PRIMARY PREVENTION OF CVD:
ROLE OF ASA AND STATIN THERAPY
MAY 2019

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Toronto Western FHT
Pharm Course Director,
PA Program, UofT
PEBC Reviewer
I have received a research grant from UTOPIAN to explore patient preferences related to STATIN therapy

I have no other conflicts of interest
ASA FOR PRIMARY PREVENTION OF CVD

FOCUSED UPDATE:
ASA FOR PRIMARY PREVENTION OF CVD

Objectives

- Briefly discuss recent trial evidence for the use of ASA in primary prevention of CVD
- Briefly review updated clinical guidelines on the use of ASA in primary prevention of CVD
- Briefly list ongoing clinical studies and potential future directions
- Discuss considerations for clinical practice
BACKGROUND

- ASA has strong evidence for use for secondary prevention of CVD
- Previously we had mixed study results on the use of ASA for primary prevention of CVD
- Guideline organizations have different recommendations regarding ASA for primary cardiovascular prevention
- ASA is commonly used for primary prevention of CVD
- Recent studies have helped clarify the role of ASA in this setting

CVD = Cardiovascular Disease
ARRIVE, ASCEND, ASPREE

[3 red X icons]
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)
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
Study excluded patients at risk of bleeding

<table>
<thead>
<tr>
<th></th>
<th>Aspirin (n=6270)</th>
<th>Placebo (n=6276)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of serious adverse events</td>
<td>1266 (20.19%)</td>
<td>1311 (20.89%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BLEEDING SERIOUS ADVERSE EVENTS BY SEVERITY</th>
<th>Aspirin</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any gastrointestinal bleed</td>
<td>61 (0.97%)</td>
<td>29 (0.46%)</td>
</tr>
<tr>
<td>Severe gastrointestinal bleed</td>
<td>4 (0.06%)</td>
<td>2 (0.03%)</td>
</tr>
<tr>
<td>Moderate gastrointestinal bleed</td>
<td>15 (0.24%)</td>
<td>5 (0.08%)</td>
</tr>
<tr>
<td>Mild gastrointestinal bleed</td>
<td>42 (0.67%)</td>
<td>22 (0.35%)</td>
</tr>
<tr>
<td>Haemorrhagic stroke</td>
<td>8 (0.13%)</td>
<td>11 (0.18%)</td>
</tr>
</tbody>
</table>
ASCEND

- Large RCT (~15,500) in UK
- ASA 100mg VS placebo
- Diabetes patients 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

Key Message:
- The CV benefits were largely counterbalanced by bleeding ADRs
- Total Population: NNT: 91 (for composite), NNH: 111 (Fatal /Major bleed)
**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
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”
Table 2. Cardiovascular Events:*  

<table>
<thead>
<tr>
<th>End Point</th>
<th>Overall (N=19,114)</th>
<th>Aspirin (N=9525)</th>
<th>Placebo (N=9589)</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of participants with event</td>
<td>no. of participants with event</td>
<td>rate per 1000 person-yr</td>
<td>no. of participants with event</td>
</tr>
<tr>
<td>Cardiovascular disease†</td>
<td>922</td>
<td>448</td>
<td>10.7</td>
<td>474</td>
</tr>
<tr>
<td>Major adverse cardiovascular event‡</td>
<td>701</td>
<td>329</td>
<td>7.8</td>
<td>372</td>
</tr>
<tr>
<td>Fatal cardiovascular disease§</td>
<td>159</td>
<td>78</td>
<td>1.8</td>
<td>81</td>
</tr>
<tr>
<td>Hospitalization for heart failure</td>
<td>171</td>
<td>88</td>
<td>2.1</td>
<td>83</td>
</tr>
<tr>
<td>Fatal or nonfatal myocardial infarction</td>
<td>355</td>
<td>171</td>
<td>4.0</td>
<td>184</td>
</tr>
<tr>
<td>Fatal or nonfatal ischemic stroke¶</td>
<td>315</td>
<td>148</td>
<td>3.5</td>
<td>167</td>
</tr>
</tbody>
</table>

No benefit for cardiovascular events
Increased risk of all cause death (NNH = 143)

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

Was this a chance finding?

