Update in Outpatient Medicine
Medical Grand Rounds
St. Charles Medical Center
September 8, 2017

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Disclosures

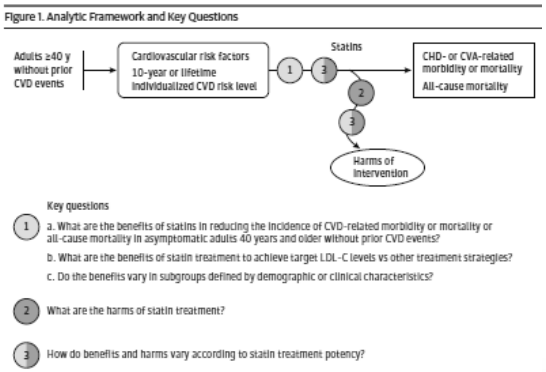
- Stock Holdings
  - Abbott Labs
  - Abbvie
  - Bristol Myers Squibb
  - GE
  - Proctor and Gamble
  - Walgreens

Topics

- Statin Intensity and Mortality in ASCVD
- Statins to prevent cardiovascular disease
- Hypertension
- Use of anticoagulants in atrial fibrillation
- Falls/Osteoporosis
- CRC Screening

USPTF Recommendation Statement
Statin Use for the Primary Prevention of Cardiovascular Disease in Adults

- Systematic review 19 RCT's enrolling 71,344 participants without prior CVD events



JAMA 2016;316:1997-2007

USPTF Recommendation Statement Statin Use for the Primary Prevention of Cardiovascular Disease in Adults

- 14% RRR all cause mortality
- 31% RRR CV mortality
- 36% RRR AMI
- No increase in adverse events
  - Evidence on the association of statins and DM mixed
  - RCT's do not conclusively support a major causative role for mylagia
  - No clear evidence of cognitive decline

USPTF Recommendation Statement Statin Use for the Primary Prevention of Cardiovascular Disease in Adults

- Initiate low to moderate dose statins in adults aged 40-75 with no history of CVD and ≥ 1 CVD risk and ≥ 10% CVD event risk using ACC pooled risk calculator
  - CVD risks- dyslipidemia (LDL > 130 or HDL ≤ 40, HTN, DM, smoking
    - Grade B recommendation
- Statin use on patients above but 7.5-10% CVD risk Grade C recommendation
- Statin use for primary prevention age > 75 Grade I

Table 1. Statin Dosing and American College of Cardiology/American Heart Association Classification of Intensity*

Statin	Total Daily Dosage, mg		
	Low Intensity (LDL-C Lowering <30%)	Moderate Intensity (LDL-C Lowering 30% to <50%)	High Intensity (LDL-C Lowering ≥50%)
Atorvastatin	NA	10-20	40-80
Fluvastatin	20-40	Twice daily: 40 Extended release: 80	NA
Lovastatin	20	40	NA
Pitavastatin	1	2-4	NA
Pravastatin	10-20	40-80	NA
Rosuvastatin	NA	5-10	20-40
Simvastatin	10	20-40	NA

Association Between Intensity of Statin Therapy and Mortality in ASCVD

- Retrospective cohort analysis 509,766 adults with ASCVD treated in the VA
- Mean follow up 492 days
- Adherence 81-83%
- Results consistent for older patients

JAMA Cardiol 2017;2(1):47-54

Association Between Intensity of Statin Therapy and Mortality in ASCVD

Figure 1. Adjusted Mortality Curves for Different Intensities of Statin Therapy

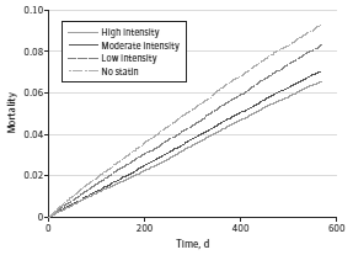
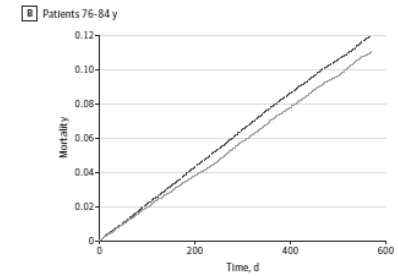


Figure 2. Adjusted Mortality Curves for High- vs Moderate-Intensity Statins by Age

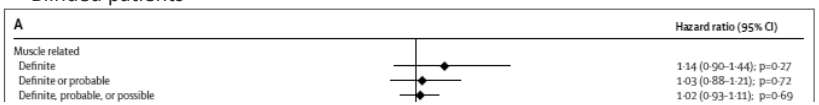


Adverse events associated with unblinded, but not blinded statin therapy- ASCOT-LLA

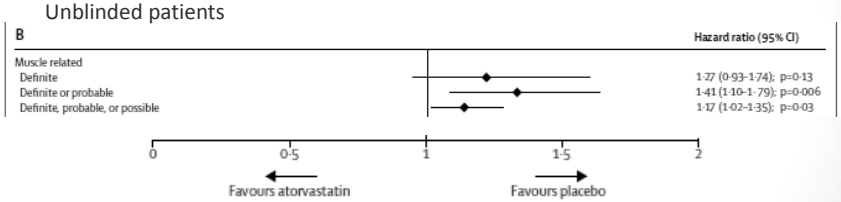
- 10,240 patients aged 40-79 with 3 or more risk factors for CVD but no history of MI or treatment for angina
  - Included patients with total cholesterol ≤ 6.5 mmol/L (approx, 250 mg/dl)
  - Included patients with previous CVA, PAD, LVH, DM
- Randomized to 10 mg atorvastatin vs. placebo
- Trial stopped for efficacy after median 3.3 years follow up. Patients then told of statin assignment and offered open label treatment

