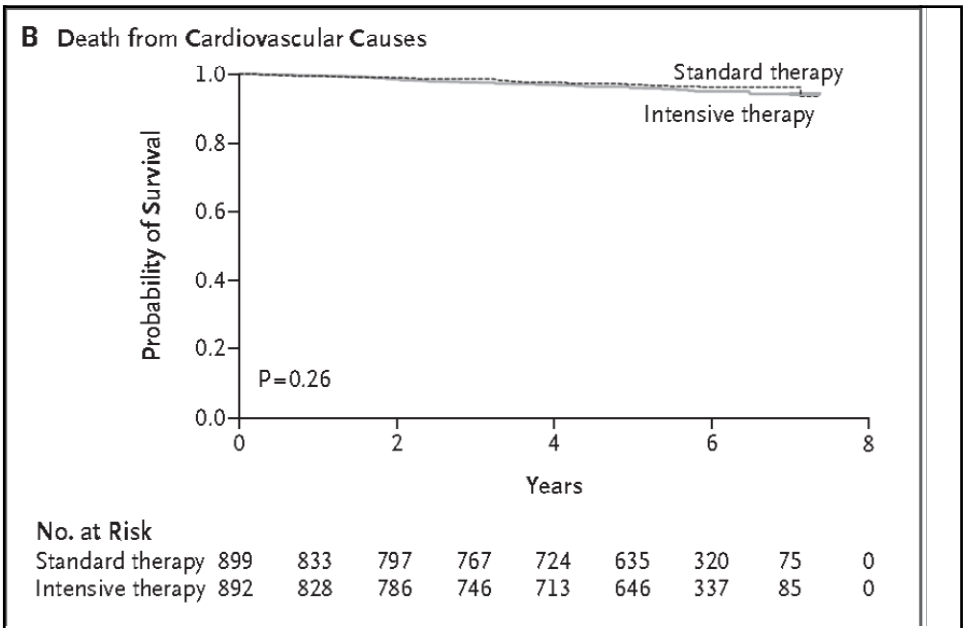
- Mortality or survival benefit
- Clinically important change experienced directly by the patient
  - Reduced pain
  - Improved functional status
  - Improved quality of life

CAST	Suppression PVCs increased risk of sudden death
CONCORDE	Improving CD4 w/ AZT did not improve HIV pts' survival
CHOIR and CREATE	Higher Hb levels w/ erythropoietin worsened dialysis pts outcomes
ENHANCE	Vytorin combination more effective in lowering lipids but no clinical benefit

ACCORD	More intensive A1C lowering worsened outcomes in type 2 DM; Increased risk death overall and CV
ADVANCE	Tighter control did not reduce cardiovascular events
VADT	No significant decrease CV events with tighter glucose control over 7.5 yrs
NICE-SUGAR	Intense glucose control increased mortality in adult ICU patients.

ACCORD Trial NEJM 6/12/08





VADT Trial NEJM 1/8/2009

Table 2. **Hypoglycemic Episodes.***

Variable	Standard Therapy (N=899)	Intensive Therapy (N=892)
	no./100 patient-yr	
Episodes with impaired consciousness	3	9
Episodes with complete loss of consciousness	1	3
Nocturnal episodes	44	152
Total episodes		
With symptoms	383	1333
Without symptoms	49	233
Relieved by food or sugar intake	421	1516
Measurement of blood glucose during episode	348	1392
With documented blood glucose <50 mg/dl (2.8 mmol/liter)	52	203

* P<0.001 for all differences between the two groups.

HEALTH AFFAIRS
The Policy Journal of the Health Sphere

ACCELERATED APPROVAL

Surrogate Endpoints And FDA's Accelerated Approval Process

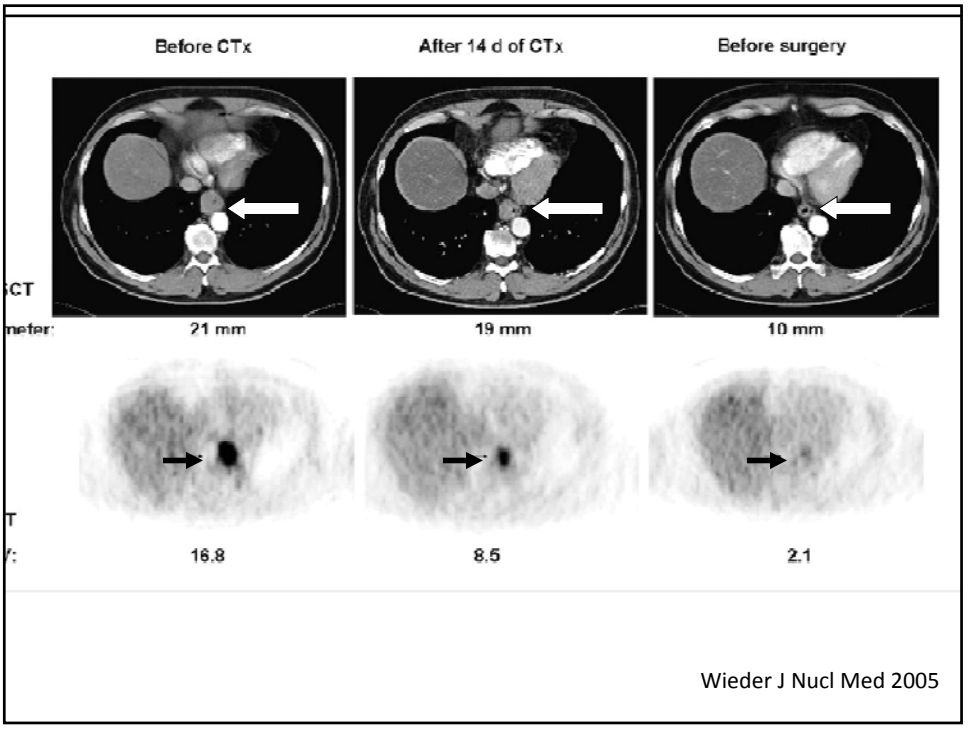
The challenges are greater than they seem.

