1   Aspirin compliance for cardiovascular disease and colorectal cancer prevention in the uninsured

2   population

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Abstract

Aspirin is an effective anti-inflammatory and antiplatelet agent as an irreversible inhibitor of cyclooxygenase. In 2016, the U.S. Preventive Services Task Force recommended aspirin for primary prevention of cardiovascular disease (CVD) and colorectal cancer (CRC) in patients aged 50 to 69 with a 10% or greater 10-year CVD risk. Due to the lack of literature describing compliance with these recommendations in the uninsured patient population, we studied the aspirin adherence for CVD and CRC prevention in several free medical clinics. We investigated the records of 8857 uninsured patients who visited nine free medical clinics in the Tampa Bay Area in 2016-2017. Aspirin compliance was assessed for patients with prior myocardial infarction (MI) or coronary artery disease (CAD). 54% (n=1467) of patients met the criteria to take aspirin for primary prevention of CVD and CRC, but just 17% of these patients aged 50-59 were on the medication. 16% percent of patients aged 60-69 were taking aspirin and significantly more men than women were on aspirin (p=0.025). Of the 306 patients who had prior MI or CAD, 50% were on the medication for secondary prevention. Among the uninsured population, there is low compliance with recommendations for aspirin usage to reduce the risk of CVD and CRC. This study demonstrates that further improvements are needed to increase adherence to current guidelines and address barriers uninsured patients may face in maintaining their cardiovascular and colorectal health.

Introduction

42

43 Cardiovascular disease (CVD) is the leading cause of death in the United States according to

44 2016 data published in the National Vitals Statistics Report from the Centers for Disease Control

45 and Prevention [1]. As an irreversible inhibitor of cyclooxygenase, aspirin is widely prescribed

46 for CVD prevention due to its effectiveness as an anti-inflammatory and antiplatelet agent [2–

47 4]. Long-term use at low doses has additionally been associated with decreased risk of

48 colorectal cancer (CRC) [5]. In 2016, the U.S. Preventative Services Task Force (USPSTF)

49 recommended aspirin for primary prevention of CVD and CRC in patients aged 50 to 69 with a

50 10% or greater 10-year CVD risk. To determine the 10-year CVD risk, the USPSTF used a

51 calculator derived from the American College of Cardiology and American Heart Association

52 (ACC/AHA) pooled cohort equations. This is a class B recommendation for 50-59 year-olds and a

53 class C recommendation for 60-69 year-olds [6]. Class B recommendations indicate that "there

54 is high certainty that the net benefit is moderate or there is moderate certainty that the net

55 benefit is moderate to substantial", whereas Class C recommendations indicate "at least

56 moderate certainty that the benefit is small" and to offer the intervention to "selected patients

57 depending on individual circumstances" [7]. Current guidelines from the AHA and American

58 College of Cardiology Foundation (ACCF) recommend aspirin for patients with prior myocardial

59 infarction (MI) or coronary artery disease (CAD) as secondary prevention of CVD [8].

60

61 Currently, no studies have examined the use of aspirin in reducing the risk of CVD and CRC in

62 the uninsured population. One study found low rates of aspirin use for primary prevention in

3

63   low-income, minority populations [9]. Several studies have reported the underutilization of

64   aspirin for primary and secondary CVD prevention among the general population, without

65   distinguishing patients' insurance status. The suboptimal rates of usage are due to both the lack

66   of physician recommendation to use aspirin and patient non-compliance with physician

67   recommendations [10–12] . Uninsured patients receive less treatment and poorer management of

68   major CVD risk factors than insured patients, despite similar prevalence of disease [13]. The cost

69   of medications is a particularly important factor in managing the health of uninsured patients.

70   The cost-effectiveness of aspirin is well-documented, augmenting its value in managing CVD in

71   uninsured patients [14].

72

73   The purpose of this study was to evaluate the compliance with USPSTF and AHA/ACCF

74   recommendations for aspirin use in the primary and secondary prevention of CVD and risk

75   reduction for CRC among uninsured patients. Our secondary purpose was to assess inappropriate

76   aspirin use by uninsured patients who do not meet criteria for its usage.

