# Aspirin for primary prevention of atherosclerotic cardiovascular disease (ASCVD) events in People with HIV

**Chris Longenecker, MD**
Director, HIV-Cardiology Clinic
Harborview Medical Center
Associate Professor of Medicine
University of Washington

Last Updated: 1/31/2023

# Disclosures

No conflicts of interest or relationships to disclose

# Disclaimer

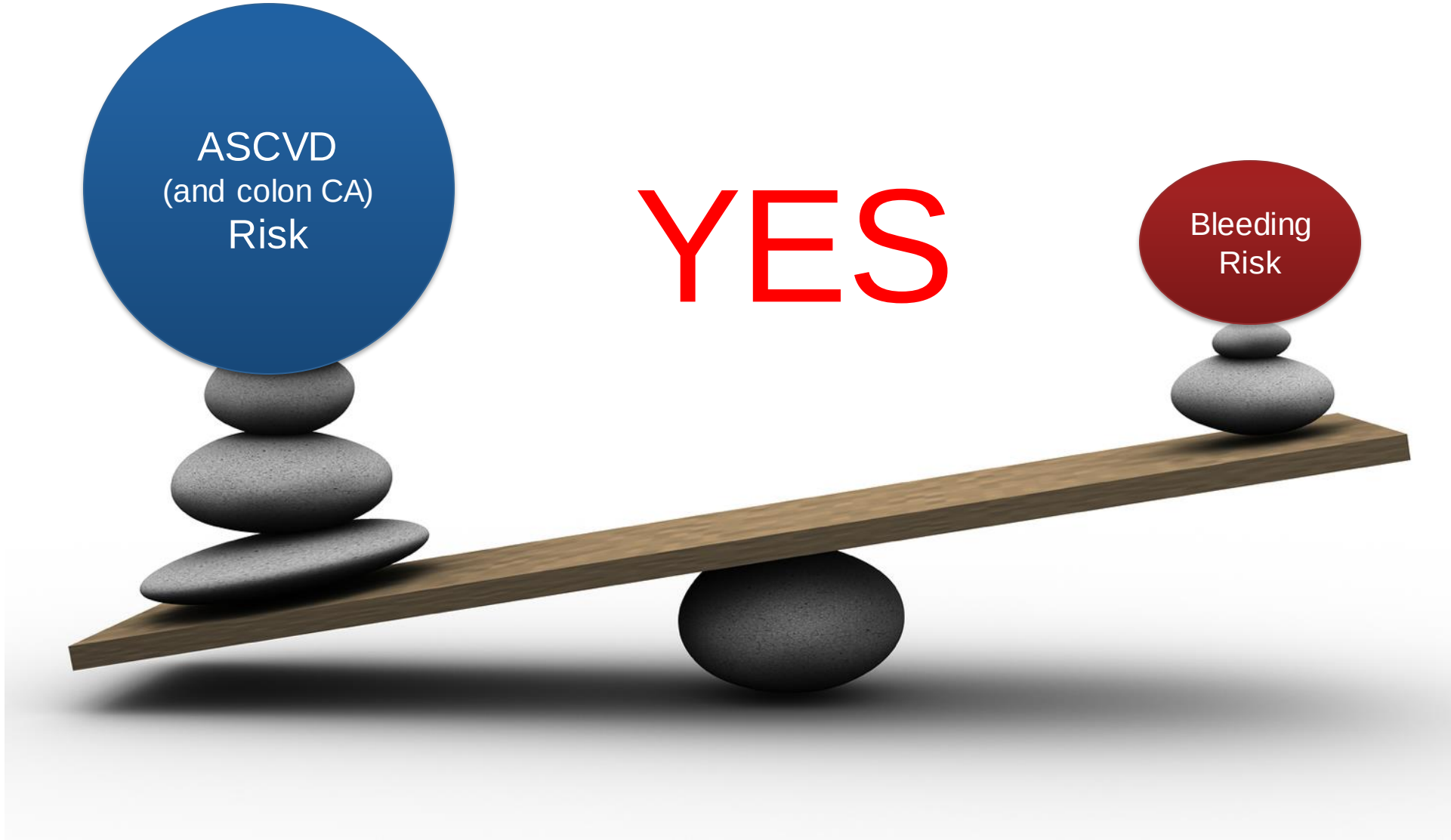
Funding for this presentation was made possible by U1OHA29296 from the Human Resources and Services Administration HIV/AIDS Bureau. The views expressed do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government. *Any trade/brand names for products mentioned during this presentation are for training and identification purposes only.*

