SWEDEHEART

Karolinska Institutet

Temporal trends in bleeding events in acute myocardial infarction –insights from the SWEDEHEART registry

Moa Simonsson, Lars Wallentin, Joakim Alfredsson, David Erlinge, Karin Hellstrom Angerud, Robin Hofmann, Thomas Kellerth, Lars Lindhagen, Annica Ravn-Fischer, Karolina Szummer, Peter Ueda, Troels Yndigegn, Tomas Jernberg

UCR

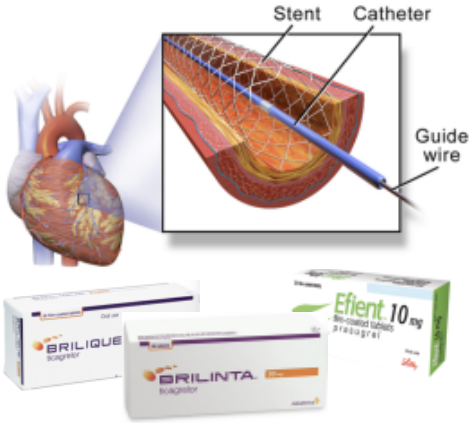
Declaration of interest

- Others (Speakers fee from Astra Zeneca, Bayer and Pfizer.)

Background

- Invasive strategies, DAPT and more efficient antithrombotic treatment has improved outcomes at the cost of increased risk of bleeding.

- Bleeding complications are associated with increased mortalilty and adverse outcomes (MI and stroke).



Szummer et al. European Heart Journal (2018) 39, 3766–3776, Szummer et al. European Heart Journal (2017) 38, 305630.
Rao SV et al. Am J Cardiol. 2005 Nov 1;96(9):1200-6. Eikelboom et al *Circulation*.2006;114:774-782

Aims

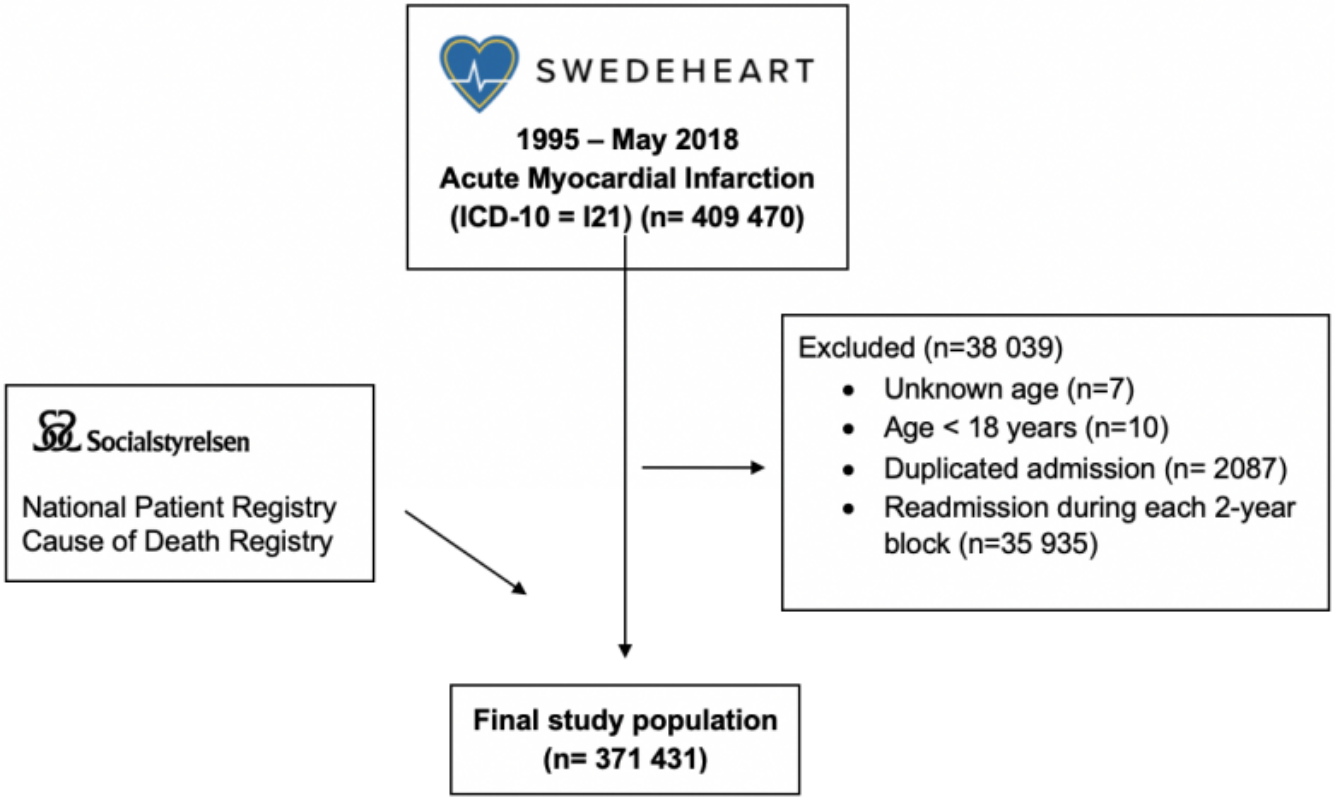
- To describe the time trends in short- and long-term bleeding events following acute myocardial infarction over the last two decades.

- To describe the bleeding trends parallel to

a) the development of antithrombotic and invasive treatment

b) ischemic outcomes.

Methods: Study population



Bleeding and ischemic outcomes

- In-hospital bleeding (non-CABG related): Fatal, intracranial or requiring blood transfusion or surgery.
- Out-of-hospital bleeding at one year: Rehospitalization with cerebral, gastrointestinal, urogenital, ear, eye or airway bleeding.

- In-hospital MI (reinfarction), CV death
- Out-of-hospital MI, stroke, CV death at one year

Baseline Characteristics 1995 -2018

- median age 73 years
- about one third female
- one quarter diabetes
- one third STEMI
- one third reduced renal function

	N=371431
Age	73 (63-81)
Female	35.8%
Previous MI	28.2%
Previous PCI	11.6%
Previous stroke	13.1%
Diabetes	24.7%
Previous bleeding	5.8%
Previous LEAD	6.2%
STEMI	33.9%
eGFR* ml/min	73 (54-89)
eGFR < 60*ml/min	32.2%

Baseline Characteristics

	1995-96 N=13979	1997-98 N=23476	1999-00 N=30021	2001-02 N=34595	2003-04 N=35393	2005-06 N=35236	2007-08 N=36640	2009-10 N=34889	2011-12 N=36030	2013-14 N=34448	2015-16 N=34236	2017-18 N=22488
Age	72 (63-79)	73 (63-79)	73 (63-80)	74 (64-81)	74 (63-81)	74 (63-82)	73 (62-81)	72 (63-81)	72 (63-81)	72 (63-81)	72 (63-81)	72 (63-80)
Female	34.5%	35.2%	36.2%	37.4%	37.2%	36.8%	36.8%	35.5%	35.6%	34.9%	34.3%	33%
Previous MI	29.4%	29.6%	28.6%	29.6%	29.2%	28.3%	27.7%	27.9%	27.7%	26.8%	27.4%	26.9%
Previous PCI	2.5%	3.5%	4.3%	5.6%	7.1%	9.4%	11.9%	14.6%	16.1%	17.7%	19.8%	20.7%
Previous stroke	10%	11.1%	11.8%	12.8%	12.7%	15.1%	14.5%	14.0%	14.1%	13.3%	12.9%	12.2%
Diabetes	21.7%	22.1%	22.9%	24.0%	24.0%	24.5%	24.8%	24.8%	25.4%	26.3%	26.9%	27.2%
Previous bleeding	3.6%	4.3%	4.5%	5.3%	5.6%	6.1%	6.1%	6.3%	6.7%	6.6%	6.7%	6.5%
Previous LEAD	5.6%	5.7%	5.9%	6.4%	6.4%	6.3%	6.1%	6.1%	6.4%	6.7%	6.3%	6.2%
STEMI	39.8%	40.3%	38.2%	33.7%	32.4%	32.0%	31.7%	33.2%	32.0%	32.5%	32.8%	34.7%
eGFR* ml/min	-	-	-	65 (48-80)	67 (49-81)	71 (52-87)	73 (53-89)	74 (54-89)	75 (55-90)	75 (55-90)	76 (56-90)	76 (57-90)
eGFR < 60* ml/min	-	-	-	43,5%	39,3%	35,1%	32,5%	31,6%	30,2%	30,4%	29,3%	28%

