HEALTHY HEART

VOLUME-10 | ISSUE-111 | FEBRUARY 05, 2019

Honorary Editor :
Dr. Milan Chag

Aspirin is available all over the world since 1899. Its benefit as antiplatelet drug for secondary prophylaxis outweigh the risk of bleeding and is widely used for this purpose. It's use for primary prophylaxis for prevention of CV events has not been clear because the bleeding risk outweighs the benefits.

Three large randomized trials were published in 2018 and have thrown more light on role of aspirin for primary prevention. These trials and the latest data is summarized in this discussion.

Should We Use Aspirin for Primary Prevention?

Aspirin is widely used all over the word since more than a century. In fact, its use has been so wide that a dictum was coined: "One Aspirin a Day Keeps the Doctor Away!" It was not uncommon that people used to take Aspirin after age 40 or 50 for primary prevention even without doctor's prescription as it used to be and is still OTC (over the counter) drug! It's role for life-long secondary prophylaxis for atherosclerotic cardiovascular, cerebrovascular and peripheral arterial disease is well established and must be continued unless contraindicated. Its role as the first time use is vital and well established in acute conditions like acute coronary syndrome, stroke, and percutaneous coronary interventions. However, its use for primary prophylaxis of cardiovascular events is not clear even in patients with high cardiovascular risk (like presence of DM, HT, dyslipidaemia or tobacco use). Marginal benefits of reduction in MI and ischemic stroke were outweighed by increased incidence of major bleeds in GI tract and increased haemorrhagic stroke. Several meta-analyses in past also showed same concern. In ESC 2018 meet, three large, randomized trials (ASCEND, ARRIVE and ASPREE) were presented and simultaneously published in NEJM and the Lancet. Later, meta-analysis on same was published this year in JAMA. These new data and their conclusions are presented here.

ASCEND (A Study of Cardiovascular Events in Diabetes: L Bowman et al. N Engl J Med August 26, 2018) was a large randomized trial where 15,840 adults who had diabetes but no evident cardiovascular disease were randomized to receive aspirin at a dose of 100 mg daily or matching placebo and followed for 7.4 years. The rate of composite of serious vascular events (MI, stroke or CV death) was 8.5% with aspirin as compared with 9.6% with placebo (rate

ratio, 0.88; 95% confidence interval [CI], 0.79 to 0.97; P = 0.01). This 12% decrease in the rate of serious vascular events came at the cost of a 29% increase in the rate of major bleeding events (4.1% with aspirin vs. 3.2% with placebo; rate ratio, 1.29; 95% CI, 1.09 to 1.52, P = 0.003). All-cause mortality was not different between the groups (rate ratio, 0.94; 95% CI, 0.85 to 1.04). GI or other cancers were also not different between the groups. The absolute lower rates of serious vascular events were of similar magnitude to the absolute higher rates of major bleeding, even among participants who had a high vascular risk (estimated 5-Yr Risk of Serious Vascular Event at Baseline of >10%) (Figure 1 and 2).

ARRIVE (Aspirin to Reduce Risk of Initial Vascular Events, J M Gaziano et al. The Lancet August 26, 2018) was a large randomized trial where 12,546 adults who had moderate risk of cardiovascular disease (10-year risk of coronary heart disease 10-20%) but no evident cardiovascular disease or diabetes were randomized to receive aspirin at a dose of 100 mg daily or matching placebo and followed for 5 years. Aspirin was not associated with a reduction in adverse cardiovascular events. The incidence of the composite primary outcome of myocardial infarction, stroke, unstable angina, transient ischemic attack, or death from cardiovascular causes was 4.3% with aspirin and 4.5% with placebo (hazard ratio, 0.96; 95% CI, 0.81 to 1.13; P = 0.60), whereas the incidence of gastrointestinal bleeding events with aspirin was twice the incidence with placebo (hazard ratio, 2.1; 95% CI, 1.36 to 3.28; P<0.001). All-cause mortality was also similar between the groups. Authors concluded that the event rate was much lower than expected, which is probably reflective of contemporary risk management strategies, making the study more representative of a low-risk population. The role of aspirin in primary prevention among patients at moderate risk could therefore not be addressed. Nonetheless, the findings with respect to aspirin's effects are consistent with those observed in the previously published low-risk primary prevention studies (Figure 3).

