

## Appendix 1: Administrative codes adopted to define conditions

Table 1. Administrative codes used to identify diagnosis of gastrointestinal bleeding.

<b>ICD-9 Code</b>	
531	Gastric ulcer
532	Duodenal ulcer
533	Peptic ulcer site unspecified*
534	Gastrojejunal ulcer
569.82	Ulceration of intestine
569.83	Perforation of intestine
578	Gastrointestinal hemorrhage†
562	Diverticula of intestine
<b>Current Procedural Terminology Code</b>	
43200, 43201, 43202, 43204, 43205, 43215, 43217, 43219, 43220, 43226, 43227, 43228, 43231, 43232, 43234, 43235, 43236, 43237, 43238, 43239, 43241, 43242, 43243, 43244, 43245, 43246, 43247, 43248, 43249, 43250, 43251, 43255, 43256, 43257, 43258, 44300, 44310, 44312, 44314, 44316, 44320, 44340, 44345, 44346, 44360, 44361, 44364, 44365, 44366, 44369, 44372, 44373, 44376, 44377, 44378, 44380, 44382, 44383, 44386, 44388, 44389, 44391, 44392, 44393, 44394	Upper gastrointestinal surgery/procedure
44389, 44391, 44392, 44393, 44394, 45300, 45305, 45307, 45308, 45309, 45315, 45317, 45320, 45330, 45331, 45333, 45334, 45335, 45355, 45378, 45379, 45380, 45381, 45382, 45383, 45384, 45385, 82270, 82271, 82272, A4773, G0394	Lower gastrointestinal surgery/procedure

\* along with an upper gastrointestinal surgery or procedure within 7 days of the ICD code.

† along with an upper or lower gastrointestinal surgery or procedure within 7 days of the ICD code.

ICD-9 = International Classification of Diseases, Ninth Revision.

Table 2. Administrative codes used to identify diagnosis of co-existing conditions at the baseline.

<b>ICD-9 Code</b>	<b>Conditions</b>
<b><i>Chronic kidney disease (585)</i></b>	
585.1	Chronic kidney disease, Stage I
585.2	Chronic kidney disease, Stage II (mild)
585.3	Chronic kidney disease, Stage III (moderate)
585.4	Chronic kidney disease, Stage IV (severe)
585.5	Chronic kidney disease, Stage V
585.6	End stage renal disease
585.9	Chronic kidney disease, unspecified
<b><i>Trauma (800-959)</i></b>	
<b><i>800-804</i></b>	<b><i>Fracture of Skull</i></b>
800	Fracture of vault of skull
801	Fracture of base of skull
802	Fracture of face bones
803	Other and unspecified skull fractures
804	Multiple fractures involving skull or face with other bones
<b><i>805-809</i></b>	<b><i>Fracture Of Spine And Trunk</i></b>
805	Fracture of vertebral column without mention of spinal cord injury
806	Fracture of vertebral column with spinal cord injury
807	Fracture of rib(s) sternum larynx and trachea
808	Fracture of pelvis
809	Ill-defined fractures of bones of trunk
<b><i>810-819</i></b>	<b><i>Fracture Of Upper Limb</i></b>
810	Fracture of clavicle
811	Fracture of scapula
812	Fracture of humerus
813	Fracture of radius and ulna
814	Fracture of carpal bone(s)
815	Fracture of metacarpal bone(s)
816	Fracture of one or more phalanges of hand
817	Multiple fractures of hand bones
818	Ill-defined fractures of upper limb
819	Multiple fractures involving both upper limbs and upper limb with rib(s) and sternum
<b><i>820-829</i></b>	<b><i>Fracture of Lower Limb</i></b>
820	Fracture of neck of femur
821	Fracture of other and unspecified parts of femur
822	Fracture of patella
823	Fracture of tibia and fibula
824	Fracture of ankle
825	Fracture of one or more tarsal and metatarsal bones
826	Fracture of one or more phalanges of foot
827	Other multiple and ill-defined fractures of lower limb
828	Multiple fractures involving both lower limbs lower with upper limb