Baseline Characteristics

	1995-96 N=13979	1997-98 N=23476	1999-00 N=30021	2001-02 N=34595	2003-04 N=35393	2005-06 N=35236	2007-08 N=36640	2009-10 N=34889	2011-12 N=36030	2013-14 N=34448	2015-16 N=34236	2017-18 N=22488
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eGFR* ml/min	-	-	-	65 (48-80)	67 (49-81)	71 (52-87)	73 (53-89)	74 (54-89)	75 (55-90)	75 (55-90)	76 (56-90)	76 (57-90)
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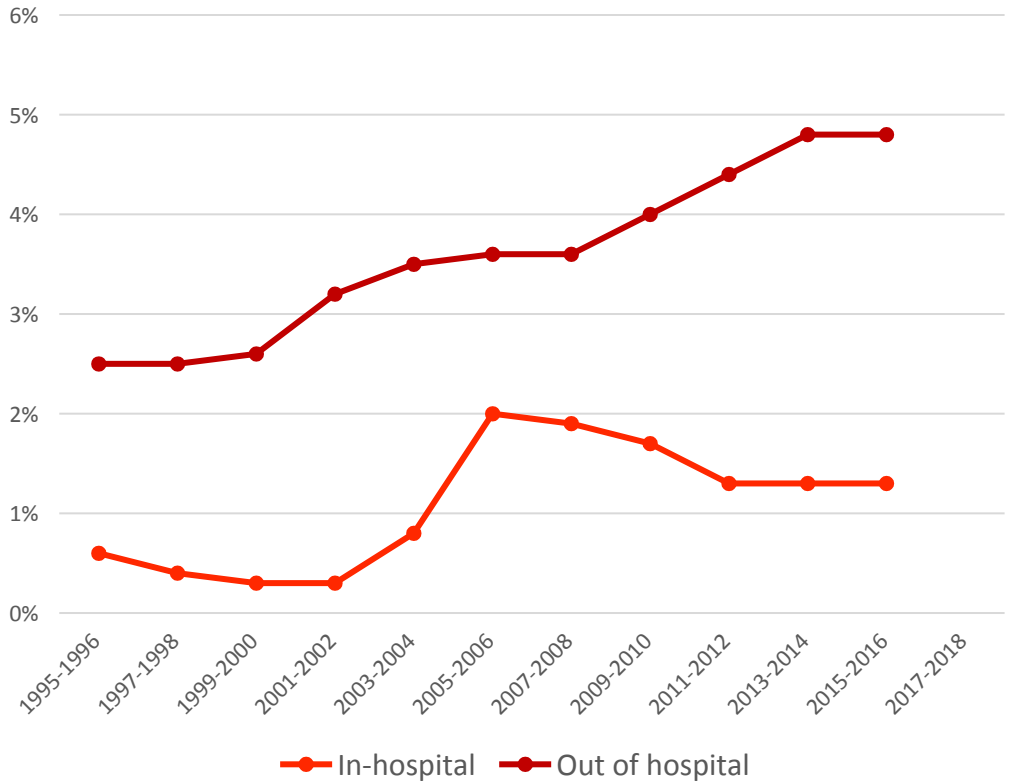
eGFR < 60* ml/min	-	-	-	43,5%	39,3%	35,1%	32,5%	31,6%	30,2%	30,4%	29,3%	28%

Bleeding trends

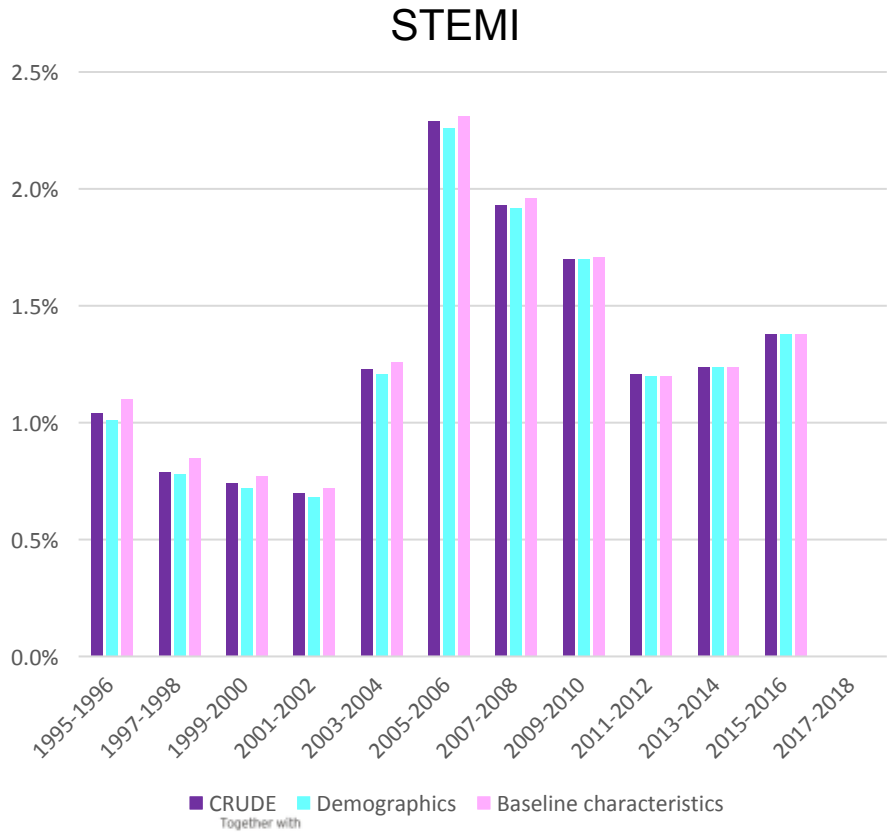
- In-hospital bleeding increased from ~ 0.5% to peak at 2% in 2005-06 and then declined to1.3%.
- Out-of-hospital bleeding increased from 2.5% to 4.8%.

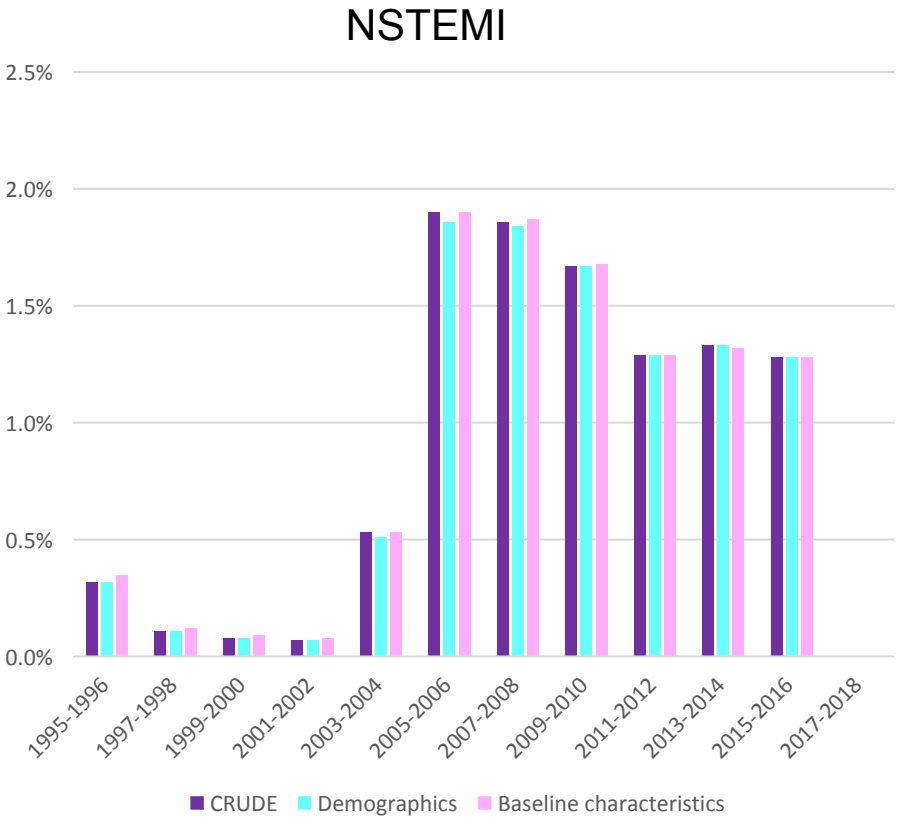


Adjusted models

- Crude
- Demographics: (Age + Gender)
- Demographics + Baseline Characteristics: (Diabetes, Hypertension, Prev MI, Prev PCI, Prev CABG, Prev CHF, Prev LEAD, Prev ischemic stroke, Prev any stroke, Prev COPD, Prev Cancer, Prev bleeding, STEMI, Pulmonary rales on adm, AF on adm, Antiplatelet therapy on adm, Beta-blockers on adm, ACEI/ARB on adm, Statin on adm)

