

## Supplementary Online Content

Schjerning Olsen A-M, Gislason GH, McGettigan P, et al. Association of NSAID use with risk of bleeding and cardiovascular events in patients receiving antithrombotic therapy after myocardial infarction. *JAMA*. doi:10.1001/jama.2015.0809.

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This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1.** ICD Codes and ATC Codes: Diagnoses, Surgical Procedures, and Pharmacotherapy Used for Defining the Study Population, Comorbidity, and Outcomes

**1A. ICD Codes**  
**Study population**

Myocardial Infarction	Defined from diagnosis	ICD8: 430 ICD10: I21-22
<b>Comorbidity</b>		
Cerebrovascular disease	Defined from diagnosis	ICD10: I60-69, ICD8: 430-438
Diabetes with complications	Defined from diagnosis	ICD10:E10-E14 ICD8: 250
Cardiac dysrhythmias	Defined from diagnosis	ICD10: I47-49, I460,I469, R001 ICD8:427
Acute renal failure	Defined from diagnosis	ICD10: N17,N19,R34 ICD8: 584
Chronic renal failure	Defined from diagnosis of chronic glomerulonephritis, chronic tubule intestinal nephropathy, non-end-stage chronic kidney disease, and diabetic and hypertensive nephropathy.	ICD10: E102, E112, E132, E142, I120, M200, M313, M319, M321B, N02-N08, N11-N12, N14, N18-N19, N26, N158-N160, N162-N164, N168, Q612-Q613, Q615, Q619 ICD8: 403, 404, 580-4, 590, 223, 25002, 40039, 59009, 59320, 75310-1, 75319
Heart failure	Defined from diagnosis plus treatment	ICD10: I110, I42, I50, J819 ICD8: 425, 4270-1 Treatment: Loop-diuretics
Malignancy	Defined from diagnoses of cancer (non-benign)	ICD10: C00-C97 ICD8: 140-208
Shock	Defined from diagnosis	ICD10: R57 ICD8: 7855
Pulmonary oedema	Defined from diagnosis	ICD10: J81.J182 ICD8: 514
Bleeding	Defined from diagnosis of gastrointestinal, intracranial, respiratory, and urinary tract bleedings; and anemia caused by bleeding.	ICD10: I60-I62, I690-I692, J942, K250, K254, K260, K264, K270, K280, K920-K922, N02, R04, R31, S064-S066

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ICD8: 430-432

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Percutaneous coronary procedure	Defined from procedure	NSCP: KFN (includes graft implantation and other coronary interventions)
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ICD8: 8<sup>th</sup> revision of the International Classification of Diseases system  
ICD10: 10<sup>th</sup> revision of the International Classification of Diseases system  
NCSP: The Nordic Medical Statistics Committees Classification of Surgical Procedures

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**Outcomes**

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Bleeding	Death from or diagnosis of gastrointestinal, intracranial, respiratory, and urinary tract bleedings; and anemia caused by bleeding.	ICD10: I60-I62, I690-I692, J942, K250, , K252 K254, K260, K264, K270, K272, K280, K920- K922, N02, R04, R31, S064-S066, D62,D50
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Combine Cardiovascular endpoint	Death from or diagnosis of thromboembolism including ischemic stroke, transient ischemic attack, and systematic arterial embolism, Re-MI, Cardiovascular death	ICD10: I63-I64, I74, G458-G459 ICD8: 430, ICD10: I21-22
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## 1B. ATC Codes