AETC AIDS Education & Training Center Program Mountain West

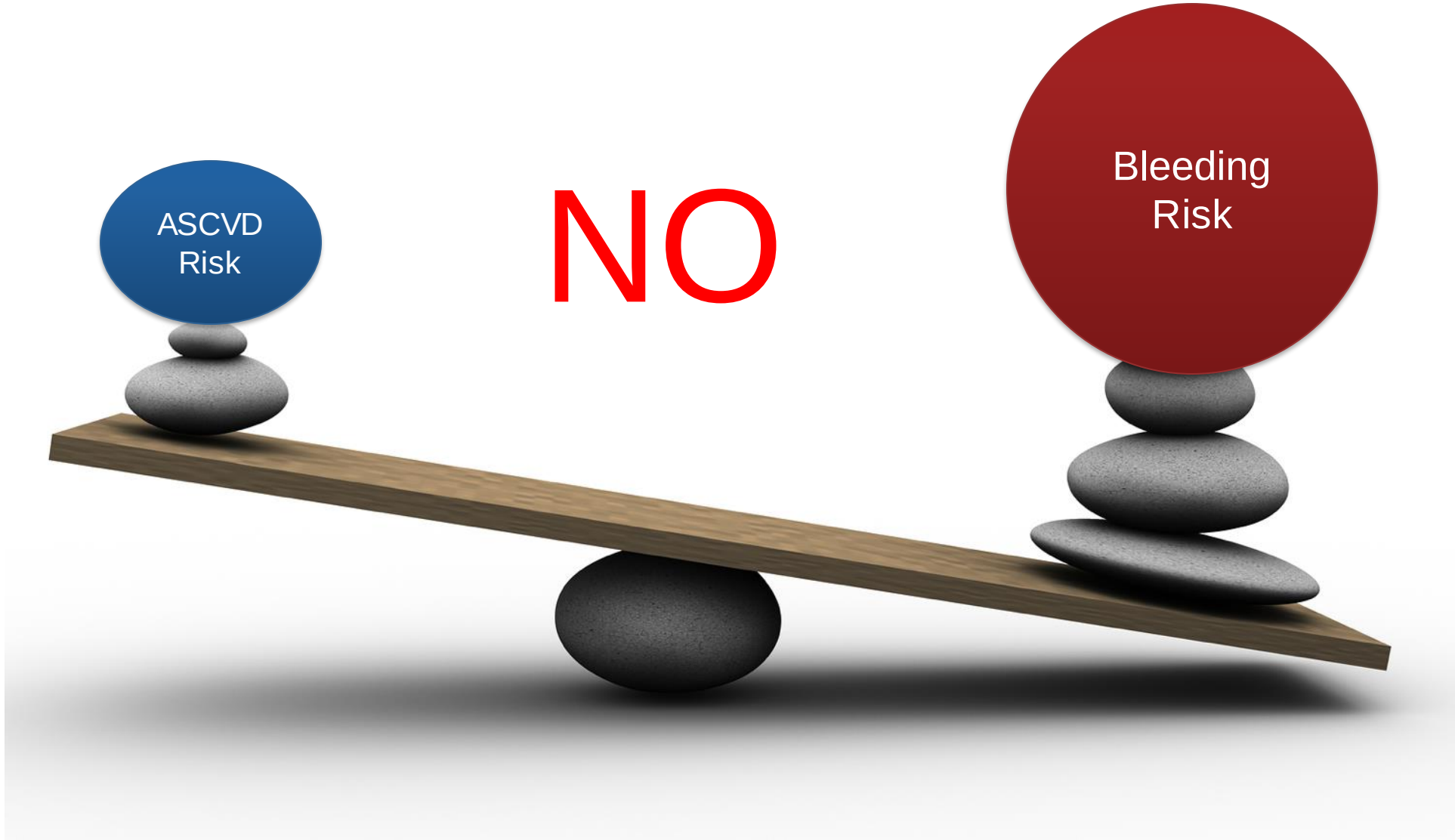
# Outline

- Aspirin for primary prevention in the general population
- Disparities in aspirin prescriptions for people with HIV (PWH)
- Abacavir
- A word on secondary prevention

# Take home message



# Take home message



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

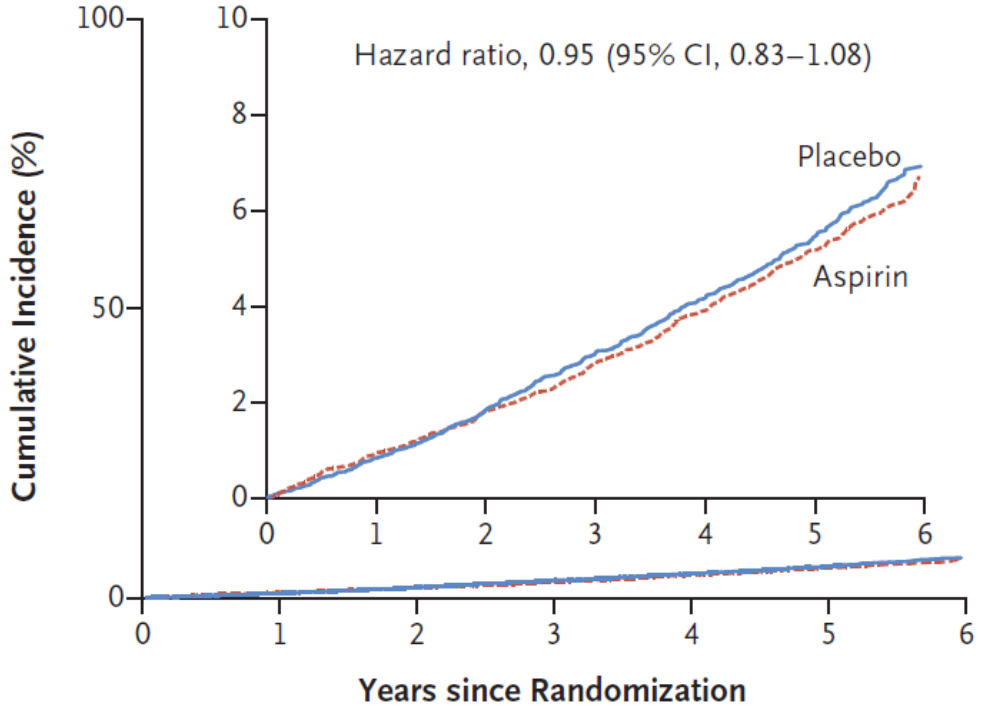
# Effect of Aspirin on Cardiovascular Events and Bleeding in the Healthy Elderly

