

Supplemental Online Content

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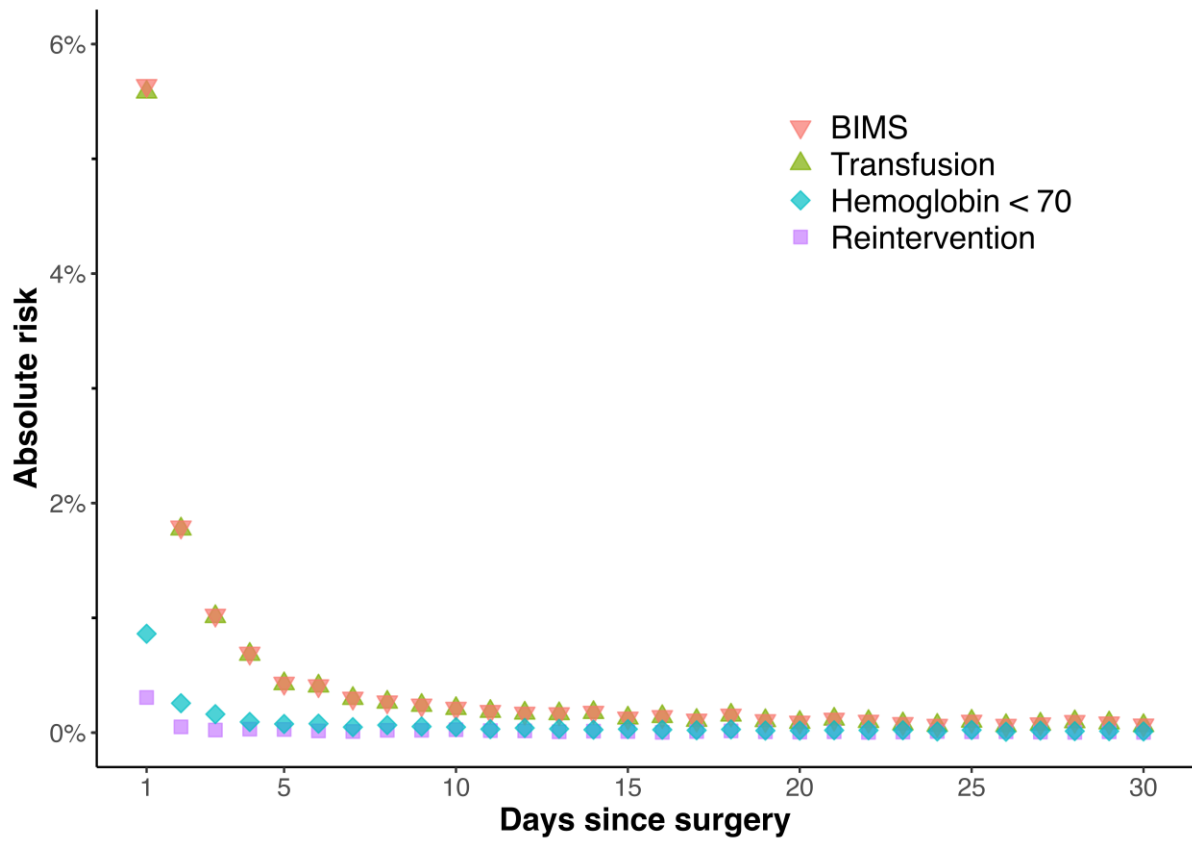
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