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

Ahmed N. Mahmoud\textsuperscript{1}‡, Mohamed M. Gad\textsuperscript{2}, Akram Y. Elgendy\textsuperscript{1}, Islam Y. Elgendy\textsuperscript{1}‡, and Anthony A. Bavry\textsuperscript{1,3}∗

\textsuperscript{1}Division of Cardiovascular Medicine, Department of Medicine, University of Florida, 1600 SW Archer Road, Gainesville, FL 32610, USA; \textsuperscript{2}Department of Cardiovascular Medicine, Heart and Vascular Institute, Cleveland Clinic, 9500 Euclid Ave, Cleveland, OH 44195, USA; and \textsuperscript{3}North Florida/South Georgia Veterans Health System, Malcom Randall Veterans Administration Medical Center, Medical Service, Cardiology Section (111D), 1601 SW Archer Road, Gainesville, FL 32608, USA

Received 28 September 2018; revised 13 October 2018; editorial decision 12 November 2018; accepted 14 November 2018; online publish-ahead-of-print 17 December 2018
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Risk Ratio (95% CI)</th>
<th>P-value</th>
<th>I²</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cause mortality</td>
<td>0.98 (0.93, 1.02)</td>
<td>0.3</td>
<td>0</td>
</tr>
<tr>
<td>Cardiovascular mortality</td>
<td>0.92 (0.83, 1.01)</td>
<td>0.08</td>
<td>0</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0.82 (0.71, 0.94)</td>
<td>0.006</td>
<td>67</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.94 (0.86, 1.02)</td>
<td>0.12</td>
<td>6</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>1.47 (1.31, 1.65)</td>
<td>&lt;0.0001</td>
<td>31</td>
</tr>
<tr>
<td>Intracranial haemorrhage</td>
<td>1.33 (1.13, 1.58)</td>
<td>0.001</td>
<td>0</td>
</tr>
</tbody>
</table>

No significant benefit if limit analysis to recent trials
UPDATED GUIDELINES
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
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?
APPLICATION TO PRACTICE
SHARING A REAL LIFE CASE
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
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.”
Clinician

PATERNALISTIC:
Information and recommendations

INFORMED MEDICAL DECISION MAKING:
Information

SHARED DECISION MAKING:
Information and recommendations

Values and preferences

Patient

STATINS FOR PRIMARY PREVENTION OF CVD
FOCUSED UPDATE:
STATINS FOR PRIMARY PREVENTION OF CVD

Objectives:

- Briefly review efficacy of STATIN therapy for Primary Prevention of CVD

- Describe new evidence related to the use of STATINs for primary prevention in elderly patients

- Briefly review potential safety risks with STATIN therapy

- Introduce select controversies throughout the talk

- Discuss considerations for clinical practice
BACKGROUND: STATINS

- Statins are the single most commonly prescribed class of treatment in the developed world

- One of the most studied therapeutic classes of medications

- Secondary prevention: standard of care. Strong evidence

- Primary prevention: significant controversy / debate
RATIONAL PRESCRIBING

- Indication
- Efficacy
- Safety
- Dosing / Monitoring / Targets
- Adherence and Other Factors
WHAT IS THE RIGHT RISK THRESHOLD?

- Guidelines from the around the world have different recommendations for STATIN use for primary prevention

- What is the right risk threshold to recommend (offer) STATIN therapy? (And is there a best way to calculate risk?)

- Most RCTs have included patients with ≥ 2 risk factors … although many patients who qualify for drug therapy may not have 2 risk factors

- Should age alone be reason enough to initiate treatment?

- Controversial: Swiss Modeling Study
  - Suggests STATINs are overprescribed for primary prevention.
  - Looked at benefits VS risks of therapy
  - Suggest a higher risk threshold be used
  - Annals of Internal Med 2019

“STATINIZATION”


• “It is uncertain whether this would be one of the greatest achievements or one of the worst disasters of medical history”

EFFICACY
Comparative effectiveness and safety of statins as a class and of specific statins for primary prevention of cardiovascular disease: A systematic review, meta-analysis, and network meta-analysis of randomized trials with 94,283 participants

Henock G Yebyo, MSc, a, b Hélène E Aschmann, MSc, a Marco Kaufmann, MSc, a and Milo A Puhan, MD, PhD a
Zurich, Switzerland and Mekelle, Ethiopia