J.J. McNeil, R. Wolfe, R.L. Woods, A.M. Tonkin, G.A. Donnan, M.R. Nelson, C.M. Reid, J.E. Lockery, B. Kirpach, E. Storey, R.C. Shah, J.D. Williamson, K.L. Margolis, M.E. Ernst, W.P. Abhayaratna, N. Stocks, S.M. Fitzgerald, S.G. Orchard, R.E. Trevaks, L.J. Beilin, C.I. Johnston, J. Ryan, B. Radziszewska, M. Jelinek, M. Malik, C.B. Eaton, D. Brauer, G. Cloud, E.M. Wood, S.E. Mahady, S. Satterfield,* R. Grimm, and A.M. Murray, for the ASPREE Investigator Group†

N Engl J Med 2018:379:1509-18

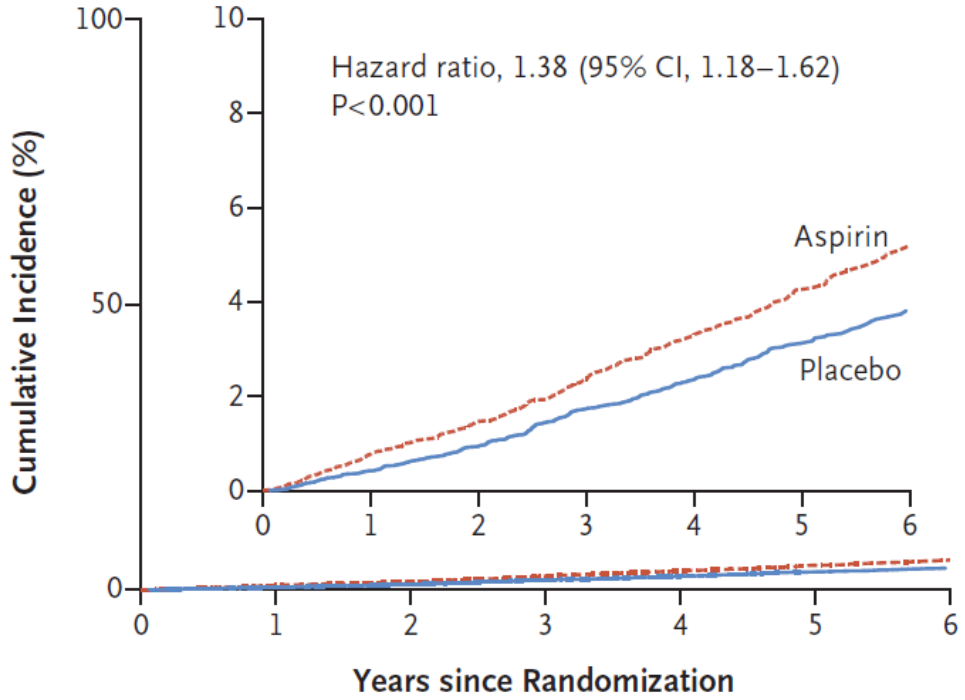
# Benefit vs. Risk in ASPREE

## ASCVD Events




| No. at Risk | | | | | | | |
|---|---|---|---|---|---|---|---|
| Aspirin | 9525 | 9322 | 9068 | 7820 | 5827 | 3568 | 1234 |
| Placebo | 9589 | 9387 | 9119 | 7843 | 5839 | 3578 | 1223 |

## Major Bleeding




| No. at Risk | | | | | | | |
|---|---|---|---|---|---|---|---|
| Aspirin | 9525 | 9337 | 9094 | 7833 | 5826 | 3574 | 1248 |
| Placebo | 9589 | 9424 | 9192 | 7930 | 5935 | 3632 | 1244 |