by Thomas R. Fleming

ABSTRACT: There is interest in approaches allowing more rapid availability of new interventions, particularly for diseases providing risks of death or serious illness. The accelerated-approval regulatory process is intended to address this need by allowing marketing of interventions shown to have strong effects on measures of biological activity, if those measures are potential "surrogates" for true measures of tangible clinical benefit. To use surrogate endpoints and the accelerated-approval process, challenging issues must be addressed to avoid compromising what is truly in the best interest of public health: the reliable as well as timely evaluation of an intervention's safety and efficacy.

Current FDA issues with Regulation of Surrogate Endpoints

- **Cancer Drugs: Objective Response Rate (ORR)**
- **Accelerated approval** (1992)
  - Formal acceptance of surrogates
  - Endpoints "reasonably likely to predict clinical benefit"
  - Early marketing approval contingent upon post-marketing studies confirming clinical benefit



Wieder J Nucl Med 2005

Table 1. Accelerated approvals based on randomized trials* JNCI 2011

Product	Date of accelerated approval	Indication	Accelerated approval end
Dexrazoxane (Zinecard)†	May 26, 1995	Cardiac protection	Cardiomyopathy
Bicalutamide (Casodex)	October 4, 1995	Stage D2‡ prostate cancer in combination with LHRH	Time to progression
Liposomal cytarabine (DepoCyt)	April 1,1999	Lymphomatous meningitis	Response rate
Celecoxib (Celebrex)	December 23, 1999	Reduction in polyps in FAP	Incidence rate
Ibritumomab (Zevalin)	February 19, 2002	Relapsed or refractory low-grade or follicular lymphoma	Response rate
Oxaliplatin (Eloxatin)	August 9, 2002	Second-line therapy for metastetic colorectal cancer in combination with FU/LV	Response rate
Anastrozole (Arimidex)†	September 5, 2002	Adjuvant treatment for postmenopausal HR-positive breast cancer	Disease-free survival
Imatinib (Gleevec)†	December 20, 2002	First-line therapy for Ph-positive CML	Progression-free survi
Pemetrexed (Alimta)	August 19, 2004	Second-line therapy for NSCLC	Response rate
Letrozole (Femara)†	October 29, 2004	Adjuvant treatment for post menopausal HR-positive breast cancer after tamoxifen	Disease-free survival
Letrozole (Femara)†	December 28, 2005	Adjuvant treatment for post menopausal HR-positive breast cancer	Disease-free survival
Thalidomide (Thalomid)	May 25, 2006	Newly diagnosed multiple myeloma	Response rate
Panitumumab (Vectibix)	September 27, 2006	Second-line therapy for EGFR-expressing metastatic colorectal cancer	Progression-free survi
Bevacizumab (Avastin)	February 22, 2008	First-line therapy in combination with chemotherapy for metastatic HER2-negative breast cancer	Progression-free survi
Pemetrexed (Alimta)	September 29, 2008	First-line therapy in combination with cisplatin for nonsquamous NSCLC	Response rate
Eltrombopag (Promacta)	November 20, 2008	Refractory ITP	Response rate
Imatinib (Gleevec)	December 19, 2008	Adjuvant treatment for GIST	Disease-free survival
Lapatinib (Tykerb)	January 29, 2010	In combination with letrozole in postmenopausal women with HR-positive, HER2-positive metastatic breast cancer for whom hormonal therapy is indicated	Progression-free survi
Nilotinib (Tasigna)	June 17, 2010	Newly diagnosed Ph-positive CML in chronic phase	Response rate