American Heart Journal, April 2019:
<table>
<thead>
<tr>
<th>Outcomes related to statins</th>
<th>RR (95% CI)</th>
<th>Quality</th>
<th>RD per 1000 over 10–yrs (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonfatal MI</td>
<td>0.62 (0.53, 0.72)</td>
<td>Very low</td>
<td>−20 (−25 to −15)</td>
</tr>
<tr>
<td>Fatal MI</td>
<td>0.72 (0.50, 1.03)</td>
<td>Moderate</td>
<td>−4 (−7 to 0)</td>
</tr>
<tr>
<td>Major CV events</td>
<td>0.74 (0.67, 0.81)</td>
<td>Very low</td>
<td>−12 (−15 to −9)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>0.75 (0.63, 0.91)</td>
<td>High</td>
<td>−6 (−9 to −2)</td>
</tr>
<tr>
<td>CVD mortality</td>
<td>0.80 (0.71, 0.91)</td>
<td>Moderate</td>
<td>−11 (−16 to −5)</td>
</tr>
<tr>
<td>Fatal stroke</td>
<td>0.79 (0.53, 1.19)</td>
<td>High</td>
<td>−2 (−4 to 2)</td>
</tr>
<tr>
<td>Nonfatal stroke</td>
<td>0.83 (0.75, 0.92)</td>
<td>Low</td>
<td>−7 (−10 to −3)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>0.84 (0.71, 1.02)</td>
<td>High</td>
<td>−3 (−6 to 0)</td>
</tr>
<tr>
<td>All–cause mortality</td>
<td>0.89 (0.85, 0.93)</td>
<td>Low</td>
<td>−14 (−20 to −9)</td>
</tr>
<tr>
<td>Trt. discontinuation</td>
<td>1.00 (0.78, 1.24)</td>
<td>Very low</td>
<td>0 (−34 to 38)</td>
</tr>
<tr>
<td>All cancers</td>
<td>1.01 (0.93, 1.09)</td>
<td>Moderate</td>
<td>+1 (−7 to 9)</td>
</tr>
<tr>
<td>Diabetes type 2</td>
<td>1.04 (0.91, 1.19)</td>
<td>Very low</td>
<td>+3 (−7 to 14)</td>
</tr>
<tr>
<td>Myopathy</td>
<td>1.08 (1.01, 1.15)</td>
<td>Low</td>
<td>+13 (2 to 24))</td>
</tr>
<tr>
<td>Headache/Nausea</td>
<td>1.13 (0.97, 1.31)</td>
<td>Moderate</td>
<td>+20 (−5 to 49)</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>1.12 (1.00, 1.26)</td>
<td>Moderate</td>
<td>+16 (0 to 36)</td>
</tr>
<tr>
<td>Hepatic dysfunction</td>
<td>1.16 (1.02, 1.31)</td>
<td>Low</td>
<td>+8 (1 to 16)</td>
</tr>
</tbody>
</table>

Favours statins: 0.6, 1.0, 1.4
Favours control: 0.6, 1.0, 1.4
EFFICACY: SELECT CONTROVERSIES

- Quality of Trial data? Influence of Drug Industry?
- True Mortality Benefit?
- Composite outcomes?
- Should we be pooling data from heterogeneous studies?
- Should we analyze/present data based on level of CVD risk?
- What is the True (Real World) Efficacy?
  - Trial F/U generally < 5 years.
  - But for many patients STATIN is lifelong.
- Data for Populations: Elderly, Women, Non-Caucasian?
CLOSE UP ON ELDERLY PATIENTS (≥75YRS)
Geriatric Experts Across Canada
Drug Classes Identified As A High Priority For
Deprescribing Guideline Development

<table>
<thead>
<tr>
<th>Rank</th>
<th>Drug</th>
<th>Number of participants (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1</td>
<td>Benzodiazepines</td>
<td>43/47 (91%)</td>
</tr>
<tr>
<td>#2</td>
<td>Atypical antipsychotics</td>
<td>38/47 (81%)</td>
</tr>
<tr>
<td>#3</td>
<td>Statins</td>
<td>22/47 (47%)</td>
</tr>
<tr>
<td>#4</td>
<td>Tricyclic antidepressants</td>
<td>21/47 (45%)</td>
</tr>
<tr>
<td>#5</td>
<td>Proton-pump inhibitors</td>
<td>20/47 (43%)</td>
</tr>
<tr>
<td>#6</td>
<td>Urinary anticholinergics</td>
<td>17/47 (36%)</td>
</tr>
<tr>
<td>#7</td>
<td>Typical antipsychotics</td>
<td>16/47 (34%)</td>
</tr>
<tr>
<td>#8</td>
<td>Cholinesterase inhibitors</td>
<td>16/47 (34%)</td>
</tr>
<tr>
<td>#9</td>
<td>Opioids</td>
<td>12/47 (26%)</td>
</tr>
<tr>
<td>#10</td>
<td>Selective serotonin reuptake inhibitors</td>
<td>9/47 (19%)</td>
</tr>
</tbody>
</table>

