

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

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23 **Abstract**

24 Aspirin is an effective anti-inflammatory and antiplatelet agent as an irreversible inhibitor of
25 cyclooxygenase. In 2016, the U.S. Preventive Services Task Force recommended aspirin for
26 primary prevention of cardiovascular disease (CVD) and colorectal cancer (CRC) in patients
27 aged 50 to 69 with a 10% or greater 10-year CVD risk. Due to the lack of literature describing
28 compliance with these recommendations in the uninsured patient population, we studied the
29 aspirin adherence for CVD and CRC prevention in several free medical clinics. We investigated
30 the records of 8857 uninsured patients who visited nine free medical clinics in the Tampa Bay
31 Area in 2016-2017. Aspirin compliance was assessed for patients with prior myocardial
32 infarction (MI) or coronary artery disease (CAD). 54% (n=1467) of patients met the criteria to
33 take aspirin for primary prevention of CVD and CRC, but just 17% of these patients aged 50-59
34 were on the medication. 16% percent of patients aged 60-69 were taking aspirin and significantly
35 more men than women were on aspirin (p=0.025). Of the 306 patients who had prior MI or CAD,
36 50% were on the medication for secondary prevention. Among the uninsured population, there is
37 low compliance with recommendations for aspirin usage to reduce the risk of CVD and CRC.
38 This study demonstrates that further improvements are needed to increase adherence to current
39 guidelines and address barriers uninsured patients may face in maintaining their cardiovascular
40 and colorectal health.

41

42 **Introduction**

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

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

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

113 **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)	0.237	104 (17.2)	40 (36.0)	0.011
Black	42 (6.7)	11 (8.7)		37 (6.1)	6 (5.4)	
Hispanic	181 (29.0)	33 (26.2)		232 (38.3)	38 (34.2)	
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)	
<i>Not Documented</i>	188 (30.1)	22 (17.5)		203 (33.6)	23 (20.7)	
Employment Status, n (%)						
Employed	156 (25.0)	40 (31.7)	0.753	143 (23.6)	37 (33.3)	0.543
Unemployed	214 (34.2)	59 (46.8)		163 (26.9)	36 (32.4)	
<i>Not Documented</i>	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)	

Race, n (%)						
Caucasian	16 (41.0)	25 (52.1)	0.974	45 (39.5)	48 (45.7)	0.977
Black	2 (5.1)	2 (4.2)		11 (9.6)	11 (10.5)	
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)	
<i>Not Documented</i>	<i>9 (23.1)</i>	<i>7 (14.6)</i>		<i>22 (19.3)</i>	<i>13 (12.4)</i>	
Employment Status, n (%)						
Employed	6 (15.4)	18 (37.5)	0.059	24 (21.1)	38 (36.2)	0.04
Unemployed	20 (51.3)	21 (43.8)		48 (42.1)	38 (36.2)	
<i>Not Documented</i>	<i>13 (33.3)</i>	<i>9 (18.8)</i>		<i>42 (36.8)</i>	<i>29 (27.6)</i>	

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

147 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

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.