N Engl J Med 2018:379:1509-18

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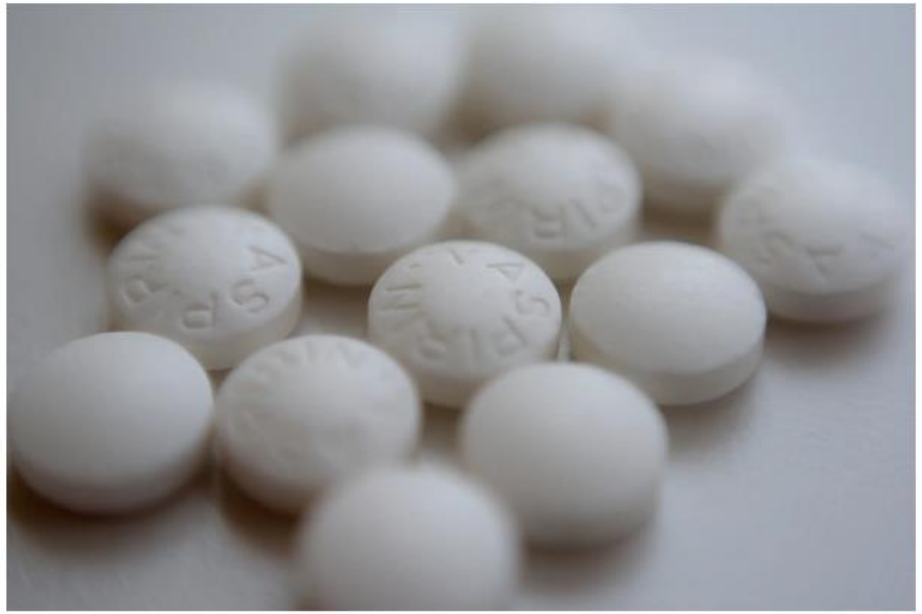
# Daily Low-Dose Aspirin No Longer Recommended by Doctors

Give this article



New guidelines suggest low-dose aspirin should not be recommended to prevent heart attacks in healthy older adults. Patrick Sison/Associated Press

By Laura M. Holson
March 18, 2019

For years, low-dose aspirin has been described as a panacea to ward off heart attacks, strokes and other cardiovascular disease.

**History of U.S. Preventive Services Task Force Recommendations on Aspirin for Primary Prevention of Cardiovascular Disease**

| Year | Recommendation | Grade* |
|---|---|---|
| 1989 | Consider for middle-aged or older men (age, ≥40) with coronary risk factors and low bleeding risk | Not graded |
| 1996 | Insufficient evidence to make recommendation for asymptomatic adults | C |
| 2002 | Strongly recommend discussion of aspirin chemoprevention with adults at excess risk for coronary disease | A |
| 2009 | Recommend aspirin for middle-aged and older men (age range, 45–79) and women (age range, 55–79) when potential benefit outweighs potential harm | A |
| | Recommend against aspirin for middle-aged men (age, <45) and women (age, <55) | D |
| | Evidence insufficient for older adults (age, ≥80) | I |
| 2016 | Recommend initiating aspirin for middle-aged adults (age, 50–59) with 10-year cardiovascular risk ≥10% | B |
| | Individualize decision to initiate aspirin for older adults (age range, 60–69) with 10-year cardiovascular risk ≥10% | C |
| | Evidence insufficient for younger and older adults (age, <50 or >70) | I |
| 2022 | Individualize decision to initiate aspirin for middle-aged adults (age range, 40–59) with 10-year cardiovascular risk ≥10% | C |
| | Recommend against initiating aspirin in older adults (age, ≥60) | D |

NEJM Journal Watch

nytimes.com and NEJM Journal Watch May 3, 2022; USPSTF JAMA. 2022;327(16):1577-1584

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**Aspirin (75 to 100 mg) compared with no aspirin in the primary prevention of cardiovascular disease and cancer**