<b>Treatment</b>		
Oral anticoagulants	ATC: B011AA03-4	Vitamin K antagonists including warfarin and phenprocoumon
Aspirin	ATC: B01AC06, N02BA01	Acetylsalicylic acid
Clopidogrel	ATC: B01AC04	
Non-steroidal anti-inflammatory drugs	ATC: M01A but excluding glucosamine (M01AX05)	<p>Including</p> <p><b>Selective COX-2 inhibitors:</b> rofecoxib (M01AH02), celecoxib (M01AH01),</p> <p><b>Non selective NSAIDs:</b> naproxen (M01AE02), diclofenac (M01AB05), ibuprofen (M01AE01)</p> <p><b>Other:</b> iclofenac (M01AB05), etodolac (M01AB08), piroxicam (M01AC01), ketoprofen (M01AE03), nabumetone (M01AX01) and indometacin (M01AB01)</p>
Statins	ATC: C10A	
Beta-blockers	ATC: C07	
Renin angiotensin system inhibitors	ATC: C09	<i>Including:</i> angiotensin-converting-enzyme inhibitors, angiotensin-II receptor blockers
Loop-diuretics	ATC: C03C	
Thiazides	ATC: C03A	
Proton-pump inhibitors	ATC: A02BC	
Oral glucose-lowering drugs	ATC: A10	
Glucocorticoids	ATC: H02AB	<i>Including:</i> prednisolon

ATC: Anatomical Therapeutic Chemical (ATC) system

**eTable 2.** Risk of Bleeding According to Antithrombotic Treatment and Concomitant Specific NSAID According to Duration (A-C)

**2A**

Overall (Sample size 90,854)												
	Rofecoxib		Celecoxib		Diclofenac		Ibuprofen		Naproxen		Other	
	Events	Crude rates	Events	Crude rates	Events.	Crude rates	Events.	Crude rates	Events.	Crude rates	Events.	Crude rates
0-14 days	3	7.8[2.5-24.2]	4	6.3[2.4-16.7]	57	9.6[7.4-12.4]	68	4.0[3.2-5.1]	4	3.8[1.4-10.1]	30	6.0 [4.2-8.6]
14-30 days	1	4.4[0.6-31.0]	4	9.5[3.6-25.2]	16	4.6[2.8-7.6]	25	2.4[1.6-3.6]	3	4.8[1.6-14.9]	15	4.8[2.9-8.0]
>30 days	1	2.1[0.3-14.8]	13	10.4[6.0-18.0]	32	4.1[2.9-5.7]	39	2.6[1.9-3.6]	3	2.2[0.7-6.9]	21	2.8[1.8-4.2]

**2B**

Single antiplatelet (Sample size 59,618)												
	Rofecoxib		Celecoxib		Diclofenac		Ibuprofen		Naproxen		Other	
	Events	Crude rates	Events.	Crude rates	Events	Crude rates	Events.	Crude rates	Events.	Crude rates	Events	Crude rates
0-14 days	0	NA	3	14.9[4.8-46.2]	16	7.5[4.6-12.2]	20	3.2[2.1-5.0]	1	2.7[0.4-19.1]	7	3.7 [1.8-7.9]
14-30 days	1	NA	2	8.2[2.0-32.7]	9	3.9[2.0-7.4]	15	2.1[1.2-3.4]	2	4.8[1.2-19.3]	7	3.3[1.6-6.8]
>30 days	0	NA	10	12.6[6.8-23.4]	21	3.7[2.4-5.6]	25	2.3[1.5-3.4]	3	3.2[1.0-9.9]	14	2.5[1.5-4.2]

**2C**

Aspirin plus clopidogrel (Sample size 13,280)												
	Rofecoxib		Celecoxib		Diclofenac		Ibuprofen		Naproxen		Other	
	Events	Crude rates	Events	Crude rates	Events	Crude rates	Events	Crude rates	Events	Crude rates	Events	Crude rates
0-14 days	1	31.9[4.4-230]	0	NA	8	15.8[7.9-31.6]	13	10.0[5.8-17.2]	1	11.2[1.6-79.4]	9	21.3 [11.1-40.9]
14-30 days	0	NA	1	13.3[1.9-94.3]	4	7.7[2.9-20.5]	5	3.6[1.5-8.7]	1	9.2[1.3-65.3]	7	11.2[4.7-27.0]
>30 days	1	15.2[2.2-110]	3	12.7[4.1-39.3]	9	9.3[4.8-17.9]	10	5.8[3.1-10.8]	0	NA	14	2.5[0.6-10.0]

**eTable 3.** Distribution of Antithrombotic Treatment at Start of Study Inception Among NSAID Users and Non-NSAIDs Users