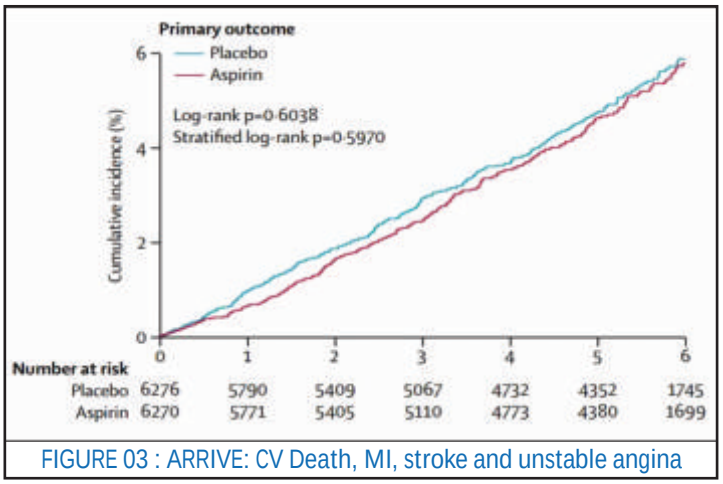

FIGURE 03 : ARRIVE: CV Death, MI, stroke and unstable angina

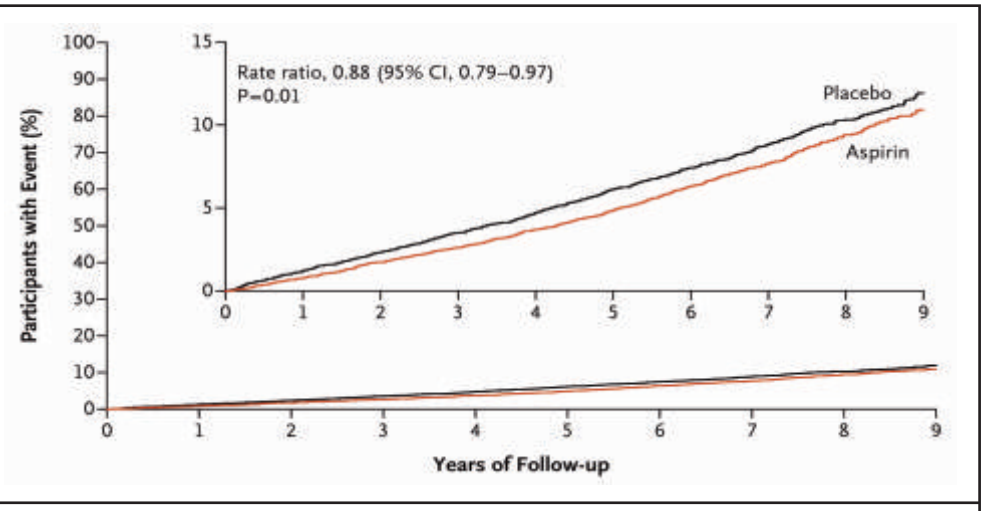

FIGURE 01 : ASCEND: The primary efficacy outcome: 3 point MACE

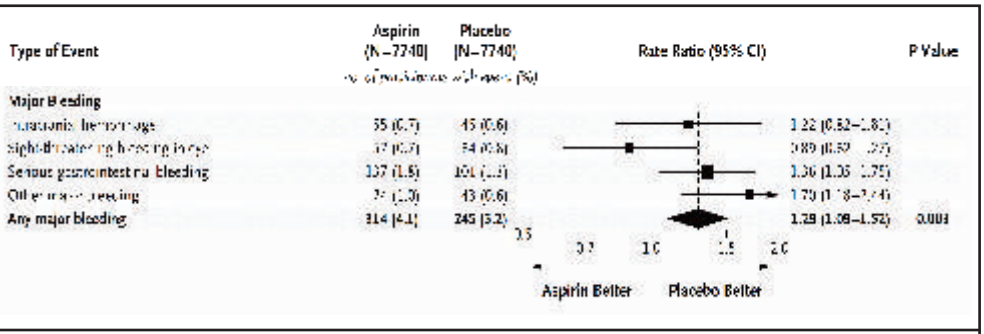

FIGURE 02 : ASCEND: The primary Safety outcome: Bleeding Events

HEALTHY HEART
VOLUME-10 | ISSUE-111 | FEBRUARY 05, 2019

ASPREE (Aspirin in Reducing Events in the Elderly, J.J. McNeil et al. N Engl J Med Sept 16, 2018) was a large randomized trial where 19,114 participants ≥ 70 years and no CV disease, dementia, and disability were randomized to receive aspirin at a dose of 100 mg daily or matching placebo and followed for 5 years. In the ASPREE trial, the use of aspirin conferred no benefit with respect to the prespecified composite primary end point of death, dementia, or persistent physical disability, an issue of considerable importance in the elderly (hazard ratio with aspirin vs. placebo, 1.01; 95% CI, 0.92 to 1.11; P = 0.79). Of the primary end-point events that occurred, half were death, 30% dementia, and 20% persistent physical disability. Similar to the ARRIVE trial, the ASPREE trial showed no evidence of a cardiovascular benefit of aspirin (hazard ratio for cardiovascular disease