APPENDIX A. SEARCH STRATEGIES

PubMed
11/30/2015-5/16/22; English Language
"Dual Anti-Platelet Therapy"[Mesh] OR "dual antiplatelet*"[tiab] OR "dual anti-platelet*"[tiab] OR DAPT[tiab] OR "double antiplatelet*"[tiab] OR "double anti-platelet*"[tiab] OR (("Platelet Aggregation Inhibitors"[Mesh] OR "Factor Xa Inhibitors"[Mesh]) AND "Drug Therapy, Combination"[Mesh:NoExp])
AND
"General Surgery"[Mesh:NoExp] OR "Surgical procedures, operative"[mh] OR surgery[tiab] OR surgeries[tiab] OR surgical[tiab] OR operation[tiab] OR operations[tiab] OR amputat*[tiab] OR amputation[Mesh]
Results: 2597

Cochrane
11/30/2015-5/16/22; English Language
[mh "Dual Anti-Platelet Therapy"] OR (([mh "Platelet Aggregation Inhibitors"] OR [mh "Factor Xa Inhibitors"]) AND [mh ^"Drug Therapy, Combination"]) OR ("dual antiplatelet*" OR "dual anti-platelet*" OR DAPT OR "double antiplatelet*" OR "double anti-platelet*"):ti,ab
AND
[mh ^"General Surgery"] OR [mh "operative surgical procedures "] OR [mh amputation] OR (surgery OR surgeries OR surgical OR operation OR operations OR amputation*):ti,ab
Results: 278

Embase:
1/1/2016-5/17/22; English
'dual antiplatelet therapy'/exp OR ("dual antiplatelet*" OR "dual anti-platelet*" OR DAPT OR "double antiplatelet*" OR "double anti-platelet*"):ti,ab OR (('antithrombocytic agent'/exp OR 'blood clotting factor 10a inhibitor'/exp) AND 'combination drug therapy'/de)
AND
"General Surgery"/de OR 'amputation'/exp OR "operative surgical procedures"/de OR (surgery OR surgeries OR surgical OR operation OR operations OR amputat*):ti,ab
Results: 2215

APPENDIX B. EXCLUDED STUDIES

No Relevant Outcome Data Presented for the Patients that were on Preoperative DAPT Comparing at Least 2 Perioperative Strategies, *N* = 38

1. Altun, G., et al., Emergency coronary bypass surgery in patients under the influence of dualantiplatelet therapy: effects of tranexamic acid and desmopressin acetate. Turk J Med Sci, 2017. 47(6).
2. Amour, J., et al., Prospective observational study of the effect of dual antiplatelet therapy with tranexamic acid treatment on platelet function and bleeding after cardiac surgery. Br J Anaesth, 2016. 117(6): p. 749-757.
3. Awada, H., et al., Pocket related complications following cardiac electronic device implantation in patients receiving anticoagulation and/or dual antiplatelet therapy: prospective evaluation of different preventive strategies. J Interv Card Electrophysiol, 2019. 54(3): p. 247-255.
4. Benkö, T., et al., One-year Allograft and Patient Survival in Renal Transplant Recipients Receiving Antiplatelet Therapy at the Time of Transplantation. Int J Organ Transplant Med, 2018. 9(1): p. 10-19.
5. Charif, F., et al., Dual antiplatelet therapy up to the time of non-elective coronary artery bypass grafting with prophylactic platelet transfusion: is it safe? J Cardiothorac Surg, 2019. 14(1): p. 202.
6. Chemtob, R.A., et al., Outcome After Surgery for Acute Aortic Dissection: Influence of Preoperative Antiplatelet Therapy on Prognosis. J Cardiothorac Vasc Anesth, 2017. 31(2): p. 569-574.
7. Christersson, C., et al., Comparison of warfarin versus antiplatelet therapy after surgical bioprosthetic aortic valve replacement. Heart, 2020. 106(11): p. 838-844.
8. Cui, R.B.J., K.S. Ng, and C.J. Young, Complications Arising From Perioperative Anticoagulant/Antiplatelet Therapy in Major Colorectal and Abdominal Wall Surgery. Dis Colon Rectum, 2018. 61(11): p. 1306-1315.
9. Dai, Y., et al., Dual antiplatelet therapy increases pocket hematoma complications in Chinese patients with pacemaker implantation. Journal of geriatric cardiology, 2015. 12(4): p. 383-387.
10. Deharo, J.C., et al., Perioperative management of antithrombotic treatment during implantation or revision of cardiac implantable electronic devices: the European Snapshot Survey on Procedural Routines for Electronic Device Implantation (ESS-PREDI). Europace, 2016. 18(5): p. 778-84.
11. Egholm, G., et al., Dual anti-platelet therapy after coronary drug-eluting stent implantation and surgery-associated major adverse events. Thromb Haemost, 2016. 116(1): p. 172-80.
12. Guo, J., et al., Effects of Sarpogrelate Combined with Aspirin in Patients Undergoing Carotid Endarterectomy in China: A Single-Center Retrospective Study. Ann Vasc Surg, 2016. 35: p. 183-8.
13. Hansson, E.C., et al., Preoperative dual antiplatelet therapy increases bleeding and transfusions but not mortality in acute aortic dissection type A repair. Eur J Cardiothorac Surg, 2019. 56(1): p. 182-188.
14. Howell, S.J., et al., Prospective observational cohort study of the association between antiplatelet therapy, bleeding and thrombosis in patients with coronary stents undergoing noncardiac surgery. Br J Anaesth, 2019. 122(2): p. 170-179.

