DOES AN ASPIRIN A DAY REALLY KEEP THE DOCTOR AWAY?

A focused update on the use of ASA for primary prevention of CVD

Oct 2019

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DISCLOSURE SLIDE

I have received a research grant from UTOPIAN to explore patient preferences related to STATIN therapy.

I am a strong believer in shared decision making

I have no other conflicts of interest

EDITORIAL

JAMA The Journal of the American Medical Association

Aspirin for Primary Prevention
Clinical Considerations in 2019

J. Michael Gaziano, MD, MPH

CLINICAL DECISIONS
INTERACTIVE AT NEJM.ORG

MAY 16, 2019

"Doctor, Should I Keep Taking an Aspirin a Day?"

OPTION 1

Recommend Continuing Aspirin

John W. McEvoy, M.B., B.Ch., M.H.S.

OPTION 2

Recommend Discontinuing Aspirin

Sigrun Halvorsen, M.D., Ph.D.

THE LANCET

The rise and fall of aspirin in the primary prevention of cardiovascular disease

Lancet 2019; 393: 2155–67

Inbar Raber, Cian P McCarthy, Muthiah Vaduganathan, Deepak L Bhatt, David A Wood, John G F Cleland, Roger S Blumenthal, John W McEvoy

Editorial

Diabetes & Vascular Disease Research
2018, Vol. 15(6) 475–476

Primary vascular prevention: The end of the road for aspirin?

RA Ajjan

The Guardian

Bitter pill: why aspirin is not such a wonder drug

New research analysis has found that for some patients the risk from the drug of increased bleeding events outweighs its benefits in preventing heart attacks and strokes

https://www.theguardian.com/lifeandstyle/shortcuts/2019/jan/23/bitter-pill-why-aspirin-is-not-such-a-wonder-drug

CBC

Healthy seniors taking low-dose Aspirin may be doing more harm than good

Large-scale study finds 'wonder drug' not working wonders

https://www.cbc.ca/news/health/aspirin-seniors-health-heart-study-1.4826801

Cardiovascular Drugs and Therapy (2018) 32:241–243
https://doi.org/10.1007/s10557-018-6803-0

EDITORIAL

Targeting Cardiovascular Disease in Patients with Chronic Kidney Disease: Is Primary Prevention with Aspirin Ready for Prime Time?

Editorial to: "Aspirin for Primary Prevention of Cardiovascular Disease and Renal Disease Progression in Chronic Kidney Disease Patients: A Multicenter Randomized Clinical Trial (AASER Study)" by M. Goicoechea et al.

June 2018

Roy O. Mathew[1] · Elvira O. Gosmanova[2] · Mandeep S. Sidhu[3]

Aspirin use may not lower risk for MI, stroke in CKD

November 20, 2018

https://susvalleypolicy.org/wp-content/uploads/2017/02/BehindTheHealines.png

OUTLINE:
FOCUSED UPDATE: ASA FOR PRIMARY PREVENTION

- Provide a brief history on the use of ASA
- Review recent trial evidence
- Discuss updated clinical guidelines
- List ongoing clinical studies and potential future directions
- Discuss application of data to clinical practice
- Share clinical experience (depending on time)
- Share takeaway messages

Watch For Slides Labelled:

RENAL PERSPECTIVE

BRIEF HISTORY

HOW DID WE GET HERE?

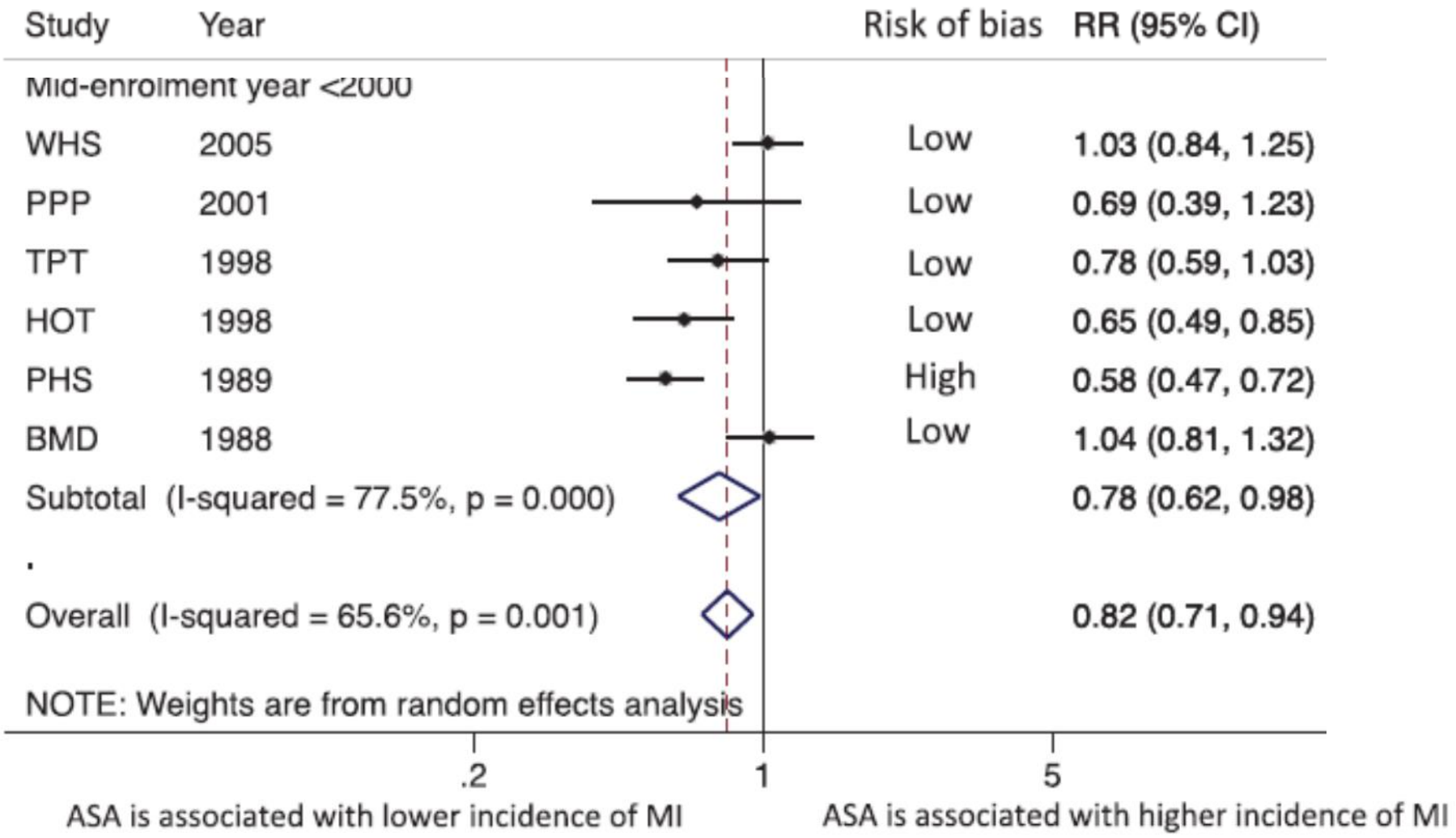
Modified: https://www.doctoroz.com/feature/dr-oz-s-complete-guide-turn-back-clock

BACKGROUND

- ASA is an old medication. First produced in 1897!
- Still one of the most commonly used medications today
- ASA is effective for secondary prevention of CVD. Considered standard of care.
- The use of ASA for primary prevention is more controversial

CVD = Cardiovascular Disease

Early Trials Of ASA For Primary Prevention



European Heart Journal (2019) 40, 607–617

BACKGROUND:

- Some early primary prevention trials found:
  - reductions in MI and stroke (although not mortality)
  - increased risk of bleeding

- In the past: Many international guidelines on primary prevention typically recommended ASA only when there was a substantial 10-yr risk of cardiovascular events

- But guideline organizations differed in their exact recommendations for ASA use

- Aside: this is a common challenge for front line clinicians.
  - Which guidelines should be followed? Which guidelines are best?
  - Patients often have multiple conditions (which may not be factored in the guidelines).