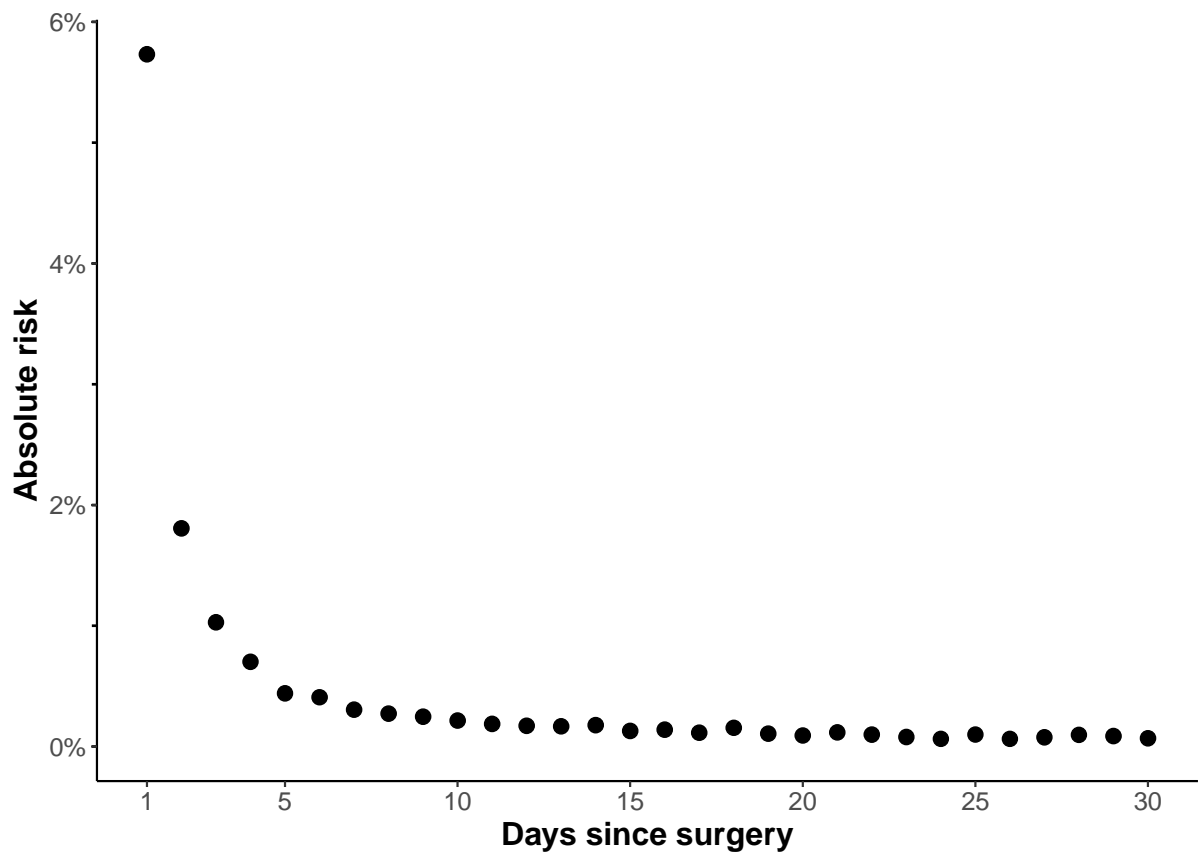
This supplemental material has been provided by the authors to give readers additional information about their work.