15. Hudson, J.S., et al., Hemorrhage associated with ventriculoperitoneal shunt placement in aneurysmal subarachnoid hemorrhage patients on a regimen of dual antiplatelet therapy: a retrospective analysis. J Neurosurg, 2018. 129(4): p. 916-921.
16. Hussain, A., et al., Is the use of dual antiplatelet therapy following urgent and emergency coronary artery bypass surgery associated with increased risk of cardiac tamponade? J Clin Transl Res, 2021. 7(2): p. 229-233.
17. Jones, D.W., et al., Dual antiplatelet therapy reduces stroke but increases bleeding at the time of carotid endarterectomy. J Vasc Surg, 2016. 63(5): p. 1262-1270.e3.
18. Kawamoto, Y., et al., Effect of antithrombic therapy on bleeding complications in patients receiving emergency cholecystectomy for acute cholecystitis. Journal of Hepato-Biliary-Pancreatic Sciences, 2018. 25(11): p. 518-526.
19. Kyuchukov, D., I. Zheleva-Kyuchukova, and G. Nachev, Antithrombotic regimens in patients after coronary artery bypass grafting and coronary endarterectomy. Pharmacia, 2020. 67(3): p. 115-120.
20. Lin, S.Y., et al., The Safety of Continuing Antiplatelet Medication Among Elderly Patients Undergoing Urgent Hip Fracture Surgery. Orthopedics, 2019. 42(5): p. 268-274.
21. Mishu, M.D., et al., Should Antiplatelet Therapy Be Withheld Perioperatively? The First Study Examining Outcomes in Patients Receiving Dual Antiplatelet Therapy in the Lower Extremity Free Flap Population. Plast Reconstr Surg, 2022. 149(1): p. 95e-103e.
22. Nagashima, Z., et al., Impact of preoperative dual antiplatelet therapy on bleeding complications in patients with acute coronary syndromes who undergo urgent coronary artery bypass grafting. J Cardiol, 2017. 69(1): p. 156-161.
23. Oh, T.K., C. Im, and I.A. Song, Antiplatelet Therapy in Patients Without a Coronary Stent and Mortality After Noncardiac Surgery. Journal of Surgical Research, 2020. 256: p. 61-69.
24. Ohya, H., et al., Comparison of the continuation and discontinuation of perioperative antiplatelet therapy in laparoscopic surgery for colorectal cancer: A retrospective, multicenter, observational study (YCOG 1603). Annals of Gastroenterological Surgery, 2021. 5(1): p. 67-74.
25. Park, S.K., et al., Risk of non-cardiac surgery after percutaneous coronary intervention with drug-eluting stents. Sci Rep, 2017. 7(1): p. 16393.
26. Plicner, D., et al., Preoperative platelet aggregation predicts perioperative blood loss and rethoracotomy for bleeding in patients receiving dual antiplatelet treatment prior to coronary surgery. Thrombosis research, 2015. 136(3): p. 519-525.
27. Rossini, R., et al., Antiplatelet therapy and outcome in patients undergoing surgery following coronary stenting: Results of the surgery after stenting registry. Catheter Cardiovasc Interv, 2017. 89(1): p. E13-e25.
28. Sadeghi, R., et al., Dual antiplatelet therapy before coronary artery bypass grafting in patients with myocardial infarction: a prospective cohort study. BMC Surg, 2021. 21(1): p. 449.
29. Schaefer, A., et al., Preoperative Ticagrelor administration leads to a higher risk of bleeding during and after coronary bypass surgery in a case-matched analysis. Interact Cardiovasc Thorac Surg, 2016. 22(2): p. 136-40.
30. Schlachtenberger, G., et al., Major Bleeding after Surgical Revascularization with Dual Antiplatelet Therapy. Thorac Cardiovasc Surg, 2020. 68(8): p. 714-722.
31. Smith, B.B., et al., Cardiac Risk of Noncardiac Surgery After Percutaneous Coronary Intervention With Second-Generation Drug-Eluting Stents. Anesth Analg, 2019. 128(4): p. 621-628.

32. Straus, S., et al., A Difference in Bleeding and Use of Blood and Blood Products in Patients who Were Preoperatively on Aspirin or Dual Antiplatelet Therapy Before Coronary Artery Bypass Grafting. Med Arch, 2018. 72(1): p. 31-35.
33. Sun, J., et al., Safety and feasibility study of holmium laser enucleation of the prostate (HOLEP) on patients receiving dual antiplatelet therapy (DAPT). World J Urol, 2018. 36(2): p. 271-276.
34. Tianchetsada, N. and A. Suwanagool, Antithrombotic management and device-related bleeding complications in patients undergoing cardiac implantable electronic device implantations: A single-center study. Journal of the Medical Association of Thailand, 2018. 101(1): p. 33-39.
35. Ueoka, K., et al., The influence of pre-operative antiplatelet and anticoagulant agents on the outcomes in elderly patients undergoing early surgery for hip fracture. J Orthop Sci, 2019. 24(5): p. 830-835.
36. Xiao, F.C., et al., Does preoperative dual antiplatelet therapy affect bleeding and mortality after total arch repair for acute type A dissection? Interact Cardiovasc Thorac Surg, 2022. 34(1): p. 120-127.
37. Yoshimoto, M., et al., Emergent cholecystectomy in patients on antithrombotic therapy. Sci Rep, 2020. 10(1): p. 10122.
38. Yoshimoto, Y., et al., Optimal use of antiplatelet agents, especially aspirin, in the perioperative management of colorectal cancer patients undergoing laparoscopic colorectal resection. World Journal of Surgical Oncology, 2019. 17(1).

Endovascular, *N* = 3

1. Chinai, N., et al., Single versus dual antiplatelet therapy following peripheral arterial endovascular intervention for chronic limb threatening ischaemia: Retrospective cohort study. PLoS One, 2020. 15(6): p. e0234271.
2. Ghamraoui, A.K., et al., Clopidogrel versus ticagrelor for antiplatelet therapy in transcarotid artery revascularization (TCAR) in the Society for Vascular Surgery Vascular Quality Initiative. J Vasc Surg, 2021.
3. Kronlage, M., et al., Anticoagulation in addition to dual antiplatelet therapy has no impact on long-term follow-up after endovascular treatment of (sub)acute lower limb ischemia. Vasa, 2019. 48(4): p. 321-329.

DAPT Interruption Not Specified, *N* = 1

1. Humenberger, M., M. Stockinger, S. Kettner, J. Siller-Matula and S. Hajdu (2019). "Impact of Antiplatelet Therapies on Patients Outcome in Osteosynthetic Surgery of Proximal Femoral Fractures." J Clin Med 8(12).

Does Not Specify Dual Antiplatelet, *N* = 1

1. Hong, S. J., M. J. Kim, J. S. Kim, E. H. Kim, J. Lee, C. M. Ahn, B. K. Kim, Y. G. Ko, D. Choi, M. K. Hong and Y. Jang (2019). "Effect of Perioperative Antiplatelet Therapy on Outcomes in Patients With Drug-Eluting Stents Undergoing Elective Noncardiac Surgery." American Journal of Cardiology **123**(9): 1414-1421.

No Outcome of Interest, *N =1*

1. Kim, C., J. S. Kim, H. Kim, S. G. Ahn, S. Cho, O. H. Lee, J. K. Park, S. Shin, J. Y. Moon, H. Won, Y. Suh, J. R. Cho, Y. H. Cho, S. J. Oh, B. K. Lee, S. J. Hong, D. H. Shin, C. M. Ahn, B. K. Kim, Y. G. Ko, D. Choi, M. K. Hong and Y. Jang (2021). "Consensus decision-making for the management of antiplatelet therapy before non-cardiac surgery in patients who underwent percutaneous coronary intervention with second-generation drug-eluting stents: A cohort study." Journal of the American Heart Association **10**(8).