U.S. Preventive Services TASK FORCE

- **Adults aged 50 to 59 years:**
  - Recommends low-dose ASA for patients (GRADE B) – provided:
    - ≥10% CVD risk (over 10 yrs)
    - Not at increased risk for bleeding,
    - Have a life expectancy of ≥ 10 years
    - Willing to take low-dose ASA daily for ≥ 10 years.

- **Adults aged 60 to 69 years:**
  - Decision is an individual one for patients who meet above criteria (GRADE C)
  - Persons who place a higher value on the potential benefits than the potential harms may choose to initiate low-dose aspirin

https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/aspirin-to-prevent-cardiovascular-disease-and-cancer

U.S. Preventive Services TASK FORCE

Guideline for:

≥10% CVD risk / 10 yrs

Not at increased risk for bleeding,

Have a life expectancy of ≥ 10 years

Initiation of low dose ASA daily for ≥ 10 years

Adults aged 50 to 59 years:

Recommends low-dose ASA for patients (GRADE B)

Adults aged 60 to 69 years:

Decision is an individual one for patients (GRADE C)

Persons who place a higher value on the potential benefits than the potential harms may choose to initiate low-dose aspirin

Age alone could qualify someone for ASA therapy

https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/aspirin-to-prevent-cardiovascular-disease-and-cancer

IT IS ESTIMATED THAT **35.8 MILLION** ADULTS IN THE US TAKE ASPIRIN FOR PRIMARY PREVENTION OF CARDIOVASCULAR DISEASE

SOME DO SO WITHOUT CONSULTING THEIR PHYSICIAN

www.thelancet.com Vol 393 May 25, 2019

WHAT ABOUT

CANADIAN GUIDELINES

Canadian Cardiovascular Society
Leadership. Knowledge. Community.

Antiplatelet Therapy for the Primary Prevention of Vascular Events

1. For men and women without evidence of manifest vascular disease, the use of ASA at any dose is not recommend for routine use to prevent ischemic vascular events (Class III, Level A).

2. For men and women without evidence of manifest vascular disease, the use of clopidogrel 75 mg daily plus ASA at any dose is not recommended to prevent ischemic vascular events (Class III, Level B).

3. In special circumstances in men and women without evidence of manifest vascular disease in whom vascular risk is considered high and bleeding risk low, ASA 75-162 mg daily may be considered (Class IIb, Level C).

Hypertension CANADA

- Consideration should be given to the addition of low-dose ASA therapy in hypertensive patients ≥50 years of age (Grade B).
    - In past: recommended that ASA be considered in all hypertensive individuals, with a Grade A rating for those ≥ 50 years of age

- Caution should be exercised if BP is not controlled (Grade C).

https://guidelines.hypertension.ca/prevention-treatment/uncomplicated-hypertension-vascular-protection/

RENAL PERSPECTIVE

BACKGROUND: RENAL PERSPECTIVE

- Patients with CKD are at high risk for cardiovascular events
  - Non-Dialysis Dependent CKD: 10X more likely to die of CVD versus general population.
  - Dialysis CKD: patients are at even higher risk for CVD

- The pathophysiology of CVD in patients with CKD may be different than general population.

- Some evidence antiplatelet agents may be less effective in patients with CKD (residual thromboxane formation)

- Patients with CKD are also at increased risk for bleeding issues

BACKGROUND: RENAL PERSPECTIVE

- Unfortunately there is great uncertainty about the benefits and risks of ASA for primary prevention in patients with CKD
  - Exclusion of patients with CKD from cardiac trials
  - Inherent limitations in published literature
  - Some of the trial results are conflicting / contradictory

- Many guidelines don't specifically address the CKD population

- Despite the gaps in knowledge and guideline recommendations - ASA is still commonly used for primary prevention in CKD setting.
  - Estimates: ~1 Million Patients With CKD use ASA for primary prevention in UK.

EARLY TRIAL DATA
RELATED TO CKD POPULATION

Study or Subgroup	Aspirin Events	Aspirin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
HARP-I	0	108	0	110		Not estimable
HOT	76	1791	110	1828	59.4%	0.71 [0.53, 0.94]
JPAD	24	342	15	290	40.6%	1.36 [0.73, 2.54]
Total (95% CI)		**2241**		**2228**	**100.0%**	**0.92 [0.49, 1.73]**
Total events	100		125			

Heterogeneity: $Tau^2 = 0.15$; $Chi^2 = 3.48$, df = 1 (P = 0.06); $I^2 = 71\%$
Test for overall effect: Z = 0.26 (P = 0.79)

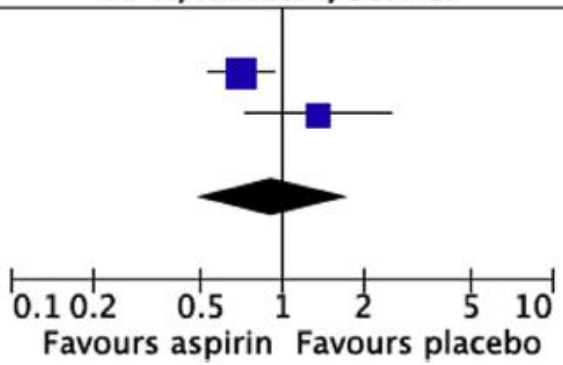


Fig. 2. Forest plot of risk ratios for CVD events using a random effects model and M-H method.

Key Message: No benefit for CVD risk reduction

Study or Subgroup	Aspirin Events	Aspirin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
HARP-I	2	108	1	110	5.9%	2.04 [0.19, 22.14]
HOT	26	1791	13	1828	76.4%	2.04 [1.05, 3.96]
JPAD	6	342	3	290	17.7%	1.70 [0.43, 6.72]
Total (95% CI)		**2241**		**2228**	**100.0%**	**1.98 [1.11, 3.52]**
Total events	34		17			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.06$, df = 2 (P = 0.97); $I^2 = 0\%$
Test for overall effect: Z = 2.30 (P = 0.02)

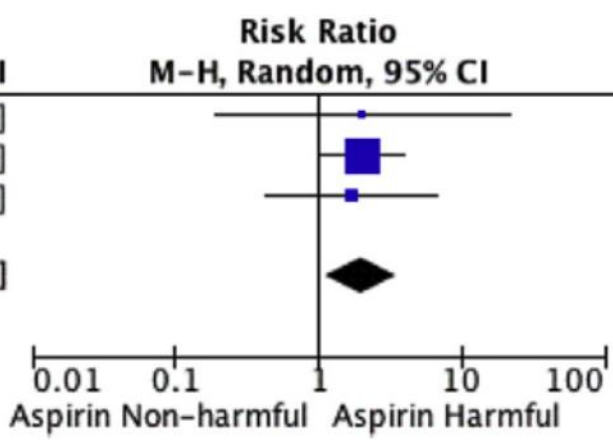


Fig. 3. Forest plot of risk ratios for major bleeding events using a random effects model and M-H method.