Table 2. Accelerated approval based on single-arm trials* JNCI 2011

Product	Date of accelerated approval	Indication	Accelerated approval endpoint(s)
Liposomal doxorubicin (Doxil)	November 17, 1995	Second-line therapy for Kaposi sarcoma	Response rate
Amifosine (Ethyol)†	March 15, 1996	Cisplatin-associated renal toxicity in patients with non–small cell lung cancer	Creatinine clearanc
Docetaxel (Taxotere)	May 14, 1996	Second-line therapy for advanced breast cancer	Response rate
Irinotecan (Camptosar)	June 14, 1996	Second-line therapy for metastatic colorectal cancer	Response rate
Capecitabine (Xeloda)	April 30, 1998	Refractory breast cancer	Response rate
Denileukin (Ontak)	February 5, 1999	Refractory CTCL	Response rate
Liposomal doxorubincin (Doxil)	June 28, 1999	Refractory ovarian cancer	Response rate
Temozolomide (Temodar)	August 11, 1999	Refractory anaplastic astrocytoma	Response rate
Gemtuzumab ozogamicin (Mylotarg)	May 17, 2000	Second-line therapy for AML in patients older than 60 y	Response rate
Alemtuzumab (Campath)	May 7, 2001	Third-line therapy for B-cell CLL	Response rate
Imatinib (Gleevec)	May 10, 2001	First-line therapy for Ph-positive CML (BC, AP) or refractory CML chronic phase	Response rate
Imatinib (Gleevec)	February 1, 2002	First-line therapy for GIST	Response rate
Gefitinib (Iressa)	May 5, 2003	Third-line therapy for NSCLC	Response rate
Bortezomib (Velcade)	May 13, 2003	Third-line therapy for multiple myeloma	Response rate
Imatinib (Gleevec)	May 20, 2003	Pediatric Ph-positive CML resistant to interferon or recurrence after stem cell transplant	Response rate
Cetuximab (Erbitux)	February 12, 2004	As a single agent for treatment of EGFR-expressing, metastatic CRC in patients who are intolerant to irinotecan-based chemotherapy	Response rate
Cetuximab (Erbitux)	February 12, 2004	In combination with irinotecan in EGFR-expressing metastatic CRC refractory to irinotecan-based chemotherapy	Response rate
Tositumomab (Bexxar)	December 22, 2004	Refractory or relapsed low-grade follicular lymphoma not treated with rituximab	Response rate
Clofarabine (Clolar)	December 28, 2004	Pediatric relapsed or refractory ALL	Response rate
Nelarabine (Arrnon)	October 28, 2005	Relapsed or refractory T-cell ALL or T-cell lymphoblastic lymphoma	Response rate

Table 4. Accelerated approvals not converted to regular approval* JNCI 2011

Product	Date of accelerated approval	Indication	Comment
Amifosine (Ethyol)	March 15, 1996	Cisplatin-associated renal toxicity in patients with non–small cell lung cancer	Failed demonstration of clinical benefit in completed trial. Indication withdrawn from the market.
Celecoxib (Celebrex)	December 23, 1999	Reduction in polyps in FAP	Confirmatory trial not completed
Gemtuzumab ozogamicin (Mylotarg)	May 17, 2000	Second-line therapy for acute myelogenous leukemia in patients older than 60 y	Failed demonstration of clinical benefit in completed trials. Drug withdrawn from the market
Gefitinib (Iressa)	May 5, 2003	Third-line therapy for non–small cell lung cancer	Failed demonstration of clinical benefit in completed trials. Limited to restricted patient distribution
Cetuximab (Erbitux)	February 12, 2004	In combination with irinotecan in EGFR-expressing metastatic colorectal cancer refractory to irinotecan-based chemotherapy	Confirmatory trial not completed
Tositumomab (Bexxar)	December 22, 2004	Refractory or relapsed low-grade follicular lymphoma not treated with rituximab	Confirmatory trial not completed
Clofarabine (Clolar)	December 28, 2004	Pediatric relapsed or refractory ALL	Confirmatory trial not completed
Nelarabine (Arrnon)	October 28, 2005	Relapsed or refractory T-cell ALL or T-cell lymphoblastic lymphoma	Confirmatory trial not completed
Thalidomide (Thalomid)	May 25, 2006	Newly diagnosed multiple myeloma	Under FDA review
Panitumumab (Vectibix)	September 27, 2006	Second-line therapy for EGFR-expressing metastatic colorectal cancer	Confirmatory trial not completed
Imatinib Gleevec	September 27, 2006	Pediatric Ph-positive CML (newly diagnosed)	Under FDA review
Nilotinib (Tasigna)	October 29, 2007	Ph-positive CML chronic phase or accelerated phase resistant or intolerant to imatinib	Under FDA review
Bevacizumab (Avastin)	February 22, 2008	First-line therapy in combination with chemotherapy for metastatic HER2-negative breast cancer	Under FDA review
Eltrombopag (Promacta)	November 20, 2008	Refractory idiopathic thrombocytopenic purpura	Confirmatory trial not completed
Fludarabine (Oforta)	December 18, 2008	B-cell CLL after at least one alkylating agent–containing regimen	Confirmatory trial not completed
Imatinib (Gleevec)	December 19, 2008	Adjuvant treatment for GIST	Confirmatory trial not completed
Bevacizumab (Avastin)	May 5, 2009	Glioblastoma progression after chemotherapy	Confirmatory trial not completed
Pralatrexate (Folotyn)	September 24, 2009	Refractory or relapsed peripheral T-cell	Confirmatory trial not completed

Skepticism towards new drugs

- 15. Be vigilant about "indications creep."

Creeping Indications
Creeping Populations

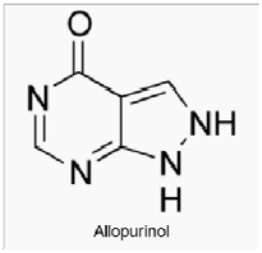
- What is precise *population studied* and *therapeutic niche*
- Not just triptans for headaches, neurontin for pain
- When should these drugs be used

Skepticism towards new drugs

- 16. Do not be seduced by elegant molecular pharmacology or drug physiology.