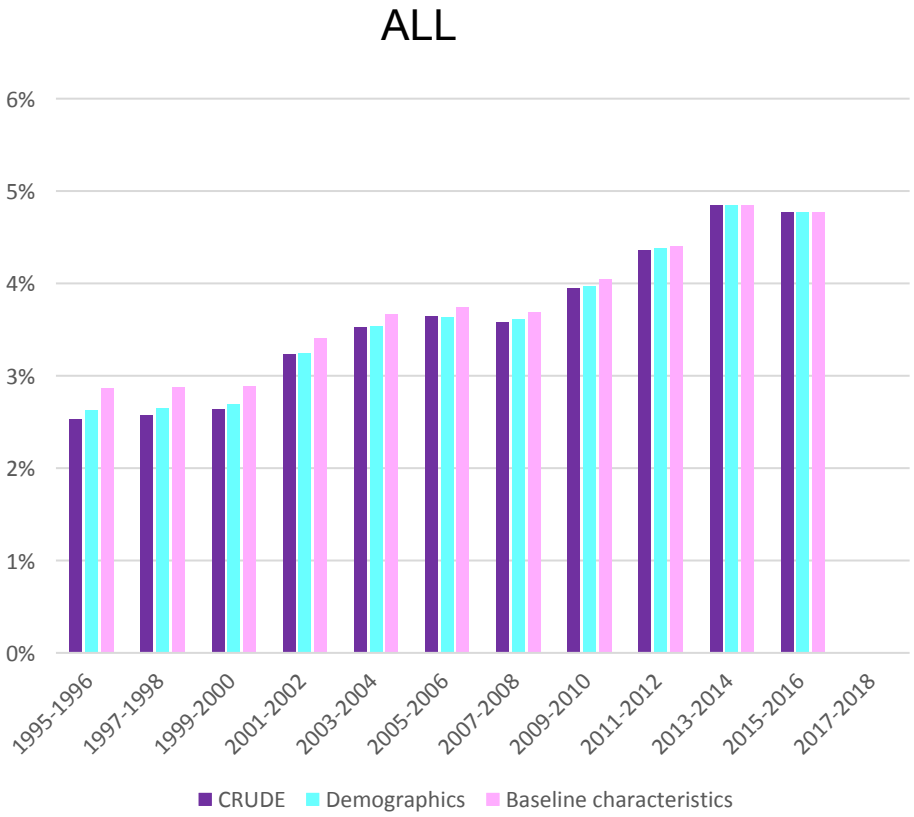
In-hospital bleeding – crude and adjusted



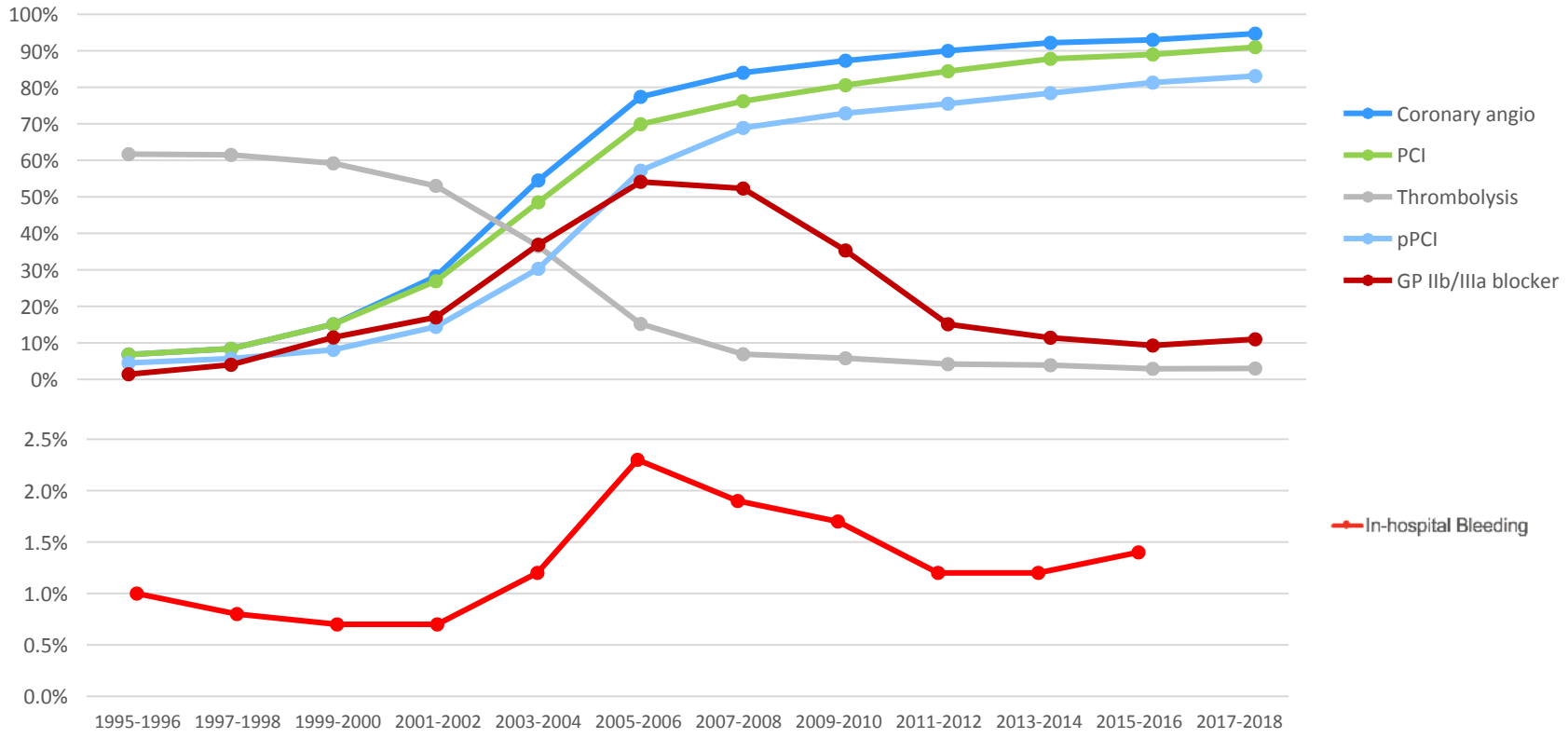


Out-of-hospital bleeding – crude and adjusted

- Adjustment had very small effects on the risk of bleeding.
- Only crude risks reported.