	and lower limb(s) with rib(s) and sternum
829	Fracture of unspecified bones
830-839	<i>Dislocation</i>
830	Dislocation of jaw
831	Dislocation of shoulder
832	Dislocation of elbow
833	Dislocation of wrist
834	Dislocation of finger
835	Dislocation of hip
836	Dislocation of knee
837	Dislocation of ankle
838	Dislocation of foot
839	Other multiple and ill-defined dislocations
840-848	<i>Sprains And Strains Of Joints And Adjacent Muscles</i>
840	Sprains and strains of shoulder and upper arm
841	Sprains and strains of elbow and forearm
842	Sprains and strains of wrist and hand
843	Sprains and strains of hip and thigh
844	Sprains and strains of knee and leg
845	Sprains and strains of ankle and foot
846	Sprains and strains of sacroiliac region
847	Sprains and strains of other and unspecified parts of back
848	Other and ill-defined sprains and strains
850-854	<i>Intracranial Injury, Excluding Those With Skull Fracture</i>
850	Concussion
851	Cerebral laceration and contusion
852	Subarachnoid subdural and extradural hemorrhage following injury
853	Other and unspecified intracranial hemorrhage following injury
854	Intracranial injury of other and unspecified nature
860-869	<i>Internal Injury Of Chest, Abdomen, And Pelvis</i>
860	Traumatic pneumothorax and hemothorax
861	Injury to heart and lung
862	Injury to other and unspecified intrathoracic organs
863	Injury to gastrointestinal tract
864	Injury to liver
865	Injury to spleen
866	Injury to kidney
867	Injury to pelvic organs
868	Injury to other intra-abdominal organs
869	Internal injury to unspecified or ill-defined organs
870-879	<i>Open Wound Of Head, Neck, And Trunk</i>
870	Open wound of ocular adnexa
871	Open wound of eyeball
872	Open wound of ear
873	Other open wound of head
874	Open wound of neck

875	Open wound of chest (wall)
876	Open wound of back
877	Open wound of buttock
878	Open wound of genital organs (external) including traumatic amputation
879	Open wound of other and unspecified sites except limbs
880-887	<i>Open Wound Of Upper Limb</i>
880	Open wound of shoulder and upper arm
881	Open wound of elbow forearm and wrist
882	Open wound of hand except finger(s) alone
883	Open wound of finger(s)
884	Multiple and unspecified open wound of upper limb
885	Traumatic amputation of thumb (complete) (partial)
886	Traumatic amputation of other finger(s) (complete) (partial)
887	Traumatic amputation of arm and hand (complete) (partial)
890-897	<i>Open Wound Of Lower Limb</i>
890	Open wound of hip and thigh
891	Open wound of knee leg (except thigh) and ankle
892	Open wound of foot except toe(s) alone
893	Open wound of toe(s)
894	Multiple and unspecified open wound of lower limb
895	Traumatic amputation of toe(s) (complete) (partial)
896	Traumatic amputation of foot (complete) (partial)
897	Traumatic amputation of leg(s) (complete) (partial)
900-904	<i>Injury to Blood Vessels</i>
900	Injury to blood vessels of head and neck
901	Injury to blood vessels of thorax
902	Injury to blood vessels of abdomen and pelvis
903	Injury to blood vessels of upper extremity
904	Injury to blood vessels of lower extremity and unspecified sites
905-909	<i>Late Effects Of Injuries, Poisonings, Toxic Effects, And Other External Causes</i>
905	Late effects of musculoskeletal and connective tissue injuries
906	Late effects of injuries to skin and subcutaneous tissues
907	Late effects of injuries to the nervous system
908	Late effects of other and unspecified injuries
909	Late effects of other and unspecified external causes
910-919	<i>Superficial Injury</i>
910	Superficial injury of face neck and scalp except eye
911	Superficial injury of trunk
912	Superficial injury of shoulder and upper arm
913	Superficial injury of elbow forearm and wrist
914	Superficial injury of hand(s) except finger(s) alone
915	Superficial injury of finger(s)
916	Superficial injury of hip thigh leg and ankle
917	Superficial injury of foot and toe(s)

918	Superficial injury of eye and adnexa
919	Superficial injury of other multiple and unspecified sites
920-924	<i>Contusion With Intact Skin Surface</i>
920	Contusion of face, scalp, and neck except eye(s)
921	Contusion of eye and adnexa
922	Contusion of trunk
923	Contusion of upper limb
924	Contusion of lower limb and of other and unspecified sites
925-929	<i>Crushing Injury</i>
925	Crushing injury of face scalp and neck
926	Crushing injury of trunk
927	Crushing injury of upper limb
928	Crushing injury of lower limb
929	Crushing injury of multiple and unspecified sites
930-939	<i>Effects Of Foreign Body Entering Through Orifice</i>
930	Foreign body on external eye
931	Foreign body in ear
932	Foreign body in nose
933	Foreign body in pharynx and larynx
934	Foreign body in trachea bronchus and lung
935	Foreign body in mouth esophagus and stomach
936	Foreign body in intestine and colon
937	Foreign body in anus and rectum
938	Foreign body in digestive system, unspecified
939	Foreign body in genitourinary tract
940-949	<i>Burns</i>
940	Burn confined to eye and adnexa
941	Burn of face head and neck
942	Burn of trunk
943	Burn of upper limb except wrist and hand
944	Burn of wrist(s) and hand(s)
945	Burn of lower limb(s)
946	Burns of multiple specified sites
947	Burn of internal organs
948	Burns classified according to extent of body surface involved
950-957	<i>Injury To Nerves And Spinal Cord</i>
950	Injury to optic nerve and pathways
951	Injury to other cranial nerve(s)
952	Spinal cord injury without evidence of spinal bone injury
953	Injury to nerve roots and spinal plexus
954	Injury to other nerve(s) of trunk excluding shoulder and pelvic girdles
955	Injury to peripheral nerve(s) of shoulder girdle and upper limb
956	Injury to peripheral nerve(s) of pelvic girdle and lower limb
957	Injury to other and unspecified nerves
958-959	<i>Certain Traumatic Complications And Unspecified Injuries</i>
958	Certain early complications of trauma