Treatment regime	No NSAID at study inception	NSAID at study inception
Total population	60,040 (100%)	1,931 (100%)
No antithrombotic treatment	2,462 (4.1%)	99(5.1%)
Aspirin	12,859(21.4%)	506(26.2%)
Clopidogrel	1,117(1.9%)	28(1.5%)
Aspirin+Clopidogrel	36,315(60.5%)	1,092(56.6%)
OAC	541(0.9%)	10(0.5%)
Single AP+OAC	2,812(4.6%)	83(4.3%)
Triple therapy	3,934(6.6%)	113(5.8%)

**eTable 4.** Type of Bleeding With and Without Concomitant NSAID Use

	No NSAID	NSAID
Overall bleeding	3675 (100%)	1613 (100%)
Cerebral	465 (12.7%)	202 (12.5%)
Gastrointestinal bleeding	1488 (40.5%)	669 (41.5%)
Urogenital bleeding	685 (18.6%)	299 (18.5%)
Respiratory bleeding	404 (11.0%)	167 (10.4%)
Anaemia caused by bleeding	633 (17.2%)	276 (17.1%)



**eFigure 1. Flowchart of Study Population**

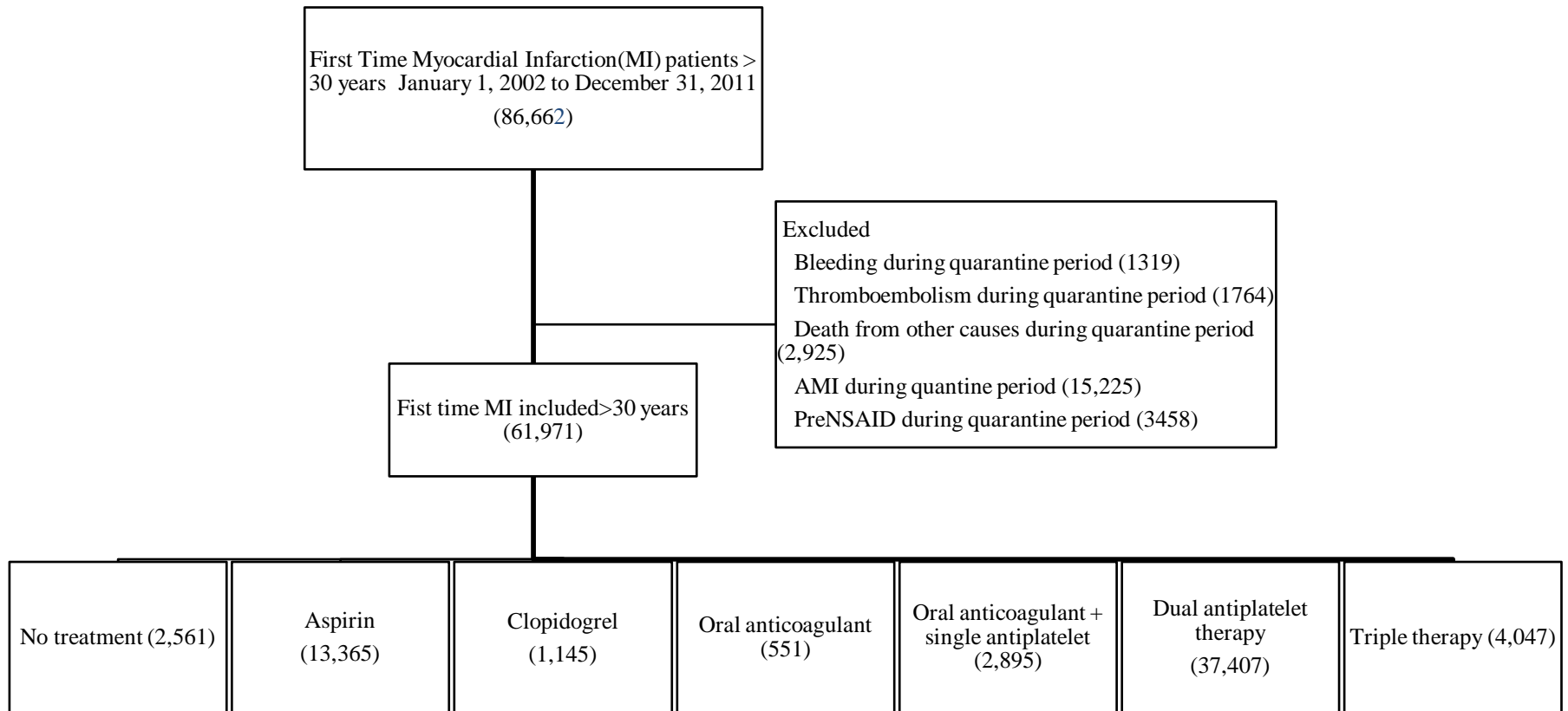
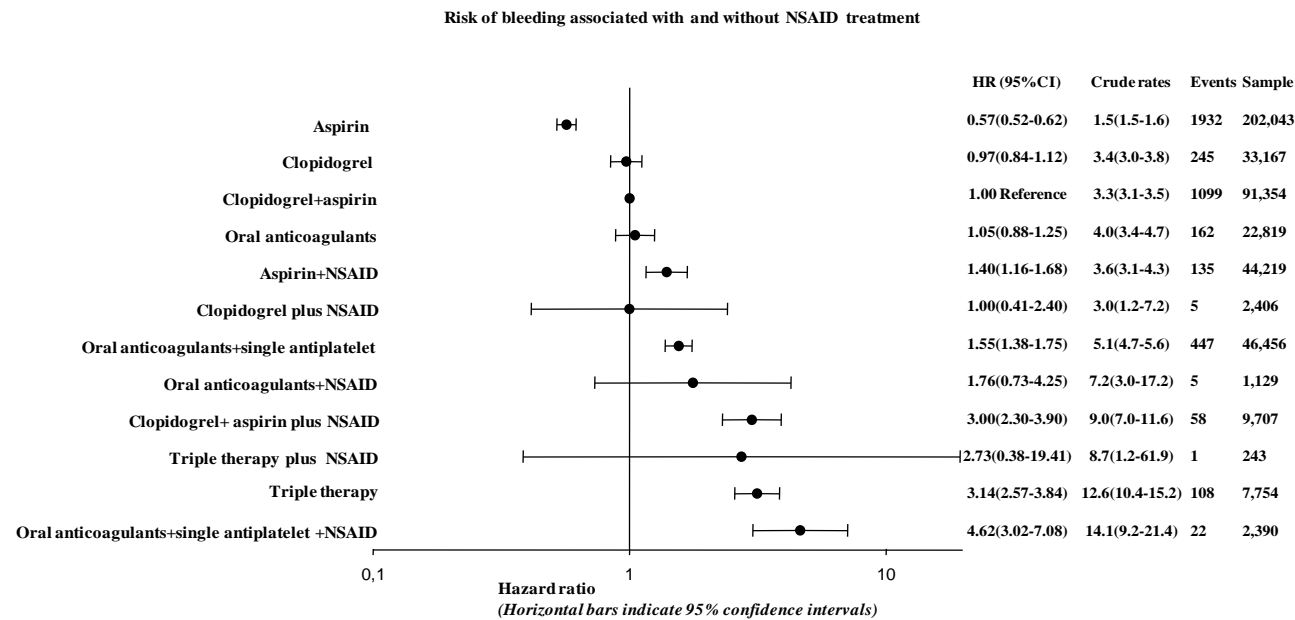


Figure legend: Flow chart of study population. Quarantine period from the day of discharge to 30 days after.

**eFigure 2.** Risk of Bleeding With and Without NSAID Use in MI Patients (New-User Design)



**Legend:** Abbreviations: NSAID, non-steroidal anti-inflammatory drug; CI, confidence interval. Reference is aspirin plus clopidogrel without NSAID (vertical line indicates reference level). New user design= excluding prevalent NSAID patients (n=4,632)