with aspirin vs. placebo, 0.95; 95% CI, 0.83 to 1.08), yet the risk of major bleeding was again 39% higher with aspirin than with placebo (hazard ratio, 1.39; 95% CI, 1.18 to 1.62; P<0.001).

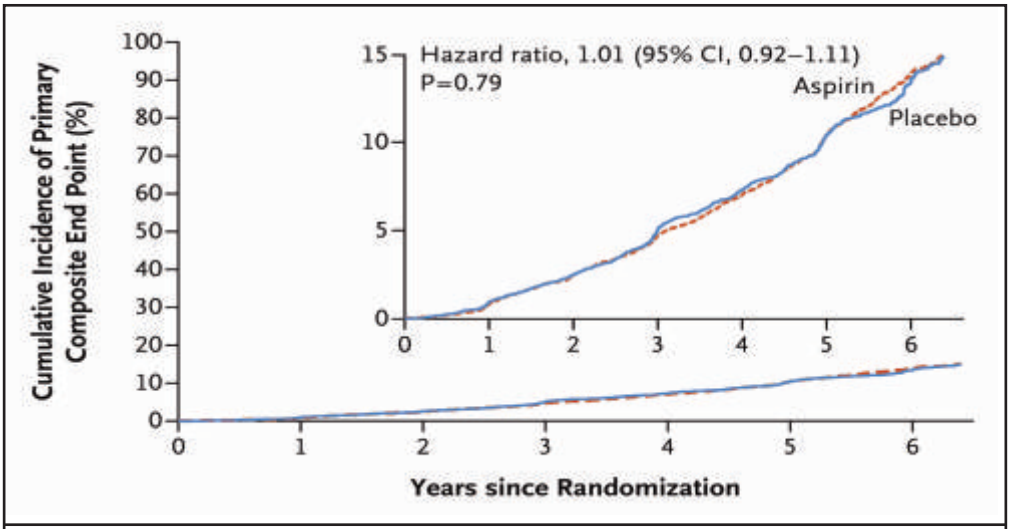

FIGURE 05 : ASPREE :
Primary Endpoint:(death from any cause, dementia, or persistent physical disability)

In ASPREE study, secondary end point of death from any cause was potentially higher with aspirin than with placebo (hazard ratio, 1.14; 95% CI, 1.01 to 1.29). This finding is at odds with the results of previous primary prevention trials of aspirin and with the results of the ASCEND and ARRIVE trials. The potentially higher mortality with aspirin was limited to the Australian cohort and was driven by an unexpectedly higher risk of cancer-related death with aspirin than with placebo (hazard ratio, 1.31; 95% CI, 1.10 to 1.56). These latter data should be interpreted with caution. No other trial has shown increased incidence of cancer with aspirin. Authors concluded that the use of low-dose aspirin as a primary prevention strategy in older adults resulted in a significantly higher risk of major haemorrhage and did not result in a significantly lower risk of cardiovascular disease than placebo. (Figure 4 and 5).