Lancet published online 5/2/2017

Blinded patients



Unblinded patients

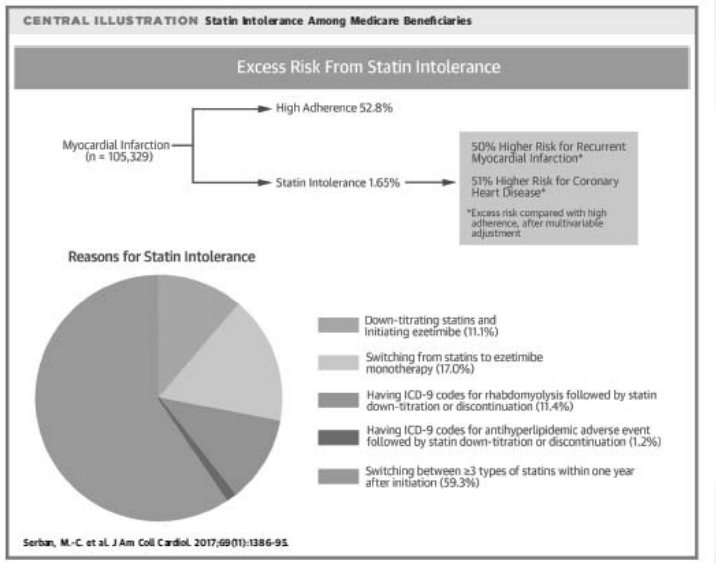


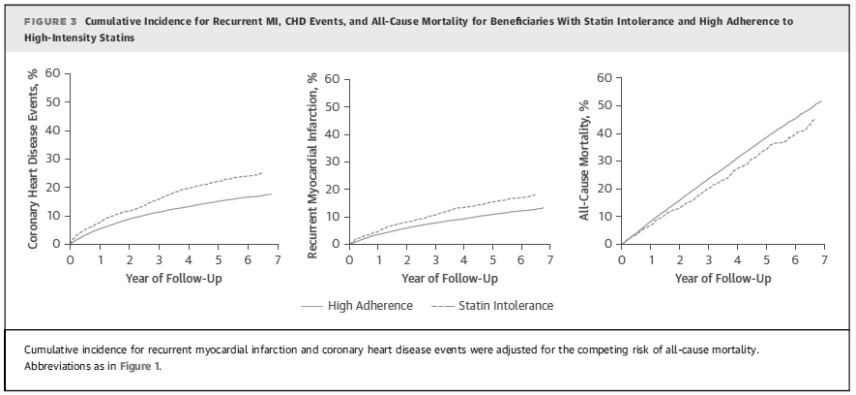
Muscle related symptoms not present during blinded phase
Cannot extrapolate to higher doses or very elderly patients

Statin Intolerance and Risk of CV Events and All Cause Mortality

- Retrospective cohort study of all Medicare beneficiaries hospitalized for AMI 2007-13, continuously enrolled 1 year before and 1 year after index event (105,329 enrollees)
  - Excluded patients with statin or other lipid lowering therapy during look back period
- Compared occurrence of MI, CHD event and all cause mortality between highly adherent (PDC ≥ 80%) and intolerant patients
- 52.8% highly adherent, 1.65% met primary definition of statin intolerance, 10.7% met secondary definition of statin intolerance

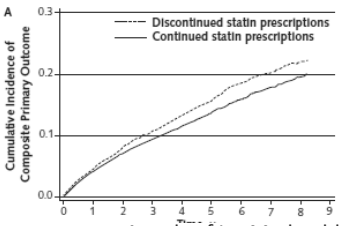
JACC 2017;69 (11):1386-95





Continued Statin Prescriptions After Adverse Reactions and Patient Outcomes

- Retrospective cohort study of 28,266 patients with a presumed adverse reaction to a statin
  - Prescribed 2000-2011
  - Continuation of statin determined through EMR review
  - Primary outcome MI, CVA, or death from any cause
  - 70.7% continued on a statin



Annals of Int Med published online July 25, 2017

Summary- Cholesterol Lowering

- USPTF endorses statin therapy for primary prevention in higher risk patients
- Statin intolerance is less frequent than believed and patients can frequently tolerate a rechallenge
  - Nocebo effect
- Patients who stop taking statins have worse outcomes, including higher mortality
- Substantial opportunity to increase prescribing and improve adherence, especially in patients with known ASCVD

Assessing Cardiovascular Risk to Guide Hypertension Diagnosis and Treatment

- Evaluated data from nonpregnant adults aged 20-79 who participated in the NHANES survey (n= 14,142)
  - Completed a mobile examination center visit
- SBP calculated by averaging up to 3 BP readings
- BP treatment status and medication type by self report
- Possibly resistant hypertension defined as taking ≥ 3 meds with at least 1 being a diuretic

JAMA Cardiol 2016:;1(8):864-871

Figure 1. Distribution of Untreated and Treated Systolic Blood Pressure (SBP) Measurements in US Adults Aged 20 to 79 Years