eFigure 1. Absolute Risk of BIMS, Postoperative Red Blood Cell Transfusion, Postoperative Hemoglobin < 70 and Bleeding Associated With Reintervention on Each Postoperative Day up to Day 30

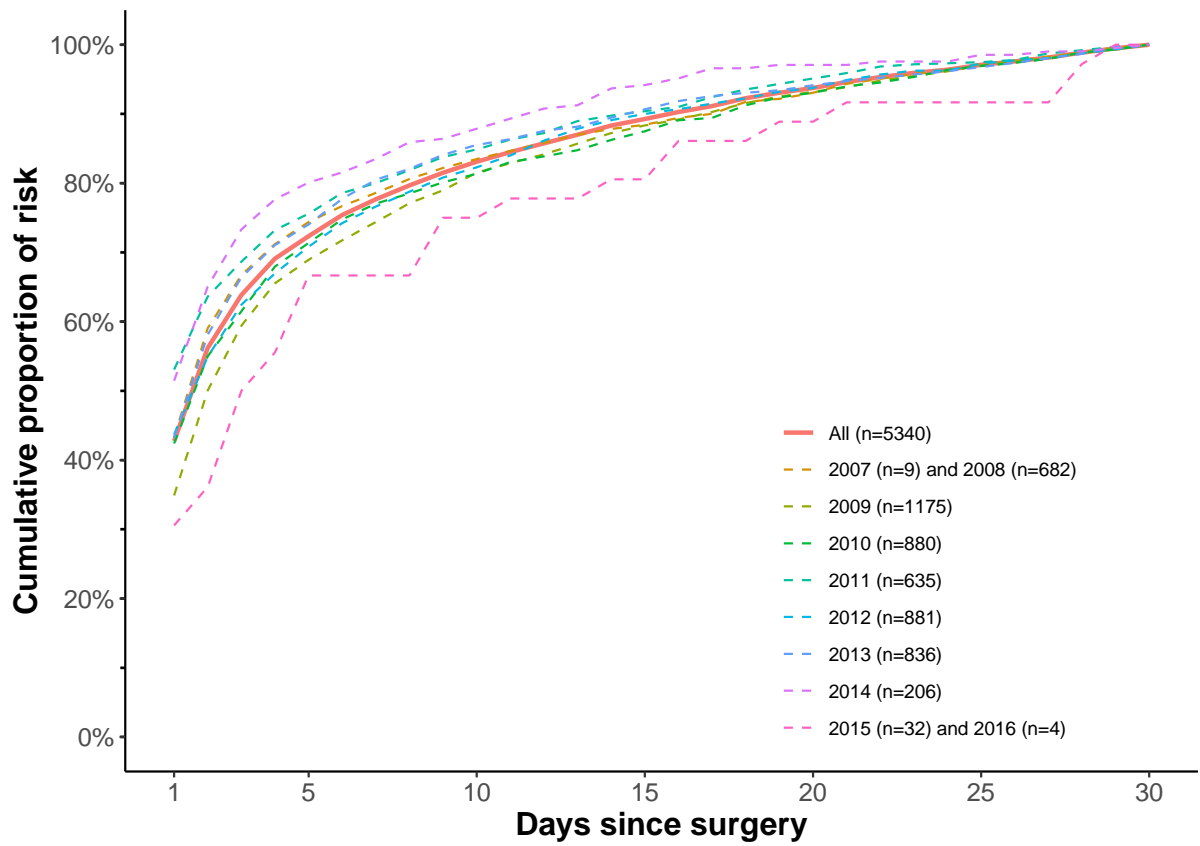


BIMS (Bleeding Independently associated with Mortality after noncardiac Surgery) is defined as a composite of postoperative transfusion, postoperative hemoglobin < 70 and bleeding associated with reintervention.