Designer drugs

- Allopurinol – 1st designer drug. No side effects since natural purine analogue



Allopurinol

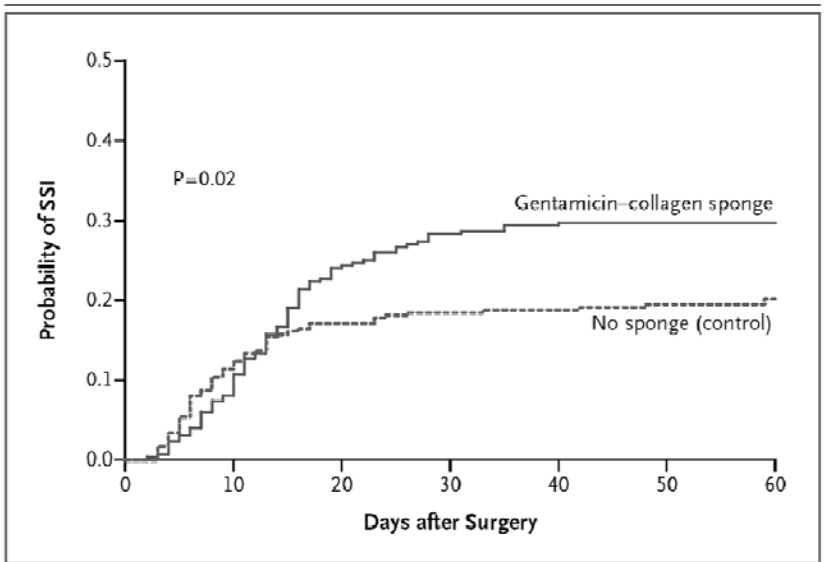


Figure 2. Kaplan–Meier Estimates of the Number of Days from Surgery to Surgical-Site Infection (SSI) within the 60-Day Postoperative Period, According to Study Group.

Table 3. **Surgical-Site Infection (SSI) and Other Postoperative End Points through Postoperative Day 60, According to Study Group.***

Characteristic	Gentamicin–Collagen Sponge (N=300)	Control (N=302)	P Value
Intention-to-treat analysis			
SSI — no. of patients (%)			
Any (primary end point)	90 (30.0)	63 (20.9)	0.01
Surgically treated	71 (23.7)	49 (16.2)	0.02
Superficial	61 (20.3)	41 (13.6)	0.03
Deep	25 (8.3)	18 (6.0)	0.26
Organ space	4 (1.3)	4 (1.3)	1.00
ASEPSIS score†			0.17
Median	0.0	0.0	
IQR	0.0–10.0	0.0–4.0	
Rehospitalization for SSI — no. of patients (%)	21 (7.0)	13 (4.3)	0.15
Visit to ER or physician for wound-related sign or symptom — no. of patients/total no. (%)	57 (19.7)	31 (11.0)	0.004
Postoperative hospital length of stay — days	6.0 (5.0–8.0)	6.0 (4.0–8.0)	0.44
Median			
IQR			

Skepticism towards new drugs

- 17. Beware of selective reporting of studies.

Gastrointestinal Toxicity With Celecoxib vs Nonsteroidal Anti-inflammatory Drugs for Osteoarthritis and Rheumatoid Arthritis

The CLASS Study: A Randomized Controlled Trial

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Lee S. Simon, MD
Theodore Pincus, MD
Andrew Whelton, MD
Robert Makuch, PhD
Glenn Eisen, MD
Naurang M. Agrawal, MD
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William W. Zhao, PhD
Jeffrey D. Kent, MD
James B. Lefkowith, MD
Kenneth M. Verburg, PhD
G. Steven Geis, PhD, MD

Context Conventional nonsteroidal anti-inflammatory drugs (NSAIDs) are associated with a spectrum of toxic effects, notably gastrointestinal (GI) effects, because of inhibition of cyclooxygenase (COX)-1. Whether COX-2–specific inhibitors are associated with fewer clinical GI toxic effects is unknown.

Objective To determine whether celecoxib, a COX-2–specific inhibitor, is associated with a lower incidence of significant upper GI toxic effects and other adverse effects compared with conventional NSAIDs.

Design The Celecoxib Long-term Arthritis Safety Study (CLASS), a double-blind, randomized controlled trial conducted from September 1998 to March 2000.

Setting Three hundred eighty-six clinical sites in the United States and Canada.

Participants A total of 8059 patients (≥18 years old) with osteoarthritis (OA) or rheumatoid arthritis (RA) were enrolled in the study, and 7968 received at least 1 dose of study drug. A total of 4573 patients (57%) received treatment for 6 months.