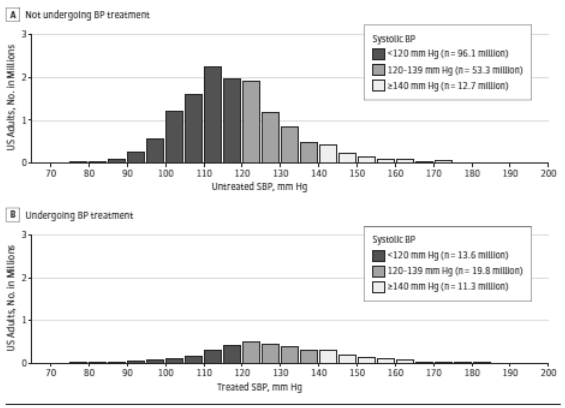
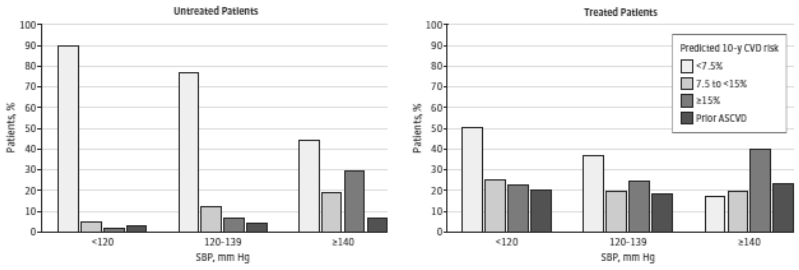


Figure 2. Cardiovascular Disease (CVD) Risk Profiles by Systolic Blood Pressure (SBP) and Treatment Status



Prevalence of prior CVD and predicted 10-year CVD risk for those free of CVD by SBP category in those not undergoing treatment and those undergoing treatment. ASCVD indicates atherosclerotic cardiovascular disease.

Assessing Cardiovascular Risk to Guide Hypertension Diagnosis and Treatment

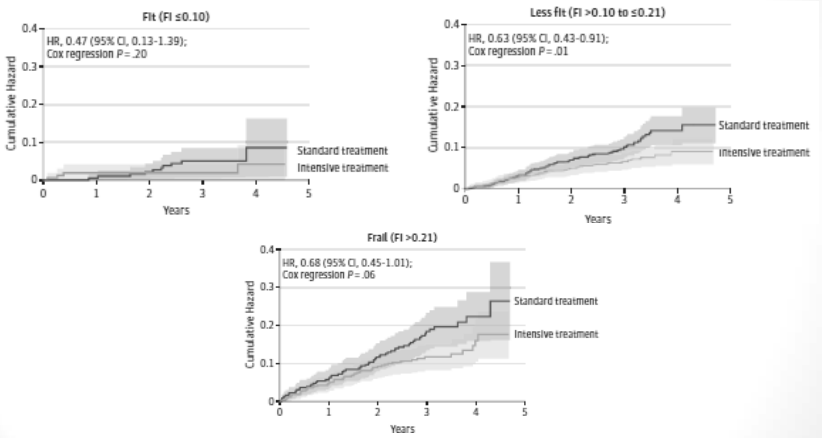
- 5.4% of US adults have an SBP ≥ 140 are taking BP meds and require intensification, 21.9% are already taking 3 or more meds with at least 1 diuretic and may have resistant hypertension
- 1.3% of US adults have SBP 120-139 and would have been SPRINT eligible, 27.2% may have treatment resistant hypertension
- These patients require careful assessment of adherence, barriers if nonadherent, or spironolactone if adherent and no contraindication

Intensive vs. Standard BP Control and CV Outcomes in Adults ≥ 75 years old

- Subset of SPRINT trial
  - 2636 community dwelling patients ≥ 75 years old with SBP 130-180 mm Hg at high risk for CVD disease
  - Clinical or subclinical CVD other than CVA
  - CKD (excluding PCKD), eGFR 20-59 ml/min
  - Framingham 10 year risk ≥ 15%
  - Age ≥ 75
  - Excluded patients with DM, CVD, LEF or symptomatic CHF, ESRD, dementia, expected survival < 3 years, unintentional weight loss > 10%, SBP < 110 following standing 1 minute, poor adherence

JAMA 2016;315(24):2673-82

Figure 2. Kaplan-Meier Curves for the Primary Cardiovascular Disease Outcome in Systolic Blood Pressure Intervention Trial (SPRINT) in Participants Aged 75 Years or Older by Baseline Frailty Status



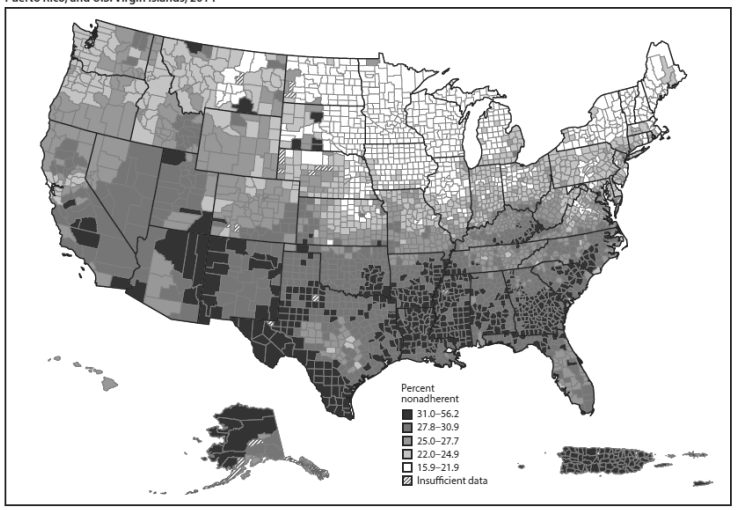
33% of intensive treated group was frail
NNT to prevent mortality or cardiac event = 60
NNH = 544

Disparities in Antihypertensive Medication Nonadherence Among Medicare Part D Beneficiaries-2014

- 70% of US adults aged ≥ 65 have HTN; 50% controlled
- Adherent patients have 45% higher rates of BP control and 38% decreased risk for a CV event
- Assessed claims for 18.5 million patients with a anti-hypertensive prescription
- 26.3% rate of nonadherence; defined as proportion of days covered metric (patient access to medication) < 80%
- Rates varied by drug class and # of meds
  - ARB<ACEI<CCB<BB<thiazide< other diuretic
  - Adherence better with fixed dose meds

MMWR September 16, 2016: 65; 967-76

FIGURE. Antihypertensive medication nonadherence* among Medicare Part D beneficiaries aged ≥65 years, by county — United States, Puerto Rico, and U.S. Virgin Islands, 2014†



* Nonadherence is defined as patients not following their health care professional's instructions concerning taking their prescribed medication. Using the proportion of days covered methodology, beneficiaries were considered nonadherent if they had access to antihypertensive medication for <80% of the days from the date of filling their first antihypertensive medication prescription through the end of 2014 or until their death in 2014.
† Additional maps of nonadherence by beneficiaries' race/ethnicity and for renin-angiotensin system antagonists and diuretics are available on the Interactive Atlas for Heart Disease and Stroke at https://www.cdc.gov/dhdsp/maps/atlas/.