Efficacy and safety of statin therapy in older people: a meta-analysis of individual participant data from 28 randomised controlled trials

Cholesterol Treatment Trialists’ Collaboration*
**Figure 2:** Effects on major vascular events per mmol/L reduction in LDL cholesterol,
Statins for primary prevention of cardiovascular events and mortality in old and very old adults with and without type 2 diabetes: retrospective cohort study

Rafel Ramos,¹ ² Marc Comas-Cufí,¹ ² Ruth Martí-Lluch,¹ ³ Elisabeth Balló,¹ ⁴ Anna Ponjoan,¹ ³ Lia Alves-Cabratosa,¹ ² Jordi Blanch,¹ ² Jaume Marrugat,⁵ ⁶ Roberto Elosua,⁵ ⁶ María Grau,⁵ ⁶ Marc Elosua-Bayes,¹ ² Luis García-Ortiz,⁷ Maria García-Gil² ⁴
No Type 2 Diabetes

Atherosclerotic Disease

Hazard ratio (95% CI)

75-84yr:
HR: 0.76 (95% CI: 0.65 to 0.89)

All Cause Mortality

Hazard ratio (95% CI)

75-84yr:
HR: 0.84 (95% CI: 0.65 to 0.89)

Only group to benefit: patients 75-84yrs with Type 2 DM
STAREE:
STATIN THERAPY FOR REDUCING EVENTS IN THE ELDERLY

- Randomized Control Trial

- Healthy elderly people (≥70 years). No history of CVD. N = 18,000

- Intervention: Atorvastatin 40mg/day VS placebo

- Primary Outcomes:
  - Death, development of dementia, development of disability
  - Major fatal or non-fatal CV event.

- Estimated completion 2023

https://clinicaltrials.gov/ct2/show/NCT02099123
SAFETY
Statin Safety and Associated Adverse Events
A Scientific Statement From the American Heart Association

Connie B. Newman, MD, FAHA, Chair; David Preiss, FRCPath, PhD; Jonathan A. Tobert, MD, PhD, FAHA;
Terry A. Jacobson, MD, FAHA, Vice Chair; Robert L. Page II, PharmD, MSPH, FAHA;
Larry B. Goldstein, MD, FAHA; Clifford Chin, MD; Lisa R. Tannock, MD, FAHA;
Michael Miller, MD, FAHA; Geetha Raghuvreer, MD, MPH, FAHA; P. Barton Duell, MD, FAHA;
Eliot A. Brinton, MD, FAHA; Amy Pollak, MD; Lynne T. Braun, PhD, FAHA;
Francine K. Welty, MD, PhD, FAHA; on behalf of the American Heart Association Clinical
Lipidology, Lipoprotein, Metabolism and Thrombosis Committee, a Joint Committee of the Council on
Atherosclerosis, Thrombosis and Vascular Biology and Council on Lifestyle and Cardiometabolic Health;
Council on Cardiovascular Disease in the Young; Council on Clinical Cardiology; and Stroke Council

February 2019.
https://www.ahajournals.org/doi/pdf/10.1161/ATV.0000000000000073
Table 7. Perspective on Benefit/Risk of Statin Therapy in 10,000 Patients on Statins for 5 Years, Achieving 2 mmol/L (77 mg/dL) Reduction in LDL-C

<table>
<thead>
<tr>
<th>Benefit*</th>
<th>Estimated Number of Patients With Benefit or Adverse Effect†</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVEs prevented (secondary prevention)</td>
<td>1000</td>
</tr>
<tr>
<td>MVEs prevented (primary prevention)</td>
<td>500</td>
</tr>
<tr>
<td>Risk</td>
<td></td>
</tr>
<tr>
<td>Newly diagnosed diabetes mellitus</td>
<td>100</td>
</tr>
<tr>
<td>Muscle symptoms without significant CK increase</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Myopathy‡</td>
<td>5</td>
</tr>
<tr>
<td>Rhabdomyolysis</td>
<td>1</td>
</tr>
<tr>
<td>Autoimmune myopathy</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Hemorrhagic stroke§</td>
<td>10</td>
</tr>
<tr>
<td>Severe liver disease</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

‡Myopathy attributable to statin therapy is defined as unexplained muscle pain or weakness accompanied by elevation in CK >10 times the upper limit of normal.

§In people with prior cerebrovascular disease taking statins, hemorrhagic stroke is possibly causally related.
AHA STATEMENT: STATIN SAFETY

“There is no convincing evidence for a causal relationship between statins and cancer, cataracts, cognitive dysfunction, peripheral neuropathy, erectile dysfunction, or tendonitis.”