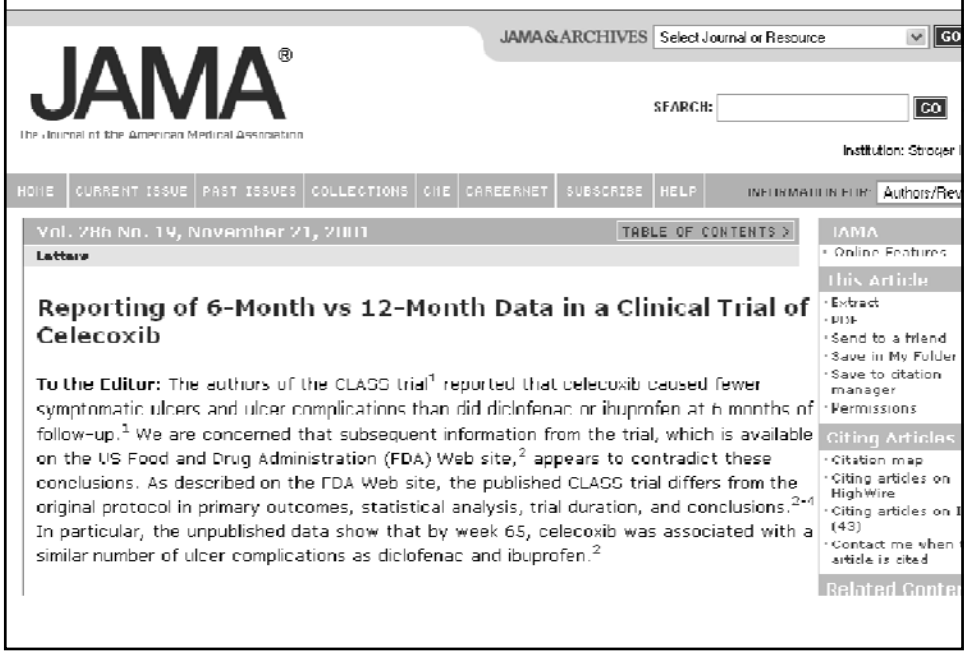
Interventions Patients were randomly assigned to receive celecoxib, 400 mg twice per day (2 and 4 times the maximum RA and OA dosages, respectively; n=3987); ibuprofen, 800 mg 3 times per day (n=1985); or diclofenac, 75 mg twice per day (n=1996). Aspirin use for cardiovascular prophylaxis (≤325 mg/d) was permitted.

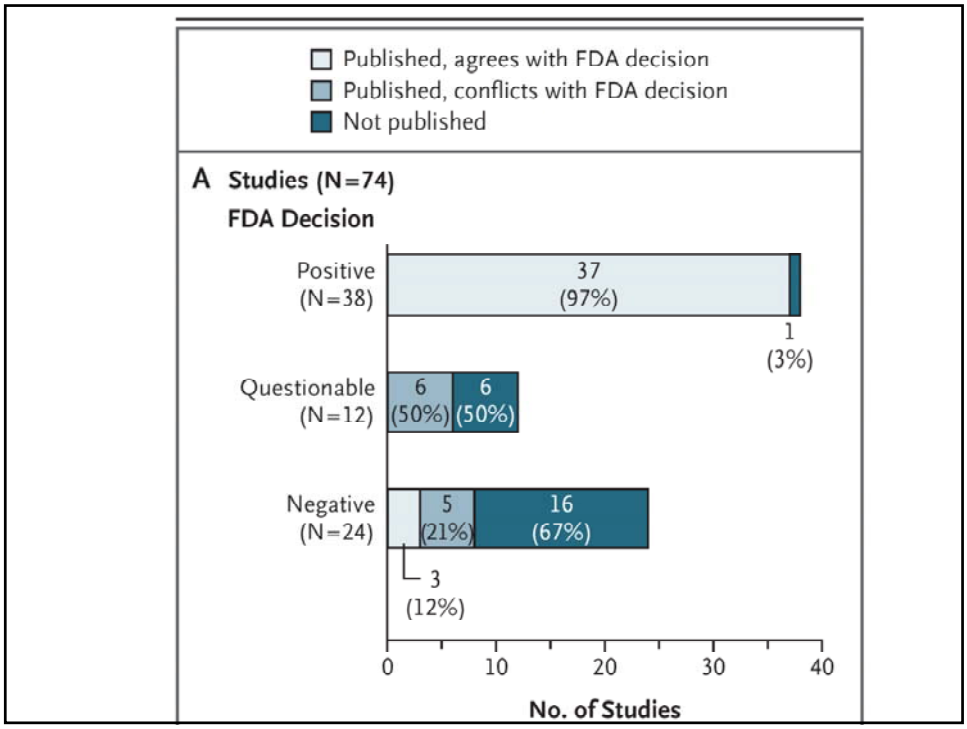
Main Outcome Measures Incidence of prospectively defined symptomatic upper GI ulcers and ulcer complications (bleeding, perforation, and obstruction) and other adverse effects during the 6-month treatment period.

Results For all patients, the annualized incidence rates of upper GI ulcer complications alone and combined with symptomatic ulcers for celecoxib vs NSAIDs were 0.76% vs 1.45% (P=.09) and 2.08% vs 3.54% (P=.02), respectively. For patients not taking aspirin, the annualized incidence rates of upper GI ulcer complications alone and combined with symptomatic ulcers for celecoxib vs NSAIDs were 0.44% vs 1.27% (P=.04) and 1.40% vs 2.91% (P=.02). For patients taking aspirin, the annualized incidence rates of upper GI ulcer complications alone and combined with symptomatic ulcers for celecoxib vs NSAIDs were 2.01% vs 2.12% (P=.92) and 4.70% vs 6.00% (P=.49). Fewer celecoxib-treated patients than NSAID-treated patients experienced chronic GI blood loss, GI intolerance, hepatotoxicity, or renal toxicity. No difference was noted in the incidence of cardiovascular events between celecoxib and NSAIDs, irrespective of aspirin use.