Key Message: Increase risk of Major Bleeding (NNH = 101 over 5 years); Minor Bleeding NNH = 35 (over 5 years)

PAST GUIDELINES:
ASA FOR PRIMARY PREVENTION IN CKD POPULATION

AJKD

Management of Traditional Cardiovascular Risk Factors in CKD: What Are the Data?

L. Parker Gregg and S. Susan Hedayati

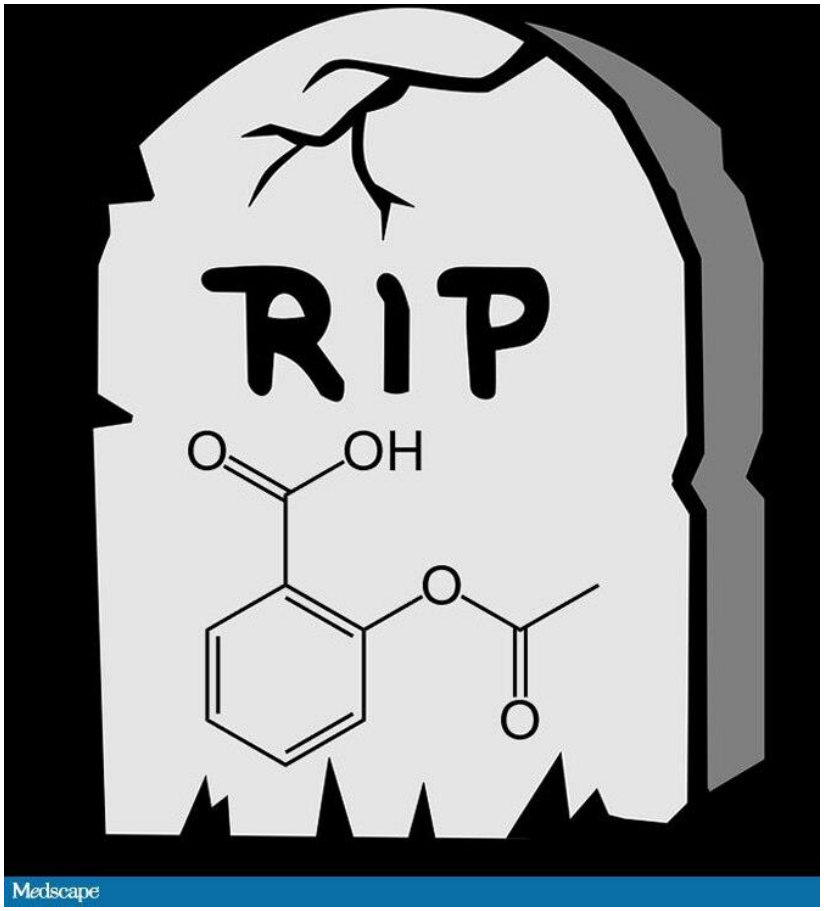
Guideline	Non-Dialysis Dependent CKD	CKD-5
ACC / AHA	Low-Dose ASA should be used in DM patients with albuminuria or other CV risk factors	-
KDIGO	Aspirin is indicated for secondary but not primary prevention	-
KDOQI	-	-

Am J Kidney Dis. 72(5): 728-744. Nov 2018

RECENT TRIAL EVIDENCE

STARTING WITH THE “BIG 3”

THE FALL OF ASPIRIN FOR PRIMARY PREVENTION?



https://img.medscapestatic.com/article/901/966/901966-figure-1.jpg?interpolation=lanczos-none&resize=670:*

ARRIVE, ASCEND, ASPREE

ARRIVE

- Large RCT (~12,500) in 7 Countries
- ASA 100mg VS placebo
- Moderate CV risk patients (Mean FRS ~ 14%)
- No CVD, No Diabetes
- Mean Age: ~64yrs, Male: ~ 70%, Caucasian ~98%
- ~43% on STATINS
- Median follow up 5 years
- Funding: Bayer

FRS = Framingham Risk Score (10yrs)

Lancet Sept 2018; 392: 1036-46

ARRIVE

Exclusion Criteria:

"Severe renal disease or damage based on the clinical judgement of the investigator"

Lancet Sept 2018; 392: 1036-46

FRS = Framingham Risk Score (10yrs)

https://clinicaltrials.gov/ct2/show/NCT00501059

	Number of events in the intention-to-treat population		
	Aspirin (n=6270)	Placebo (n=6276)	Hazard ratio (95% CI); p value
Myocardial infarction, stroke, cardiovascular death, unstable angina, or transient ischaemic attack	269 (4·29%)	281 (4·48%)	0·96 (0·81–1·13); p=0·6038
Myocardial infarction, stroke, or cardiovascular death	208 (3·32%)	218 (3·47%)	0·95 (0·79–1·15); p=0·6190
Myocardial infarction*	95 (1·52%)	112 (1·78%)	0·85 (0·64–1·11); p=0·2325
Non-fatal myocardial infarction	88 (1·40%)	98 (1·56%)	0·90 (0·67–1·20); p=0·4562
Stroke*	75 (1·20%)	67 (1·07%)	1·12 (0·80–1·55); p=0·5072
Cardiovascular death	38 (0·61%)	39 (0·62%)	0·97 (0·62–1·52); p=0·9010
Unstable angina	20 (0·32%)	20 (0·32%)	1·00 (0·54–1·86); p=0·9979
Transient ischaemic attack	42 (0·67%)	45 (0·72%)	0·93 (0·61–1·42); p=0·7455
Any death	160 (2·55%)	161 (2·57%)	0·99 (0·80–1·24); p=0·9459

*Fatal or non-fatal.

Table 2: Efficacy endpoints in the intention-to-treat

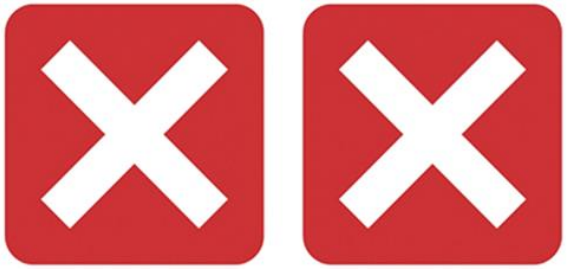
Key Message: No significant difference in any of the efficacy endpoints.
Limitation: lower than expected event rate
Per Protocol Analysis (Controversial): some benefit in MI reduction

https://www.thelancet.com/article/S0140-6736(18)31924-X/fulltext

	Aspirin (n=6270)	Placebo (n=6276)
Total number of serious adverse events	1266 (20·19%)	1311 (20·89%)
Bleeding serious adverse events by severity		
Any gastrointestinal bleed **NNH 196**	61 (0·97%)	29 (0·46%)
Severe gastrointestinal bleed	4 (0·06%)	2 (0·03%)
Moderate gastrointestinal bleed	15 (0·24%)	5 (0·08%)
Mild gastrointestinal bleed	42 (0·67%)	22 (0·35%)
Haemorrhagic stroke	8 (0·13%)	11 (0·18%)

Study excluded patients at risk of bleeding

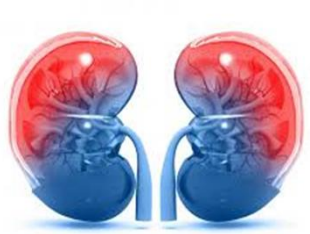
ASCEND



- Large RCT (~15,500) in UK
- ASA 100mg VS placebo
- Patients with DM, without CVD
- Mostly: Low (~40%) to Moderate CV Risk (~40%)
- Mean Age: 63yrs, Male: ~ 63%, Caucasian ~97%
- ~75% on STATINS, by end of trial ~ 25% on PPI
- Follow up 7.4 years
- Funded: mainly British Heart Foundation