| Outcomes | Number of participants (studies), follow-up | Certainty of the evidence (GRADE) | Relative effect (95% CI) | Anticipated absolute effects over 10 years | |
|---|---|---|---|---|---|
| | | | | Risk with placebo | Risk difference with aspirin* |
| **Total mortality**<br>Follow-up: range 3.8 to 10 years[1-4] | 161,660 (13 RCTs) | ⨁⨁⨁<br>**MODERATE**<br>due to imprecision¶ | **RR 0.97**<br>(0.93 to 1.02) | **60-year-old person**Δ | |
| | | | | 83 per 1000Δ | 2 fewer per 1000<br>(6 fewer to 2 more) |
| **Myocardial infarction (MI)**<br>Nonfatal events<br>Follow-up: range 3.8 to 10 years[1,2,4] | 142,566 (12 RCTs) | ⨁⨁⨁⨁<br>**HIGH** | **RR 0.83**<br>(0.76 to 0.90) | **Low cardiovascular risk population**◇ | |
| | | | | 27 per 1000§ | 5 fewer per 1000<br>(6 fewer to 3 fewer) |
| | | | | **Moderate cardiovascular risk population**◇ | |
| | | | | 83 per 1000§ | 14 fewer per 1000<br>(20 fewer to 8 fewer) |
| | | | | **High cardiovascular risk population**◇ | |
| | | | | 136 per 1000§ | 23 fewer per 1000<br>(33 fewer to 14 fewer) |
| **Stroke**<br>Includes nonfatal ischemic and hemorrhagic strokes<br>Follow-up: range 3.8 to 10 years[1,2,4] | 127,433 (12 RCTs) | ⨁⨁⨁<br>**MODERATE**<br>due to imprecision¶ | **RR 0.95**<br>(0.85 to 1.06) | **Low cardiovascular risk population**◇ | |
| | | | | 23 per 1000§ | 1 fewer per 1000<br>(3 fewer to 1 more) |
| | | | | **Moderate cardiovascular risk population**◇ | |
| | | | | 65 per 1000§ | 3 fewer per 1000<br>(10 fewer to 4 more) |
| | | | | **High cardiovascular risk population**◇ | |
| | | | | 108 per 1000 | 5 fewer per 1000<br>(16 fewer to 6 more) |
| **Major extracranial bleed**¶¶<br>Follow-up: range 3.8 to 10 years[1,2,4-6] | 155,911 (11 RCTs) | ⨁⨁⨁⨁<br>**HIGH** | **RR 1.46**<br>(1.32 to 1.62) | **Low cardiovascular risk population**‡ | |
| | | | | 8 per 1000§ | 4 more per 1000<br>(3 more to 5 more) |
| | | | | **Moderate cardiovascular risk population**‡ | |
| | | | | 24 per 1000§ | 11 more per 1000<br>(8 more to 15 more) |
| | | | | **High cardiovascular risk population**‡ | |
| | | | | 40 per 1000§ | 18 more per 1000<br>(13 more to 25 more) |
| **Colorectal cancer** (incidence)<br>Follow-up: median 18.3 years[7] | 14,033 (4 RCTs) | ⨁⨁<br>**LOW**<br>due to imprecision† and risk of bias△△ | **HR 0.76**<br>(0.60 to 0.96) | **Low colorectal cancer risk population: Anticipated absolute effect over 20 years**◇◇ | |
| | | | | 30 per 1000** | 7 fewer per 1000<br>(12 fewer to 1 fewer) |
| | | | | **Moderate colorectal cancer risk population** | |
| | | | | 53 per 1000** | 12 fewer per 1000<br>(21 fewer to 2 fewer) |
| | | | | **High colorectal cancer risk population** | |
| | | | | 100 per 1000** | 23 fewer per 1000<br>(39 fewer to 4 fewer) |

## Low Risk

- 5 fewer MIs
- 1 fewer strokes
- 4 more major bleeds
- 7 fewer colon cancers

## High Risk

- 23 fewer MIs
- 3 fewer strokes
- 18 more major bleeds
- 23 fewer colon cancers

**UpToDate.com "Aspirin in the primary prevention of cardiovascular disease and cancer"**

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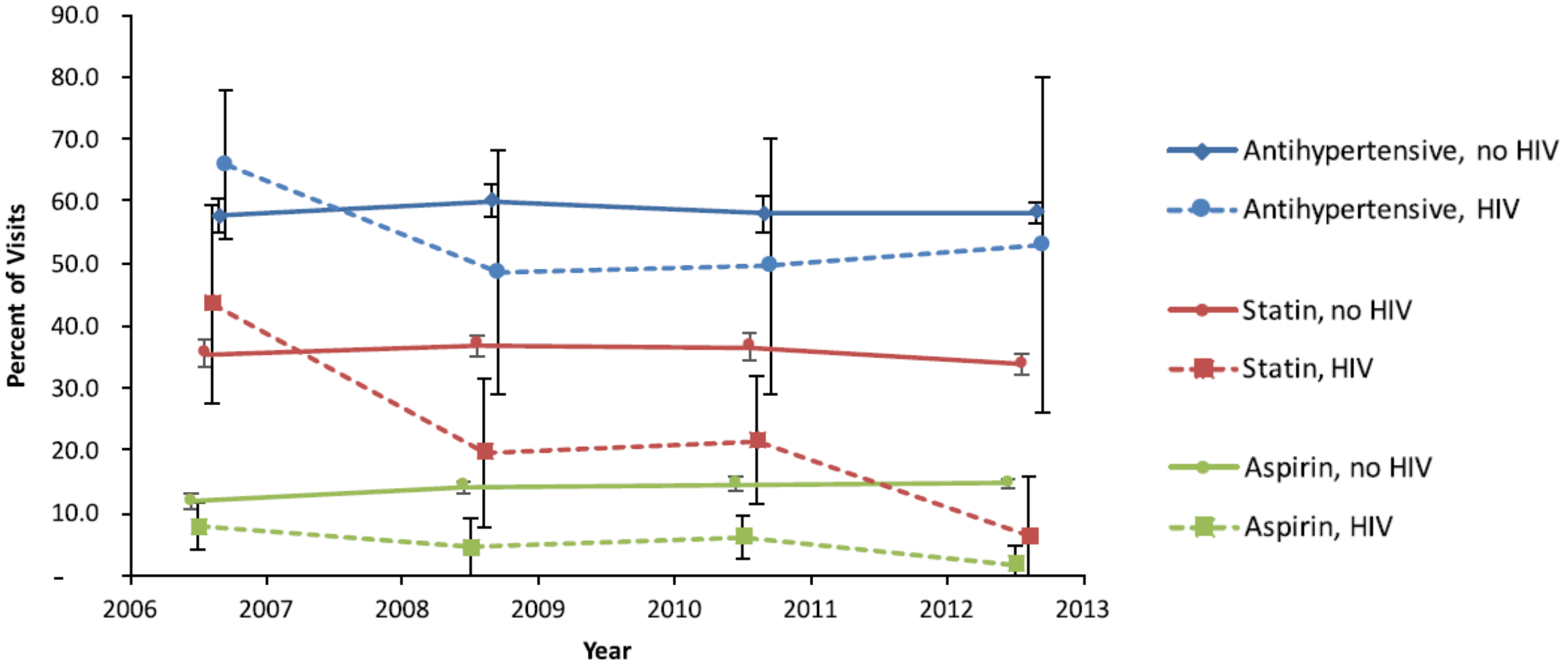
# What about PWH?