In-hospital bleeding and treatment STEMI



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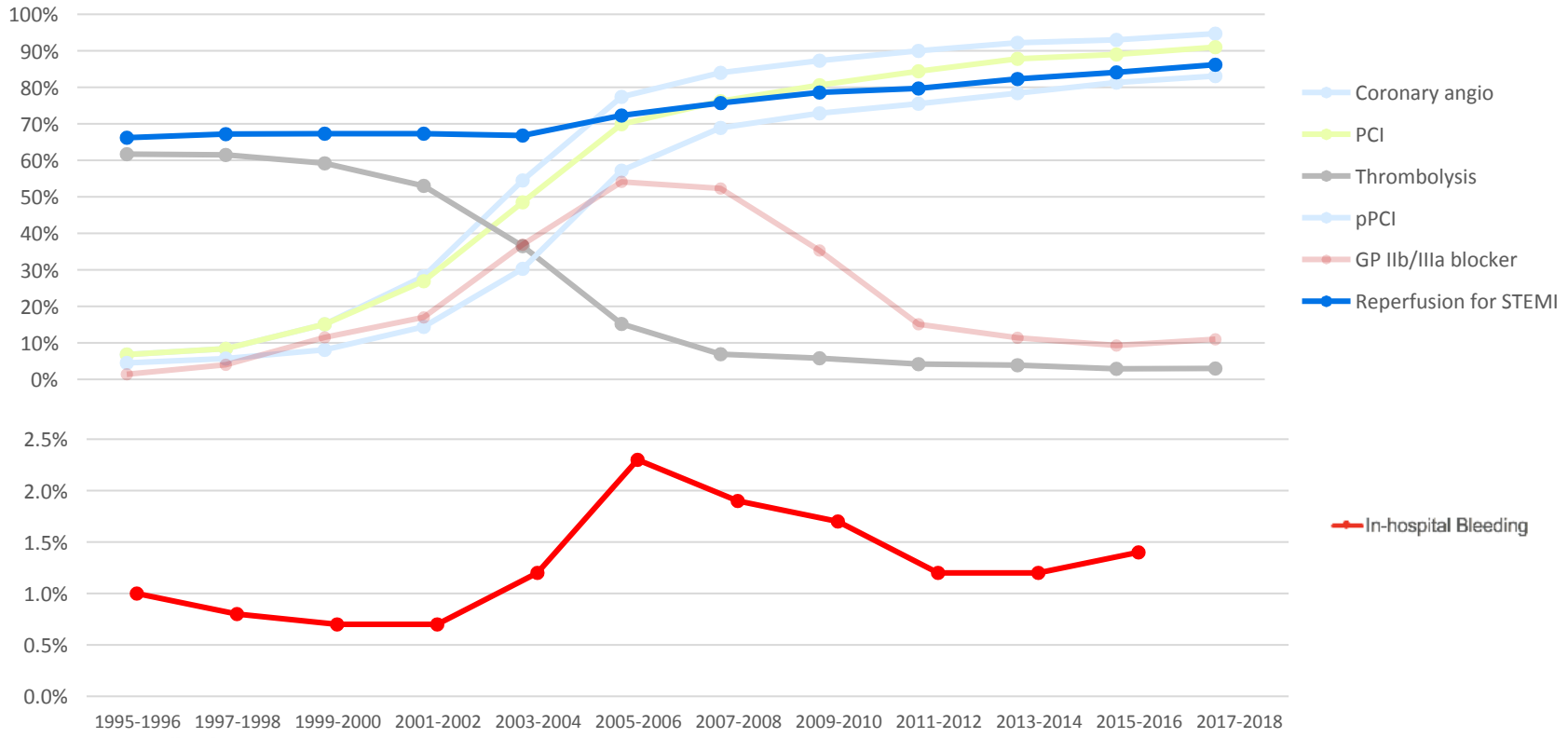