NEJM Oct 2018 https://www.nejm.org/doi/pdf/10.1056/NEJMoa1804988; Am Heart Journal; April 2018

ASCEND

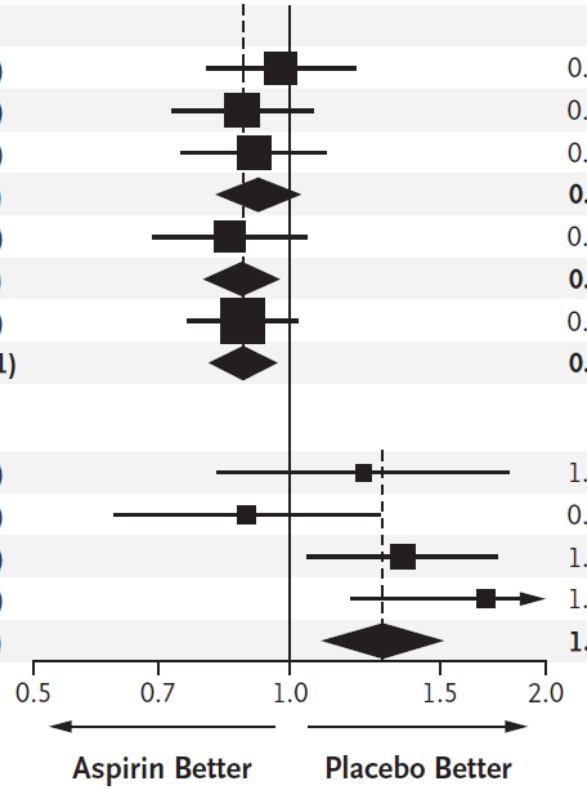


Measurement	Aspirin (N=7740)		Placebo (N=7740)	
eGFR (ml/min/1.73m^2)$^+$				
≥90	2265	(29%)	2258	(29%)
≥60 <90	1986	(26%)	2030	(26%)
<60	649	(8%)	627	(8%)
No usable sample collected	2840	(37%)	2825	(36%)
Mean (SD)	85.2	(21)	85.2	(21)
Urinary albumin/creatinine ratio (mg/mmol)				
≥3	621	(8%)	627	(8%)
<3	4267	(55%)	4259	(55%)
No usable sample collected	2852	(37%)	2854	(37%)
Median (IQR)	0.56	(0.00-1.33)	0.55	(0.18-1.34)

Exclusion: "No other predominant life-threatening medical problem … that might limit compliance with 5 yrs of study treatment"

https://www.nejm.org/doi/suppl/10.1056/NEJMoa1804988/suppl_file/nejmoa1804988_appendix_1.pdf

Type of Event	Aspirin (N=7740)	Placebo (N=7740)	Rate Ratio (95% CI)	P Valu
	no. of participants with event (%)			
Vascular Outcomes				
Nonfatal myocardial infarction	191 (2.5)	195 (2.5)	0.98 (0.80–1.19)	
Nonfatal presumed ischemic stroke	202 (2.6)	229 (3.0)	0.88 (0.73–1.06)	
Vascular death excluding intracranial hemorrhage	197 (2.5)	217 (2.8)	0.91 (0.75–1.10)	
Any serious vascular event excluding TIA	**542 (7.0)**	**587 (7.6)**	**0.92 (0.82–1.03)**	
TIA	168 (2.2)	197 (2.5)	0.85 (0.69–1.04)	
Any serious vascular event including TIA ★	**658 (8.5)**	**743 (9.6)**	**0.88 (0.79–0.97)**	**0.01**
Any arterial revascularization	340 (4.4)	384 (5.0)	0.88 (0.76–1.02)	
Any serious vascular event or revascularization	**833 (10.8)**	**936 (12.1)**	**0.88 (0.80–0.97)**	
Major Bleeding				
Intracranial hemorrhage	55 (0.7)	45 (0.6)	1.22 (0.82–1.81)	
Sight-threatening bleeding in eye	57 (0.7)	64 (0.8)	0.89 (0.62–1.27)	
Serious gastrointestinal bleeding	137 (1.8)	101 (1.3)	1.36 (1.05–1.75)	
Other major bleeding	74 (1.0)	43 (0.6)	1.70 (1.18–2.44)	
Any major bleeding ★	**314 (4.1)**	**245 (3.2)**	**1.29 (1.09–1.52)**	**0.003**



Key Message:

- **NNT (for SVE including TIA) = 91**
- **NNH for Major Bleed = 111**
- **The benefits were largely counterbalanced by bleeding ADRs**

ASPREE

- Large RCT (~19,000) primarily from Australia
- ASA 100mg VS placebo
- Elderly patients without CVD
- Majority "Not Frail", ~11% had Diabetes
- Mean Age: 74, Female: ~ 56%, Caucasian ~91%
- ~34% on STATINS, ~25% on PPI – at trial entry
- Median follow up 4.7 years (trial stopped for futility)
- Funding: mainly National Institute on Aging

NEJM October 2018

ASPREE

Table 1. Demographic Characteristics, Cardiovascular Risk Factors, and Treatment of the Participants at Randomization.*

Variable	Aspirin (N=9525)	Placebo (N=9589)
	no. (%)	
Chronic kidney disease**	2456 (26)	2464 (26)

** Chronic kidney disease was defined as an estimated glomerular filtration rate of less than 60 ml per minute per 1.73 m^2 or a ratio of albumin (in milligrams per liter) to creatinine (in millimoles per liter) in urine of 3 or more.

Exclusion: "A serious intercurrent illness likely to cause death within the next 5 years"

NEJM October 2018

Table 2. Composite Primary End Point, Including the Components, and Secondary End Points of Death, Dementia, Persistent Physical Disability, and Major Hemorrhage.*

End Point	Aspirin (N = 9525)		Placebo (N = 9589)		Hazard Ratio (95% CI)	P Value
	no. of participants with event	*rate per 1000 person-yr*	*no. of participants with event*	*rate per 1000 person-yr*		
Primary end point†	921	21.5	914	21.2	1.01 (0.92–1.11)	0.79
Death from any cause	480	11.2	431	10.0	—	—
Dementia	274	6.4	275	6.4	—	—
Persistent physical disability	167	3.9	208	4.8	—	—
Secondary end points‡						
Death from any cause	558	12.7	494	11.1	1.14 (1.01–1.29)	—
Dementia	283	6.7	292	6.9	0.98 (0.83–1.15)	—
Persistent physical disability	188	4.9	224	5.8	0.85 (0.70–1.03)	—
Major hemorrhagic event	361	8.6	265	6.2	1.38 (1.18–1.62)	<0.001
Clinically significant bleeding	312	7.4	225	5.3	—	—
Hemorrhagic stroke	49	1.2	40	0.9	—	—

No benefit in all cause death, dementia, persistent physical disability

But there was increased risk of major bleeding.