Nonadherence to Antihypertensive Treatment

- Consider in uncontrolled patients on 3 medication classes
- Strategies to promote adherence
  - Use fixed dose combinations (start on ACE/ARB + diuretic)
    - Oregon only used in 5.3% patients
  - Prescribe 90 day supply to reduce pharmacy trips
  - Synchronize refills
  - Promote technology aids to follow medication schedule

Oral Anticoagulant Therapy in Patients with Atrial Fibrillation

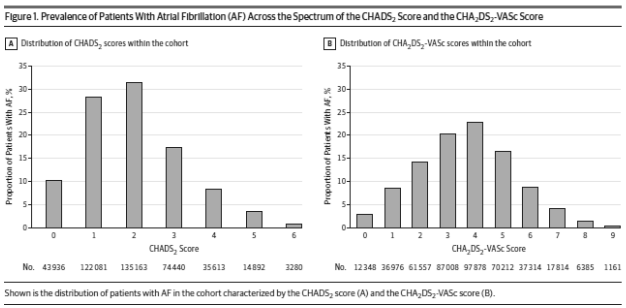
Insights from the NCDR PINNACLE Registry

429,417 patients with atrial fibrillation from 144 cardiology practices participating in the ACC PINNACLE registry

- $CHADS_2$
  - CHF
  - Hypertension
  - Age ≥ 75
  - Diabetes Mellitus
  - TIA or CVA (2 points)
- CHA_2DS_2VASc
  - CHF
  - Hypertension
  - Age ≥ 65 (1 point)
    ≥ 75 (2 points)
  - Diabetes mellitus
  - TIA or CVA (2 points)
  - CVD or PAD
  - Female Sex

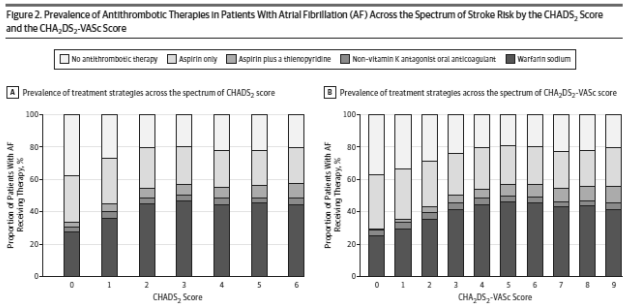
Over 50% of PHP patients with stroke and known history of atrial fibrillation did not fill a prescription for an anticoagulant

JAMA Cardiology 2016;(1):55-62

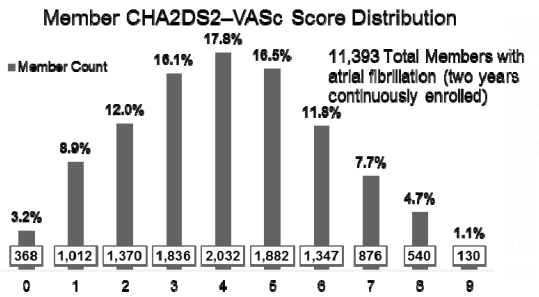


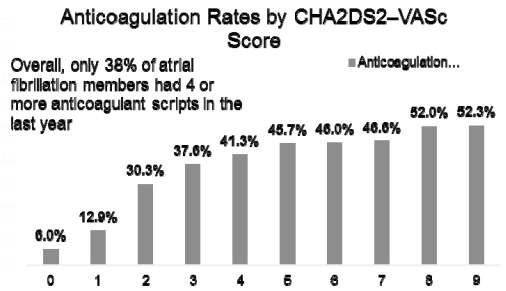
Stroke rates per year

0 points 0.2%	5 points 7.2%
1 point 0.6%	6 points 9.7%
2 points 2.2%	7 points 11.2%
3 points 3.3%	8 points 10.8%
4 points 4.8%	9 points 12.2%



PHP CHA2DS2-VASc Stroke Prediction Model





Association of preceding anti-thrombotic treatment and severity if stroke in patients with AF

- Retrospective observational study if 94,474 patient with acute ischemic stroke and known AF admitted 10/12-3/15 at hospitals participating in Get With the Guidelines program.
- Outcomes NIHSS score and in hospital mortality
- >95% patients high risk CHA_2DS_2-VASc ≥ 2
  - 28.6% of untreated patients and 35.9% of patients only on anti-platelet therapy had prior CVA or TIA
- Most common documented reasons for lack of anti-coagulation were risk of bleeding and falls

JAMA 2017;317:1057-1067

Association of preceding anti-thrombotic treatment and severity if stroke in patients with AF