Not at Least 2 Comparison Groups of Patients on DAPT, *N = 1*

1. Hu, S. B., Y. Hai, J. F. Tang, T. Liu, B. X. Liang and B. Q. Xue (2019). "Risk of bleeding in patients with continued dual antiplatelet therapy during orthopedic surgery." Chin Med J (Engl) **132**(8): 943-947.

Single Arm with Bridging, *N = 1*

1. Dargham, B. B., A. Baskar, I. Tejani, Z. Cui, S. Chauhan, J. Sum-Ping, R. A. Weideman and S. Banerjee (2019). "Intravenous Antiplatelet Therapy Bridging in Patients Undergoing Cardiac or Non-Cardiac Surgery Following Percutaneous Coronary Intervention." Cardiovasc Revasc Med 20(9): 805-811.

TAVR, *N =1*

1. Hioki, H., Y. Watanabe, K. Kozuma, Y. Nara, H. Kawashima, A. Kataoka, M. Yamamoto, K. Takagi, M. Araki, N. Tada, S. Shirai, F. Yamanaka and K. Hayashida (2017). "Pre-procedural dual antiplatelet therapy in patients undergoing transcatheter aortic valve implantation increases risk of bleeding." Heart 103(5): 361-367.

Unavailable, *N = 1*

1. Zhang, J., F. Huang, J. Yang, Q. Wu, Y. Liu, Y. Zhou, Y. Zou and E. Zhu (2015). "Impact of preoperative dual antiplatelet therapy on perioperative bleeding in patients undergoing off-pump coronary artery bypass grafting." National medical journal of china **95**(24): 1934-1937.

APPENDIX C. RISK OF BIAS IN NON-RANDOMISED STUDIES – OF INTERVENTIONS (ROBINS-I)

Bias Domains Included in ROBINS-I

Pre-intervention	Risk of bias assessment is mainly distinct from assessments of randomized trials
Bias due to confounding	Baseline confounding occurs when one or more prognostic variables (factors that predict the outcome of interest) also predicts the intervention received at baseline ROBINS-I can also address time-varying confounding, which occurs when individuals switch between the interventions being compared and when post-baseline prognostic factors affect the intervention received after baseline
Bias in selection of participants into the study	When exclusion of some eligible participants, or the initial follow-up time of some participants, or some outcome events is related to both intervention and outcome, there will be an association between interventions and outcome even if the effects of the interventions are identical This form of selection bias is distinct from confounding—A specific example is bias due to the inclusion of prevalent users, rather than new users, of an intervention
At intervention	Risk of bias assessment is mainly distinct from assessments of randomized trials
Bias in classification of interventions	Bias introduced by either differential or non-differential misclassification of intervention status Non-differential misclassification is unrelated to the outcome and will usually bias the estimated effect of intervention towards the null Differential misclassification occurs when misclassification of intervention status is related to the outcome or the risk of the outcome, and is likely to lead to bias
Post-intervention	Risk of bias assessment has substantial overlap with assessments of randomized trials
Bias due to deviations from intended interventions	Bias that arises when there are systematic differences between experimental intervention and comparator groups in the care provided, which represent a deviation from the intended intervention(s) Assessment of bias in this domain will depend on the type of effect of interest (either the effect of assignment to intervention or the effect of starting and adhering to intervention)
Bias due to missing data	Bias that arises when later follow-up is missing for individuals initially included and followed (such as differential loss to follow-up that is affected by prognostic factors); bias due to exclusion of individuals with missing information about intervention status or other variables such as confounders
Bias in measurement of outcomes	Bias introduced by either differential or non-differential errors in measurement of outcome data. Such bias can arise when outcome assessors are aware of intervention status, if different methods are used to assess outcomes in different intervention groups, or if measurement errors are related to intervention status or effects
Bias in selection of the reported result	Selective reporting of results in a way that depends on the findings and prevents the estimate from being included in a meta-analysis (or other synthesis)

APPENDIX D. QUALITY ASSESSMENT FOR INCLUDED OBSERVATIONAL STUDIES

Author, Year	Bias Due to Confounding	Bias in Selection of Participants	Bias in Classification of Interventions	Bias Due to Deviations from Intended Interventions	Bias Due to Missing Data	Bias in Measurement of Outcomes	Bias in Selection of Reported Results
Cao, 2022[23]	Moderate	Low	Low	Low	Low	Low	Low
Cheng, 2020[27]	Moderate	Low	Low	Low	Moderate	Low	Moderate
De Servi, 2016[28]	High	Low	Moderate	Low	Low	Low	Low
Della Corte, 2017[18]	Moderate	Low	Low	Moderate	Low	Low	Moderate
Doğan, 2017[25]	Moderate	Moderate	Low	Low	Low	Low	Low
Gielen, 2015[29]	Moderate	Moderate	Low	Low	Low	Moderate	Low
Hansson, 2016[30]	Moderate	Low	Low	Low	Low	Low	Low
Heidari, 2016[21]	High	High	Low	Low	Low	Moderate	Moderate
Irie, 2019[22]	Moderate	Moderate	Low	Low	Low	Low	Low
Kacar, 2018[19]	Moderate	Low	Low	Low	Moderate	High	High
Kapoor, 2022[31]	High	Moderate	Low	Low	Low	Moderate	Low
Kim, 2020[24]	Moderate	Moderate	Low	Low	Low	Low	Low
Kremke, 2019[16]	Low	Moderate	Low	Low	Low	Low	Moderate
Nardi, 2021[17]	Moderate	Moderate	Low	Low	Low	Moderate	Low
Shahid, 2021[20]	High	Moderate	Low	Low	Low	High	Moderate
Tarrant, 2020[15]	Moderate	Moderate	Low	Low	Low	Moderate	Low
Vuilliomenet, 2019[32]	Moderate	Low	Low	Low	Low	Moderate	Moderate
Zhu, 2018[33]	High	Moderate	Low	Low	Low	Moderate	Moderate