Major Bleeding NNH =97

Reminder: they excluded patients at "high risk for bleeding"

NEJM Oct 2018 https://www.nejm.org/doi/pdf/10.1056/NEJMoa1800722?articleTools

Table 2. Cardiovascular Events.*

End Point	Overall (N = 19,114)	Aspirin (N = 9525)		Placebo (N = 9589)		Hazard Ratio (95% CI)
	no. of participants with event	*no. of participants with event*	*rate per 1000 person-yr*	*no. of participants with event*	*rate per 1000 person-yr*	
Cardiovascular disease†	922	448	10.7	474	11.3	0.95 (0.83–1.08)
Major adverse cardiovascular event‡	701	329	7.8	372	8.8	0.89 (0.77–1.03)
Fatal cardiovascular disease§	159	78	1.8	81	1.9	0.97 (0.71–1.33)
Hospitalization for heart failure	171	88	2.1	83	1.9	1.07 (0.79–1.44)
Fatal or nonfatal myocardial infarction	355	171	4.0	184	4.3	0.93 (0.76–1.15)
Fatal or nonfatal ischemic stroke¶	315	148	3.5	167	3.9	0.89 (0.71–1.11)

No benefit for cardiovascular events

NEJM Oct 2018 https://www.nejm.org/doi/pdf/10.1056/NEJMoa1805819

Table 1. Mortality According to the Underlying Cause of Death.*

Cause of Death	Overall (N = 19,114)	Aspirin (N = 9525)	Placebo (N = 9589)	Hazard Ratio (95% CI)
	no. of deaths	*no. of deaths (%)*		
Any **NNH 143**	1052	558 (5.9)	494 (5.2)	1.14 (1.01–1.29)
Cancer† **NNH 125**	522	295 (3.1)	227 (2.3)	1.31 (1.10–1.56)
Cardiovascular disease, including ischemic stroke‡	203	91 (1.0)	112 (1.2)	0.82 (0.62–1.08)
Major hemorrhage, including hemorrhagic stroke§	53	28 (0.3)	25 (0.3)	1.13 (0.66–1.94)
Other¶	262	140 (1.5)	122 (1.3)	1.16 (0.91–1.48)
Insufficient information‖	12	4 (<0.1)	8 (0.1)	—

Increased risk of all cause death (NNH = 143)

Surprisingly – death related to cancer was increased (NNH 125)

Was this a chance finding?

NEJM Oct 2018. https://www.nejm.org/doi/pdf/10.1056/NEJMoa1803955

WERE THERE ANY RECENT RCTS THAT FOCUSED ON CKD PATIENTS

Cardiovascular Drugs and Therapy (2018) 32:255–263
https://doi.org/10.1007/s10557-018-6802-1

ORIGINAL ARTICLE

Aspirin for Primary Prevention of Cardiovascular Disease and Renal Disease Progression in Chronic Kidney Disease Patients: a Multicenter Randomized Clinical Trial (AASER Study)

- Multicenter, Open Label, RCT
- Conducted in Spain
- N = 111
- GFR 15-60 ml/min
- Intervention: ASA 100mg/day VS usual therapy
- Follow up ~ 65 months
- **Limitations: small sample size, open label, low event rate**

Table 2 Distribution of cardiovascular events in the two groups. *PAD* peripheral arterial disease, *MI* myocardial infarction, *HF* heart failure

	Cardiovascular Event (n)					Total
Group	MI	Stroke	HF	PAD	Fatal MI	
Standard (n=61)	7	2	4	3	1	17(28%)
ASA (n=50)	0	4	1	0	0	5(10%)

No statistical difference in primary composite CV outcome (p=0.069)

ASA benefit in reducing Fatal / Non-Fatal MI (ARR: 13%; p=0.014)

No differences in major / minor bleeding

Secondary Outcome: AASER Study

ASA reduced the risk for renal events (p=0.016)

- Standard Group: 17/61 (28%),
- ASA Group 3/50 (6%)

Definition:

- Doubled SCR, ≥50% decrease in eGFR OR Renal Replacement Therapy

Table 3 eGFR changes in standard and ASA group (baseline and at the end of the study) (all patients)

eGFR (ml/min/1.73 m^2)	Baseline	End of the study
Standard group ($n = 50$)	38 ± 10	28 ± 13*
ASA group ($n = 61$)	40 ± 11	40 ± 19

*$p < 0.001$ vs baseline eGFR

UPDATED META-ANALYSIS

ESC European Society of Cardiology

European Heart Journal (2019) **40**, 607–617
doi:10.1093/eurheartj/ehy813

FASTTRACK CLINICAL RESEARCH

Efficacy and safety of aspirin for primary prevention of cardiovascular events: a meta-analysis and trial sequential analysis of randomized controlled trials

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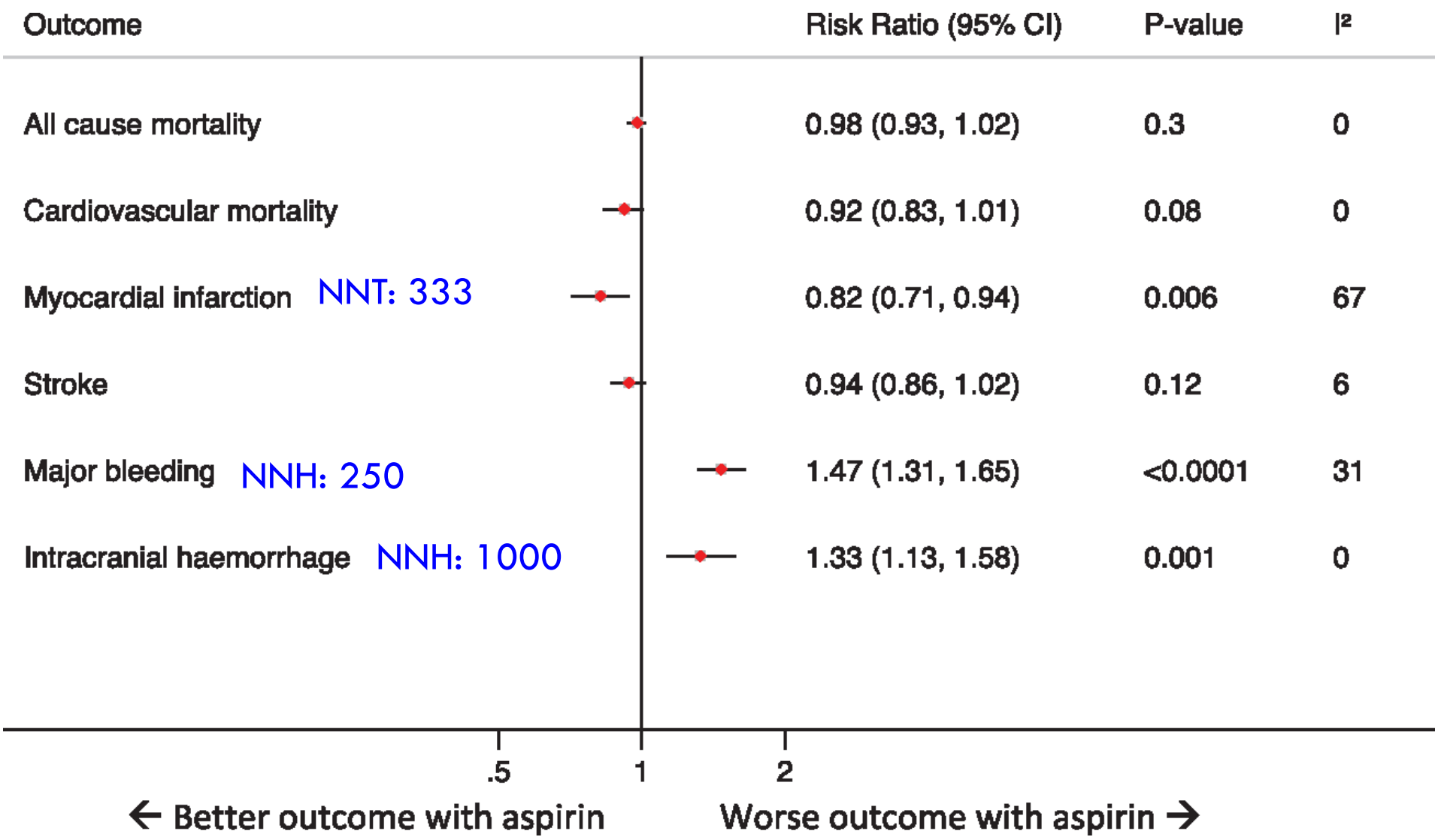
ESC European Society of Cardiology