77

78   **Methods**

79   We conducted a retrospective chart review that included 8857 uninsured patients who visited

80   nine free medical clinics in the Tampa Bay Area between January 1, 2016 and December 31,

81   2017. Age, sex, race, employment status, and history of MI, CAD, cerebrovascular accident, and

82   gastrointestinal ulcers were recorded. Cholesterol levels, blood pressure, diabetic status, and

83   smoking status were used to calculate 10-year Framingham risk scores [15]. The Framingham

84   risk score predicts the risk of developing hard coronary heart disease (myocardial infarction or

85   coronary death) within 10 years. Framingham scores, rather than the ACC/AHA pooled cohort

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86   equations, were used to determine 10-year CAD risk because the patient information collected

87   through our chart review did not include all data points required by the pooled cohort equations.

88   The data for total cholesterol was not available, however low density lipoprotein cholesterol

89   levels were available. As a result, Framingham risk scores were more representative of the CVD

90   risk for our population of patients.

91

92   Ten-year Framingham risk scores for CAD were calculated for only the 50-69 year-old

93   population to determine which patients qualified to take aspirin for primary prevention of CVD

94   and CRC. Records of patients with a 10% or greater risk score were reviewed to determine if

95   they were taking aspirin for primary prevention of CVD and CRC, and records of patients with

96   prior MI or CAD were reviewed to determine if they were taking aspirin for secondary

97   prevention of CVD.

98

99   The secondary aim of this study was to evaluate inappropriate use of aspirin, which we defined

100   as patients taking aspirin with no history of MI, CAD, or cerebrovascular accident, having less

101   than a 10% 10-year Framingham risk score, or having gastrointestinal (GI) ulcers. Although

102   current guidelines from the AHA and American Stroke Association recommend aspirin for

103   patients with a history of ischemic stroke [16], increased risk of bleeding, including history of GI

104   ulcers, is a contraindication for aspirin usage [6]. Given the limited data set, our parameters

105   defining inappropriate aspirin use did not incorporate the various other factors that increase risk

106   of bleeding, such as bleeding disorders, severe liver disease, renal failure, and thrombocytopenia.

107

108   The data was edited and analyzed using IBM SPSS Statistics software. P-values for categorical

109   data, such as demographics, were determined using Chi-squared and Fisher's exact test. This

110   study was approved by the University of South Florida Institutional Review Board for the

111   Protection of Human Subjects.

112

Results

114   Of the 8857 patients, 1773 met the USPSTF and AHA/ACCF criteria for taking aspirin. Of the

115   2724 (30.8%) patients who were 50-69 years old and met the USPSTF criteria, 1467 (53.9%)

116   had a 10% or greater 10-year Framingham risk score, the threshold to take aspirin for primary

117   prevention of CVD and CRC. Three hundred six patients (3.5%) had a history of MI or CAD,

118   meeting AHA/ACCF criteria to use aspirin for secondary prevention of CVD (Fig. 1).

119   **Fig. 1** Details of sample development.

120

121   Of the 1467 patients who met the criteria to take aspirin for primary prevention of CVD and

122   CRC, 751 were aged 50-59 and 716 were aged 60-69. In the 50-59 year age group, 16.8%

123   (126/751) of the patients were taking aspirin, and sex, race, or employment status did not differ

124   between aspirin users and non-users. In the 60-69 year age group, 15.5% (111/716) were taking

125   aspirin (Fig. 2), significantly more men than women were taking aspirin (p=0.025), and

126   Caucasians were more likely to be taking aspirin than patients of other races (p=0.011) (Table 1).

127

128   **Fig. 2** Patients who met criteria and were taking aspirin.

129

130   **Table 1** Patient predictors for aspirin use as primary prevention.

