



RACP Foundation Research Awards

FINAL REPORT

Project / Program Title	Epidemiology of Clinically Significant Bleeding in the Elderly	
Name	Dr Suzanne Mahady	
Award Received	2019 Vincent Fairfax Family Foundation Research Establishment Fellowship	
Report Date	1 April 2020	
Chief Investigator / Supervisor	Professor John McNeil	
Administering Institution	Monash University	
Funding Period	Start Date:	1 February 2019
	Finish Date:	31 December 2019

PROJECT SUMMARY

Older people are at higher risk of serious bleeding events, which is further increased with the use of aspirin. We used data from a large clinical trial of 19,114 persons, where aspirin was given to half of the participants and placebo was given to the remaining participants. We then measured the increased risk of serious bleeding (i.e. bleeding that resulted in hospitalisation or transfusion) when people are taking aspirin, as well as other risk factors for bleeding. Overall, we found that aspirin increases risk of gastrointestinal bleeding by around 60%. This risk is further increased with advancing age, smoking and kidney disease.

PROJECT AIMS / OBJECTIVES

1. To quantify the absolute risk of upper gastrointestinal bleeding in an elderly population at baseline and with aspirin
2. To quantify the absolute risk of lower gastrointestinal bleeding in an elderly population at baseline and with aspirin
3. To identify covariates that define high risk groups for bleeding
4. To quantify the risk of intracerebral bleeding
5. To derive a risk prediction model for bleeding events for use as a bedside decision aid

SIGNIFICANCE AND OUTCOMES

Older people have a greater risk of bleeding than younger people, and aspirin is also known to increase bleeding risk. Our analysis, derived from a large aspirin primary prevention trial makes an important contribution to understanding the risks of gastrointestinal bleeding resulting from low dose aspirin use. This has not been studied before using trial based data in healthy older people. Our prospective and systematic capture of bleeding events reduces bias and makes it unlikely any substantial bleeding events were missed.

We found that the increased risk with aspirin is modest for those 70-80 years old who appear healthy and without significant comorbidity. However, the risk does increase substantially with age over 80 years. Other risk factors (apart from age and aspirin) are NSAID use, smoking, truncal obesity, hypertension and kidney disease. Understanding the epidemiology of bleeding with and without aspirin in older people is important due to the high prevalence of aspirin use in the population, and the substantial morbidity and costs associated with serious bleeding events. These data will help inform individual decision making for people considering aspirin for primary prevention, and is useful for policy makers when considering guidance on aspirin for the wider population.

Following from this are the above 2 projects examining bleeding specifically in subgroups with CKD, and overall bleeding events in older people. The latter topic is important to inform incidence of other bleeding types such as haematuria and epistaxis with aspirin, which frequently result in hospital presentations in older persons.

PUBLICATIONS / PRESENTATIONS

1. Mahady SE et al. Major gastrointestinal bleeding in older persons using aspirin: incidence and risk factors in the ASPREE randomized controlled trial. This has been accepted as an oral presentation at the international Gastroenterology conference in Chicago titled "DDW 2020".
2. Mahady SE et al. Major gastrointestinal bleeding in older persons using aspirin: incidence and risk factors in the ASPREE randomized controlled trial. This study is completed and is currently under review at an international gastroenterology specialty journal.
3. Mahady SE, Margolis KL, Chan AT et al. Major gastrointestinal bleeding in older persons using aspirin: incidence and risk factors in the ASPREE randomized controlled trial; Australian Gastroenterology Week 2019; awarded as "Poster of Merit".
4. Mahady SE, Woods RL, Wolfe R, Nelson MR, Murray AM, McNeil JJ. Aspirin for primary prevention in adults older than 70 years is not supported by high quality trial data and may cause harm. American Journal of Medicine. Accepted March 2020.

My bleeding research also led to a collaboration on a related project which is under review as follows:

Wolfe R, Wetmore J...Mahady SE et al. Effects of aspirin in older adults with chronic kidney disease: a subgroup analysis of the ASPirin in Reducing Events in the Elderly (ASPREE) randomized clinical trial. Submitted, under review at Kidney International with invitation to resubmit after amendments.

In total, there is 1 publication, 2 further publications under review, an international oral presentation and a poster of merit at an Australian Gastroenterology Conference derived from this project.

Others outputs:

1. I have been awarded a further fellowship to study bleeding outcomes in 2020 (Bridging Postdoctoral Fellowship, Monash University)
2. International oral presentation at a gastroenterology conference, as written above and poster presentation at the Australian Gastroenterology Week (AGW).
3. Presentation on this topic at Harvard Medical School: Clinical Translational & Epidemiology Unit, Harvard Medical School & MGH, 1/5/19
4. Presentation on this topic at Gastroenterology Grand Rounds, Massachusetts General Hospital, Boston, 7/5/2019
5. Invited Speaker on aspirin and bleeding, Melbourne Liver Group, San Remo, March 2019.

ACKNOWLEDGEMENTS

The publication (#2 above) is currently under review and has acknowledged the VFFF fellowship as supporting myself (first author).