APPENDIX E. EVIDENCE TABLE

Author Year Study design # Institutions: Propensity (Y/N)	**Procedure(s)**	**Pre-op DAPT Sample: n (%) Comparison Groups**	**Patient Characteristics Indication for DAPT, % Time Since Indication Age, Years Mean (SD) Gender [%Male or Female]**	**Bleeding Outcomes (Total or Specify) [Report N (%), Mean (SD) or Specify] Chest tube Drainage (cc, Total): RBC Transfusions (Total): Plt Transfusions (Total): Intraop Blood Loss Volume (cc): Reoperation: Hematoma: TIMI-defined Bleeding: BARC Type:**			**Thrombotic/Cardiovascular Outcomes (30d or Specify) MACE: MALE: Acute MI: Stroke: Revascularization/Reintervention: Major Amputation: CV Death: All-cause Death:**			**Statistical Methods Adjustment? [If Y: Propensity, Multivariable Regression, other? What Were Adjustment Variables?]**	**Comments**
				Continued DAPT (or DAPT held ≤ 2d)	Discontinued DAPT (or DAPT held > 2d)	Bridged / Other:	Continued DAPT (or DAPT held ≤ 2d)	Discontinued DAPT (or DAPT held > 2d)	Bridged / Other:		
Gielen, 2015[29] Observational 7 N	CABG	290 (27%) Groups: -DAPT held <2d before surgery (n=98) -DAPT held <1d before surgery (n=192)	Indication: Unclear, likely CAD Time:unclear Age: 65 (10) Gender: 83% male	Mean Blood Loss at 48 h: Day -2: 623 mL (IQR 485-913) vs Day -1: 715 mL, IQR (513-1078 mL) Plt transfusion: Day -2: 10% Day -1 : 41%				>2d, ASA+Clop MACE: OR, OR LCI, OR UCI: 0.849, 0.635, 1.135		Not propensity matched, Multiple linear regressions using the logarithm of 48-h blood loss as the dependent variable and the effect of the variable stop day was modelled.	MACCE data is not directly compared between DAPT and other groups. Linear regression using this group on only Median blood loss/Plt transfusion
Zhu, 2018[33] Observational 1 N	CABG	120/180 (66%) Groups: Treatment group: >1wk DAPT (n=60) Discontinuation: hx DAPT but dc'd >1wk before surgery (n=60) Control: no hx DAPT (n=60)	DAPT indication is CAD + PCI Age: (48.5±3.2) Male: 130/180	Cont DAPT at least 7 d before surgery Chest Tube Drainage (total, SD): 1456.8 mL, (680.3 mL) RBC Transfusion: 9.1, (11.2) Plt Transfusion: 0.5, (1.9)	Held DAPT at least 7 d before surgery (discontinue) Chest Tube Drainage (total, SD): 1254.8 mL (457 mL) RBC transfusion: 6.5 (3.2) Plt Transfusion 0.1 (0.6)					N	
Kapoor, 2022[31] Observational 1 N	CABG	1200 (100%) Discontinue >6 d (n=468) D/C 3-5 d (n=621) D/C <2 d (n=111)	"Ages 31-70, no significant diff in age between groups" No gender reported No time since indication reported	< 2 d RBC transfusion (packed cell volume mL, SD): 34.78, 3.89 CT Drainage (mL, SD): 283.682, 191.915 Re-operation: 10	3-5 d RBC transfusion (packed cell volume mL, SD): 35.05, 5.7 CT Drainage (total mL, SD): 216.475, 188.928 Re-operation (Count): 5 6 d RBC transfusion (packed cell volume mL, SD): 28.84, 6.61 CT Drainage (total mL, SD): 333.939, 258.845 Re-operation (Count): 16					No adjustment. Mean/std deviation, ANOVA, chi squared.	

Author Year Study design # Institutions: Propensity (Y/N)	**Procedure(s)**	**Pre-op DAPT Sample: n (%) Comparison Groups**	**Patient Characteristics Indication for DAPT, % Time Since Indication Age, Years Mean (SD) Gender [%Male or Female]**	**Bleeding Outcomes (Total or Specify) [Report N (%), Mean (SD) or Specify] Chest tube Drainage (cc, Total): RBC Transfusions (Total): Plt Transfusions (Total): Intraop Blood Loss Volume (cc): Reoperation: Hematoma: TIMI-defined Bleeding: BARC Type:**		**Thrombotic/Cardiovascular Outcomes (30d or Specify) MACE: MALE: Acute MI: Stroke: Revascularization/Reintervention: Major Amputation: CV Death: All-cause Death:**		**Statistical Methods Adjustment? [If Y: Propensity, Multivariable Regression, other? What Were Adjustment Variables?]**	**Comments**
Nardi, 2021[17] Observational 1 N	CABG (on or off pump)	333 (100%) Group A: Discontinuing DAPT (ASA + Clopidogrel/Ticagrelor) > 72 hours or 3–4 days (n=159) Group B: Discontinuing Clopidogrel/Ticagrelor (maintaining ASA when possible) 48–72 hours or 2–3 days (n=126) Group C: Discontinuing Clopidogrel/Ticagrelor (maintaining ASA or both agents) < 24 hours or 0–1 days (n=48)	Indication: Coronary artery disease Time: Unspecified Age: A: 67 (8.5), B: 68 (9.8), C: 65 (11.4) Gender (%male): A: 89%, B: 83%, C: 90%	Group C Chest tube drainage (24hrs): 698mL (SD 409) RBC transfusions (total): 0.8u (SD 1.2) Plt transfusions (total): 4 (8.33%) Reoperation for bleeding: 4 (8.33%)	Group A Chest tube drainage (24hrs): 511mL (SD 254) RBC transfusions (total): 0.7u (SD 1.4) Plt transfusions (total): 4 (2.52%) Reoperation for bleeding: 2 (1.25%) Group B Chest tube drainage (24hrs): 507mL (SD 206) RBC transfusions (total): 1.3u (SD 4.6) Plt transfusions (total): 5 (3.97%) Reoperation for bleeding: 2 (1.59%)	Group C Acute MI: 0 All-cause death: 0	Group A Acute MI: 0 All-cause death: 3 (1.87%) Group B Acute MI: 0 All-cause death: 1 (0.79%)	Variables were compared in an unadjusted analysis. Separate univariate analysis and a logistic regression model were used for additional results not pertinent to the review and so not reported here.	
Tarrant, 2020[15] Observational 1 Y	Hip surgery (following low energy proximal femur fracture)	122 (100%) Compares day of operation after last antiplatelet agent dose (time as continuous variable, 0-9d) (n=122)	Indication: Ischemic heart disease (61%), cerebrovascular disease (31%), peripheral vasular disease (5%), other (3%) Time: Unspecified Age: 83.1 (66-98) Gender: 63% female	Results reported as OR for each day of operative delay after antiplatelet dose RBC transfusions: 1 (0.87-1.15)		OR for each day of operative delay after antiplatelet dose: All-cause death: 1.32 (1.03-1.68)		Y: propensity matched on age, sex, Charleston comorbidity index, Nottingham hip fracture score, procedure (arthroplasty: yes/no)	The results were reported as odds ratios of increased risk per day for relevant outcomes as opposed to quantity/ number of events per comparison groups.