Characteristic	50-59 Years			60-69 Years		
	Not taking aspirin (n=625)	Taking aspirin (n=126)	P-value	Not taking aspirin (n=625)	Taking aspirin (n=126)	P-value
Gender, n (%)						
Male	322 (51.5)	68 (54.0)	0.616	242 (40.0)	57 (51.4)	0.025
Female	303 (48.5)	58 (46.0)		363 (60.0)	54 (48.6)	
Race, n (%)						
Caucasian	196 (31.4)	56 (44.4)		104 (17.2)	40 (36.0)	
Black	42 (6.7)	11 (8.7)		37 (6.1)	6 (5.4)	
Hispanic	181 (29.0)	33 (26.2)	0.237	232 (38.3)	38 (34.2)	0.011
Asian	15 (2.4)	2 (1.6)		26 (4.3)	4 (3.6)	
Other	3 (0.5)	2 (1.6)		3 (0.5)	0 (0)	
Not Documented	*188 (30.1)*	*22 (17.5)*		*203 (33.6)*	*23 (20.7)*	
Employment Status, n (%)			0.753			0.543
Employed	156 (25.0)	40 (31.7)		143 (23.6)	37 (33.3)	
Unemployed	214 (34.2)	59 (46.8)		163 (26.9)	36 (32.4)	
Not Documented	*255 (40.8)*	*27 (21.4)*		*299 (49.4)*	*38 (34.2)*	

131

132 Of the 306 patients who met criteria to take aspirin for secondary prevention of CVD, 50%

133 (153/306) were taking aspirin. 55.2% (48/87) of patients who had a prior MI and 47.9%

134 (105/219) of patients who had a history of CAD were taking aspirin (Fig. 2). The effects of sex

135 and race on compliance with aspirin recommendations were not statistically significant. Among

136 patients with a history of CAD, those who were currently employed were more likely to be

137 taking aspirin (p=0.04) (Table 2).

138

139 **Table 2** Patient predictors for aspirin use as secondary prevention.

Characteristic	MI Patients			CAD Patients		
	Not taking aspirin (n=39)	Taking aspirin (n=48)	P-value	Not taking aspirin (n=114)	Taking aspirin (n=105)	P-value
Gender, n (%)						
Male	28 (71.8)	36 (75.0)	0.736	65 (57.0)	70 (66.7)	0.165
Female	11 (28.2)	12 (25.0)		48 (42.1)	35 (33.3)	

7

Race, n (%)						
Caucasian	16 (41.0)	25 (52.1)		45 (39.5)	48 (45.7)	
Black	2 (5.1)	2 (4.2)	0.974	11 (9.6)	11 (10.5)	0.977
Hispanic	11 (28.2)	13 (27.1)		30 (26.3)	26 (24.8)	
Asian	1 (2.6)	1 (2.1)		6 (5.3)	7 (6.7)	
Other	0 (0)	0 (0)		0 (0)	0 (0)	
Not Documented	*9 (23.1)*	*7 (14.6)*		*22 (19.3)*	*13 (12.4)*	
Employment Status, n (%)			0.059			0.04
Employed	6 (15.4)	18 (37.5)		24 (21.1)	38 (36.2)	
Unemployed	20 (51.3)	21 (43.8)		48 (42.1)	38 (36.2)	
Not Documented	*13 (33.3)*	*9 (18.8)*		*42 (36.8)*	*29 (27.6)*	

140

141   To assess the inappropriate use of aspirin, we excluded 1467 patients aged 50-69 who had a 10%

142   or greater 10-year Framingham risk score, 306 patients with a history of MI or CAD, and 144

143   patients with a history of stroke. 172 (2.5%) of the remaining 6919 patients were inappropriately

144   taking aspirin. 6 (6.3%) of 96 patients with history of GI ulcers were taking aspirin, despite an

145   increased risk of bleeding.

146

Discussion

148   Our results demonstrate suboptimal rates of aspirin use in the prevention of CVD and CRC

149   according to current guidelines. Although 53.9% (1467/2724) of uninsured patients met criteria

150   to be on an aspirin regimen for primary prevention, only 16.2% (237/1467) of them were taking

151   the medication. Among uninsured patients with a history of MI or CAD, 50% (153/306) were

152   taking aspirin.