STATS/EBM Expert: Caution "No significant benefit if limit analysis to recent trials"

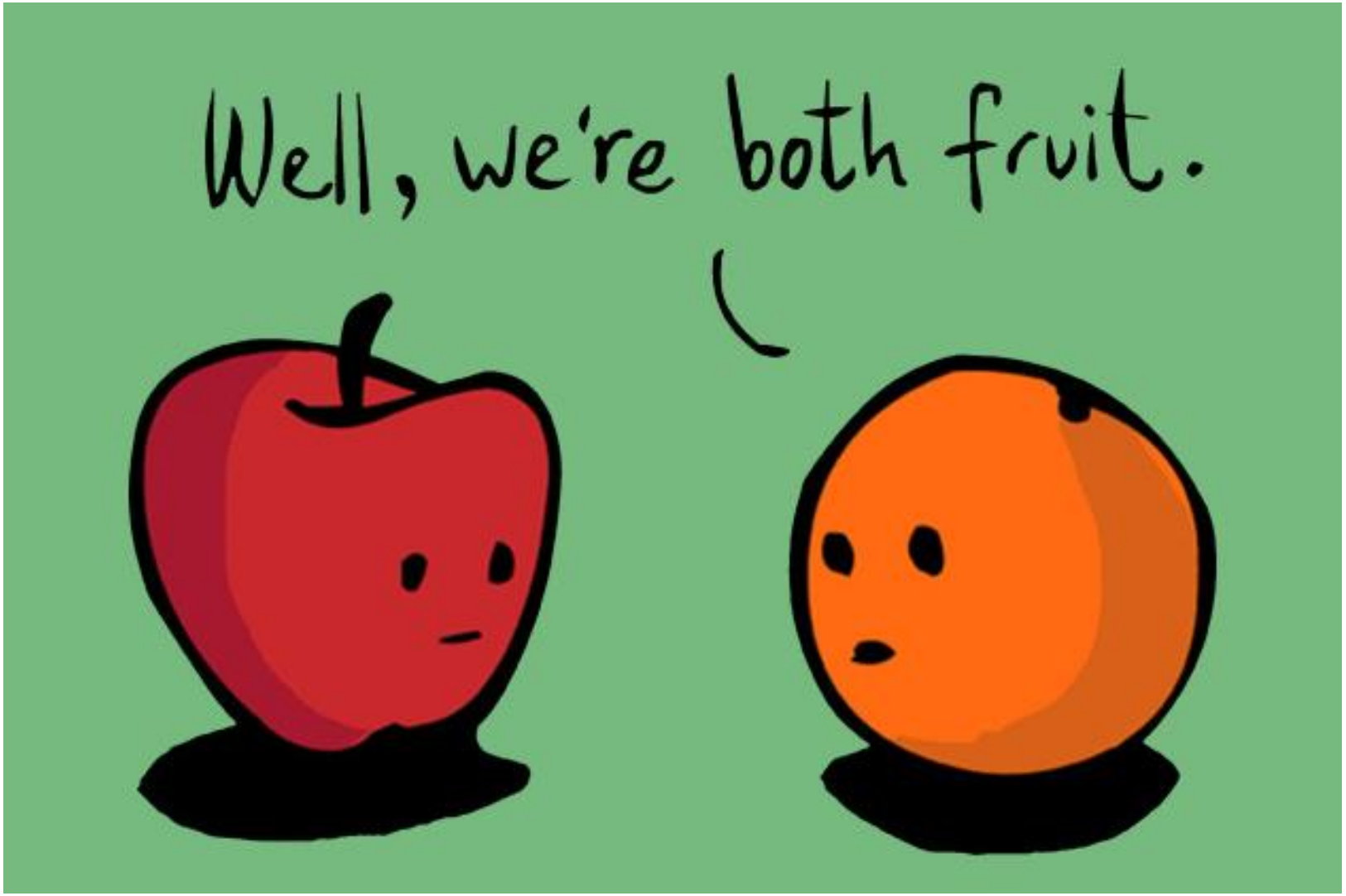
BMC Nephrology

RESEARCH ARTICLE

Effect of antiplatelet therapy on cardiovascular and kidney outcomes in patients with chronic kidney disease: a systematic review and meta-analysis

Xiaole Su[1,2], Bingjuan Yan[2], Lihua Wang[2], Jicheng Lv[3], Hong Cheng[1] and Yipu Chen[1*]

Su *et al. BMC Nephrology* (2019) 20:309
https://doi.org/10.1186/s12882-019-1499-3



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UPDATED GUIDELINE

2019 ACC/AHA GUIDELINE ON THE PRIMARY PREVENTION OF CVD

Age 40-70yrs

- Low Dose ASA might be considered for primary prevention in select higher ASCVD adults who are not at increased bleeding risk.

Age > 70yrs

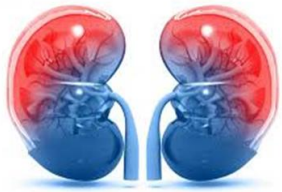
- Low-dose ASA should NOT be administered on a routine basis for primary prevention

Patients at increased risk of bleeding (any age)

- Low-dose ASA should NOT be administered for primary prevention

https://www.acc.org/latest-in-cardiology/ten-points-to-remember/2019/03/07/16/00/2019-acc-aha-guideline-on-primary-prevention-gl-prevention

ACC/ AHA: Avoid ASA



"Most important is to avoid aspirin in persons with increased risk of bleeding including a history of GI bleeding or peptic ulcer disease, bleeding from other sites, age >70 years, thrombocytopenia, coagulopathy, **chronic kidney disease**, and concurrent use of nonsteroidal anti-inflammatory drugs, steroids, and anticoagulants. "