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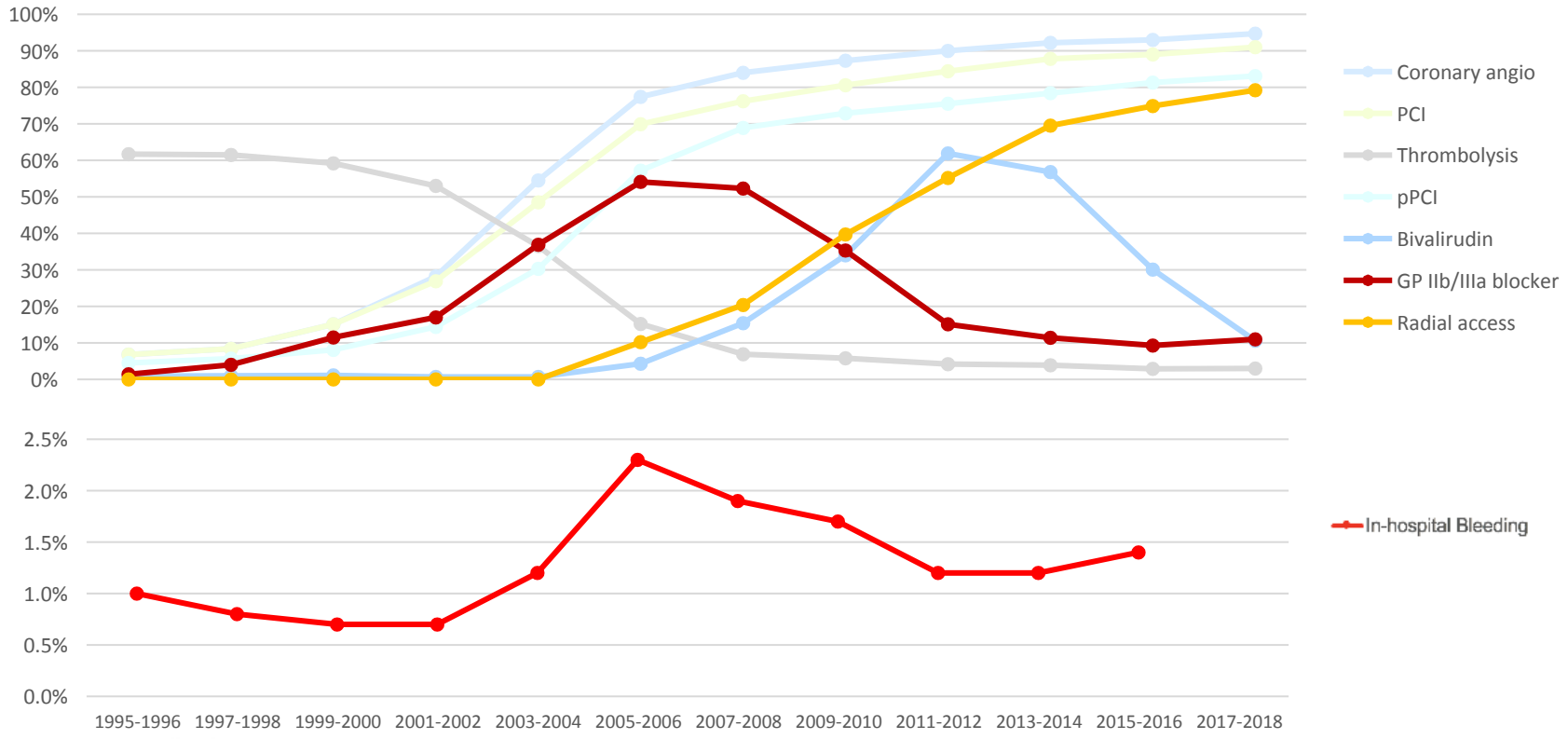
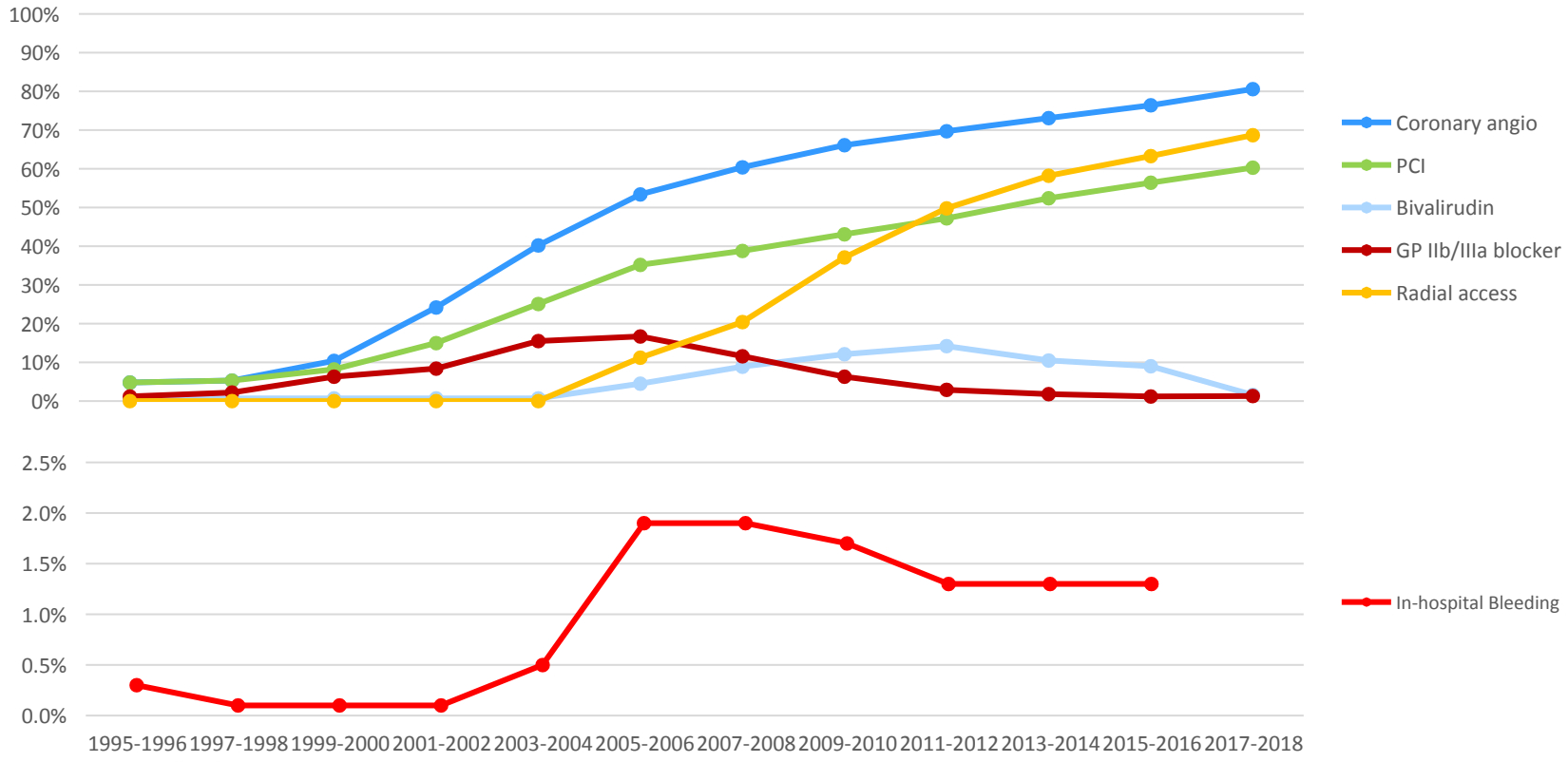
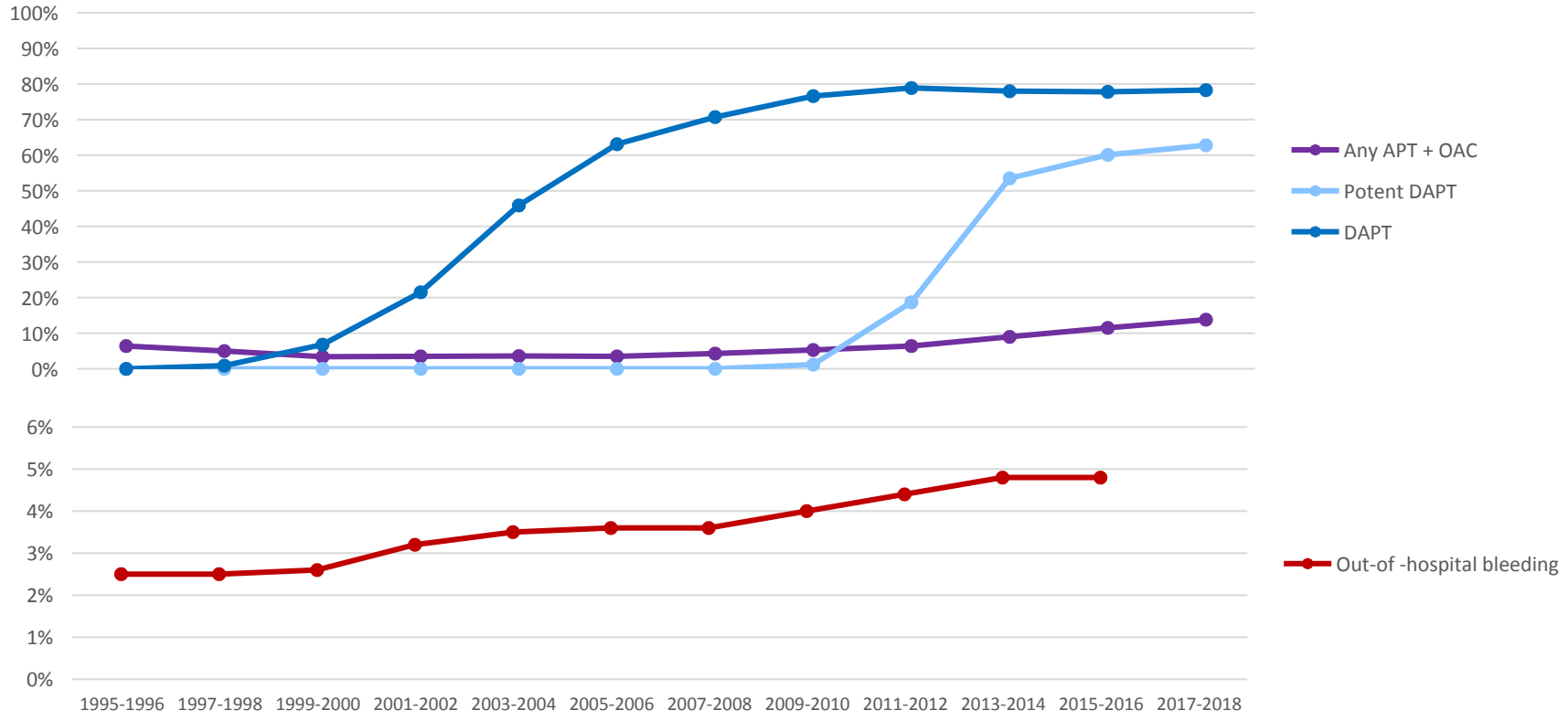