153

154   Previous studies reported underutilization of aspirin for the primary and secondary prevention of

155   CVD in the general population. One study reported 40.9% of patients were told by their

156   physician to take aspirin for primary prevention, with 79% complying. Comparably, 75.9% of

157   patients were told by their physician to take aspirin for secondary prevention, with 89.9%

158   complying [12]. Despite the seeming underuse of CVD risk score calculators, such as the

159   Framingham risk score calculator, providers may be considering the risk of GI bleeding and

160   hemorrhagic stroke associated with an aspirin regimen when evaluating patients. A low dose

161   aspirin regimen was found to increase the risk of GI bleeding by 58% and hemorrhagic stroke by

162   27% in patients using the medication for primary prevention of CVD [17]. Consideration of the

163   bleeding risks could play a role in the under-prescription of aspirin.

164

165   Within the general population, aspirin use is lower than that recommended by current guidelines.

166   Our results showed that uninsured patients had even lower rates of use than the general

167   population, indicating room to improve compliance to guidelines. These findings bring up the

168   question of why uninsured patients have suboptimal rates of aspirin use. Lack of health insurance

169   and a low socioeconomic status have been associated with medication non-adherence [18,19].

170   However, there is limited information regarding provider prescribing patterns in free medical

171   clinics. A combination of poor medication adherence and provider prescribing patterns could be

172   a possible explanation for the discrepancy between aspirin use among the uninsured and general

173   patient populations.

174

175   We also found inappropriate use of aspirin. Among patients in our study, 2.5% (172/6919) did

176   not meet guideline criteria but were taking aspirin. This result contrasts with that from a previous

177   study using a national database, which reported that 11.6% of patients were inappropriately

178   taking aspirin for primary prevention of CVD [20]. However, that study used older guideline

9

179   criteria that defined inappropriate aspirin use as an aspirin regimen in patients with a less than

180   6% 10-year risk of a CVD event. The 4% difference in guideline criteria could account for the

181   variance in frequency. The association between lack of health insurance and medication non-

182   adherence could also contribute to the lower rate of inappropriate aspirin use among uninsured

183   patients compared to the general population.

184

185   The results of our study highlight the need to educate uninsured patients and their providers of

186   the value of aspirin and current clinical guidelines regarding its use. Aspirin is an inexpensive

187   preventive measure, thus it is a valuable and cost-effective tool to prevent CVD and CRC in the

188   uninsured population. The National Heart, Lung, and Blood Institute reported that educational

189   outreach visits, along with audit and feedback strategies, were effective methods to improve

190   clinical practice guideline implementation [21]. These interventions could be used in free

191   medical clinics to address the suboptimal rates of aspirin use. Further studies are needed to

192   improve our understanding of the discrepancy in rates of aspirin use between uninsured patients

193   and the general population. Emphasis should be placed on developing solutions to minimize the

194   gap between these two populations.

195

196   The 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease

197   recommends considering aspirin for primary prevention in certain patients aged 40-70 who are

198   not at increased risk of bleeding. New studies demonstrating a lack of benefit have influenced the

199   evolving opinion on the beneficial effects of aspirin on primary prevention of CVD [22]. Despite

200   the changing views on aspirin, our study indicates that uninsured patients will still be taking

201   aspirin at lower rates than the general population unless interventions are implemented.

202

203   This study has several limitations. Patient races were not consistently recorded in medical

204   records, thus we could not fully assess relationships between race and aspirin use. Additionally,

205   our limited dataset did not include comprehensive information regarding factors that can lead to

206   increased risk of bleeding. As a result, it is conceivable that many more patients were

207   inappropriately on low-dose aspirin. The retrospective chart review conducted for this study did

208   not allow us to discern whether physicians discussed potential aspirin regimens with qualified

209   patients. Furthermore, we could not assess if concerns regarding risk of bleeding were addressed

210   in those conversations or if patients decided not to adhere to an aspirin regimen.

211

212   In conclusion, patients without health insurance are taking aspirin for the prevention of CVD and

213   CRC at suboptimal rates. Aspirin is underutilized among this population even in comparison to

214   the general population. Further improvements are needed to increase adherence to current

215   guidelines and address barriers uninsured patients may face in maintaining their cardiovascular

216   and colorectal health.