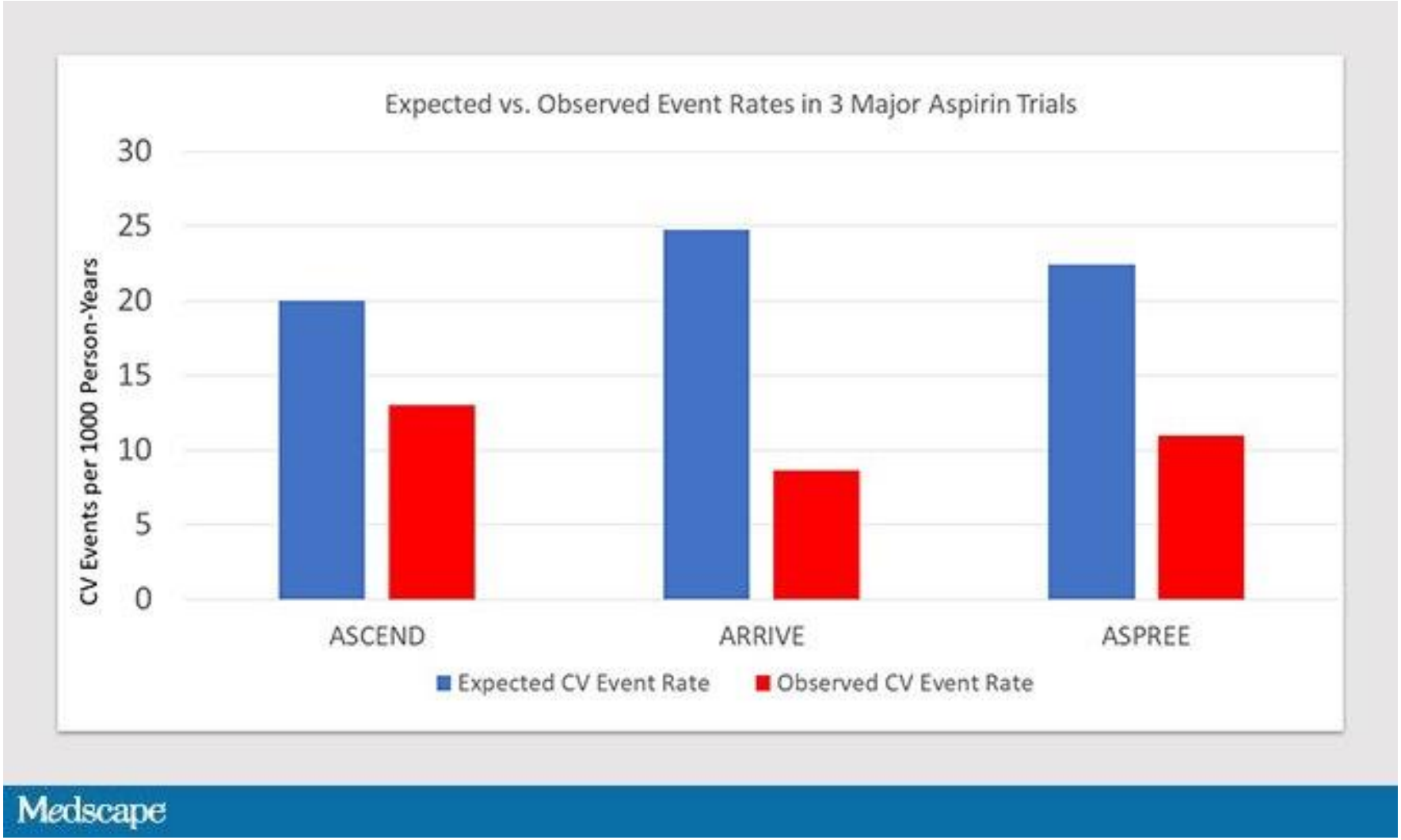
https://www.acc.org/latest-in-cardiology/ten-points-to-remember/2019/03/07/16/00/2019-acc-aha-guideline-on-primary-prevention-gl-prevention

FUTURE STUDIES
OUTSTANDING QUESTIONS

FUTURE STUDIES AND OUTSTANDING QUESTIONS

- Do we need new cardiovascular risk calculators?
- Will ASA provide additional benefit to STATIN therapy?
  - Ongoing Study: ACCEPT-D (DM patients on Simvastatin)
- Optimal dose of ASA (to balance efficacy VS safety)?
  - Is it the same for everyone?
  - Ongoing: ANDAMAN (Daily VS BID), ADAPTABLE (81mg VS 325mg)
- Are there specific populations that may benefit from ASA?
  - Prediction tools to help us select patients? (efficacy + safety).
- Will ASA be (partially) resurrected for primary prevention?

NEED FOR NEW RISK CALCULATORS?

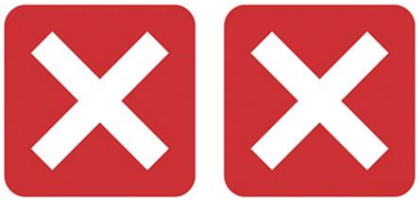


https://img.medscapestatic.com/article/901/966/901966-figure-7.jpg?interpolation=lanczos-none&resize=670:*

RENAL PERSPECTIVE

POTENTIAL OPPORTUNITY: POST- HOC REVIEW?

ASCEND



Number of Patients With CKD: 1276

ASPREE

Number of Patients With CKD: 4920

ATTACK TRIAL

ASPIRIN TO TARGET ARTERIAL EVENTS IN CKD

- **Objective:** to determine if low dose ASA reduces major vascular events in people with CKD without pre-existing CVD.
- **Design:** open label, multicenter, RCT
- **Location:** primary care centers in the UK
- **Population** (N ~25,000):
  - CKD GFR Category 1-4.
  - Exclude: History of CVD, at risk of bleeding
- **Intervention:**
  - ASA 75mg daily VS standard of care
  - Stratified by: stratified by age, diabetes and CKD severity
- **Expected completion:** 2025

https://www.southampton.ac.uk/attack-trial/about/about-attack.page

IMPLICATIONS FOR CLINICAL PRACTICE


EXPERT
COMMENTARY

NEJM COMMENTARY:

Dr Schwenk and Dr Brett (Deputy editor/ Editor in Chief NEJM)

- *"pinpointing an individual patient's 10-year CV risk is difficult (given the controversies about accuracies of risk calculators), and individualizing 10-year risk for major bleeding is equally difficult. An alternative perspective would be for clinicians to inform patients that the most-recent trials — performed in contemporary patient populations — weigh against a net benefit for aspirin in primary prevention, regardless of baseline CV risk."*

https://www.jwatch.org/na48372/2019/02/06/aspirin-primary-prevention-new-meta-analysis

NEJM COMMENTARY:

Dr Paul Ridker, Center for CV Disease Prevention,
Brigham and Women's Hospital, Boston

- *"Thus, beyond diet maintenance, exercise, and smoking cessation, the best strategy for the use of aspirin in the primary prevention of cardiovascular disease may simply be to prescribe a statin instead."*

https://www.nejm.org/doi/pdf/10.1056/NEJMe1812000

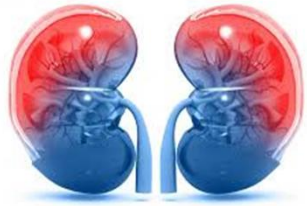
EXPERT COMMENTARY

DR'S DAD AND WEINER
(TUFTS MEDICAL CENTER, BOSTON)

2017 (Pre-AASER): "*High quality prospective data assessing the efficacy and safety of low-dose aspirin for primary CVD prevention in patients with kidney disease do not exist. Given different trade-offs in advanced kidney disease, particularly in dialysis, where the risk for bleeding may be higher, life expectancy is far shorter at all ages than for the general population, and the mechanism of CVD may differ from the general population … there are no convincing data to recommend aspirin for primary prevention in advanced CKD at the current time*"

Am J Kidney Dis. 2017;69(3):337-340

AJKD



Management of Traditional Cardiovascular Risk Factors in CKD: What Are the Data?

L. Parker Gregg and S. Susan Hedayati

2018 (Pre-AASER): *"Overall, existing data do not support the use of aspirin for primary prevention of CV events in NDD-CKD because the bleeding risk may equal or outweigh the uncertain benefits."*

"There is insufficient evidence to support routine Aspirin use in dialysis dependent patents"

Am J Kidney Dis. 72(5): 728-744. Nov 2018

AJKD

Management of Traditional Cardiovascular Risk Factors in CKD: What Are the Data?