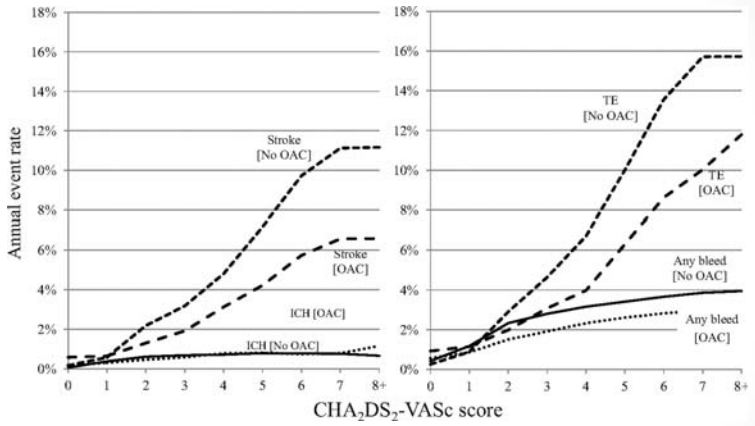
Preceding anti-platelet therapy

	None	Anti-plt	Warfarin INR ≤ 2	Warafarin INR ≥ 2	NOAC
Mod-severe CVA	27.1%	24.8%	25.8%	15.8%	17.5%
In-hosp mortality	9.3%	8.1%	8.8%	6.4%	6.3%

Clinical characteristics comprising the HAS-BLED Bleeding Risk Score

Letter	Clinical characteristic*	Points	HAS-BLED score (total points)	Bleeds per 100 patient-years¶
H	Hypertension (ie, uncontrolled blood pressure)	1	0	1.13
A	Abnormal renal and liver function (1 point each)	1 or 2	1	1.02
S	Stroke	1	2	1.88
B	Bleeding tendency or predisposition	1	3	3.74
L	Labile INRs (for patients taking warfarin)	1	4	8.70
E	Elderly (age greater than 65 years)	1	5 to 9	Insufficient data
D	Drugs (concomittant aspirin or NSAIDs) or alcohol abuse (1 point each)	1 or 2		
		Maximum 9 points		

Relation between CHA2DS2-VASc scores and annual event rates of ischemic stroke and intracranial hemorrhage (ICH; left) and more widely defined thromboembolic events and bleedings (right) in relation to use of oral anticoagulation (OAC; n=159 013).



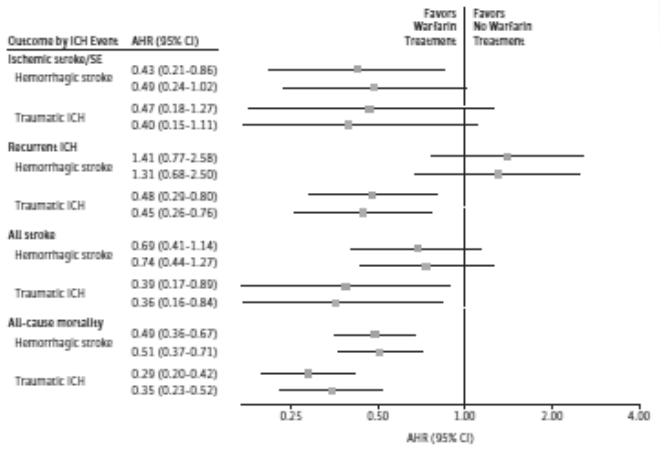
Leif Friberg et al. Circulation. 2012;125:2298-2307

Outcomes Associated With Resuming Warfarin Treatment After Hemorrhagic Stroke or Traumatic Intracranial Hemorrhage in Patients with Atrial Fibrillation

- Observational cohort study using data from Danish nationwide databases
- Identified patients with spontaneous intracranial hemorrhage or traumatic intracranial hemorrhage
- Median follow up 279 days

JAMA Intern Med 2017;177(4) 563-570

Figure 2. Forest Plots of Studied Outcomes and Associations With Resumption or No Resumption of Warfarin Treatment



In patients with hemorrhagic stroke, resuming warfarin decreases the rate of recurrent stroke, but have an increased risk of recurrent intracranial hemorrhage.

Patients with traumatic ICH have fewer strokes and ICH with warfarin resumption

Table 1. Stroke Prophylaxis Treatment Recommendations, Based on Maximizing QALYs*

Variable	Risk of Upper GI Tract Bleeding, %/y	Risk of Stroke, %/y†	QALYs: Warfarin Therapy	QALYs: Aspirin Therapy	QALYs: NT	Antithrombotic Treatment Recommendations	General Recommendations
Recent resolved GI tract bleeding (with *Helicobacter pylori* testing and treatment)							
Aged 65-75 y‡							
No RF		4.3	11.13	10.52	10.12	Warfarin	
≥1 RF		5.7	10.68	9.70	9.18	Warfarin	
Aged >75 y§	1.2						None
No RF		4.3	8.08	7.71	7.47	Warfarin	
≥1 RF		8.1	7.36	6.43	6.02	Warfarin	
Concurrent NSAID and misoprostol or PPI use or COX-2–specific NSAID use							
Aged 65-75 y‡							
No RF		4.3	10.75	10.35	9.98	Warfarin	
≥1 RF		5.7	10.27	9.55	9.06	Warfarin	
Aged >75 y§	2.3						None
No RF		4.3	7.84	7.60	7.39	Warfarin or aspirin	
≥1 RF		8.1	7.09	6.35	5.96	Warfarin	
Concurrent conventional NSAID use							
Aged 65-75 y‡							
No RF		4.3	10.12	10.02	9.71	Warfarin or aspirin	Assess the need for NSAIDs, consider a switch to an alternative analgesic, and consider the addition of misoprostol or PPIs
≥1 RF		5.7	9.62	9.25	8.82	Warfarin	
Aged >75 y§	4.5						
No RF		4.3	7.44	7.39	7.21	Warfarin, aspirin, or NT	
≥1 RF		8.1	6.66	6.19	5.83	Warfarin	

Risk of stroke exceeds risk of bleeding in almost all patients with risk factors

Patient with atrial fibrillation and 5% risk of stroke/year would need to fall 300 times a year to have an equivalent risk of subdural hematoma