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218   # Acknowledgements

223

224   # References

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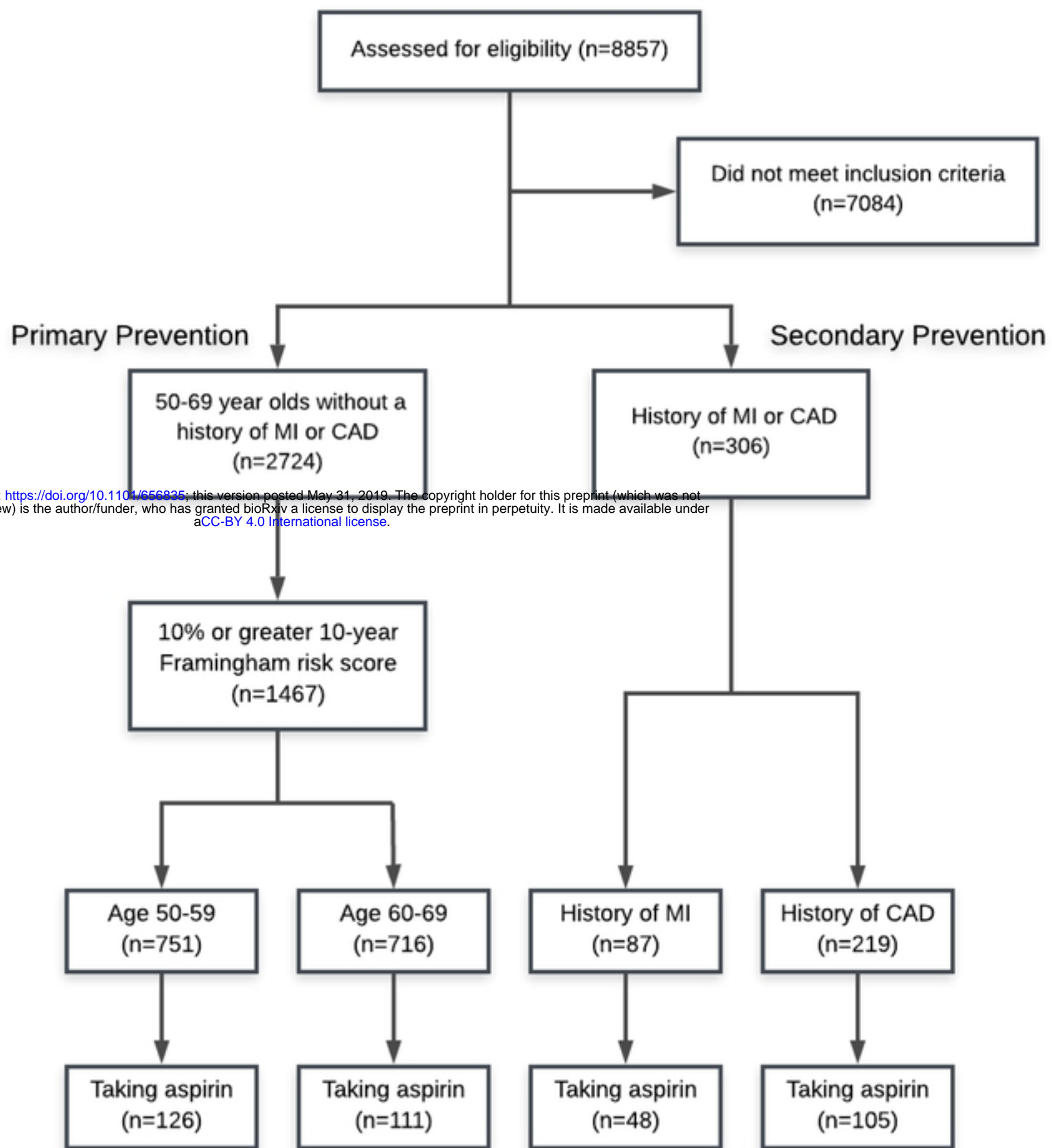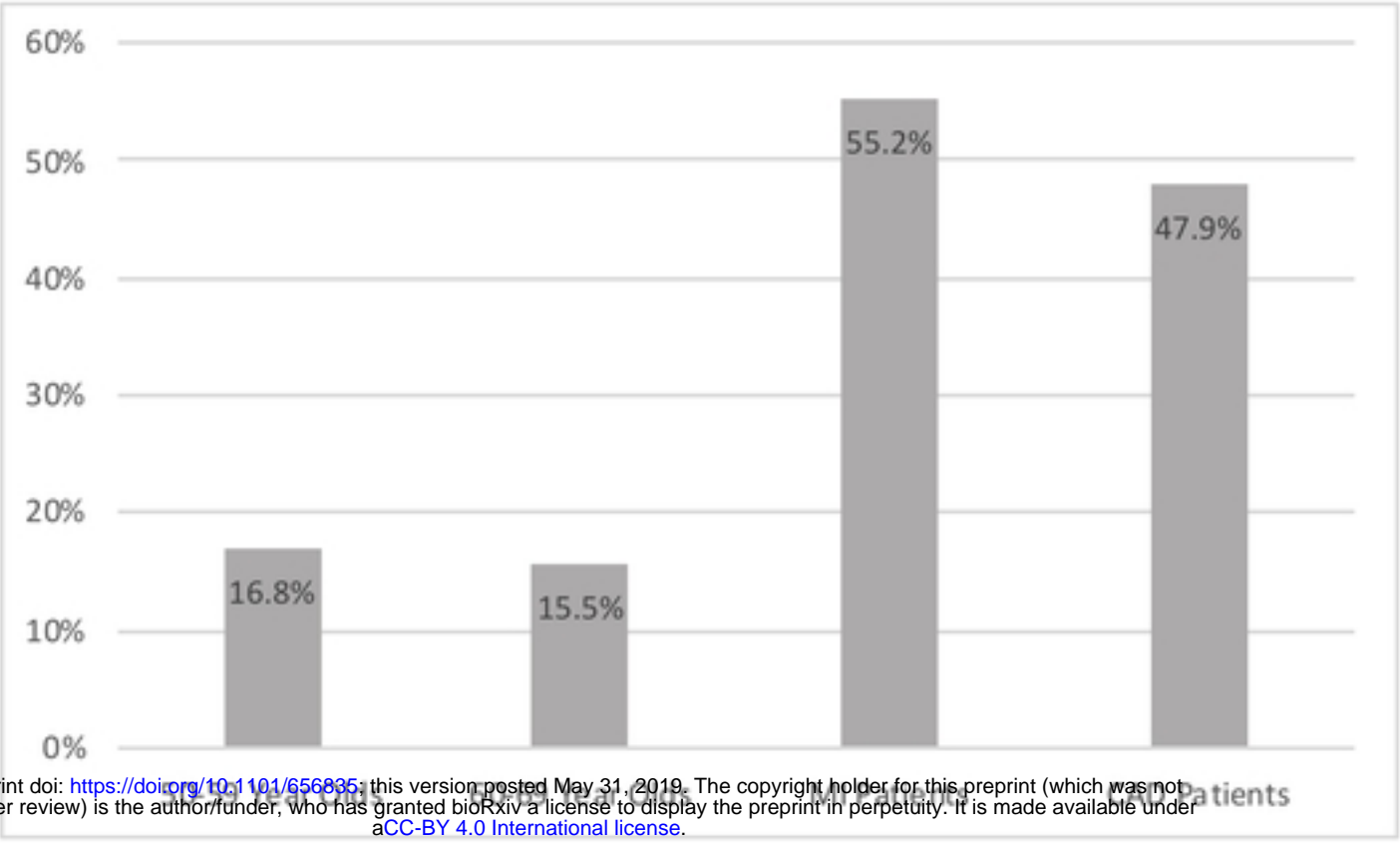295   doi:10.1016/j.jacc.2019.03.010

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Figure1

Figure2