In-hospital bleeding and treatment NSTEMI

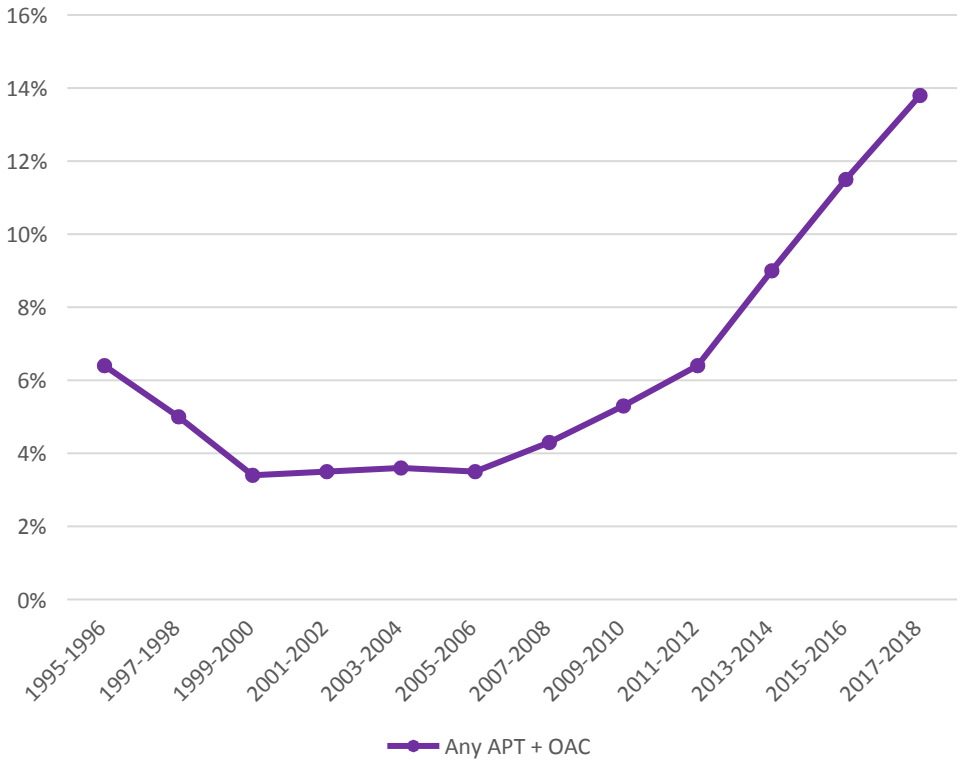


Out-of-hospital bleeding and treatment ALL



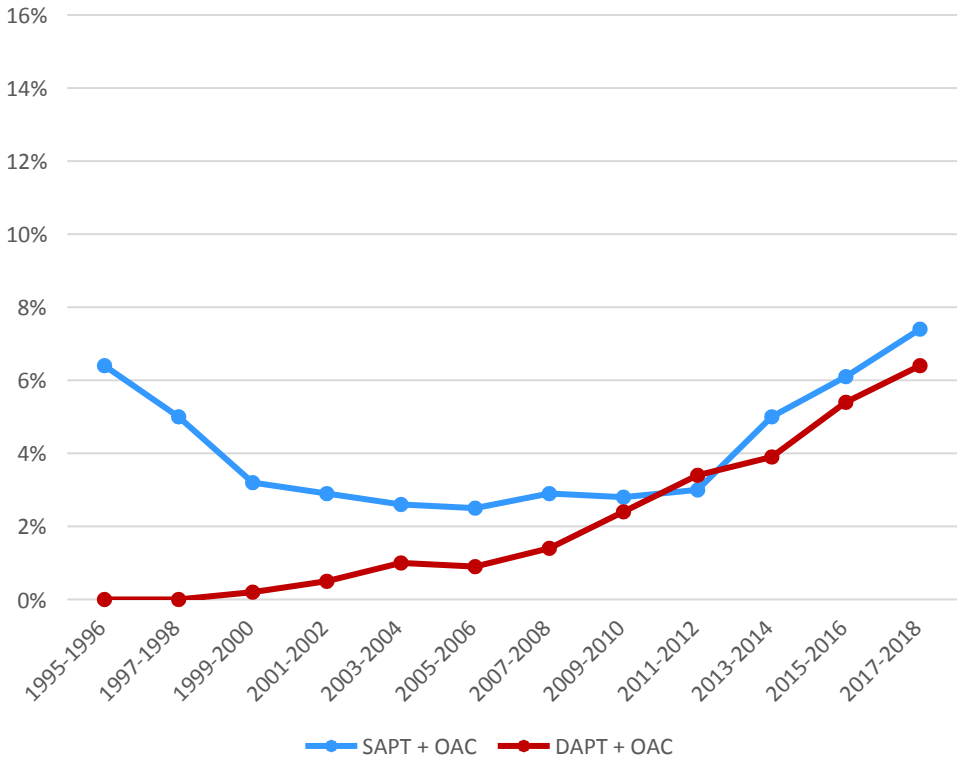
Combination Therapy

- Combination therapy (Any APT + OAC) doubled from 7% to 14%



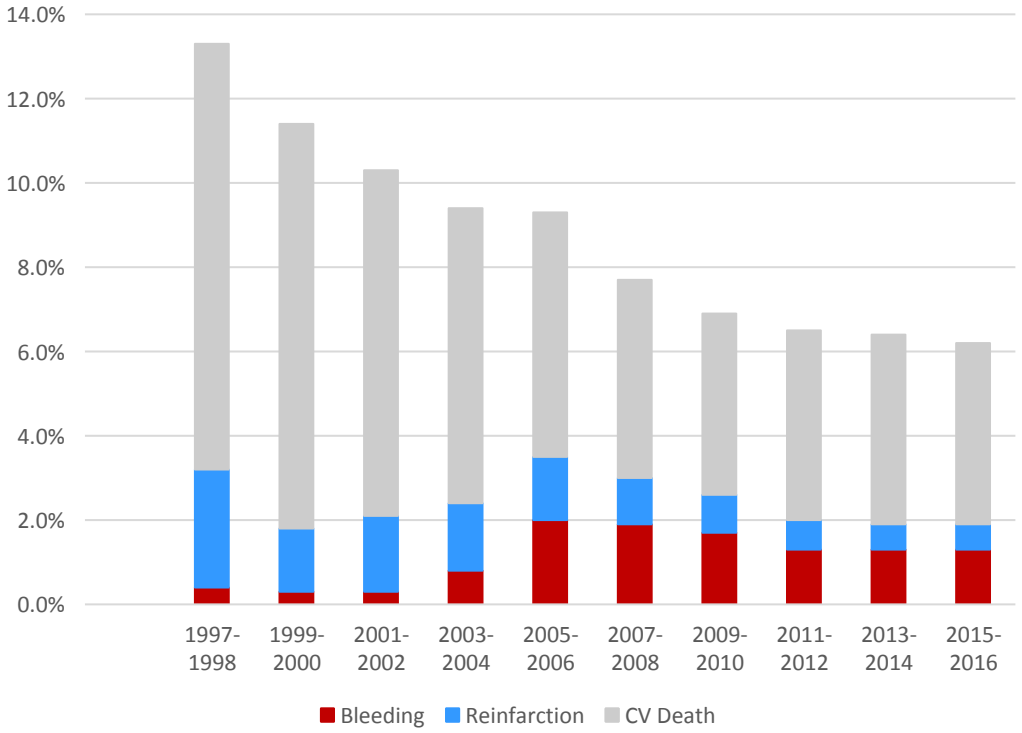
Combination Therapy

- Triple therapy (DAPT +OAC) increased from 0% to 5%
- Double therapy almost equally common as triple in the last years



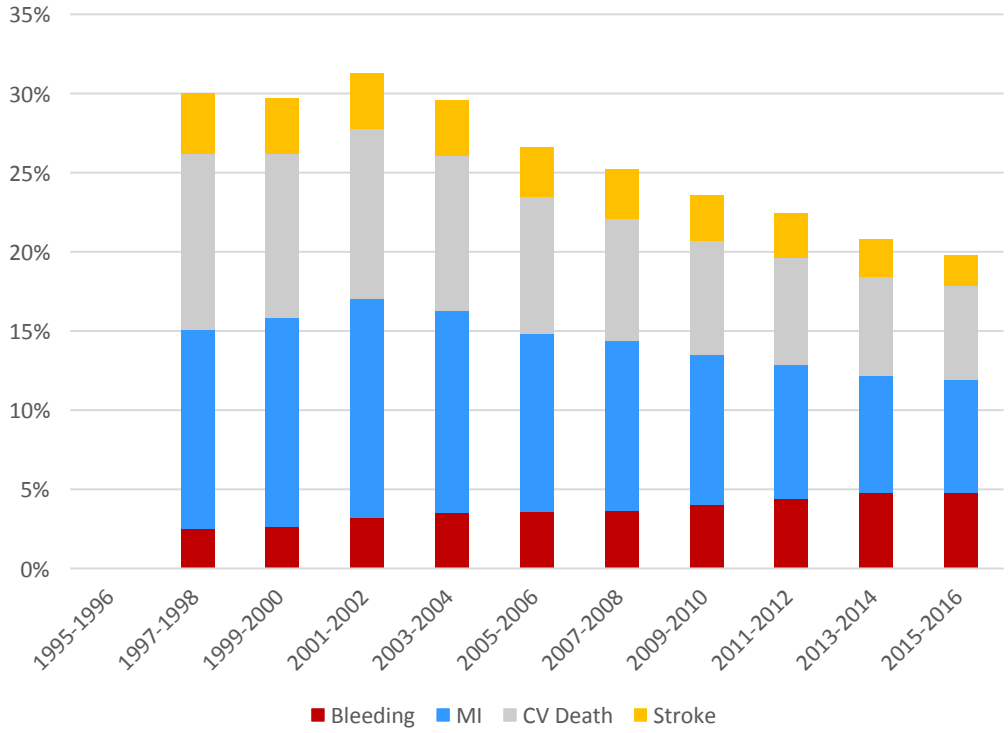
In-hospital bleeding and ischemic events added

- In-hospital bleeding doubled (absolute increase ~1%).
- Ischemic outcomes more than halved (absolute decrease ~ 8%).



Out-of-hospital bleeding and ischemic events added

- Out-of-hospital bleeding doubled (absolute increase 2.3%).
- Ischemic outcomes halved (absolute decrease > 10%).



Limitations

- Observational design
  – unmeasured residual confounders
  – caution regarding causality or effect.

- No standardized bleeding definitions. Outcomes not adjudicated.

- The registration patterns may have changed over time.

Conclusions

- Over a 20-year period the introduction of invasive and potent antithrombotic treatment has been associated with an increase in both in-hospital and out-of-hospital bleeding.
- Simultaneously there has been a substantial greater reduction of ischemic events including improved survival.
- Future optimal treatments: Reduction of bleeding risk without compromise in ischemic protection (personalized antithrombotic treatment, new secondary prevention drugs)?

Acknowledgements

- Thanks to all at Uppsala Clinical Research centre (UCR) for continuous maintaining and updating the registry.

- Thanks to to all collaborators and hospitals of the SWEDEHEART registry: Alingsås, Arvika Avesta, Bollnäs, Borås, Danderyd, Eksjö, Enköping, Eskilstuna, Fagersta, Falun, Gällivare, Gävle, Halmstad, Helsingborg, Hudiksvall, Hässleholm, Jönköping, Kalix, Kalmar, Karlshamn, Karlskoga, Karlskrona, Karlstad, Karolinska, Katrineholm, Kiruna, Kristianstad, Kungälv, Köping, Landskrona, Lidköping, Lindesberg, Linköping, Ljungby, Lund, Lycksele, Malmö, Mora, Motala, Mölndal, Norrköping, Norrtälje, Nyköping, Oskarshamn, Piteå , Sahlgrenska, Skellefteå, Skövde, Sollefteå. St Göran, Sunderbyn, Sundsvall, Södersjukhuset, Södertälje, Torsby, Trelleborg, Trollhättan, Umeå, Uppsala, Varberg, Visby, Värnamo, Västervik, Västerås, Växjö, Ystad, Ängelholm, Örebro, Örnsköldsvik, Östersund, Östra