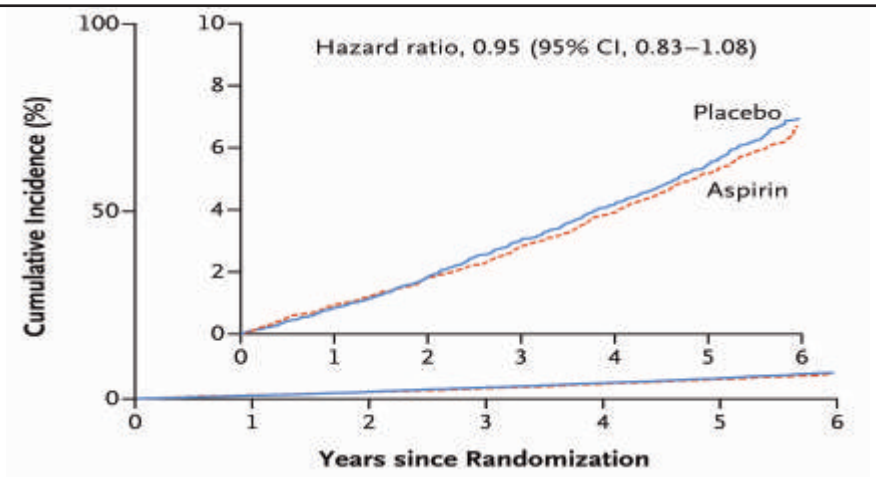

FIGURE 04 : ASPREE: Cumulative Incidence of 3-point MACE and HHF

Conclusion:

From these three trials and Metaanalysis of Aspirin in primary prevention (Figure 6) for cardiovascular events, for primary prevention, in which risk is determined largely by age and the presence or absence of diabetes, the benefit–risk ratio for prophylactic aspirin in current practice

is exceptionally small compared to risk of increased bleeding. If we really want to advocate something for primary prevention beyond healthy lifestyle of diet, exercise and tobacco free life, is use of Statin in persons with high cardiovascular risk. In primary prevention trials, the use of statins was associated with a 25% decrease in the risk of major vascular events for every 1 mmol per litre (approximately 38 mg/dL) decrease in the LDL cholesterol level (rate ratio with statin vs. placebo, 0.75; 95% CI, 0.69 to 0.82) without any serious side-effects (Figure 7).

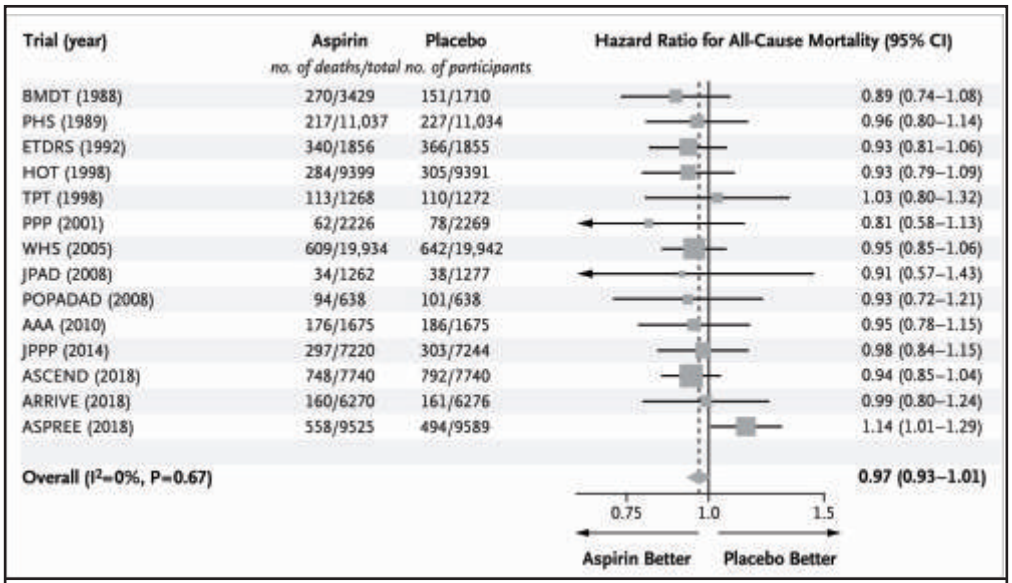

FIGURE 06 :
Meta-analysis: Aspirin and All-Cause Mortality in 14 Primary Prevention Trials