217

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223

224 **References**

- 225 1. Heron M. Deaths: Leading Causes for 2016. *Natl Vital Stat Rep.* 2018;67: 1–77.
- 226 2. Patrono C, Ciabattini G, Patrignani P, Pugliese F, Filabozzi P, Catella F, et al. Clinical
227 pharmacology of platelet cyclooxygenase inhibition. *Circulation.* 1985;72: 1177–1184.
- 228 3. O’Brien JR. EFFECTS OF SALICYLATES ON HUMAN PLATELETS. *The Lancet.* 1968;291: 779–
229 783. doi:10.1016/S0140-6736(68)92228-9
- 230 4. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-
231 analysis of individual participant data from randomised trials. *The Lancet.* 2009;373: 1849–
232 1860. doi:10.1016/S0140-6736(09)60503-1
- 233 5. Friis S, Riis AH, Erichsen R, Baron JA, Sørensen HT. Low-Dose Aspirin or Nonsteroidal Anti-
234 inflammatory Drug Use and Colorectal Cancer Risk: A Population-Based, Case-Control
235 Study. *Ann Intern Med.* 2015;163: 347–355. doi:10.7326/M15-0039
- 236 6. Bibbins-Domingo K, U.S. Preventive Services Task Force. Aspirin Use for the Primary
237 Prevention of Cardiovascular Disease and Colorectal Cancer: U.S. Preventive Services Task
238 Force Recommendation Statement. *Ann Intern Med.* 2016;164: 836–845.
239 doi:10.7326/M16-0577
- 240 7. Grade Definitions - US Preventive Services Task Force [Internet]. [cited 13 May 2019].
241 Available: <https://www.uspreventiveservicestaskforce.org/Page/Name/grade-definitions>
- 242 8. Sidney C, Smith J, Benjamin EJ, Bonow RO, Braun LT, Creager MA, Franklin BA, et al.
243 AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients With Coronary
244 and Other Atherosclerotic Vascular Disease: 2011 Update. *Circulation.* 2011; Available:
245 <https://www.ahajournals.org/doi/10.1161/cir.0b013e318235eb4d>
- 246 9. Coon SA, Brooks AD, Wolff SE. Primary prevention aspirin use in high-risk patients: A
247 pharmacist intervention and comparison of risk stratification tools. *Journal of the*
248 *American Pharmacists Association.* 2017;57: 585–590. doi:10.1016/j.japh.2017.07.003
- 249 10. Malayala SV, Raza A. Compliance with USPSTF recommendations on aspirin for prevention
250 of cardiovascular disease in men. *International Journal of Clinical Practice.* 2016;70: 898–
251 906. doi:10.1111/ijcp.12869
- 252 11. Stafford RS, Monti V, Ma J. Underutilization of aspirin persists in US ambulatory care for
253 the secondary and primary prevention of cardiovascular disease. *PLoS Med.* 2005;2: e353.
254 doi:10.1371/journal.pmed.0020353
- 255 12. Mainous AG, Tanner RJ, Shorr RI, Limacher MC. Use of aspirin for primary and secondary
256 cardiovascular disease prevention in the United States, 2011–2012. *J Am Heart Assoc.*
257 2014;3. doi:10.1161/JAHA.114.000989

- 258 13. Brooks EL, Preis SR, Hwang S-J, Murabito JM, Benjamin EJ, Kelly-Hayes M, et al. Health
259 insurance and cardiovascular disease risk factors. *Am J Med.* 2010;123: 741–747.
260 doi:10.1016/j.amjmed.2010.02.013
- 261 14. Gaspoz J-M, Coxson PG, Goldman PA, Williams LW, Kuntz KM, Hunink MGM, et al. Cost
262 effectiveness of aspirin, clopidogrel, or both for secondary prevention of coronary heart
263 disease. *N Engl J Med.* 2002;346: 1800–1806. doi:10.1056/NEJM200206063462309
- 264 15. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults.
265 Executive Summary of The Third Report of The National Cholesterol Education Program
266 (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In
267 Adults (Adult Treatment Panel III). *JAMA.* 2001;285: 2486–2497.
- 268 16. Kernan Walter N., Ovbiagele Bruce, Black Henry R., Bravata Dawn M., Chimowitz Marc I.,
269 Ezekowitz Michael D., et al. Guidelines for the Prevention of Stroke in Patients With Stroke
270 and Transient Ischemic Attack. *Stroke.* 2014;45: 2160–2236.
271 doi:10.1161/STR.0000000000000024
- 272 17. Whitlock EP, Burda BU, Williams SB, Guirguis-Blake JM, Evans CV. Bleeding Risks With
273 Aspirin Use for Primary Prevention in Adults: A Systematic Review for the U.S. Preventive
274 Services Task Force. *Ann Intern Med.* 2016;164: 826–835. doi:10.7326/M15-2112
- 275 18. Mochari H, Ferris A, Adigopula S, Henry G, Mosca L. Cardiovascular disease knowledge,
276 medication adherence, and barriers to preventive action in a minority population. *Prev
277 Cardiol.* 2007;10: 190–195.
- 278 19. Wamala S, Merlo J, Bostrom G, Hogstedt C, Agren G. Socioeconomic disadvantage and
279 primary non-adherence with medication in Sweden. *Int J Qual Health Care.* 2007;19: 134–
280 140. doi:10.1093/intqhc/mzm011
- 281 20. Hira RS, Kennedy K, Nambi V, Jneid H, Alam M, Basra SS, et al. Frequency and practice-
282 level variation in inappropriate aspirin use for the primary prevention of cardiovascular
283 disease: insights from the National Cardiovascular Disease Registry’s Practice Innovation
284 and Clinical Excellence registry. *J Am Coll Cardiol.* 2015;65: 111–121.
285 doi:10.1016/j.jacc.2014.10.035
- 286 21. Chan WV, Pearson TA, Bennett GC, Cushman WC, Gaziano TA, Gorman PN, et al. ACC/AHA
287 Special Report: Clinical Practice Guideline Implementation Strategies: A Summary of
288 Systematic Reviews by the NHLBI Implementation Science Work Group: A Report of the
289 American College of Cardiology/American Heart Association Task Force on Clinical Practice
290 Guidelines. *J Am Coll Cardiol.* 2017;69: 1076–1092. doi:10.1016/j.jacc.2016.11.004
- 291 22. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, et al. 2019
292 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the
293 American College of Cardiology/American Heart Association Task Force on Clinical Practice