FOR PATIENTS WITH MUSCULOskeletal disorders, conventional nonsteroidal anti-inflammatory drugs (NSAIDs) are a mainstay of clinical care.[1-3] Well-established limitations of NSAID therapy, however, include the risk of developing significant injury to the upper gastrointestinal (GI) tract.[4-10] The

Silverstein, F. et al. (2000). Gastrointestinal toxicity with Celocoxib vs NSAIDs for osteoarthritis and rheumatoid arthritis. *JAMA*, 284,1247-1255.





E. Work w/pts for shared agenda

- Do not automatically accede to requests for drugs pt heard advertised
- Consider non adherence before adding rx
- Avoid restarting previously unsuccessful drugs
- Discontinue meds not needed; not working
- Respect pt' own reservations about drugs

Work w/ patient for a shared agenda

- 18. Do not hastily or uncritically succumb to patient requests for drugs, especially drugs they have heard advertised.

Work w/ patient for a shared agenda

- 19. Avoid mistakenly prescribing additional drugs for "refractory" problems, failing to appreciate the potential for patient nonadherence.

Drugs don't work in patients who don't take them.
— C. Everett Koop, M.D.

Intensifying Therapy for Hypertension Despite Suboptimal Adherence

Adam J. Rose, Dan R. Berlowitz, Meredith Manze, Michelle B. Orner, Nancy R. Kressin

bstract—More intensive management can improve control blood pressure (BP) in hypertensive patients. However, many would posit that treatment intensification (TI) is not beneficial in the face of suboptimal adherence. We investigated whether the effect of TI on BP varies by adherence. We enrolled 819 patients with hypertension, managed in primary care at an academically-affiliated inner-city hospital. We used the following formula to characterize TI: (visits with a medication change−visits with elevated BP)/total visits. Adherence was characterized using electronic monitoring devices ("MEMS caps"). Patients who returned their MEMS caps (671) were divided into quartiles of adherence, whereas patients who did not return their MEMS caps (148) had "missing" adherence. We examined the relationship between TI and the final systolic blood pressure (SBP), controlling for patient-level covariates. In the entire sample, each additional therapy increase per 10 visits predicted a 2.0 mm Hg decrease in final SBP ($P<0.001$). After stratifying by adherence, in the "best" adherence quartile each therapy increase predicted a 2.1-mm Hg decrease in final SBP, followed by 1.8 for the "next-best" adherence quartile, 2.3 in the third quartile, and 2.4 in the "worst" adherence quartile. The effect size for patients with "missing" adherence was 1.6 mm Hg. The differences between the group with "best" adherence and the other 4 groups were not statistically significant. In this observational study, treatment intensification was associated with similar BP improvement regardless of the patient's level of adherence. A randomized trial could further examine optimal management of patients with suboptimal adherence. (***Hypertension*. 2009;54:524-529.)**

Key Words: hypertension ■ adherence ■ medication therapy management ■ quality of care ■ ambulatory care

Importance of Therapy Intensification and Medication Nonadherence for Blood Pressure Control in Patients With Coronary Disease

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Background: Despite the importance of blood pressure (BP) control in secondary prevention, a significant proportion of patients with coronary disease have uncontrolled BP.

Methods: This retrospective cohort study of patients with coronary disease (N=10 447) evaluated the impact of medication nonadherence and therapy intensification on reaching target BP goals. Medication adherence was calculated as the proportion of days covered for filled prescriptions of antihypertensive medications. Therapy intensification included dosage increase or increase in number of antihypertensive medications. The primary outcome was uncontrolled systolic BP (SBP) over time, using a latent class model that incorporated longitudinal SBP data and assigned patients to SBP trajectory groups. Multivariable regression evaluated the association between medication nonadherence (ie, proportion of days covered, <0.80) and therapy intensification with SBP control over time, with adjustment for demographics and clinical characteristics.

Results: Three SBP trajectory groups were identified: (1) patients with BP that remained controlled (ie, SBP, ≤140 mm Hg) over time (n=9114 [87.2%]), (2) patients with high BP that became controlled (n=779 [7.5%]), and (3) patients with BP that remained high over time (n=554 [5.3%]). In multivariable analyses, therapy intensification (odds ratio, 1.31; 95% confidence interval, 1.01-1.70) and medication nonadherence (odds ratio, 1.73; 95% confidence interval, 1.34-2.24) were associated with uncontrolled BP compared with high SBP that became controlled over time.

Conclusions: These findings suggest that medication nonadherence can help explain why BP levels remained elevated despite intensification of antihypertensive medications. Successful BP control is seen with a combination of intensification and adherence, suggesting that therapy intensification must be coupled with interventions to enhance medication adherence.