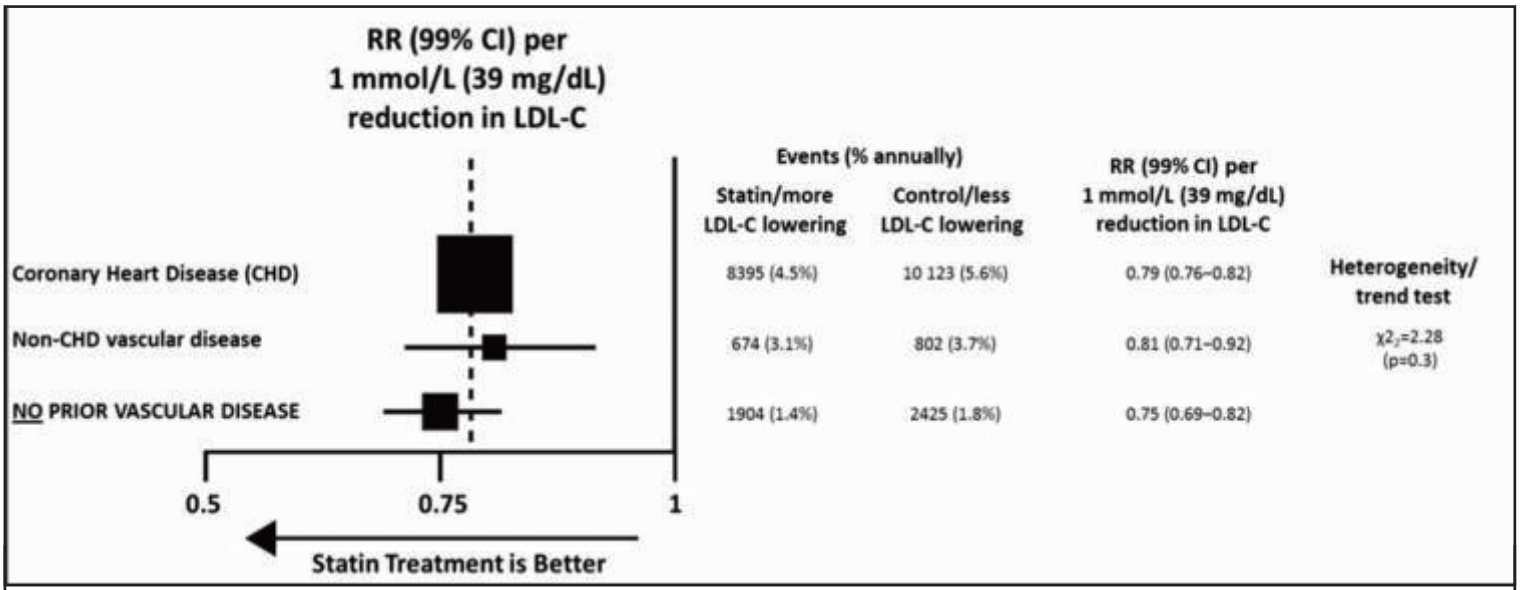

FIGURE 07 : META ANALYSIS OF STATIN TRIALS

References:

1. ASCEND: Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus. Louise Bowman et al. N Engl J Med 2018; 379:1529-1539
2. ARRIVE: Aspirin to Reduce Risk of Initial Vascular Events, J M Gaziano et al. The Lancet August 26, 2018
3. ASPREE: Effect of Aspirin on All-Cause Mortality in the Healthy Elderly. John J. McNeil et al. N Engl J Med 2018; 379:1519-1528
4. Editorial: Paul M Ridker. Should Aspirin Be Used for Primary Prevention in the Post-Statin Era? N Engl J Med 2018; 379:1572-1574

CIMS®
CARE INSTITUTE OF MEDICAL SCIENCES
Earning Trust with World-Class Practices

HEALTHY HEART
VOLUME-10 | ISSUE-111 | FEBRUARY 05, 2019

JIC 2020
Joint International Conference
January 3-5, 2020

Organized by
GMERS Medical College, Sola, Ahmedabad

Supported by
CIMSRE
Care Institute Medical Society for Research and Education

In Association with
सह वीर्यम करवावहै
United We Create Glory
ESTD 1970

Annual Scientific Symposium
25th Year of Academics

Key Dates

January - 2020

3 4 5

with Enhanced Scientific Education

Be the First to Register to win Early Bird Prize

- **To win early bird prize**
- **To be assured of exposure to an excellent Scientific Programme**
- **To save costs/time**
- **To not miss out on registration opportunity**