959	Injury other and unspecified
<b><i>H pylori infection</i></b>	
041.86	Helicobacter pylori (H. pylori) infection

ICD-9 = International Classification of Diseases, Ninth Revision.

**Appendix 2: Standardized Differences between groups before and after the application of ATT weighting**

	Original Sample		ATT Weighting	
	Dabigatran vs. Warfarin	Rivaroxaban vs. Warfarin	Dabigatran vs. Warfarin	Rivaroxaban vs. Warfarin
<b>Age Group</b>				
Continuous	0.358	0.022	-0.047	-0.043
18-44	-0.294	-0.216	0.012	0.003
45-64	-0.146	0.066	0.015	0.003
55-64	0.088	0.181	0.011	-0.003
65+	0.233	-0.123	-0.030	-0.001
Female	-0.333	0.092	0.002	-0.005
<b>Region</b>				
East	-0.019	-0.274	-0.005	-0.002
Mid-West	-0.158	-0.070	0.004	-0.001
South	0.186	0.304	-0.002	0.003
West	-0.037	-0.157	0.002	-0.003
<b>Clinical/Medication Indicators</b>				
Renal Failure	-0.040	-0.162	-0.005	-0.003
Trauma	-0.261	0.101	0.005	-0.010
Helicobacter Pylori infection	0.019	0.010	0.002	0.000
<b>Bleeding Risk</b>				
HAS_BLED score	0.242	-0.013	-0.045	0.001
<b>CCS</b>				
Continuous	-0.291	-0.166	0.003	-0.004
<=5	0.098	-0.210	0.001	-0.032
6-10	0.172	0.102	0.009	0.003
11-15	-0.006	0.245	-0.009	0.032
16-20	-0.097	-0.006	-0.021	-0.022
21-25	-0.129	-0.083	-0.008	0.024
>=26	-0.185	-0.306	0.044	-0.035
NSAID use	-0.211	0.428	0.013	-0.011
PPI use	-0.022	-0.009	-0.003	0.000
Steroid use	-0.081	-0.077	0.003	-0.001

CCS=clinical classification system; NSAID=non-steroidal anti-inflammatory drug; PPI=proton pump inhibitor



**Appendix 3: Hazard Ratios of all variables included in the Cox Proportional Hazard Models**

	Dabigatran (ref: Warfarin)	Rivaroxaban (ref: Warfarin)
N	44,514	41,256
Warfarin	1	1
Exposure (Dabigatran/ Rivaroxaban)	1.21 (0.96–1.53)	0.98 (0.36-2.69)
Sex		
Male	1	1
Female	0.64** (0.49 – 0.85)	0.43** (0.25 – 0.71)
Region of Residence		
South	1	1
East	1.15 (0.78 – 1.69)	1.50 (0.85 – 2.62)
Mid-West	1.15 (0.87 – 1.52)	1.66 (0.86 – 3.18)
West	0.89 (0.60 – 1.32)	0.85 (0.47 – 1.52)
Co-morbidity and co-medications		
Use of PPI	0.87 (0.65 – 1.16)	1.59 (0.87 – 2.90)
Use of Steroids	1.19 (0.85 – 1.66)	1.09 (0.58 – 2.05)
Renal Failure	0.82 (0.46 – 1.47)	4.10* (1.09 – 15.4)
Trauma	0.77 (0.53 – 1.11)	0.66 (0.39 – 1.11)

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H Pylori infection	0.01** (0.00-0.04)	0.05** (0.01 – 0.41)
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\*:  $p \leq 0.05$ , \*\*:  $p \leq 0.01$

Age groups, CCS categories, and NSAID use as stratification factors and others as regression covariates