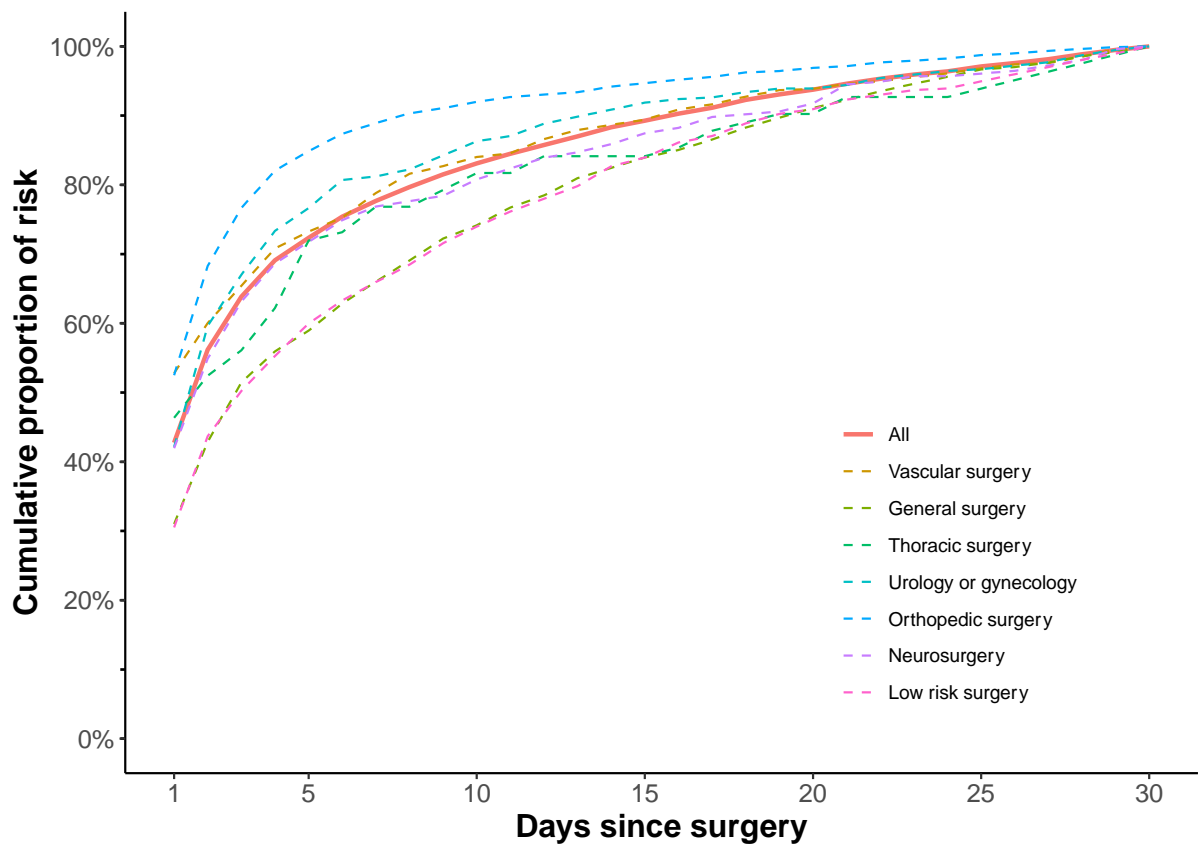
eFigure 2. Absolute Risk of Major Bleeding on Each Postoperative Day up to Day 30



eFigure 3. Sensitivity Analysis of Cumulative Proportion of Risk for Major Bleeding by Patient Recruitment Year



eFigure 4. Sensitivity Analysis of Cumulative Proportion of Risk for Major Bleeding by Surgical Specialty



eTable 1. Cumulative Proportion of Risk (%) of Events up to Postoperative Day 30

	1 d	2 d	3 d	4 d	5 d	6 d	7 d	14 d	21 d	30 d
Major bleeding*	42.7	56.2	63.9	69.1	72.4	75.4	77.7	88.3	94.6	100
BIMS	42.6	56.1	63.9	69.1	72.3	75.4	77.7	88.3	94.6	100
Transfusion	42.6	56.2	63.9	69.1	72.3	75.4	77.7	88.3	94.6	100
Hg < 70	39.9	51.8	59.3	63.6	67.1	70.7	72.9	86.5	93.8	100
Reintervention	44.5	51.8	55.1	59.5	63.5	65.7	67.2	84.3	92.7	100
Death**	32.0	36.0	40.0	44.0	48.0	52.0	56.0	88.0	92.0	100

*A composite of BIMS and bleeding associated with reintervention

**Very low number of events (n=25)

eTable 2. Confidence Intervals for Outcomes

Post-operative day	Lower limit (95% CI)	Risk* (%)	Upper limit (95% CI)
Major bleeding			
1	40.9	42.7	44.6
2	54.3	56.2	58.1
3	62.0	63.9	65.7
4	67.2	69.1	70.9
5	70.5	72.4	74.2
6	73.5	75.4	77.3
7	75.8	77.7	79.5
14	86.5	88.3	90.2
21	92.7	94.6	96.5
30		100	
BIMS			
1	40.7	42.6	44.5
2	53.4	56.1	58.0
3	62.0	63.9	65.7
4	67.2	69.1	71.0
5	70.5	72.3	74.2
6	73.5	75.4	77.3
7	75.8	77.7	79.5
14	86.4	88.3	90.2
21	92.7	94.6	96.4
30		100	
Transfusion			
1	40.7	42.6	44.5
2	54.3	56.2	58.0
3	62.0	63.9	65.8
4	67.2	69.1	71.0
5	70.4	72.3	74.2
6	73.5	75.4	77.3
7	75.8	77.7	79.6
14	86.5	88.3	90.2
21	92.8	94.6	96.5
30		100	
Hg < 70			
1	35.3	39.9	44.6
2	47.2	51.8	56.4
3	54.6	59.3	63.9
4	58.9	63.6	68.2
5	62.4	67.1	71.7
6	66.0	70.7	75.3
7	68.2	72.9	77.5
14	81.9	86.5	91.1
21	89.2	93.8	98.5
30		100	
Reintervention			
1	36.3	44.5	52.7
2	43.6	51.8	60.0
3	46.9	55.1	63.3
4	51.3	59.5	67.7
5	55.3	63.5	71.7
6	57.5	65.7	73.9
7	58.9	67.2	75.4
14	76.1	84.3	92.5
21	84.5	92.7	100
30		100	