Upto April 30, 2019

Visit www.jicindia.org for more information

"JIC India" Application Available

ANDROID APP ON Google play | Download on the App Store

Conference Secretariat

CIMS Hospital, Nr. Shukan Mall, Off Science City Road, Sola, Ahmedabad - 380060. Ph.: +91-79-3010 1059/1060
Fax : +91 -79-2771 2770 (M) +91 -98250 66664, 98250 66668
Email: communication@cimshospital.org | www.jicindia.org

HEALTHY HEART
VOLUME-10 | ISSUE-111 | FEBRUARY 05, 2019

CIMS®
CARE INSTITUTE OF MEDICAL SCIENCES
Earning Trust with World-Class Practices

Healthy Heart Registered under RNI No. GUJENG/2008/28043
Published on 5th of every month
Permitted to post at PSO, Ahmedabad-380002 on the 12th to 17th of every month under
Postal Registration No. GAMC-1725/2018-2020 issued by SSP Ahmedabad valid upto 31st December, 2020
Licence to Post Without Prepayment No. PMG/HQ/055/2018-20 valid upto 31st December, 2020

If undelivered Please Return to :

CIMS Hospital, Nr. Shukan Mall,

Off Science City Road, Sola, Ahmedabad-380060.

Ph. : +91-79-2771 2771-72

Fax: +91-79-2771 2770

Mobile : +91-98250 66664, 98250 66668

Subscribe "Healthy Heart" : Get your "Healthy Heart", the information of the latest medical updates only ` 60/- for one year.
To subscribe pay ` 60/- in cash or cheque/DD at CIMS Hospital Pvt. Ltd. Nr. Shukan Mall, Off Science City Road, Sola, Ahmedabad-380060. Phone : +91-79-3010 1059 / 3010 1060. Cheque/DD should be in the name of : "CIMS Hospital Pvt. Ltd."
Please provide your complete postal address with pincode, phone, mobile and email id along with your subscription

CIMS Learning Centre 2019

For any query, please email on :
clccommunications@cimshospital.org

Echocardiography Fellowship Programme

Registration Fees : ` 35,000/-*

Course Directors : Dr. Satya Gupta / Dr. Milan Chag / Dr. Tejas V. Patel / Dr. Vineet Sankhla
Date : One Week (Monday to Saturday)
Duration : 6 days
Number of Seats : 15
Venue : CIMS Auditorium

Programme Overview:

Sights and Sounds of Echocardiography at CIMS Hospital is a premier education course for Echocardiologists, Fellows in training, and Physicians in clinical practice. Over the past few years, we have trained and taught more than 1000 candidates. This unique programme is intended for those who want to learn Echocardiography right from basics. Overall programme includes lectures on basics of Echocardiography, theoretical and practical aspects of Ischemic, Valvular and Congenital Heart Disease in relation to Echocardiography and hands-on supervised training. This is the star educational programme of the CIMS Learning Centre and has been appreciated worldwide.

Online registration & payment on www.cims.org /clc

Programme Highlights:

- 6 days extensive teaching of echocardiography
- Easy access to faculty members
- Supervised hands-on practice
- Provision of course materials (Textbook of Echocardiography)

Schedule of Echocardiography Fellowship 2019

Month	Start Date	End Date
June	24-06-2019	29-06-2019
September	23-09-2019	28-09-2019
November	25-11-2019	30-11-2019

> Certificate of attendance will be given at the end of the course.

* Hotel Registration Separate

CIMS Hospital : Regd Office: Plot No.67/1, Opp. Panchamrut Bunglows, Nr. Shukan Mall, Off Science City Road, Sola, Ahmedabad - 380060.
Ph. : +91-79-2771 2771-72 Fax: +91-79-2771 2770.
CIMS Hospital Pvt. Ltd. | CIN : U85110GJ2001PTC039962 | info@cims.org | www.cims.org

Printed, Published and Edited by Dr. Keyur Parikh on behalf of the CIMS Hospital
Printed at Hari Om Printery, 15/1, Nagori Estate, Opp. E.S.I. Dispensary, Dudheshwar Road, Ahmedabad-380004.
Published from CIMS Hospital, Nr. Shukan Mall, Off Science City Road, Sola, Ahmedabad-380060.