Author Year Study design # Institutions: Propensity (Y/N)	**Procedure(s)**	**Pre-op DAPT Sample: n (%) Comparison Groups**	**Patient Characteristics Indication for DAPT, % Time Since Indication Age, Years Mean (SD) Gender [%Male or Female]**	**Bleeding Outcomes (Total or Specify) [Report N (%), Mean (SD) or Specify] Chest tube Drainage (cc, Total): RBC Transfusions (Total): Plt Transfusions (Total): Intraop Blood Loss Volume (cc): Reoperation: Hematoma: TIMI-defined Bleeding: BARC Type:**		**Thrombotic/Cardiovascular Outcomes (30d or Specify) MACE: MALE: Acute MI: Stroke: Revascularization/Reintervention: Major Amputation: CV Death: All-cause Death:**	**Statistical Methods Adjustment? [If Y: Propensity, Multivariable Regression, other? What Were Adjustment Variables?]**	**Comments**
Cheng, 2020[27] Observational 1 N	CABG (off pump)	2012 (100%) Compares day of DAPT (ASA + Clopidogrel) discontinuation preoperation (time as continuous variable, 0-5d) 0d (n=220) 1d (n=240) 2d (n=360) 3d (n=332) 4d (n=428) 5d (n=432)	Indication: Coronary artery disease Time: Unspecified Age: 61.9 (9.1) Gender: 24.7% female	0 days Chest tube drainage (mL): 610 (50) RBC transfusions (units): 3.3 (0.4) Reoperation: 13 (5.9%) BARC 4 major bleeding event within 7d: 64 (29.1%) 1 day Chest tube drainage (mL): 660 (50) RBC transfusions (units): 3 (0.3) Reoperation: 9 (3.6%) BARC 4 major bleeding event within 7d: 59 (24.6%) 2 days Chest tube drainage (mL): 600 (40) RBC transfusions (units): 2.8 (0.9) Reoperation: 17 (4.7%) BARC 4 major bleeding event within 7d: 70 (19.4%)	3 days Chest tube drainage (mL): 595 (45) RBC transfusions (units): 2.5 (0.7) Reoperation: 6 (1.8%) BARC 4 major bleeding event within 7d: 43 (13%) 4 days Chest tube drainage (mL): 590 (40) RBC transfusions (units): 2.5 (0.5) Reoperation: 10 (2.3%) BARC 4 major bleeding event within 7d: 62 (14.5%) 5 days Chest tube drainage (mL): 560 (35) RBC transfusions (units): 2.6 (0.6) Reoperation: 10 (2.3%) BARC 4 major bleeding event within 7d: 56 (13%)		Y: Univariable associations between clinical outcomes and study variables were analyzed using binary logistic regression.	This study included a subgroup analysis of incidence of myocardial ischemia, however did not analyze ischemic outcome by DAPT use, so it was not relevant to this review.
Irie, 2019[22] Observational 1 N	Non-cardiac surgery (emergent, procedure performed within 24hrs of diagnosis)	133 (100%) Compares ASA + different P2Y12 inhibitors Groups: Clopidogrel (n=86) Ticlodipine (n=37) Prasugrel (n=10) *All patients received ASA < 5d and P2Y12 < 7d before emergent surgery	Indication: PCI (100%) Time: 982d (0-6433) Age: 74 (38-90) Gender: 73.7% male	Clopidogrel Life threatening or major bleed: 12 (14%) Ticlodipine Life threatening or major bleed: 3 (8.1%) Prasugrel Life threatening or major bleed: 3 (30%)		Restarting antiplatelet agents earlier than 2d postoperatively Life threatening or major bleed: 11 (8.3%)		Multiple methods: Kaplan-Meier method to describe survival until 180 days after surgery, log-rank test to compare survival between the groups. Multivariable logistic regression. Cox proportional hazard model and estimated hazard ratios (HRs). Covariates were also evaluated for collinearity.	The majority of the results in this study were not useful to our review because the authors' analysis comprised of factors associated with a bleeding and non-bleeding group as opposed to a comparison of DAPT strategies. Additionally,

Author Year Study design # Institutions: Propensity (Y/N)	Procedure(s)	Pre-op DAPT Sample: n (%) Comparison Groups	Patient Characteristics Indication for DAPT, % Time Since Indication Age, Years Mean (SD) Gender [%Male or Female]	Bleeding Outcomes (Total or Specify) [Report N (%), Mean (SD) or Specify] Chest tube Drainage (cc, Total): RBC Transfusions (Total): Plt Transfusions (Total): Intraop Blood Loss Volume (cc): Reoperation: Hematoma: TIMI-defined Bleeding: BARC Type:	Thrombotic/Cardiovascular Outcomes (30d or Specify) MACE: MALE: Acute MI: Stroke: Revascularization/Reintervention: Major Amputation: CV Death: All-cause Death:	Statistical Methods Adjustment? [If Y: Propensity, Multivariable Regression, other? What Were Adjustment Variables?]	Comments
							patients received ASA and a P2Y12 inhibitor preop (given urgent nature of surgeries) and medication management consisted of P2Y12 type and restarting agents post op.