Arch Int Med 2003;163:1580-1586

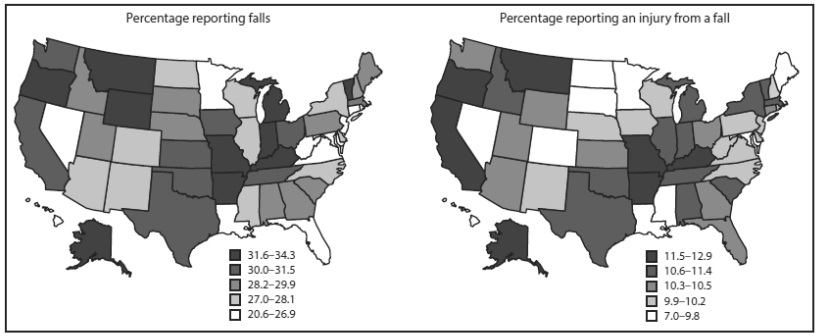
Conclusions

- Use of anticoagulants to prevent thromboembolic events is low
- Benefits exceed risks in almost all patients
- Risks of bleeding often overestimated

Falls and Falls Injuries in Adults ≥ 65-United States 2014

- 2.8 million ED visits for fall related injuries, 800,000 hospitalizations, 27,000 deaths
- CDC analyzed data from the Behavioral Risk Factor Surveillance System Survey
  - 147,319 respondents
- 28.7% of older adults reported a fall
  - 37.5% of those who fell restricted activity at least 1 day or sought medical attention
- Only 58% of PHP members recall their provider asking about falls

MMWR Sept. 23, 2016/65(37);993-98



* Injuries resulting from falls that caused respondents to limit their regular activities for ≥1 days or to go see a doctor.

Prevention of Falls in Older People Living in the Community

- Risk factors
  - Gait and Balance
  - Frailty
  - Co-morbidities
  - Polypharmacy
  - Visual impairment
  - CV causes i.e. syncope, orthostatic hypotension, cerebrovascular disease
  - DM
- Interventions
  - TUG test (abnormal >12 s)
  - Medication review
  - Exercise program such as Tai Chi
  - PT eval, especially if fear of falling or TUG test positive
  - Vitamin D 800 IU daily or test and supplement in patients with low levels
    - 17% reduction in falls
  - Calcium 1000-1200 mg daily
    - Evidence stronger in institutionalized people

BMJ 2016;353:i1419

Patterns of Prescription Drug Use Before and After a Fragility Fracture

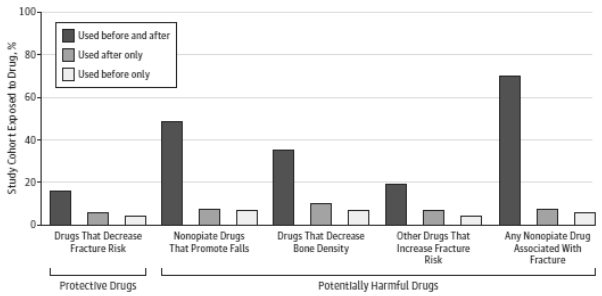
- Retrospective cohort study using a 40% sample of FFS Medicare beneficiaries
- 168,133 patients who sustained a hip, wrist, or shoulder fracture
  - Community dwelling at time of fracture and for at least 30 days within 4 months of fracture
- 76% of patients were exposed to at least 1 non-opiate drug that increased fracture risk

JAMA IM 2016;176:1531-1538

Table 1. Drugs Associated With Increased Risk of Fracture by Proposed Mechanism

Proposed Mechanism of Increased Fracture Risk	Cohort Use Prior to Fracture, %
Increased Risk of Falls	
Benzodiazepines	2.8
Barbiturates	1.2
Sedative-hypnotics (nonbenzodiazepine)[a]	10.8
Opiates	35.5
Selective serotonin reuptake inhibitors[a]	26.4
Tricyclic antidepressants	4.8
Anti-Parkinson disease drugs	5.6
Centrally acting antihypertensives	3.9
Nitrates	8.6
Nonnitrate anti-anginal agents	1.4
Thiazide diuretics	23.4
Thiazide-like diuretics	2.9
Decreased Bone Density	
Inhaled glucocorticoids	7.0
Oral glucocorticoids[a]	9.8
Proton pump inhibitors[a]	25.6
H2 receptor antagonists	5.6
Thiazolidinediones[a]	5.7
Anticonvulsants	9.3
Unclear Primary Mechanism	
Atypical antipsychotics[a]	5.2
Early-generation antipsychotics	1.8
Loop diuretics	21.0

Figure. Use of Drugs That Affect Fracture Risk Before and After Fracture



Risk of hip, subtrochanteric, and femoral shaft fractures among mid and long term uses of alendronate

- Danish national registry of 61,990 incident users of alendronate from 1996-2007
- Outcomes were incident fractures of the hip, subtrochanteric femur, and the femoral shaft
  - One case control study for hip fracture
  - One case control study for subtrochanteric and femoral shaft fracture
- 29.4% completed 5 years of treatment with a medication possession ratio of ≥ 80%