L. Parker Gregg and S. Susan Hedayati

2018 (Pre-AASER): *"As practicing nephrologists, we are therefore left with the challenging conundrum of whether evidence to support such management is lacking because robust trials do not yet exist, whether our patients are different from the general population, or worse yet, it is just too late to intervene"*

Am J Kidney Dis. 72(5): 728-744. Nov 2018

Targeting Cardiovascular Disease in Patients with Chronic Kidney Disease: Is Primary Prevention with Aspirin Ready for Prime Time?

Editorial to: "Aspirin for Primary Prevention of Cardiovascular Disease and Renal Disease

Roy O. Mathew [1] · Elvira O. Gosmanova [2] · Mandeep S. Sidhu [3]

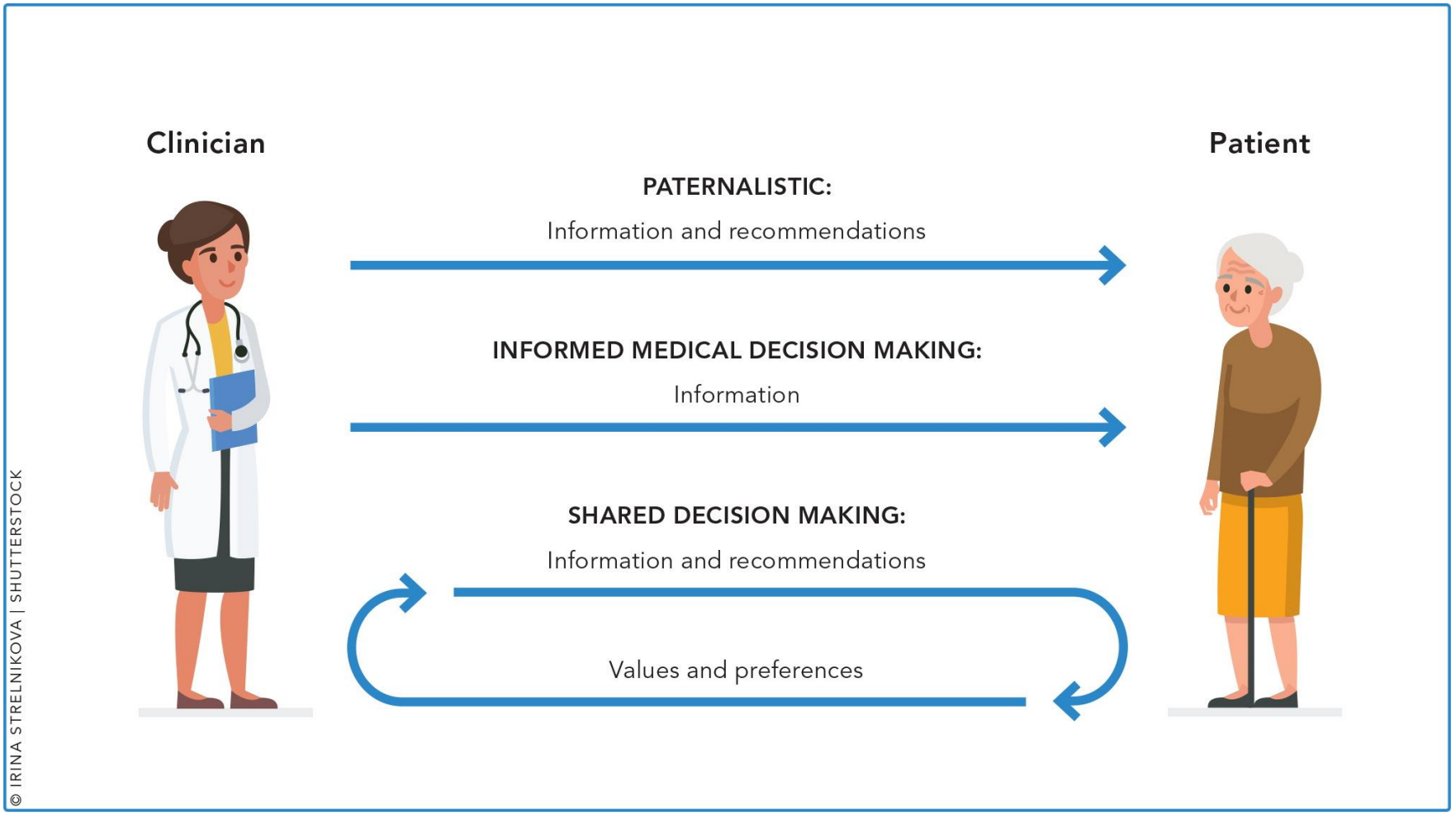
- *"Although Aspirin appears to reduce coronary events, the results should be interpreted with caution given the study's small sample size and low rate of CVD events in the aspirin arm, which raises a concern of incomplete ascertainment of CVD events."*
- *"A larger RCT should be conducted … before aspirin can be uniformly recommended for patients with severe CKD"*

Cardiovascular Drugs and Therapy (2018) 32:241–243

MY APPROACH

IMPORTANCE OF SHARED DECISION MAKING

Shared Decision Making



https://www.aafp.org/fpm/2017/0500/p5.html

Asking "What Matters to You?" Should Be an Always Event

http://www.ihi.org/communities/blogs/PublishingImages/mdrydacb.yaf.1e880535-d855-4727-a8c1-27ee672f115d.1330272.png
http://www.ihi.org/communities/blogs/why-asking-what-matters-to-you-should-be-an-always-event?utm_campaign=tw&utm_source=hs_email&utm_medium=email&_hsenc=p2ANqtz-8IZv9JiK-mtsxAsab0ZI9y3czKwgPSZZKGJMcBVbAaKSfNtLmWCC_VH0NMPiqUqkZReeNP

- The vast majority of patients actively seek information about their health.

- Offer to discuss the issue with your patients
  - For those already on ASA for primary prevention
  - For those who are considering ASA for primary prevention

- Review benefits, risks, and uncertainties. Involve patients in the treatment decision.

Alston et al. Institute of Medicine, 2012

https://fosteringandadoption.rip.org.uk/wp-content/uploads/2014/03/dfe_key_messages_icon.jpg

SHARING REAL LIFE CASES

(DEPENDING ON TIME)

Do You Have Any Real Life Cases You Wish To Share

http://health.sunnybrook.ca/wp-content/uploads/2014/11/doctor-elderly-patient.jpg
https://catalyst.nejm.org/shared-decision-making-good-clinical-care/

Patient Safety Tip: Need For Detective Work!

THE TAKEAWAYS

My Takeaways (Part 1)

- In the past - guideline organizations differed on their exact recommendations for ASA use in the primary prevention of CVD (in general population and CKD population)
- Despite this – ASA was commonly prescribed for this indication
- Major RCTs and Meta-Analyses were published in the last year that shed some new light on the benefits VS risks of ASA in this setting
- There is still, however, much to be learned related to CKD population
- Many experts recommend against routine use of ASA for primary prevention (risks > benefit for many patients). It will be interesting to see how recommendations evolve over time as more studies are conducted

My Takeaways (Part 2)

- Remember Shared Decision Making: discuss benefits, risks and uncertainties. Involve patients in the decision

- When R/A patients:
  - Carefully consider indication(s): may require some detective work
  - For primary prevention: many patients may not wish to use ASA after a shared decision making discussion. (especially seniors or those without DM). Some high risk patients may still wish therapy despite the risks / limitations in current data.
  - For secondary prevention patients: revisit the importance of long term ASA

- Hopefully future studies will provide more clear guidance to patients / providers RE: ASA for primary prevention

https://s3-eu-west-1.amazonaws.com/stm-stmvalidation/uploads/20160928082101/QA770.jpg