Author Year Study design # Institutions: Propensity (Y/N)	**Procedure(s)**	**Pre-op DAPT Sample: n (%) Comparison Groups**	**Patient Characteristics Indication for DAPT, % Time Since Indication Age, Years Mean (SD) Gender [%Male or Female]**	**Bleeding Outcomes (Total or Specify) [Report N (%), Mean (SD) or Specify] Chest tube Drainage (cc, Total): RBC Transfusions (Total): Plt Transfusions (Total): Intraop Blood Loss Volume (cc): Reoperation: Hematoma: TIMI-defined Bleeding: BARC Type:**		**Thrombotic/Cardiovascular Outcomes (30d or Specify) MACE: MALE: Acute MI: Stroke: Revascularization/Reintervention: Major Amputation: CV Death: All-cause Death:**	**Statistical Methods Adjustment? [If Y: Propensity, Multivariable Regression, other? What Were Adjustment Variables?]**	**Comments**
Vuilliomenet, 2019[32] Observational 1 N	CABG (emergency or urgent)	262 (78%) Groups: Time of ticagrelor, prasugrel or clopidogrel d/c before surgery: <24h (n=101) 24-48h (n=92) 48-72h (n=21) >72h (n=48)	Indication: ACS (100%) Time: ACS within 10 days Age: Ticagrelor (65.1 (11.0)) Prasugrel (62.8(9.0)) Clopidogrel (67.7(10.9)) Gender: Ticagrelor (89% male) Prasugrel (85%) Clopidogrel (78%)	d/c ticagrelor <24h Chest tube drainage (cc): 1220 (1197.0) any transfusion (units): 2.5 (17.9) reoperation: d/c prasugrel <24h Chest tube drainage (cc): 1320 (1934.4) any transfusion (units): 2 (22.5) reoperation: d/c clopidogrel <24h Chest tube drainage (cc): 1190 (494.3) any transfusion (units): 1 (6.0) reoperation: d/c ticagrelor 24-48h Chest tube drainage (cc): 1220 (440.0) any transfusion (units): 1 (4.1) reoperation: d/c prasugrel 24-48h Chest tube drainage (cc): 1050 (742.5) any transfusion (units): 1 (5.2) reoperation: d/c clopidogrel 24-48h Chest tube drainage (cc): 830 (1319.0) any transfusion (units): 1 (10.6) reoperation:	d/c ticagrelor 48-72h Chest tube drainage (cc): 1100 (260.8) any transfusion (units): 1 (4.5) reoperation: d/c prasugrel 48-72h Chest tube drainage (cc): 1050 (0) any transfusion (units): 0 (0) reoperation: d/c clopidogrel 48-72h Chest tube drainage (cc): 820 (766.7) any transfusion (units): 1 (1.3) reoperation: d/c ticagrelor >72h Chest tube drainage (cc): 700 (350.7) any transfusion (units): 0 (1.63) reoperation: d/c prasugrel >72h Chest tube drainage (cc): 750 (587.8) any transfusion (units): 0 (3.1) reoperation: d/c clopidogrel >72h Chest tube drainage (cc): 900 (35.5) any transfusion (units): 0 (2.2) reoperation:	(note: mortality data not reported by time of discontinuation, only by type of DAPT agent, so not included as DAPT type was not varied)	multivariable linear regression only for predictors of 24h chest tube output	

Author Year Study design # Institutions: Propensity (Y/N)	**Procedure(s)**	**Pre-op DAPT Sample: n (%) Comparison Groups**	**Patient Characteristics Indication for DAPT, % Time Since Indication Age, Years Mean (SD) Gender [%Male or Female]**	**Bleeding Outcomes (Total or Specify) [Report N (%), Mean (SD) or Specify] Chest tube Drainage (cc, Total): RBC Transfusions (Total): Plt Transfusions (Total): Intraop Blood Loss Volume (cc): Reoperation: Hematoma: TIMI-defined Bleeding: BARC Type:**		**Thrombotic/Cardiovascular Outcomes (30d or Specify) MACE: MALE: Acute MI: Stroke: Revascularization/Reintervention: Major Amputation: CV Death: All-cause Death:**		**Statistical Methods Adjustment? [If Y: Propensity, Multivariable Regression, other? What Were Adjustment Variables?]**	**Comments**
Kremke, 2018[16] Observational 3 Y	CABG and/or single valve surgery	90 (50%) Groups: Time of ticagrelor d/c before surgery compared to ASA control group: <72h (n=42) 72-120h (n=48)	Indication: not specified Time: not specified Age: DAPT: 68, control: 69 Gender: DAPT: 78% male, control: 80% male	d/c ticagrelor <72h major bleeding: 48% reoperation: 29%	d/c ticagrelor >72h major bleeding: 17% reoperation: 10%			Propensity score matching among DAPT group to ASA only control group (by sex, age insulin-dependent DM, COPD, PAD< CNS disease, prior cardiac surgery, critical preop state, unstable angina, reduced LVEF, recent MI, acute surgery, surgery type, ECMO time preop aprotinin use)	
Kacar, 2017[19] Observational 1 N	CABG (within 10d of ACS)	123 (100%) Groups: Clopidogrel discontinuation before surgery continued (clopidogrel held 1-4 days before surgery) (n=65) discontinued (clopid held 5-10d before surgery) (n=57)	Indication: PCI, 100% Time: Within 10 days Age: Continued: 61.8 (8.1), Discontinued: 60.8 (9.6) Gender: Continued: 68.4% male, Discontinued: 66.7% male	continued (clopidogrel held 1-4 days before surgery) Chest tube drainage (cc, total): 0.65L (in 48hrs) RBC transfusions (total): 0.64L Reoperation: 1	discontinued (clopid held 5-10d before surgery) (n=57) Chest tube drainage (cc, total): 0.68L (in 48hrs) RBC transfusions (total): 0.47L Reoperation: 1	continued (clopidogrel held 1-4 days before surgery) All-cause death: 0	discontinued (clopid held 5-10d before surgery) All-cause death: 0	no multivariable models for outcomes of interest reported	

Author **Year** **Study design** **# Institutions:** **Propensity (Y/N)**	**Procedure(s)**	**Pre-op DAPT Sample: n (%)** **Comparison Groups**	**Patient Characteristics** **Indication for DAPT, %** **Time Since Indication** **Age, Years Mean (SD)** **Gender [%Male or Female]**	**Bleeding Outcomes (Total or Specify) [Report N (%), Mean (SD) or Specify]** **Chest tube Drainage (cc, Total):** **RBC Transfusions (Total):** **Plt Transfusions (Total):** **Intraop Blood Loss Volume (cc):** **Reoperation:** **Hematoma:** **TIMI-defined Bleeding:** **BARC Type:**	**Thrombotic/Cardiovascular Outcomes (30d or Specify)** **MACE:** **MALE:** **Acute MI:** **Stroke:** **Revascularization/Reintervention:** **Major Amputation:** **CV Death:** **All-cause Death:**	**Statistical Methods Adjustment?** **[If Y: Propensity, Multivariable Regression, other? What Were Adjustment Variables?]**	**Comments**
Altun, 2017[34] RCT 1 N	CABG	Pre-Op DAPT: 54, 100% TnX-A (n = 18) TnX-A+Des (n = 16) Des (n = 10) Control (n = 10)	ACS, 100% Male TnX-A 84%, 65.8 ± 6.1 TnX-A+Des 88%, 65.6 ± 11.3 Des 90%, 66.4 ± 9.3 Control 90%, 57.9 ± 14.6	DAPT in all groups TnX-A Total Blood Loss (chest tube drainage mL, SD): 535, 116.8 RBC transfusion (erythro suspe mL): 125, 128.6 Platelet sus (mL): 0, 0 TnX-A + Des Total Blood Loss (chest tube drainage mL, SD): 574, 75.5 RBC transfusion (erythro suspe mL): 93.7, 125 Platelet sus (mL): 0, 0 Des alone Total Blood Loss (chest tube drainage mL, SD): 1430, 257.6 RBC transfusion (erythro suspe mL): 675, 237.1 Platelet sus (mL): 0, 0 Control (no drug) Total Blood Loss (chest tube drainage mL, SD): 1767.5, 293.2. RBC transfusion (erythro suspe mL): 900, 268.7 Platelet sus (mL): 120, 209.7		N	