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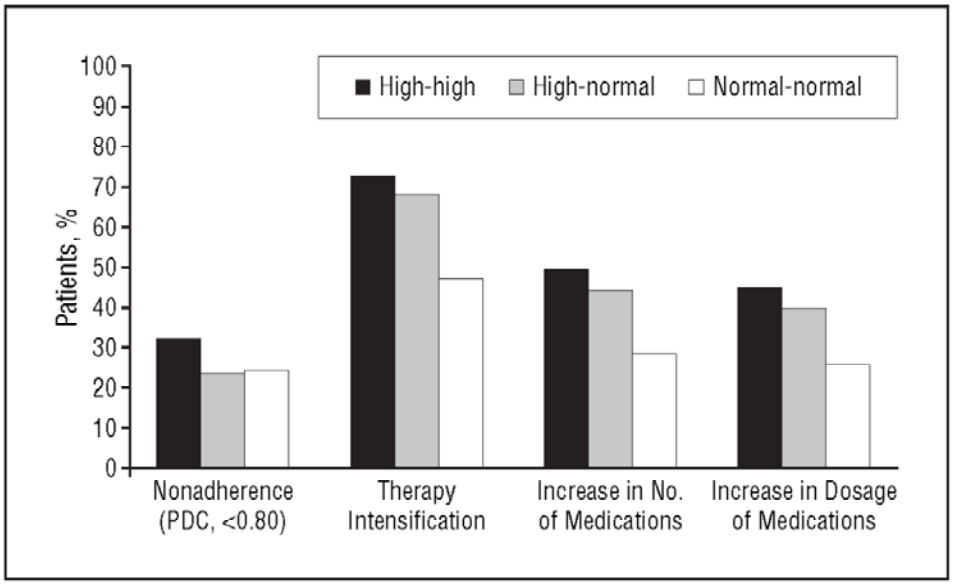
CORONARY ARTERY DISEASE (CAD) is common and affects more than 13 million patients in the United States.[1] Uncontrolled

than 50% of patients with CAD in clinical practice have their BP at levels recommended by national guidelines.[4,5]

Previous studies have focused mainly on patient characteristics associated with

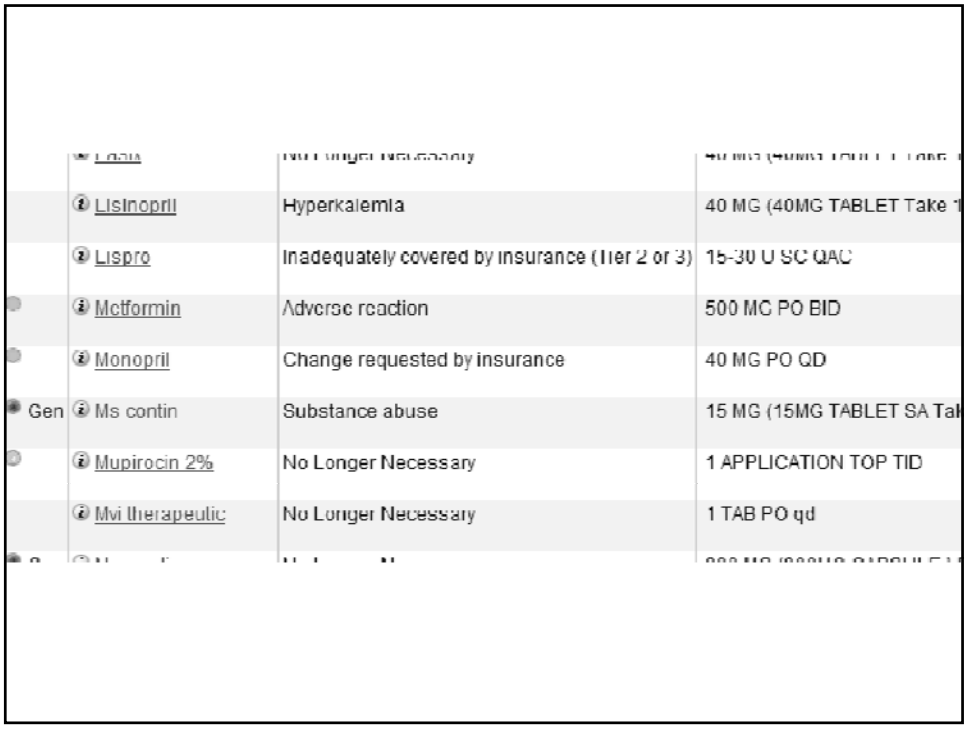


Medication adherence and therapy intensification across the 3 BP control groups PDC indicates proportion of days covered.

Ho Arch Int Med 2008

Work w/ patient for a shared agenda

- 20. Avoid (either knowingly, or unknowingly because of lack of complete drug history) repeating prescriptions for drugs a patient has previously tried unsuccessfully or had an adverse reaction.



	Lisinopril	Hyperkalemia	40 MG (40MG TABLET Take 1
	Lispro	Inadequately covered by insurance (Tier 2 or 3)	15-30 U SC QAC
	Metformin	Adverse reaction	500 MG PO BID
	Monopril	Change requested by insurance	40 MG PO QD
Gen	Ms contin	Substance abuse	15 MG (15MG TABLET SA Tal
	Mupirocin 2%	No Longer Necessary	1 APPLICATION TOP TID
	Mvi therapeutic	No Longer Necessary	1 TAB PO qd

Work w/ patient for a shared agenda

- 21. Discontinue drugs that are not working or no longer needed.

- Geriatrics- the art of taking older adults off drugs they no longer need

Shaughnessy- Am Fam Physician 2007

Work w/ patient for a shared agenda

- 22. Work with patients' desires to be conservative with medications

F. Consider long-term, broader impacts

- Weigh not just short term benefits but also long-term pt outcomes & ecologic impacts
- Recognize improved prescribing systems and better monitoring may outweigh marginal benefits of new drugs.

