

## B. Statement of Grounds

### 7. Risk/Benefit Evaluation

#### United States Preventive Task Force

Based on the meta-analysis of the five primary prevention studies, the United States Preventive Services Task Force (USPSTF) stated that the balance of benefits and harms is most favorable in patients whose risk for CHD is greater than or equal to 3% over 5 years <sup>10, 21</sup>.

Outcome	Estimated 5-Year Risk for CHD Events at Baseline		
	1%	3%	5%
CHD events avoided, n	3 (1-4)	8 (4-12)	14 (6-20)
Hemorrhagic strokes precipitated, n	1 (0-2)	1 (0-2)	1 (0-2)
Major gastrointestinal bleeding events precipitated, n	3 (2-4)	3 (2-4)	3 (2-4)

(Adapted from USPSTF)

The Task Force estimates, over a 5-year period, that treating 1000 patient with a moderately high risk (5%) would prevent 14 events. Alternatively, treating 1000 low risk patients would only result in the prevention of 3 events. The use of daily low-dose aspirin is estimated to result in 1 hemorrhagic stroke and 3 major bleeding events among 1000 patients regardless of cardiovascular risk. Therefore, the benefit for patients at a 5-year cardiovascular risk of 3% begins to outweigh risk. Of 1000 patients treated 8 CHD events will be avoided while 4 adverse events will be experienced.

#### American Heart Association

The American Heart Association (AHA) published a position statement on aspirin use in the prevention of a first MI <sup>11</sup>. Its current recommendation endorses the use of aspirin for persons with a risk of 10% over 10 years to improve the likelihood of a positive balance of coronary risk reduction over bleeding and hemorrhagic stroke.

The statement further identifies that it applies largely to adults with risk factors including but not limited to smoking, hypertension, elevated cholesterol, obesity and diabetes and its intent is to aid primary care providers in their assessment, management, and follow-up of patients who are at increased risk of developing CHD. This message continues to support the need for adults to pursue a healthy lifestyle and minimize risk factors.

Although these two guidelines differ slightly in the exact level of risk required to initiate an aspirin regimen they both conclude that patients who are deemed at increased risk and are not contraindicated should be offered aspirin for prevention of a first MI.

### **Eidelman/Hennekens**

Eidelman, et al. <sup>25</sup> performed an analysis of the data contained in the five available primary prevention trials. They found a statistically significant reduction of 32% for nonfatal MI and a 15% reduction in the risk of any important vascular event. Overviews of secondary and primary prevention trials suggest that aspirin treatment results in a risk of 1 to 2 hemorrhagic strokes per 1000 patient. The authors' conclusion follows that of the American Heart Association, in that the benefits of aspirin outweigh the risk when the risk for a cardiovascular event is  $\geq 10\%$  for 10 years.

### **Methods to evaluate risk**

A number of methods are available to assist physicians in evaluating their patient's CV risk. One of the most well known and most commonly referenced tools was established by the Framingham study <sup>26</sup>. A coronary prediction algorithm was developed to predict the probability of a CV event in people according to their risk factors <sup>27</sup>.

The risk factors studied in Framingham consisted of cigarette smoking, hypertension, elevated serum cholesterol, low levels of high-density lipoprotein (HDL), diabetes mellitus and age. In addition to these, other factors have been well accepted in contributing to coronary disease risk. Obesity, physical inactivity, family history of premature CHD and hypertriglyceridemia are also important when determining risk <sup>28</sup>.

Most tools are based on the Framingham algorithm which was originally limited to a white middle class population. However, D'Agostino and colleagues <sup>29</sup> concluded

that the sex-specific Framingham CHD prediction functions perform well among whites and blacks in different settings and can be applied to other ethnic groups after recalibration.

Some risk calculators include [www.med-decisions.com](http://www.med-decisions.com), [www.riskscore.org.uk](http://www.riskscore.org.uk), and [www.chd-taskforce.com](http://www.chd-taskforce.com). These internet-based tools vary slightly in their approach. They all take into account age, cholesterol, blood pressure, smoking status and diabetes status. In addition to the risk factors common to all, [www.chd-taskforce.com](http://www.chd-taskforce.com) includes triglycerides and family history, but not sex. The two other calculators consider left ventricular dysfunction (LVD) in the risk calculation. It is important to note that these tools do not take into account the timing and duration of smoking, diabetes or LVD.

Another well recognized tool in predicting coronary risk is the Sheffield Table. A revised and validated version of the table was published in the British Journal of Medicine in March 2000 by Wallis and colleagues<sup>30</sup>. The revised Sheffield Table takes into account sex, age, serum cholesterol:HDL ratio, hypertension, smoking and diabetes. It allows physicians to determine whether their patients fall into a 10-year risk of 15% or 30%. These categories are in line with joint guidelines, of four British societies and British Hypertension Society guidelines which recommend aspirin and treatment of mild hypertension when risk reaches 15% over 10 years<sup>31,32</sup>.

## Lauer

Michael Lauer published an algorithm<sup>33</sup> taking into account the “outlying” risk factors such as target organ damage and poor physical fitness. A 10-year risk via the Framingham scoring system is calculated and then outcome is divided into three scenarios. A risk of less than or equal to 0.6% per year would not necessitate prophylactic aspirin use. The second group comprises those who fall between 0.7% and 1.4% per year. These moderate risk patients are then examined further to determine whether they have treated hypertension with target organ damage, diabetes or poor physical fitness. Strong patient preference is also figured. Obesity has been left out of this algorithm but can be considered when deciding upon a patient of moderate risk. The final group, those at a per year risk of greater than 1.5%, are recommended to take prophylactic aspirin.

In addition, Lauer examined the number needed to treat for five years given various base-line risks of MI. A total of 256, 88 and 53 treated patients are needed to

prevent one MI without a major bleeding event with coronary risks of 0.5%, 1.0% and 1.5% per year, respectively. This further emphasizes the increased efficacy of an aspirin regimen as the risk increases in the subject population. Lauer endorses the use of Framingham as a risk assessment tool and emphasizes the need for physicians to determine risk when evaluating patients.

### **Conclusion**

Aspirin is effective at reducing risk of a first MI in men and women and should be recommended for all who have a 10 year risk of a CVD event of 10% or more. A number of risk calculators are available for physicians to evaluate the CVD risk of their patients.

Expanding the professional labeling of aspirin to include patients at risk for a first MI will provide a cost effective, safe treatment option with the potential to prevent life altering coronary events. Recent recommendations demonstrate that the benefits of aspirin treatment outweigh risks in an appropriate population. Risk evaluation and long term aspirin use in common medical practice are key to an effective primary prevention strategy for cardiovascular event reduction.