ATRIUM CARDIOLOGY COLLABORATIVE

@atriumcc

Does a Low Dose Aspirin Really Keep the Doctor Away?

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Objective

- Given a patient without established cardio- or cerebrovascular disease, discuss the role of low-dose aspirin for primary prevention

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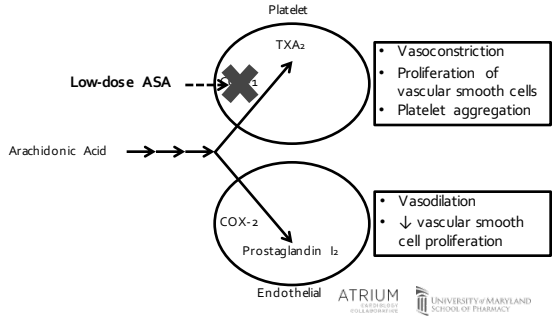
Mechanism for Prevention



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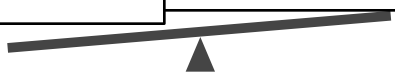
The Dilemma

Risk Factors for Cardiovascular Disease

- Age (per decade)
- Male sex
- DM
- Current smoker
- HTN (mean BP increase of 20 mmHg)
- Dyslipidemia
- BMI

Risk Factors for Bleeding

- Prior dyspepsia, PUD, or GI bleed
- Medications (NSAID, OAC, steroid)
- *H. pylori* infection
- History of heavy alcohol use
- Bleeding disorder
- Age, DM, smoking, HTN, BMI



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Lancet. 2009;373:1849-60. Hellenic J Cardiol. 2015;56:461-74.

Controversy? Comparing the Guidelines

	UK CKS-NICE (2013)	USPSTF (2009)	AHA (2011)	ADA (2016)	CCS (2010)	WHO (2007)
Age (y/o)	--	Men 45-79 Women 55-79	-	Most patients ≥50	<70	--
Population	HTN pts over 50 with: - 20% CVD risk - Reduced renal function	CHD Risk (Men) ≥4% (45-59) ≥9% (60-69) ≥12% (70-79) Stroke Risk (Women) ≥3% (55-59) ≥8% (60-69) ≥11% (70-79)	CVD risk ≥6-10%	CVD risk >10% and not at ↑ risk of bleeding Highest risk: - Most ≥5 plus - Another risk factor	CHD risk ≥20%	CVD risk ≥30%

ADA: American Diabetes Association; AHA: American Heart Association; CCS: Canadian Cardiovascular Society; CKS-NICE: Clinical Knowledge Summaries-National Institute for Health and CareExcellence; USPSTF: United States Preventative Services Task Force; WHO: World Health Organization

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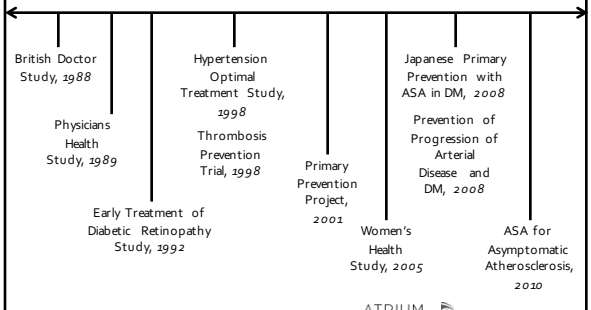
Adapted from AHRQ Publication No. 13-05195-EF-1; Diabetes Care 2016;39(Suppl. 1):S1-S2

Historical Evaluation



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ATT Meta-analysis (2009)

- Analyzed 6 primary prevention trials and 16 secondary prevention trials
- Population:
  - Mostly healthy volunteers (67,086 patients)
  - Risk factors for CVD (3 trials): HTN, dyslipidemia, DM, obesity, family history of CVD, or elderly (28,784 patients)
- ASA dosing
  - 75 mg daily (2 trials)
  - 100 mg daily (1 trial) and every other day (1 trial)
  - 325 mg every other day (1 trial)
  - 500 mg daily (1 trial)

Lancet. 2009;373:1849-60.

ATT Meta-analysis

Benefit	Risk
• Any major coronary event • 0.28 vs 0.34 %/yr • 0.82 (0.75-0.90) • Any stroke • 0.20 vs 0.21 %/yr • 0.95 (0.85-1.06) • Any vascular death • 0.19 vs 0.19 %/yr • 0.97 (0.87-1.09) • Any serious vascular event • 0.51 vs 0.57 %/yr • 0.88 (0.82-0.94)	• Major GI and other extracranial bleeds • 0.10 vs 0.07% • 1.54 (1.30-1.82)
NNT= 3125*	NNH=5681

*NNT based on any serious vascular event data as events/person years.

Lancet. 2009;373:1849-60.

Updates Since ATT Meta-analysis

- Aspirin in Asymptomatic Atherosclerosis-AAA (2010)
  - 50-75 y/o with ABI < 0.99 (mean 0.85)
  - ASA 100 mg daily vs placebo
  - Initial fatal or nonfatal coronary event, stroke, or revascularization: no difference
  - Bleeding: no difference
    - 2.0% vs 1.2% with major hemorrhage
- 2 trials in diabetic patients
  - POPADAD
  - JPAD

JAMA. 2010;303(9):841-848.