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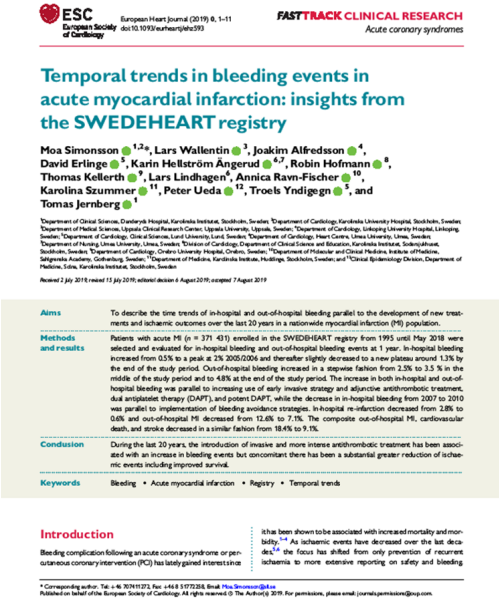
10.1093/eurheartj/ehz593



ESC European Society of Cardiology
European Heart Journal (2019) 0, 1–11
doi:10.1093/eurheartj/ehz593
FASTTRACK CLINICAL RESEARCH
Acute coronary syndromes

Temporal trends in bleeding events in acute myocardial infarction: insights from the SWEDEHEART registry

Moa Simonsson[1,2]*, Lars Wallentin[3], Joakim Alfredsson[4], David Erlinge[5], Karin Hellström Ängerud[6,7], Robin Hofmann[8], Thomas Kellerth[9], Lars Lindhagen[9], Annica Ravn-Fischer[10], Karolina Szummer[11], Peter Ueda[12], Troels Yndigegn[5], and Tomas Jernberg[1]

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Received 2 July 2018; revised 15 July 2019; editorial decision 6 August 2019; accepted 7 August 2019

Aims To describe the time trends of in-hospital and out-of-hospital bleeding parallel to the development of new treatments and ischaemic outcomes over the last 20 years in a nationwide myocardial infarction (MI) population.

Methods and results Patients with acute MI (n = 371 431) enrolled in the SWEDEHEART registry from 1995 until May 2018 were selected and evaluated for in-hospital bleeding and out-of-hospital bleeding events at 1 year. In-hospital bleeding increased from 0.5% to a peak at 2% 2005/2006 and thereafter slightly decreased to a new plateau around 1.3% by the end of the study period. Out-of-hospital bleeding increased in a stepwise fashion from 2.5% to 3.5 % in the middle of the study period and to 4.8% at the end of the study period. The increase in both in-hospital and out-of-hospital bleeding was parallel to increasing use of early invasive strategy and adjunctive antithrombotic treatment, dual antiplatelet therapy (DAPT), and potent DAPT, while the decrease in in-hospital bleeding from 2007 to 2010 was parallel to implementation of bleeding avoidance strategies. In-hospital re-infarction decreased from 2.8% to 0.6% and out-of-hospital MI decreased from 12.6% to 7.1%. The composite out-of-hospital MI, cardiovascular death, and stroke decreased in a similar fashion from 18.4% to 9.1%.

Conclusion During the last 20 years, the introduction of invasive and more intense antithrombotic treatment has been associated with an increase in bleeding events but concomitant there has been a substantial greater reduction of ischaemic events including improved survival.

Keywords Bleeding • Acute myocardial infarction • Registry • Temporal trends

Introduction

Bleeding complication following an acute coronary syndrome or percutaneous coronary intervention (PCI) has lately gained interest since it has been shown to be associated with increased mortality and morbidity.[1–3] As ischaemic events have decreased over the last decades,[4,5] the focus has shifted from only prevention of recurrent ischaemia to more extensive reporting on safety and bleeding

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This accompanying article is online

Backupslides

Comparison of bleeding incidence

- bleeding definition used
- population studied
- time period studied and duration of follow up
- antithrombotic treatment used
- type of follow-up and completeness of reporting of bleeding events

Baseline Characteristics 1998-2018

- NSTEMI patients older (74 vs 70 years), more often female and overall higher burden of comorbidity
- More high bleeding risk criteria

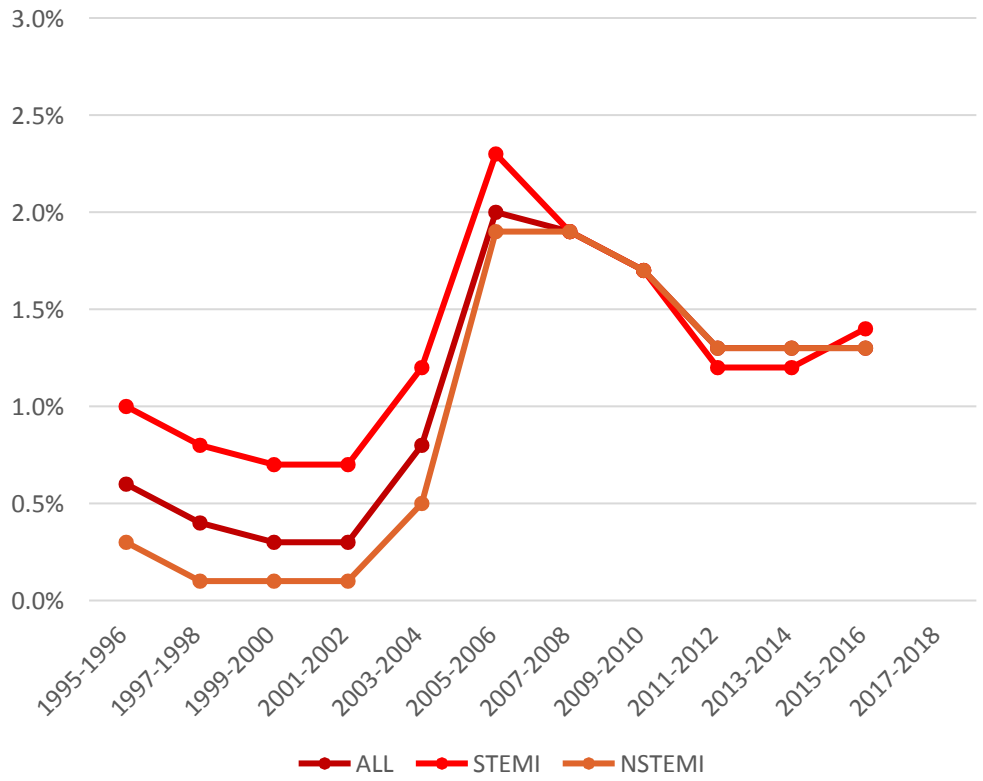
	ALL 1995-2018 N=371431	STEMI 1995-2018 N=125868	NSTEMI 1995-2018 N=245563
Age	73 (63-81)	70 (60-79)	74 (65-82)
Female	35.8%	33.2%	37.1%
Previous MI	28.2%	17.9%	33.5%
Previous PCI	11.6%	7.6%	13.6%
Previous stroke	13.1%	9.6%	15%
Diabetes	24.7%	20.1%	27.1%
Previous bleeding	5.8%	4.5%	6.5%
Previous LEAD	6.2%	3.8%	7.4%
STEMI	33.9%	100%	0%
eGFR* ml/min	73 (54-89)	78 (59-92)	71 (51-87)
eGFR < 60*ml/min	32.2%	25.5%	35.4

Antithrombotic treatment on admission

	N=13979	N=23476	N=30021	N=34595	N=35393	N=35236	N=36640	N=34889	N=36030	N=34448	N=34236	N=22488
	1995-96	1997-98	1999-00	2001-02	2003-04	2005-06	2007-08	2009-10	2011-12	2013-14	2015-16	2017-18
Mono APT on admission	33.6%	38.0%	40.2%	42.6%	40.6%	39.5%	37.9%	37.1%	36.1%	34.9%	32.6%	29.9%
DAPT on admission	0.0%	0.1%	0.3%	1.2%	3.3%	4.5%	4.9%	4.9%	4.8%	4.3%	3.8%	3.5%
OAC on admission	4.5%	4.5%	4.6%	5.3%	5.2%	5.3%	5.6%	5.4%	5.6%	6.9%	8.7%	9.8%