Author Year Study design # Institutions: Propensity (Y/N)	**Procedure(s)**	**Pre-op DAPT Sample: n (%) Comparison Groups**	**Patient Characteristics Indication for DAPT, % Time Since Indication Age, Years Mean (SD) Gender [%Male or Female]**	**Bleeding Outcomes (Total or Specify) [Report N (%), Mean (SD) or Specify] Chest tube Drainage (cc, Total): RBC Transfusions (Total): Plt Transfusions (Total): Intraop Blood Loss Volume (cc): Reoperation: Hematoma: TIMI-defined Bleeding: BARC Type:**		**Thrombotic/Cardiovascular Outcomes (30d or Specify) MACE: MALE: Acute MI: Stroke: Revascularization/Reintervention: Major Amputation: CV Death: All-cause Death:**	**Statistical Methods Adjustment? [If Y: Propensity, Multivariable Regression, other? What Were Adjustment Variables?]**	**Comments**
Doğan, 2017[25] Observational 1 N	Renal transplant	106 (100%) Compares groups with variable timing since stent placement interruption Groups: DES-Early 3mo from DES implantation (n=41) DES-Late- 3-12mo from DES implantation BMS- at least 1mo from BMS implantation *Interruption defined as holding ASA and Clopidogrel 5-7d before transplant	Indication: Stable angina, unstable angina, or NSTEMI Timing: Variable per group Age: BMS: 58.17 (5.4), DES-Early: 54.55 (6.6), DES-Late: 56.63 (6.9) Gender (%male): BMS: 75%, DES-Early: 65.9%, DES-Late: 65.9%			DES-Early MACE: 2 (4.9%) Acute MI: 1 (2.4%) CV Death: 0 All-Cause Death: 1 (2.4%) DES-Late MACE: 3 (7.3%) Acute MI: 2 (2.9%) CV Death: 0 All-Cause Death: 1 (2.4%) BMS MACE: 2 (8.3%) Acute MI: 1 (4.2% CV Death: 1 (4.2%) All-Cause Death: 2 (8.3%)	No adjustment	All patients had DAPT held 5-7 days prior to surgery. The timing since DAPT indication was varied.
Della Corte, 2017[18] Observational 1 N	CABG	226 (100%) Groups: time of d/c clopidogrel or ticagrelor 0-3 days (n=34) >3 days (n=192)	Indication: not specified Time: not specified Age: 63 (9) Gender: 80.5% male	d/c clopidogrel 0-3d Post-op blood loss: 700 (205.9) d/c ticagrelor 0-3d Post-op blood loss: 800 (577.8)	d/c clopidogrel >4d Post-op blood loss: 625 (264.4) d/c ticagrelor >4d Post-op blood loss: 560 (270.4)		multivariable logistic regression	Other outcomes (including transfusions, reexploration) only compared clopidogrel versus ticagrelor groups instead of comparing time to agent discontinuation so are not reported here

Author **Year** **Study design** **# Institutions:** **Propensity (Y/N)**	**Procedure(s)**	**Pre-op DAPT** **Sample: n (%)** **Comparison Groups**	**Patient Characteristics** **Indication for DAPT, %** **Time Since Indication** **Age, Years Mean (SD)** **Gender [%Male or Female]**	**Bleeding Outcomes (Total or Specify) [Report N (%), Mean (SD) or Specify]** **Chest tube Drainage (cc, Total):** **RBC Transfusions (Total):** **Plt Transfusions (Total):** **Intraop Blood Loss Volume (cc):** **Reoperation:** **Hematoma:** **TIMI-defined Bleeding:** **BARC Type:**	**Thrombotic/Cardiovascular Outcomes (30d or Specify)** **MACE:** **MALE:** **Acute MI:** **Stroke:** **Revascularization/Reintervention:** **Major Amputation:** **CV Death:** **All-cause Death:**	**Statistical Methods** **Adjustment?** **[If Y: Propensity, Multivariable Regression, other?** **What Were Adjustment Variables?]**	**Comments**
De Servi, 2015[28] Observational 3 N	Cardiac/ Vascular/ Uro/ Abd/ Thoracic/ Ortho/ Other	Pre-Op DAPT: (100%) Bridge P2Y12 inhibitor with i.v. tirofiban.(n=87) Control (continue or d/c P2Y12 inhibitor without Bridge) (n=227)	DAPT Indication : PCI 6-12 months, 100% Time (days): Bridge: 104 [5–365]; control: 105 [0–360] Age: Bridge: 67.4 [25–83]; control: 69.2 [41–90] Gender: Bridge: 64 (73.6% male), Control: 180 (79.3% male)	Bridge TIMI major bleeding 5 (5.7%) Any transfusion 22 (25.9%) Control (no bridge) TIMI major bleeding: 36 (15.8%) Any transfusion: 76 (33.5%)	Bridge MACCE: 2 (2.3%) Stroke: 0 Death: 0 MI: 2 (2.34%) Control (no bridge) MACCE: 17 (7.5%) Stroke: 0 Death: 6 (2.6%) MI: 12 (5.3%)	multivariable logistic regression (only used for net adverse cardiac events which was not abstracted for consistency across studies) Nearest-neighbor matching, the bridge therapy did not show a statistically significant effect on overall MACE (4% lower in the treated sample, p = 0.199).	