ASPIRIN IN PATIENTS WITH DIABETES

Summary of Diabetic Trials

Trial	Design	Population	Clinical Outcomes	Bleeding
POPADAD	RCT, double blind, 2x2 factorial, placebo controlled, multicenter	1276 pts with DM and ABI ≤0.99 without CVD ≥40 y/o 100 mg ASA daily vs placebo	No evidence of reduction in CV events or mortality	No difference in GI bleed (4.4% vs 4.9%) or GI symptoms (11.4% vs 14.7%)
JPAD	RCT, open label, multicenter	2539 pts with DM 30-85 y/o 81 mg or 100 mg ASA daily vs placebo	Did not reduce risk of atherosclerotic events	No significant difference in hemorrhagic stroke and GIB

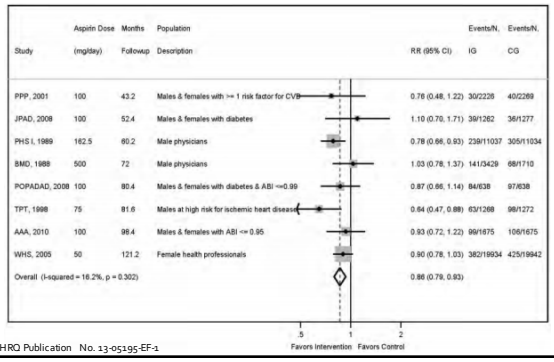
BMJ. 2008;337:a1840. JAMA. 2008;300(18):2134-41.

Summary of Diabetic Trials

Trial	Population	Clinical Outcomes	Bleeding
JPAD sub-group: Renal Disease	2523 pts with DM 30-85 y/o 3 groups: - eGFR ≥90 ml/min/1.73m^2 - eGFR 60-89 ml/min/1.73m^2 - eGFR <60 ml/min/1.73m^2	Incidence of atherosclerotic events (fatal and nonfatal IHD, stroke, and PAD) significantly lower in ASA group	Event rates low and not significant
JPAD sub-group: Hypertension	2539 pts with DM 30-85 y/o 2 groups: - SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg - SBP < 140 mmHg and/or DBP < 90 mmHg	ASA may reduce cerebrovascular events in DM pts with higher blood pressure	Event rates low and not compared in the study

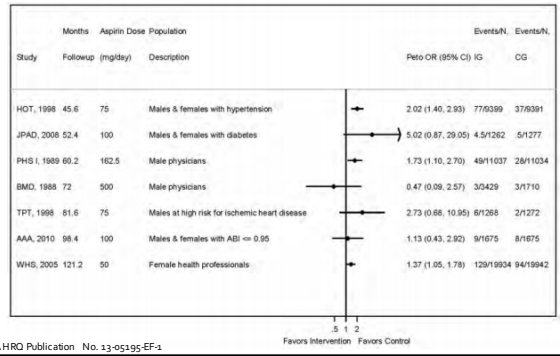
Diabetes Care. 2001;34:280-5. Circ J. 2012;76:1526-32.

Nonfatal MI/Coronary and Stroke Events



AHRQ Publication No. 13-05195-EF-1

Major GI Bleeding



AHRQ Publication No. 13-05195-EF-1

Patient Case

- JP is a 55 y/o WM presents to your outpatient clinic asking about starting 81 mg ASA because he heard it will prevent a heart attack on Dr. Oz.
- PMH: HTN and PUD
- Non-smoker
- Medications: Lisinopril 10 mg daily, Pantoprazole 40 mg daily
- BP 142/88 mmHg Chol 192 mg/dL LDL 98 mg/dL HDL 47 mg/dL

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Patient Case

- Would you recommend ASA 81 mg daily?
  - Yes
  - No

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Patient Case

- DJ is a 62 y/o WF was admitted to the hospital with hypertensive urgency and is being prepared for discharge after control of her BP.
- PMH: HTN, CKD (eGFR 65 ml/min/1.73m^2), DM
- Non-smoker
- Medications: Lisinopril 40 mg daily, Furosemide 40 mg daily, Amlodipine 10 mg daily, Metformin 1000 mg BID
- BP 154/98 mmHg Chol 214 mg/dL LDL 130 mg/dL HDL 40 mg/dL

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Patient Case

- Would you recommend ASA 81 mg daily?
  - Yes
  - No

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Take Home Points

- Heterogenous data
- Compare risk vs. benefit in each patient
- Overall recommendations

Population	Recommendation
CVD risk high, bleed risk low	ASA 81mg daily
CVD risk high, bleed risk high	ASA 81mg daily with increased monitoring for bleeding
CVD risk moderate	Discussion with patient and evaluation of bleeding risks
CVD risk low	Do not give ASA, reassess regularly to determine risks

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Future Directions

- ASCEND
  - 2x2 comparison of pts ≥ 40 y/o with DM and no previous history of vascular disease
    - ASA 100 mg daily vs placebo + Omega-3 1 gm daily vs placebo
  - Non-fatal MI, non-fatal stroke or TIA, or vascular death
- ACCEPT-D
  - Open label trial of pts ≥ 50 y/o with DM on simvastatin
    - ASA 100 mg daily plus Simvastatin vs. Simvastatin alone
  - Cardiovascular death, non-fatal MI, non-fatal stroke, and hospital admission for CV causes
- ASPREE
  - 19,000 men ≥ 70 y/o (≥65 y/o non-US minorities)
    - ASA 100 mg daily vs placebo
  - All cause mortality, dementia incidence, or physical disability

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Trials. 2007;8:21; Contemp Clin Trials. 2013;36(2):555-64. https://clinicaltrials.gov/ct2/show/NCT00135226

Questions?

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