294 Guidelines. Journal of the American College of Cardiology. 2019;
295 doi:10.1016/j.jacc.2019.03.010

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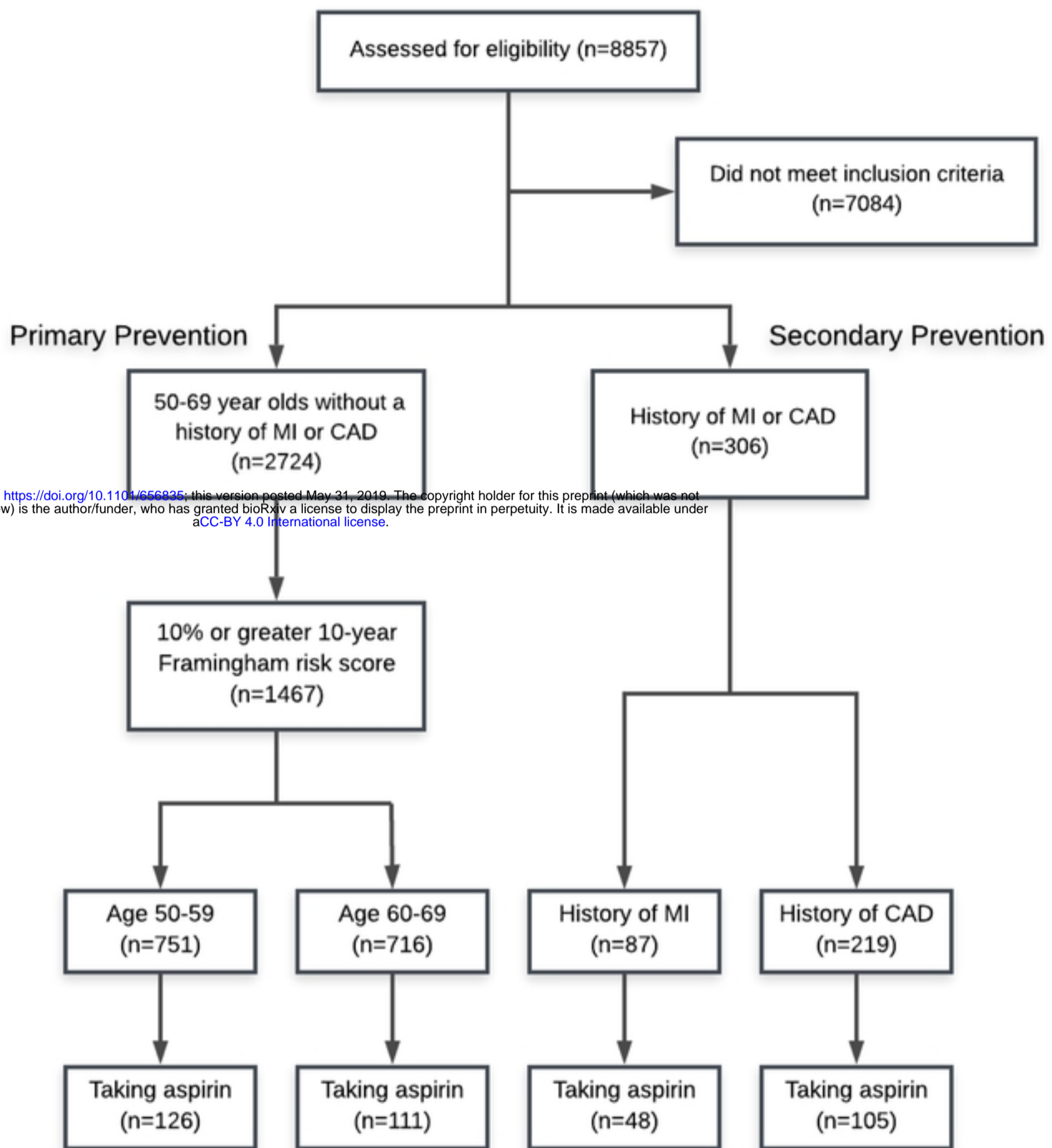
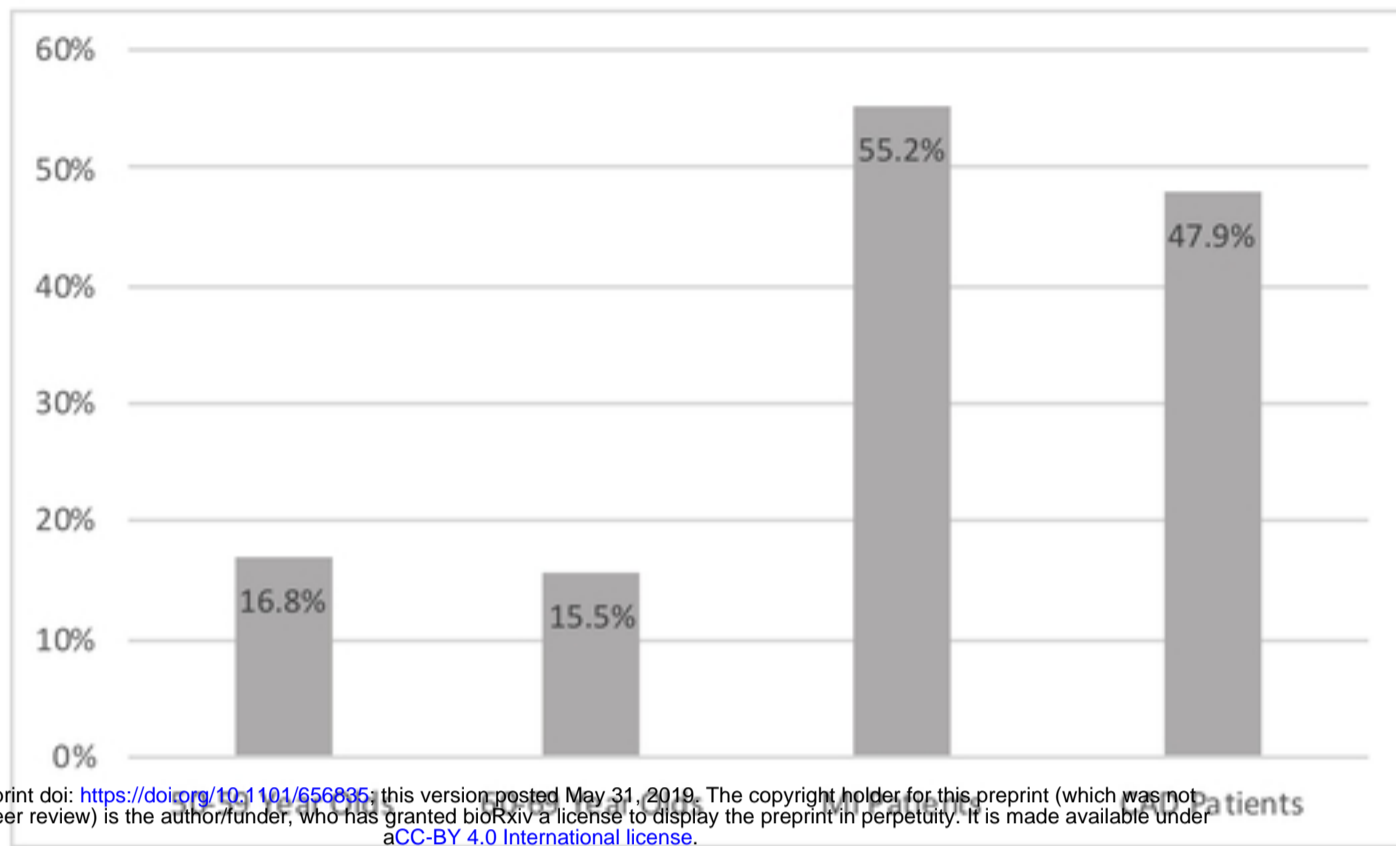


Figure 1



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