Consider longer-term, broader impacts

- 23. Think beyond short term drug effects, which may be beneficial, but also consider longer term benefits and risks.

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Long Term Efficiacy?

- Anti-fungals
- Obesity drugs
- 1st generation anti-psychotics
- DES
- Ecology of drugs in water supply

Consider longer-term, broader impacts

- 24. Look for opportunities to improve local prescribing systems, changes that can make prescribing and medication use safer.

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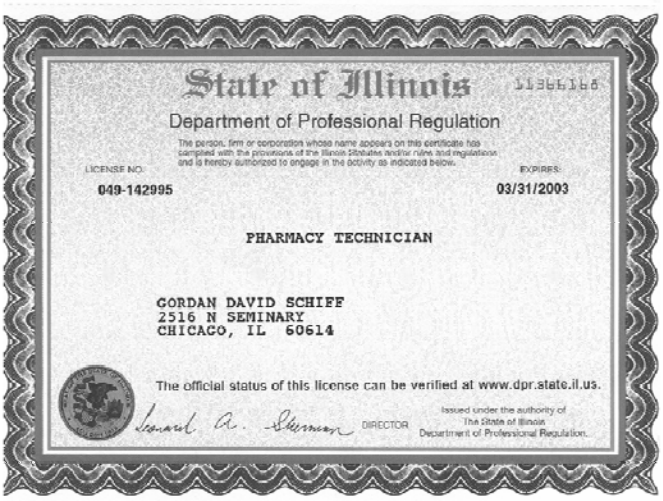

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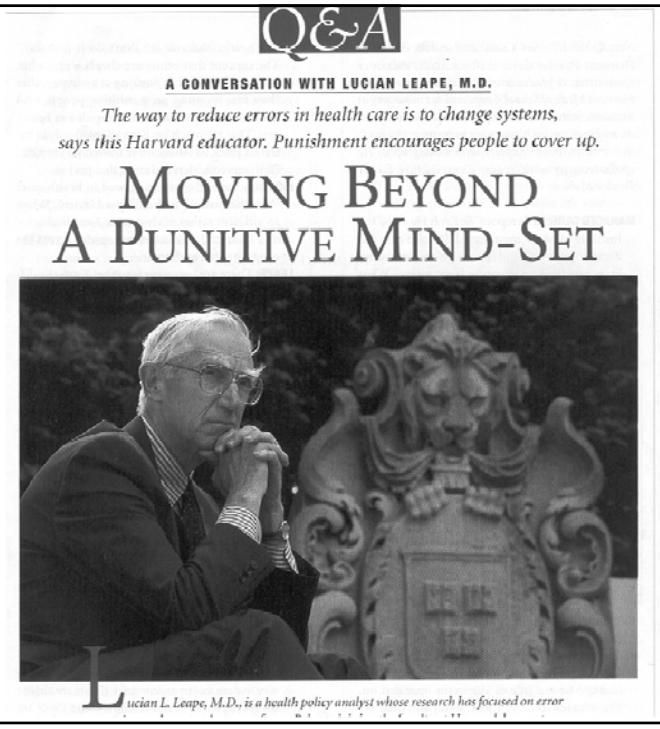

Q&A

A CONVERSATION WITH LUCIAN LEAPE, M.D.

The way to reduce errors in health care is to change systems, says this Harvard educator. Punishment encourages people to cover up.

MOVING BEYOND A PUNITIVE MIND-SET

Lucian L. Leape, M.D., is a health policy analyst whose research has focused on error

- "The pharmacist is the single most underused resource in the modern hospital

Lucian L. Leape, MD Harvard School of Public Health. ACP Observer 3/2000

Hey, we're just in the middle here Don't blame or preach to pharmacists

What can *we* do anyway?

1. Help patient articulate their (often legitimate) concerns and to be a sounding board – Hear out patient
2. Help delineate options/alternatives to better understand their diseases, choices, options - Not practicing medicine, but legitimate pharmacy patient education role
3. Help pts define questions they want to ask MD. – empowering patients who have questions
4. More serious cases, obligation to posing questions to doctor directly -known allergy, overdose, but also selected cases of drug selection.
   - ❖ Takes courage, diplomacy: how to define, achieve this ideal

More (business) is Better? …or Less is More (business)

- Realign pharmacists incentives, thinking
- More drugs – more wasted inventory
  - Recalls, shelf space, expired drugs
- Knowledge, familiarity w/ essential drugs
  - ↓ errors, anticipate problems, less to learn/recall
- Patient trust - not just pushing or filling drugs
  - Long term relationships better model
- New drugs, less faith, more evidence

- What's in it for us?

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Conservative Prescribing = Liberation for Pharmacists

- Lack of Conservative Prescribing has led to various dyfunctionalities undermining quaility of work of life of pharmacists.
- Hassles and calls to Doctors
  - –Symptoms/consequences of Cons Rx Failure
  - – "Prior auth"
  - – "Not covered"
  - – "Tier 3"
  - – "Non preferred brand"
  - – "Switches"

Conclusions

- From "newer is better" to "fewer and more time-tested is best" to achieve better balance
- Need for new paradigm and role for pharmacy: overcoming complacency and understanding and advocating best rx for patients, and questioning where not
- We need to figure out how to operationalize this together……starting now!