BMJ 2016;353:i3365

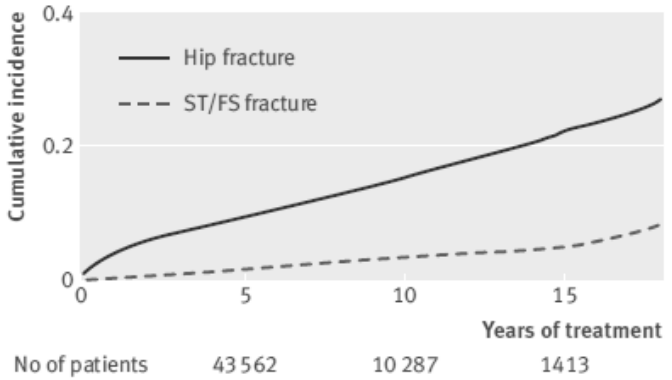
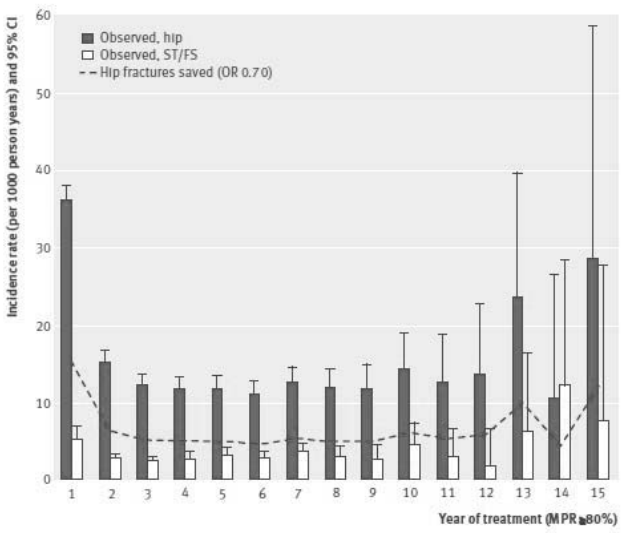


Fig 2 | Kaplan-Meier cumulative incidence plot of hip fracture and subtrochanteric and femoral shaft fracture (ST/FS) as function of time for all people treated with alendronate irrespective of adherence



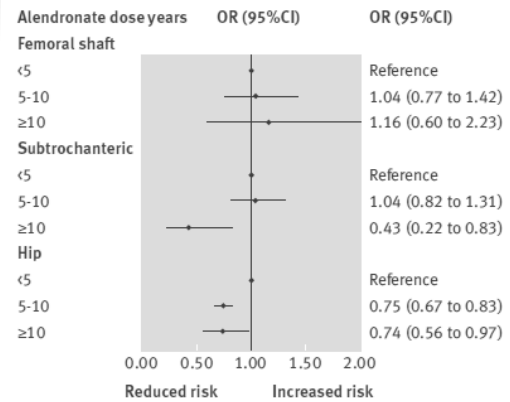


Fig 4 | Subanalysis of femoral shaft fractures, subtrochanteric fractures, and hip fractures. Nested case-control analysis adjusted for covariates in tables 2 and 3

NNT to prevent hip fractures after additional 5 years of alendronate= 38

NNH harm 1449

Conclusions

- Benefits of long term bisphosphonates far exceed the risks
- Under treatment is common in high risk patients
  - Over 50% of PHP patients with known osteoporosis and previous fracture who sustain a hip fracture are not treated with a bisphosphonate

Effectiveness of Screening Colonoscopy to Prevent CRC age 70-79

- Population based, prospective study 1,332,692 average risk FFS Medicare beneficiaries without colonoscopy within 5 years
  - Selected cohort who used other preventive services
  - Over 85% had Charlson co-morbidity score < 1
- Outcomes
  - 8 year incidence of CRC
  - Stage reported, but not mortality
  - 30 day adverse outcomes

Annals of Int Med2017;166(1):18-26

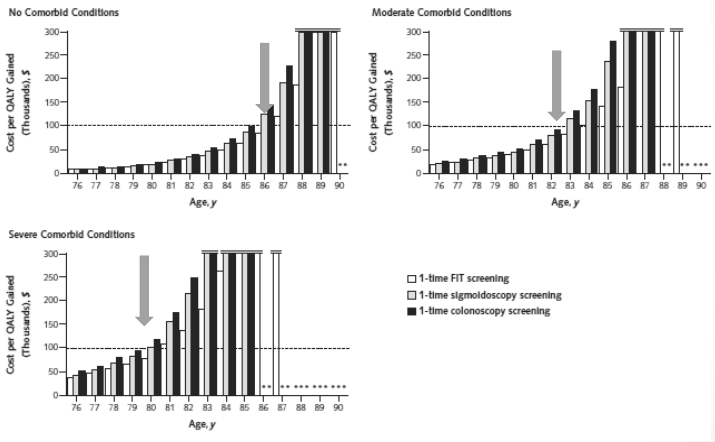
Effectiveness of Screening Colonoscopy to Prevent CRC age 70-79

	Age 70-74 Screened	Age 70-74 Unscreened	Age 75-79 Screened	Age 75-79 Unscreened
8 year incidence CRC	2.19%	2.62%	2.84%	2.92%
Adverse events	5.6/10,000		10.3/10,000	

Adverse events: Arrythmia>CHF>Syncope/hypotension>N/V
Bleeding requiring transfusion/perforation uncommon

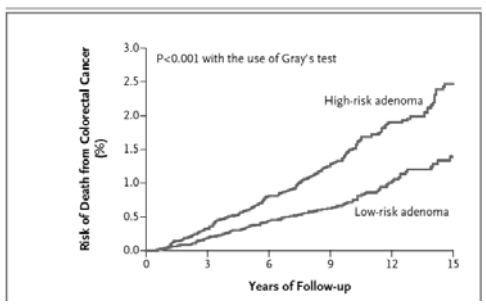
	Ages 70-74		Ages 75-79	
	Colonoscopy	No screening	Colonoscopy	No screening
Stage 0	84 (15.1)	986 (8.5)	73 (13.4)	1,025 (7.7)
Stage I	200 (35.9)	2,821 (24.2)	217 (39.8)	3,311 (24.9)
Stage II	105 (18.9)	3,017 (25.9)	105 (19.3)	3,653 (27.4)
Stage III	131 (23.5)	2,856 (24.5)	113 (20.7)	3,129 (23.5)
Stage IV	37 (6.6)	1,976 (17.0)	37 (6.8)	2,195 (16.5)