February 2019.
https://www.ahajournals.org/doi/pdf/10.1161/ATV.0000000000000073
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Statin Dose</th>
<th>RR or OR [95% CI]</th>
<th>ARI NNH</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Withdrawal due to adverse effects</td>
<td>High* vs low#</td>
<td>1.3 [1.2, 1.4]</td>
<td>2.1% 47 (3.4 yr)</td>
<td>13</td>
</tr>
<tr>
<td>Muscle damage (CK elevation &gt;10x normal)</td>
<td>High* vs low#</td>
<td>10.0 [1.3, 78.0]</td>
<td>0.07% 1534 (3.4 yr)</td>
<td>13</td>
</tr>
<tr>
<td>Liver enzyme elevation</td>
<td>High* vs low#</td>
<td>4.8 [3.3, 6.2]</td>
<td>1.2% 86 (3.4 yr)</td>
<td>13</td>
</tr>
<tr>
<td>Newly diagnosed diabetes</td>
<td>High* vs low#</td>
<td>1.12 [1.04, 1.22]</td>
<td>1.0% 105 (4 yr)</td>
<td>14</td>
</tr>
<tr>
<td>Newly diagnosed diabetes</td>
<td>All doses</td>
<td>1.09 [1.02, 1.17]</td>
<td>0.4% 250 (4 yr)</td>
<td>15</td>
</tr>
</tbody>
</table>

* High dose - simvastatin 80 mg, atorvastatin 40-80 mg.
# Low dose - simvastatin 20 mg, pravastatin 40 mg, atorvastatin 10 mg.
RR- relative risk, OR- odds ratio, ARI- absolute risk increase, NNH- number of people needed to treat to harm one person.

https://www.ti.ubc.ca/2014/05/28/statins-proven-and-associated-harms/
SAFETY: SELECT CONTROVERSIES

- RCTs suggest no significant excess of major adverse events (is this true?)
- Skepticism persists about whether trials captured ADRs reliably

How can CHD decrease, but not total Serious Adverse Events (SAEs)?
- All CHD events are SAEs and are counted in both categories (CHD + SAE)
- A reduction in major CHDs should be reflected in a reduction in total SAEs
- The fact that it is not suggests that other SAEs are increased by STATINS

---

<table>
<thead>
<tr>
<th># RCTs</th>
<th>RR* [95%CI]</th>
<th>ARR %</th>
<th># RCTs</th>
<th>RR* [95%CI]</th>
<th>ARR %</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>0.74 [0.68-0.80]</td>
<td>1.0</td>
<td>6</td>
<td>0.99 [0.96-1.03]</td>
<td>nil</td>
</tr>
</tbody>
</table>

SAFETY: SELECT CONTROVERSIES

- Clinicians and patients suggest that ADRs may be more common than those described in clinical trials.

- To some extent this may be explained by the use of a “run in period” in some STATIN trials.

- What is the long term safety?

- Information on potential statin harms is accumulating and concerning but also less systematically collected. What is the real world data?

- Given Diabetes may be dose related, should this impact our approach to dosing?

- Key Message: more uncertainty regarding safety VS benefits
EXPERT
COMMENTARY
“while disputes over individual numbers are important, the leading protagonists in the statin wars seem, above all, to be suffering under a grand delusion that all patients think like they do. On the one hand, we have clinicians and researchers insisting that no sane patient would refuse a safe simple treatment that reduces their chances of a heart attack by one in 200; on the other, we have clinicians and researchers insisting that one in 200 is a laughable and trivial benefit, which no sensible patient could ever care about. In reality, all patients are different, and we all – as doctors or as patients - weigh up different factors differently…. we need to recognise that different patients have different priorities: different to each other and, sometimes, very different to our own”
APPROACH TO PRACTICE
CLINICIAN

PATERNALISTIC:
Information and recommendations

INFORMED MEDICAL DECISION MAKING:
Information

SHARED DECISION MAKING:
Information and recommendations
Values and preferences

PATIENT

SAMPLE TOOLS AND RESOURCES

- **MAYO Clinic Shared Decision Aid**
  - Online Tool: [https://statindecisionaid.mayoclinic.org/](https://statindecisionaid.mayoclinic.org/)

- **Best CV risk Calculator:**
Simplified lipid guidelines

Prevention and management of cardiovascular disease in primary care

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http://www.cfp.ca/content/cfp/61/10/857.full.pdf