# Aspirin is prescribed less often for PWH




Ladapo et al, J Am Heart Assoc, 2017

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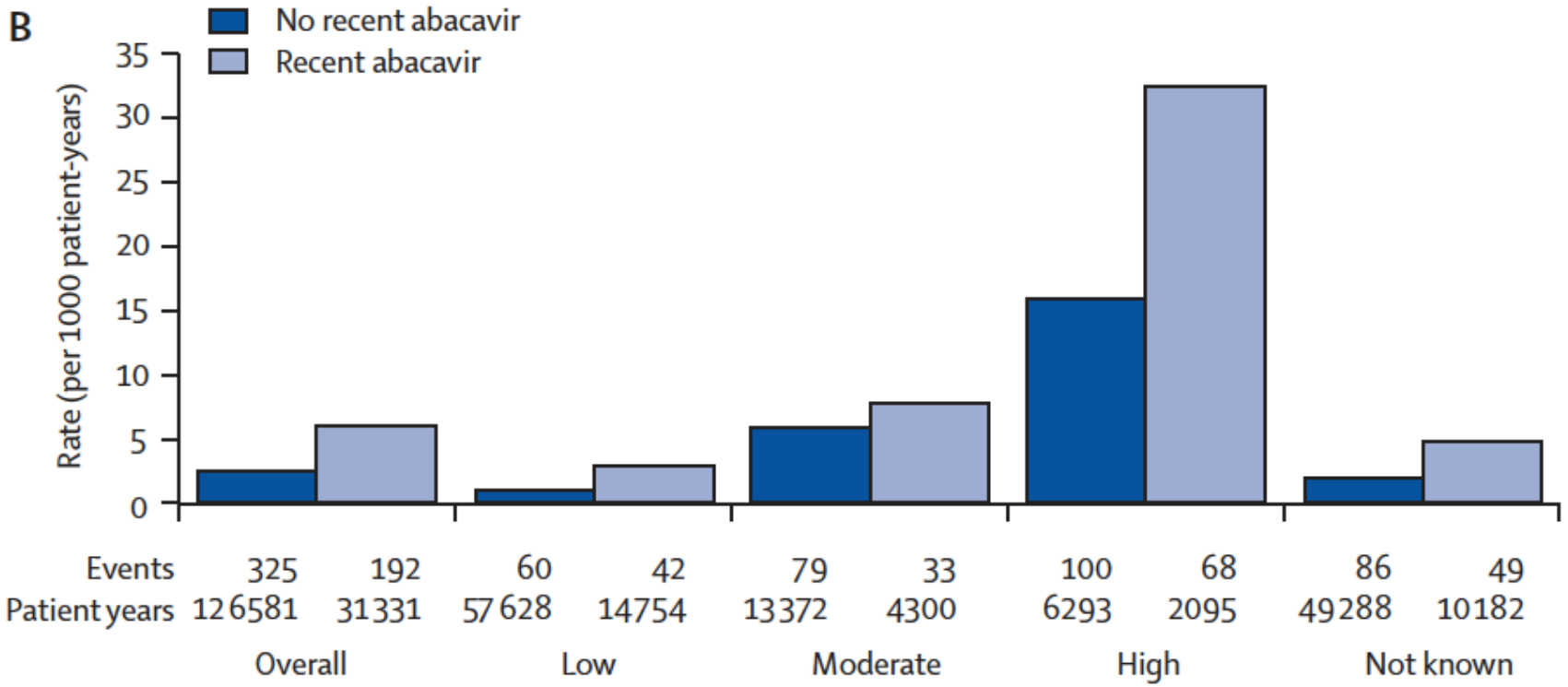
SPECIAL CONSIDERATIONS:

# Abacavir

# Abacavir

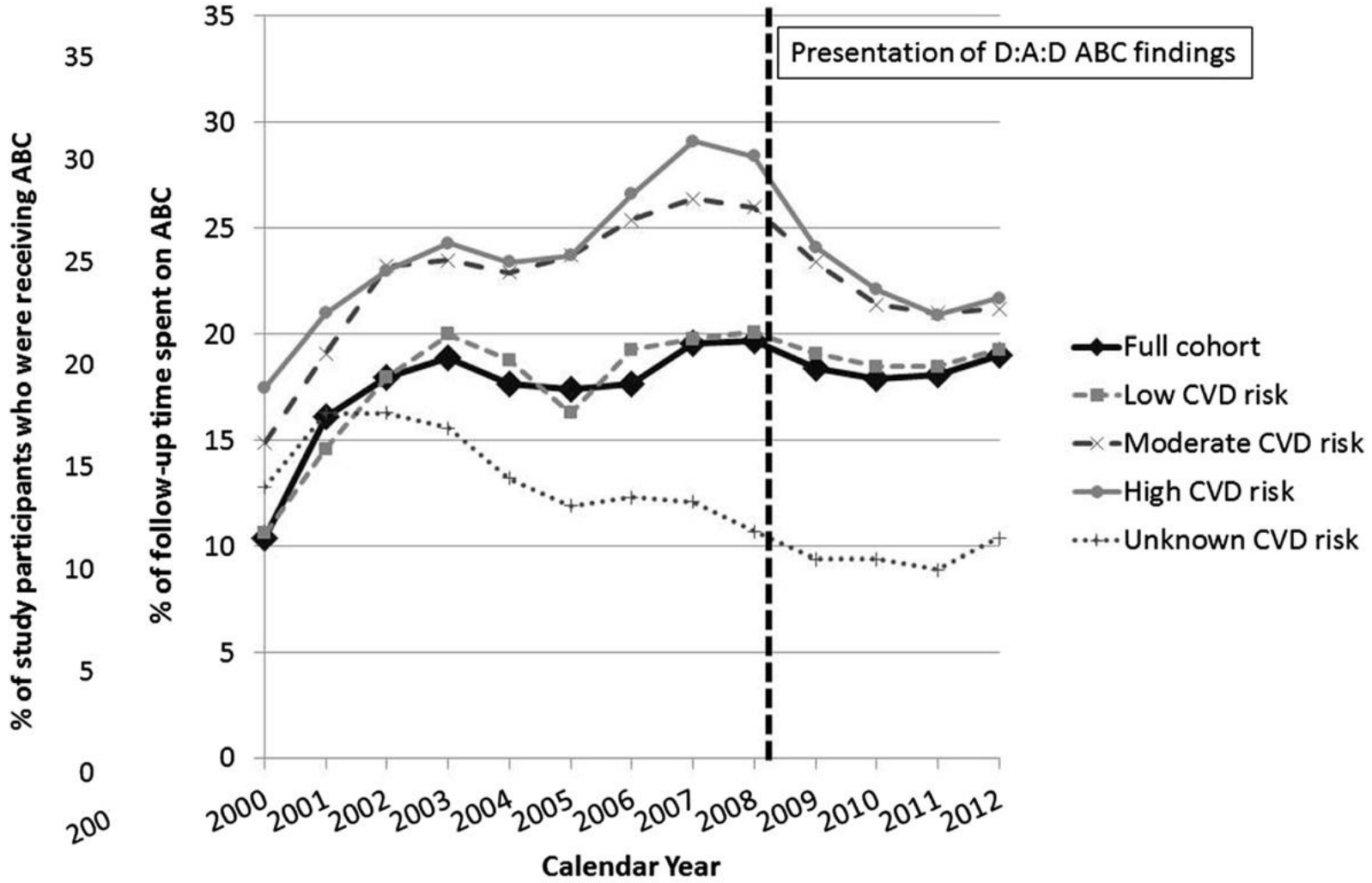
- Original D:A:D study of NRTI risk
- Recent (<6 months)—but not cumulative—use associated with risk (RR 1.9 for abacavir and 1.5 for didanosine)




Sabin et al, Lancet 2008

# Abacavir

- Adjusted RR of MI while on ABC ~2.0
- No difference in pre- vs. post-2008 periods