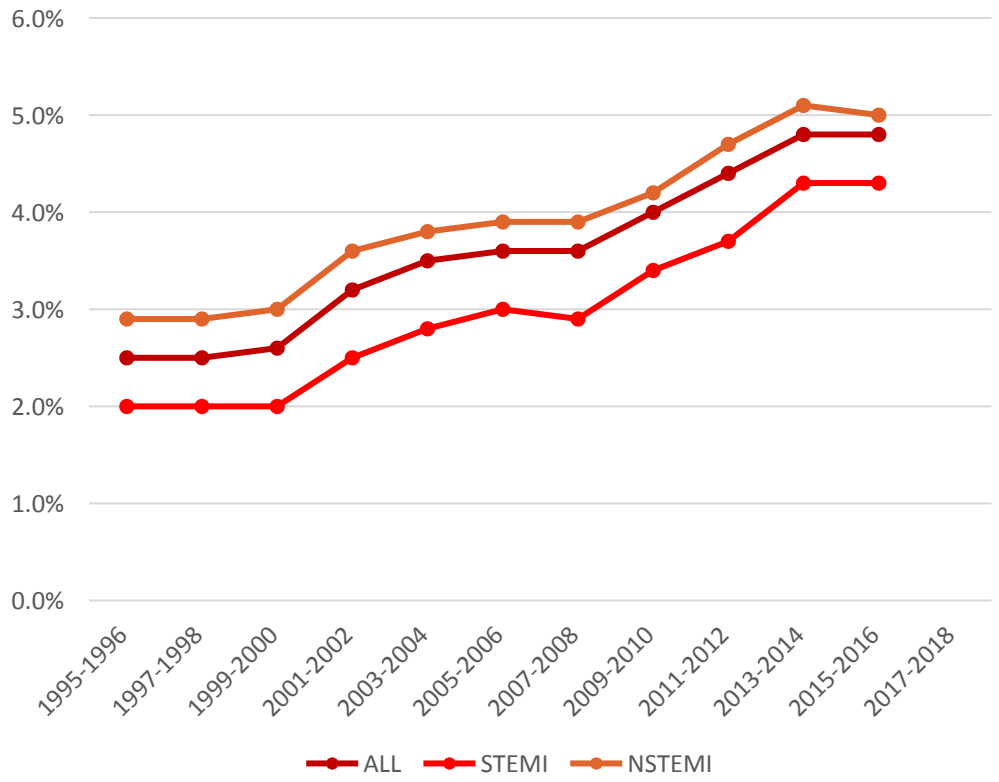
Bleeding trends in-hospital per subgroup

- In-hospital bleeding more common in STEMI patients in the first decade
- In-hospital bleeding equal in STEMI and NSTEMI patients in the last decade

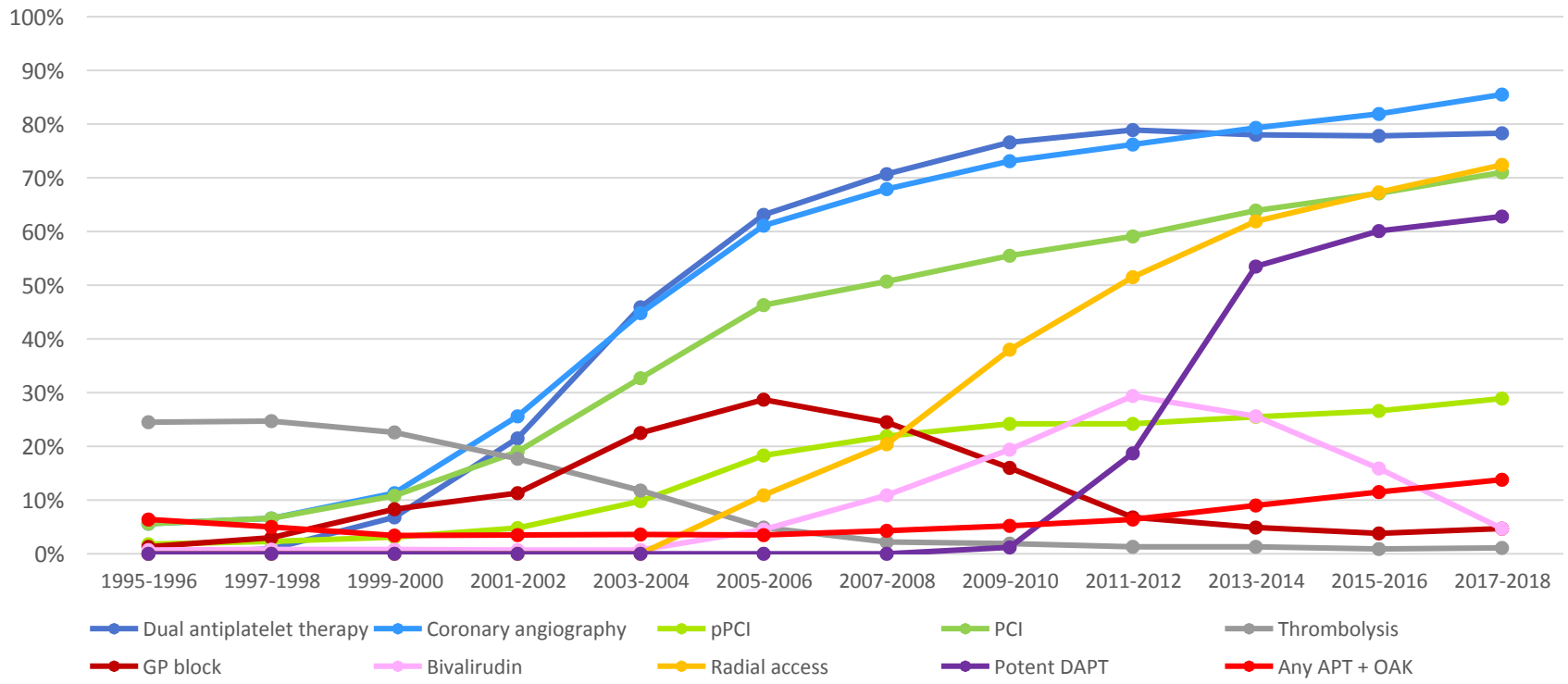


Bleeding trends out of-hospital per subgroup

- Out-of-hospital bleeding was more common in NSTEMI patients during the whole study period

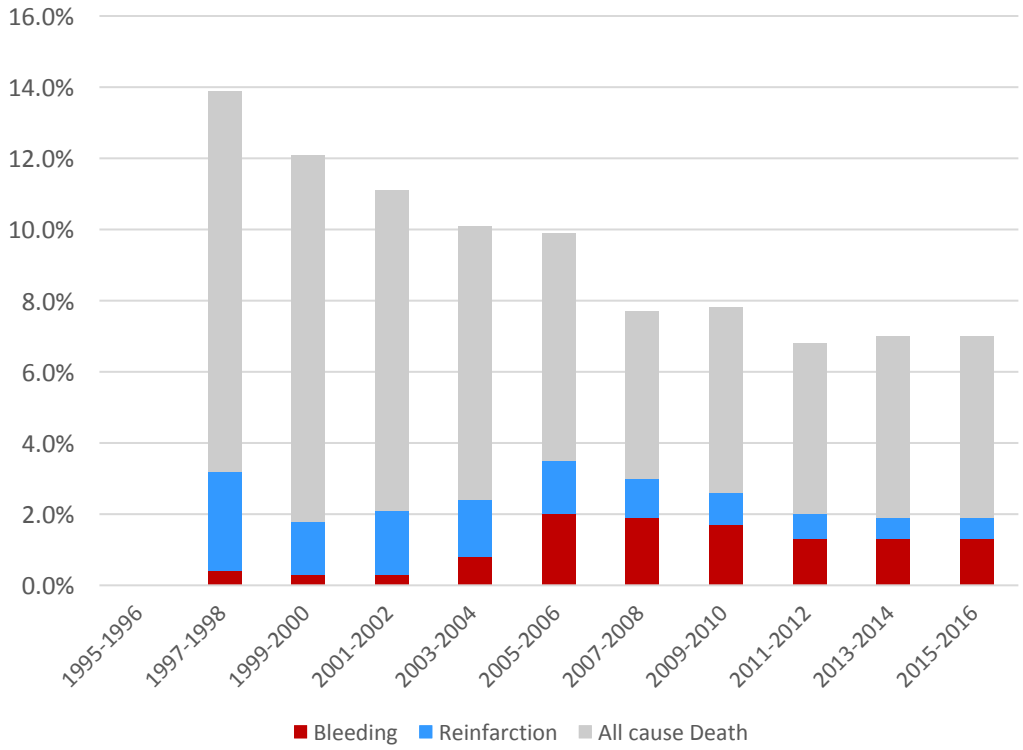


Treatment ALL



In-hospital bleeding and ischemic events added (all-cause death)

- All cause death 10,7% to 5,1%
- (CV death 10,1% to 4,3%)



Out-of-hospital bleeding and ischemic events added (all-cause death)

- All cause death 13,7% to 9,5% and no change 2013/14 to 2015/16
- (CV death 11,1% to 6%)