Death			
1	4.8	32	59.2
2	8.8	36	63.2
3	12.8	40	67.2
4	16.8	44	71.2
5	20.8	48	75.2
6	24.8	52	79.2
7	28.8	56	83.2
14	60.8	88	100
21	72.8	92	100
30		100	

*Cumulative proportion of risk of the event

eTable 3. Results of the Secondary Analysis for Late vs Early Postoperative Major Bleeding

Early bleeding is defined as BIMS or reintervention within the first 2 postoperative days (1) and late as BIMS or reintervention after the first 2 postoperative days (0).

Characteristic	OR ¹	95% CI ¹	p-value
Female	1.49	1.28, 1.74	<0.001
Age			
45 - 64	—	—	
65 - 79	0.90	0.77, 1.07	0.2
80+	0.87	0.69, 1.09	0.2
BMI			
18.5 - 24.9	—	—	
< 18.5	0.76	0.57, 1.02	0.067
25 - 29.9	0.95	0.80, 1.13	0.6
30+	0.81	0.66, 0.99	0.040
Preoperative hemoglobin			
>= 130	—	—	
120-130	1.13	0.91, 1.41	0.3
110-120	1.13	0.91, 1.41	0.3
100-110	1.13	0.89, 1.43	0.3

Characteristic	OR [†]	95% CI [†]	p-value
90-100	1.07	0.83, 1.38	0.6
80-90	1.41	1.00, 1.99	0.048
70-80	1.39	0.75, 2.58	0.3
<70	1.16	0.45, 3.06	0.8
Tobacco use within 6 months	1.02	0.82, 1.26	0.9
GFR			
>=90	—	—	
60-89	0.89	0.72, 1.11	0.3
30-59	0.88	0.67, 1.17	0.4
15-29	0.80	0.49, 1.31	0.4
<15 or dialysis	0.68	0.41, 1.12	0.13
NSAID/COX-2-inhibitor <24h	1.00	0.75, 1.34	>0.9
NSAID/COX-2-inhibitor 7d to >24h	0.97	0.75, 1.26	0.8
ASA, Ticlopidine or Plavix 1d	1.20	0.84, 1.72	0.3
ASA, Ticlopidine or Plavix 7d to >24h	0.90	0.71, 1.15	0.4
Statin <24h	0.88	0.64, 1.20	0.4
Statin 7d to >24h	1.06	0.80, 1.43	0.7

Characteristic	OR [†]	95% CI [†]	p-value
Prophylactic SC AA <24h	1.04	0.81, 1.32	0.8
Prophylactic SC AA 7d to >24h	0.66	0.49, 0.90	0.007
DOAC or Therapeutic subc. or IV antithrombotic agent <24h	0.43	0.21, 0.89	0.021
DOAC or Therapeutic subc. or IV antithrombotic agent 7d to >24h	1.31	0.87, 2.00	0.2
Surgical procedure			
Major hip or pelvic surgery	—	—	
Low risk surgeries	0.49	0.38, 0.64	<0.001
Thoracic aorta reconstruction	0.69	0.24, 2.03	0.5
Aorta-iliac reconstruction	1.12	0.66, 1.95	0.7
Peripheral vascular reconstruction without aortic cross-clamping	0.68	0.43, 1.10	0.12
Extracranial cerebrovascular surgery	0.51	0.19, 1.40	0.2
EVAR	0.89	0.40, 2.06	0.8
Complex visceral resection	0.46	0.32, 0.65	<0.001
Partial or total colectomy, or stomach surgery	0.48	0.35, 0.64	<0.001
Other intra-abdominal surgery	0.37	0.26, 0.52	<0.001