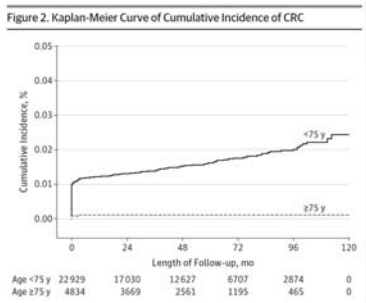
Simulation model of CRC Screening in Previously Unscreened Elderly Patients



Ann Intern Med 2014;160:750-759

Marginal Benefit for More Frequent Surveillance of Low Risk Polyps





NEJM 2014;371:799-807

JAMA IM 2014:174:1675-1682

Summary- Colonoscopy for CRC Screening in the Elderly

- Patients aged 70-74 have small reduction in CRC incidence and small risk of adverse events
- Patients aged 75 and older have no significant benefit in reducing CRC incidence and have small risk of adverse events
- Decisions for screening should consider results of past screening and presence of chronic illness
- Older patients with normal or low risk findings on colonoscopy (i.e. 1-2 polyps < 1 cm) should consider stopping surveillance or changing to stool based test (i.e. FIT)

Multitarget Stool DNA Testing for CRC Screening

- 12,776 patients age 50-84 at average risk for CRC enrolled at 90 sites
  - Excluded patients with previous colonoscopy within 9 years, + fecal blood in past 6 months.
- 9989 participants could be fully evaluated
  - 1168 did not undergo colonoscopy
  - 723 had insufficient stool or other sample issues
  - 304 had incomplete colonoscopy

NEJM 2014; 370: 1287-97

Multitarget Stool DNA Testing for CRC Screening

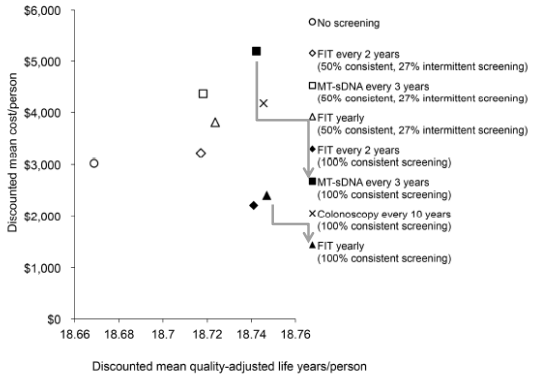
	Stool DNA	FIT
Colon cancer sensitivity	92.3%	73.8%
Advanced precancerous lesions	42.4%	23.8%
All nonadvanced adenomas, negative colonoscopy specificity	86.6%	94.9%
Advanced precancerous lesions, cancer specificity	89.8%	96.4%

Specificity for multitarget stool DNA further reduced in the elderly

Comparative Effectiveness and Cost Effectiveness of a Multi-target Stool DNA Test to Screen for Colonic Neoplasia

- Markov model to compare effectiveness of Multi-target DNA test vs. FIT vs. colonoscopy
  - Patients entered the model at age 50, screened from age 50-80 and followed until age 100
- Assumed Medicare costs
  - FIT $19 per test
  - Multi-target stool DNA $496 per test
  - Added $153 per cycle to FIT for cost of program to ensure follow up

Gastroenterology 2016 http://dx.doi.org/10.1016/S0016-5085(16)30703-X



Incremental cost/QALY comparing MT-sDNA to FIT well over $1 million/QALY

One time testing at age 70 MT-sDNA vs. FIT cost $27,884/QALY

Table. Characteristics of Colorectal Cancer Screening Strategies[a]

Screening Method	Frequency[b]	Evidence of Efficacy	Other Considerations
Stool-Based Tests			
gFOBT	Every year	RCTs with mortality end points: High-sensitivity versions (eg, Hemoccult SENSA) have superior test performance characteristics than older tests (eg, Hemoccult II)	Does not require bowel preparation, anesthesia, or transportation to and from the screening examination (test is performed at home)
FIT[c]	Every year	Test characteristic studies: Improved accuracy compared with gFOBT Can be done with a single specimen	Does not require bowel preparation, anesthesia, or transportation to and from the screening examination (test is performed at home)
FIT-DNA	Every 1 or 3 y[d]	Test characteristic studies: Specificity is lower than for FIT, resulting in more false-positive results, more diagnostic colonoscopies, and more associated adverse events per screening test Improved sensitivity compared with FIT per single screening test	There is insufficient evidence about appropriate longitudinal follow-up of abnormal findings after a negative diagnostic colonoscopy; may potentially lead to overly intensive surveillance due to provider and patient concerns over the genetic component of the test
Direct Visualization Tests			
Colonoscopy[e]	Every 10 y	Prospective cohort study with mortality end point	Requires less frequent screening Screening and diagnostic follow-up of positive findings can be performed during the same examination
CT colonography[e]	Every 5 y	Test characteristic studies	There is insufficient evidence about the potential harms of associated extracolonic findings, which are common
Flexible sigmoidoscopy	Every 5 y	RCTs with mortality end points: Modeling suggests it provides less benefit than when combined with FIT or compared with other strategies	Test availability has declined in the United States
Flexible sigmoidoscopy with FIT[c]	Flexible sigmoidoscopy every 10 y plus FIT every year	RCT with mortality end point (subgroup analysis)	Test availability has declined in the United States Potentially attractive option for patients who want endoscopic screening but want to limit exposure to colonoscopy

USPTF CRC Screening Update JAMA 2016;315: 275

Questions?