**Appendix 4: Hazard Ratios Derived from Cox Proportional Hazard Models with Different Covariates-inclusion Methods**

	Dabigatran (ref: Warfarin)	Rivaroxaban (ref: Warfarin)
N	44,514	41,256
Crude HR <sup>1</sup>	1.20 (0.96–1.52)	0.95 (0.31–2.94)
Adjusted HR <sup>2</sup>	1.20 (0.95–1.52)	0.95 (0.32–2.86)
Adjusted HR <sup>3</sup>	1.21 (0.96–1.53)	0.98 (0.36–2.69)
Adjusted HR <sup>4</sup>	1.29* (1.00–1.65)	1.06 (0.34–3.30)

\*:  $p \leq 0.10$  \*\*:  $p \leq 0.05$

<sup>1</sup>: No control variables

<sup>2</sup>: All control variables as regression covariates

<sup>3</sup>: Age groups, CCS categories, and NSAID use as stratification factors and others as regression covariates

<sup>4</sup>: All control variables as stratification factors

**Appendix 5: Hazard Ratios Derived from Cox Proportional Hazard Models with Different Wash-out Periods**

	Dabigatran (ref: Warfarin)	Rivaroxaban (ref: Warfarin)
N	44,514	41,256
Wash-out Period: 7 Days		
Crude HR <sup>1</sup>	1.21 (0.94–1.56)	0.83 (0.22–3.12)
Adjusted HR <sup>2</sup>	1.25* (0.97–1.62)	0.76 (0.24–2.42)
Wash-out Period: 14 Days		
Crude HR <sup>1</sup>	1.20 (0.96–1.52)	0.95 (0.31–2.94)
Adjusted HR <sup>2</sup>	1.21 (0.96–1.53)	0.98 (0.36–2.69)
Wash-out Period: 30 Days		
Crude HR <sup>1</sup>	1.22* (0.99–1.51)	0.89 (0.33–2.41)
Adjusted HR <sup>2</sup>	1.13 (0.91–1.40)	0.99 (0.40–2.47)
Wash-out Period: 45 Days		
Crude HR <sup>1</sup>	1.23** (1.01–1.50)	0.85 (0.35–2.08)
Adjusted HR <sup>2</sup>	1.11 (0.91–1.36)	1.10 (0.47–2.56)

\*: p≤0.10 \*\*: p≤0.05

<sup>1</sup>: No control variables

<sup>2</sup>: Age groups, CCS categories and NSAID use as stratification factors and others as regression covariates

**Appendix 6: Hazard Ratios Derived from Cox Proportional Hazard Models Censoring GI Bleeding from Hospitalization Records**

	Dabigatran (ref: Warfarin)	Rivaroxaban (ref: Warfarin)
<b>All Sample</b>		
N	44,514	41,256
Crude HR <sup>1</sup>	1.18 (0.91–1.51)	1.34 (0.41–4.36)
Adjusted HR <sup>2</sup>	1.19 (0.91–1.54)	1.36 (0.49–3.75)
<b>Non-Elderly</b>		
N	34,038	32,099
Crude HR <sup>1</sup>	1.26 (0.90–1.75)	1.71 (0.37–7.83)
Adjusted HR <sup>2</sup>	1.26 (0.90–1.77)	1.52 (0.50–4.60)
<b>Elderly</b>		
N	10,476	9,157
Crude HR <sup>1</sup>	1.08 (0.73–1.60)	0.80 (0.12–5.38)
Adjusted HR <sup>2</sup>	1.08 (0.73–1.62)	0.67 (0.22–2.04)

<sup>1</sup>: No control variables

<sup>2</sup>: Age groups, CCS categories and NSAID use as stratification factors and others as regression covariates

**Appendix 7: Hazard Ratios Derived from Cox Proportional Hazard Models Adding the HAS-BLED Risk Score**

	Dabigatran (ref: Warfarin)	Rivaroxaban (ref: Warfarin)
<b><i>All Sample</i></b>		
N	44,514	41,256
Adjusted HR <sup>1</sup>	1.21 (0.96–1.53)	0.98 (0.36–2.67)
<b><i>Non-Elderly</i></b>		
N	34,038	32,099
Adjusted HR <sup>1</sup>	1.35 (0.99–1.84)	1.03 (0.34–3.17)
<b><i>Elderly</i></b>		
N	10,476	9,157
Adjusted HR <sup>1</sup>	1.08 (0.76–1.54)	0.62 (0.18–2.09)

<sup>1</sup>: Age groups, CCS categories and NSAID use as stratification factors and others as regression covariates

**Appendix 8: Cohort exit reason by drug type**

Exit reason	Dabigatran	Rivaroxaban	Warfarin
Inpatient	13.23%	12.13%	15.52%
Bleeding	2.49%	0.24%	1.60%
Loss of enrollment	15.02%	8.37%	10.36%
End of observation	19.16%	19.16%	11.80%
Loss of continuous RX exposure	46.30%	59.43%	59.40%
Switch drug	3.81%	0.67%	1.32%