Sabin et al, BMC Med 2016

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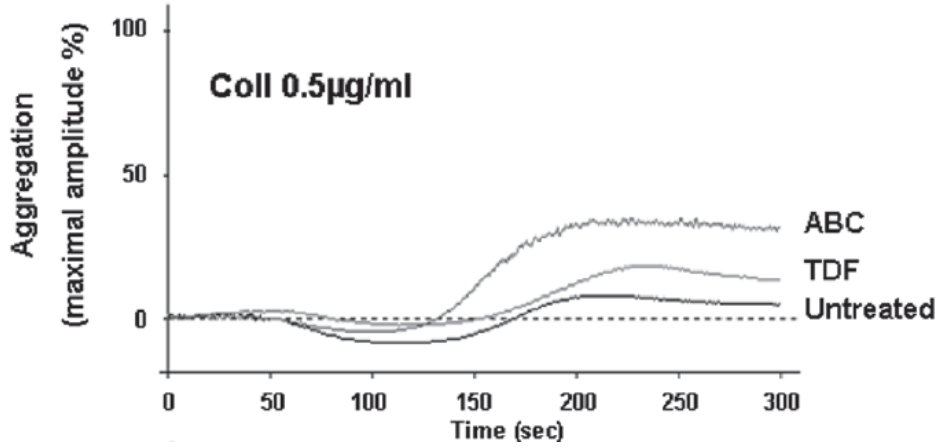
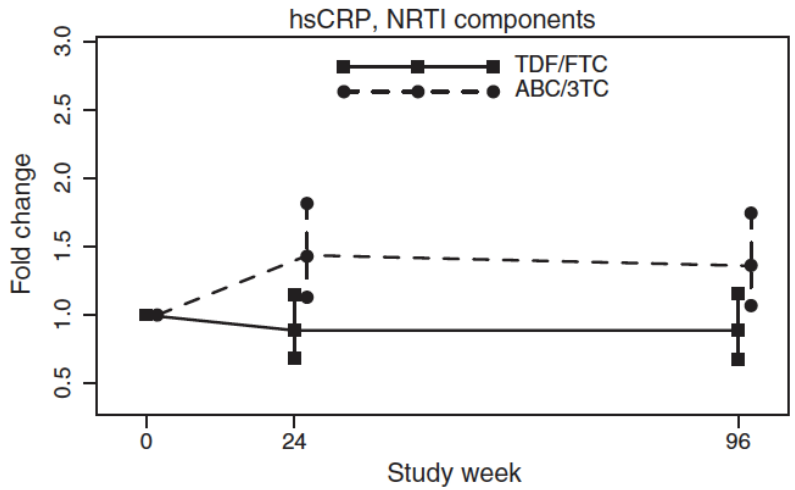
# Abacavir

- Mechanisms?
  - Platelet reactivity
  - Inflammation
- D:A:D analysis of recurrent MI
  - NO increased risk of continued abacavir use after first MI
    - Cumulative post-MI exposure RR 0.86 (95% CI 0.68-1.10)
    - Recent post-MI exposure RR 1.19 (0.82-1.71)
  - ? Role of aspirin




* Higher platelet aggregation by light transmission aggregometry after stimulation in ABC treated patients compared to TDF




* More inflammation? Higher hsCRP with ABC vs. TDF in A5224s

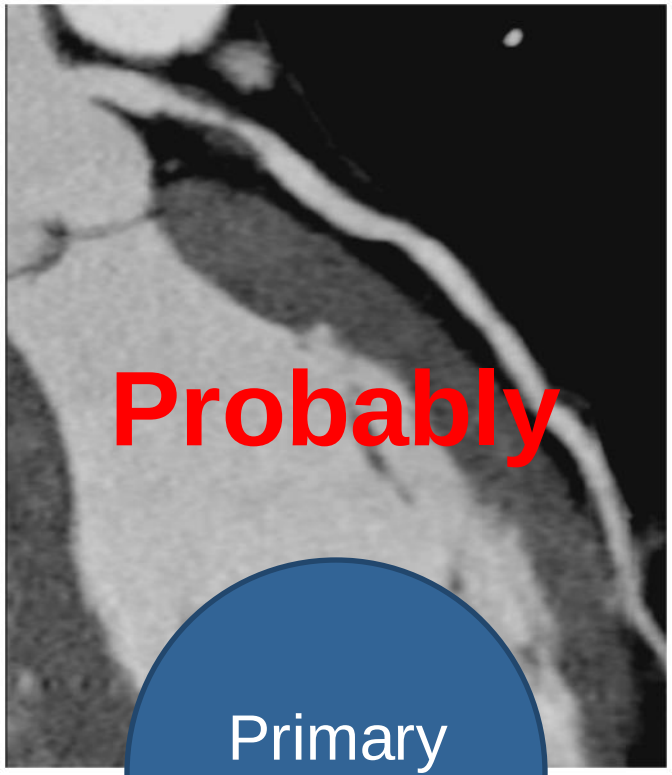
Falcinelli et al, Thromb Haemost 2013; McComsey et al, AIDS 2012; Sabin et al, AIDS 2017

# A word on secondary prevention

# "… for healthy people" does NOT apply for patients with established ASCVD

## Primary Prevention


Healthy
No prior ASCVD event




## Secondary Prevention


Post-MI
Post-stroke
Symptomatic PAD

# Other anti-platelet therapy and boosted ART

- P2Y12 inhibitors
  - Ticagrelor contraindicated due to CYP3A4 metabolism
  - Clopidogrel and Prasugrel are prodrugs converted to active metabolites by CYP3A4 & 2C19 in the liver
    - The AUC and Cmax of both active metabolites are reduced by ~50% in patients on cobicistat or ritonavir
    - However, prasugrel's antiplatelet effect is preserved (compared to clopidogrel, which is significantly reduced)
  - Prasugrel is the usually the best choice for patients on a protease inhibitor or cobicistat

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# In Conclusion

- Individualize decision to initiate aspirin for primary prevention of ASCVD events
- In middle-aged adults with HIV (40-59)
- With 10-year ASCVD risk >10%
- ***Or on abacavir***
- ***Or with significant subclinical coronary disease on CT ("Primary +")***

Generally, avoid aspirin for primary prevention among older adults with HIV (>60 years old)

# Acknowledgment

This Mountain West AIDS Education and Training (MWAETC) program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $3,098,654 with 0% financed with non-governmental sources.

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