Characteristic	OR [†]	95% CI [†]	p-value
Major head and neck resection for non-thyroid tumor	1.18	0.68, 2.08	0.6
Lobectomy	0.33	0.13, 0.82	0.016
Other thoracic surgery	0.76	0.35, 1.78	0.5
Visceral resection	0.80	0.50, 1.28	0.3
Cytoreductive surgery	0.22	0.11, 0.45	<0.001
Hysterectomy	1.36	0.71, 2.81	0.4
Radical hysterectomy	0.86	0.31, 2.62	0.8
Radical prostatectomy	1.09	0.50, 2.53	0.8
Transurethral prostatectomy	0.99	0.49, 2.05	>0.9
Internal fixation of femur	1.10	0.75, 1.62	0.6
Knee arthroplasty	1.31	0.98, 1.74	0.067
Above knee amputation	0.64	0.35, 1.18	0.15
Lower leg amputation	0.68	0.36, 1.30	0.2
Craniotomy	0.62	0.33, 1.15	0.12
Major spine surgery	1.02	0.65, 1.59	>0.9
Recruitment year			
2009	—	—	

Characteristic	OR [†]	95% CI [†]	p-value
2007	0.14	0.01, 0.92	0.079
2008	1.03	0.79, 1.36	0.8
2010	1.37	1.05, 1.79	0.021
2011	1.30	0.94, 1.81	0.12
2012	1.02	0.75, 1.38	>0.9
2013	1.18	0.86, 1.62	0.3
2014	1.28	0.79, 2.09	0.3
2015	0.27	0.10, 0.71	0.008
2016	1.53	0.06, 40.7	0.8
Study center			
2	—	—	
1	0.69	0.36, 1.37	0.3
3	0.25	0.15, 0.43	<0.001
4	1.67	0.90, 3.29	0.12
5	0.27	0.18, 0.42	<0.001
6	1.49	0.88, 2.60	0.15
10	0.39	0.28, 0.54	<0.001

Characteristic	OR [†]	95% CI [†]	p-value
11	0.67	0.37, 1.25	0.2
21	0.19	0.12, 0.32	<0.001
22	0.21	0.10, 0.44	<0.001
31	0.84	0.44, 1.65	0.6
35	0.18	0.07, 0.45	<0.001
40	0.31	0.21, 0.45	<0.001
41	0.35	0.24, 0.51	<0.001
42	0.22	0.14, 0.33	<0.001
43	0.14	0.07, 0.27	<0.001
45	0.52	0.21, 1.37	0.2
46	0.50	0.29, 0.90	0.020
49	0.20	0.11, 0.38	<0.001
51	0.29	0.19, 0.44	<0.001
52	0.38	0.25, 0.58	<0.001
60	0.29	0.19, 0.47	<0.001
80	0.23	0.14, 0.38	<0.001
81	1.73	0.96, 3.30	0.079

Characteristic	OR [†]	95% CI [†]	p-value
82	2.69	1.42, 5.31	0.003
90	0.54	0.19, 1.64	0.3
92	0.61	0.37, 1.02	0.055

OR, odds ratio; CI, Confidence Interval; GFR, glomerular filtration rate; NSAID, nonsteroidal anti-inflammatory drug; COX-2, cyclooxygenase-2; BMI, body mass index; ASA, acetylsalicylic acid, SC AA, subcutaneous antithrombotic agent, DOAC, direct oral anticoagulant; EVAR, endovascular aneurysm repair

Study center 36 (n = 1) and pneumonectomy (n = 3) were excluded from the table due to low event counts. The OR, 95% CI and p-value for them is available from the corresponding author upon reasonable request.

BIMS (Bleeding Independently associated with Mortality after noncardiac Surgery) is defined as a composite of postoperative transfusion, postoperative hemoglobin < 70 and bleeding associated with reintervention.