Hansson, 2015 Observational 8 Y	CABG	Pre-Op DAPT Ticagrelor+ASA n = 1266 (56.4%) Clopidogrel+ASA n = 978, 43.5%	DAPT indication- ACS Time: Unspecified Clop+ASA Age: 68.4 +/- 9.5 Gender: 775/978 (79.2%) Tica + ASA Age: 67.8 +/- 9.4 Gender: 995/1266 (78.5%)	d/c clopidogrel 0-24 hours Blood Loss (mL, SD): 663, 627 RBC Transfusion (units, SD): 4.9, 6.8 Platelet Transfusion (units, SD): 1.5, 2.3 d/c clopidogrel 24-48 hours Post op blood loss (mL, SD): 714, 462 RBC Transfusion (units, SD): 3.4, 4.5 Platelet Transfusion (units, SD): 0.94, 1.5 d/c ticagrelor 0-24 hours Blood Loss (mL): 813, 478 RBC Transfusion (units, SD): 6.9, 9.8 Platelet Transfusion (units, SD): 3.2, 3.7 d/c ticagrelor 24-48 hours Post op blood loss (mL, SD): 641, 337 RBC Transfusion (units, SD): 4.4, 5.7 Platelet Transfusion (units, SD):1.6, 2.2	d/c clopidogrel 48-72 hours Post op blood loss (mL, SD): 659, 313 RBC Transfusion (units, SD): 2.8, 3.5 Platelet Transfusion (units, SD): 0.79,1.4 d/c clopidogrel 72-96 hours Post op blood loss (mL, SD): 682, 462 RBC Transfusion (units, SD): 3, 5.3 Platelet Transfusion (units, SD): 0.68, 1.4 d/c clopidogrel 96-120 hours Post op blood loss (mL, SD): 701, 454 RBC Transfusion (units, SD): 2.3, 2.9 Platelet Transfusion (units, SD): 0.51, 1 d/c clopidogrel >120 hours Post op blood loss (mL, SD): 555, 313 RBC Transfusion (units, SD): 1.7, 3 Platelet Transfusion (units, SD): 0.25, 0.84 d/c ticagrelor 48-72 hours Post op blood loss (mL, SD): 709, 707 RBC Transfusion (units, SD): 4, 9.9 Platelet Transfusion (units, SD): 1.8, 3.7 d/c ticagrelor 72-96 hours		Y: Multivariable logistic regression

Post op blood loss (mL, SD): 630, 541
RBC Transfusion (units, SD): 1.7, 3.2
Platelet Transfusion (units), SD: 0.44, 0.81

d/c ticagrelor 96-120 hours

Post op blood loss (mL, SD): 550, 296
RBC Transfusion (units), SD: 1.3, 2.1
Platelet Transfusion (units, SD): 0.32, 0.9

d/c ticagrelor >120 hours

Post op blood loss (mL, SD): 534, 363
RBC Transfusion (units, SD): 1.6, 3.2
Platelet Transfusion (units, SD): 0.24, 0.95

Author Year Study design # Institutions: Propensity (Y/N)	**Procedure(s)**	**Pre-op DAPT Sample: n (%) Comparison Groups**	**Patient Characteristics Indication for DAPT, % Time Since Indication Age, Years Mean (SD) Gender [%Male or Female]**	**Bleeding Outcomes (Total or Specify) [Report N (%), Mean (SD) or Specify] Chest tube Drainage (cc, Total): RBC Transfusions (Total): Plt Transfusions (Total): Intraop Blood Loss Volume (cc): Reoperation: Hematoma: TIMI-defined Bleeding: BARC Type:**		**Thrombotic/Cardiovascular Outcomes (30d or Specify) MACE: MALE: Acute MI: Stroke: Revascularization/Reintervention: Major Amputation: CV Death: All-cause Death:**		**Statistical Methods Adjustment? [If Y: Propensity, Multivariable Regression, other? What Were Adjustment Variables?]**	**Comments**
Cao, 2021[23] Observational 1 N	Non-cardiac surgery	747 (81.7%) Groups: DAPT interruption (any kind) (n=297) No DAPT interruption (n=312) ASA + P2Y12 interruption (n=128) Only P2Y12 interruption (n=152)	Indication: PCI, 100% Time: <1yr since PCI Age: Not specified Gender: 67.6% male	No DAPT interruption Bleeding (defined as requiring >2u RBC transfusion): 26 (8.3%)	DAPT interruption (any kind) Bleeding (defined as requiring >2u RBC transfusion): 40 (13.5%) ASA + P2Y12 interruption Bleeding (defined as requiring >2u RBC transfusion): 25 (19.5%) Only P2Y12 interruption Bleeding (defined as requiring >2u RBC transfusion): 14 (9.3%)	No DAPT interruption: MACE: 11 (3.5%) Acute MI: 3 (1%) All-cause death: 8 (2.6%)	DAPT interruption (any kind) MACE: 8 (2.7%) Acute MI: 2 (0.7%) All-cause death: 6 (2%) ASA + P2Y12 interruption MACE: 5 (3.9%) Acute MI: 1 (0.8%) All-cause death: 4 (3.1%) Only P2Y12 interruption MACE: 2 (1.3%) Acute MI: 1 (0.7%) All-cause death: 1 (0.7%)	Y: Multivariable logistic regression. Variables for risk-adjustment: age, sex, urgent/emergent surgery, risk category (low, intermediate or high), and ASA-PS class.	
Shahid, 2021[20] Observational 1 N	CABG	192 (100%) Group A: d/c clopidogrel < 48h (n=102) Group B: d/c clopidogrel 48-120h before surgery (n=89)	ACS, 100% Male TnX-A group 84%, 65.8 ± 6.1 TnX-A+Des 88%, 65.6 ± 11.3 Des 90%, 66.4 ± 9.3 Control 90%, 57.9 ± 14.6	Group A: d/c clopidogrel < 48h Chest tube drainage (cc, total): 602.25 (200) Any transfusion: 33 (32%) Reoperation: 3 (2.9%)	Group B: d/c clopidogrel 48-120h Chest tube drainage (cc, total): 609.87 (200) Any transfusion 25 (28.1%) Reoperation: 1 (1.1%)	Group A: d/c clopidogrel < 48h All-cause death: 7 (6.8%)	Group B: d/c clopidogrel 48-120h All-cause death: 2 (2.2%)	N, all data are unadjusted	

Author Year Study design # Institutions: Propensity (Y/N)	**Procedure(s)**	**Pre-op DAPT Sample: n (%) Comparison Groups**	**Patient Characteristics Indication for DAPT, % Time Since Indication Age, Years Mean (SD) Gender [%Male or Female]**	**Bleeding Outcomes (Total or Specify) [Report N (%), Mean (SD) or Specify] Chest tube Drainage (cc, Total): RBC Transfusions (Total): Plt Transfusions (Total): Intraop Blood Loss Volume (cc): Reoperation: Hematoma: TIMI-defined Bleeding: BARC Type:**		**Thrombotic/Cardiovascular Outcomes (30d or Specify) MACE: MALE: Acute MI: Stroke: Revascularization/Reintervention: Major Amputation: CV Death: All-cause Death:**		**Statistical Methods Adjustment? [If Y: Propensity, Multivariable Regression, other? What Were Adjustment Variables?]**	**Comments**
Kim, 2020[24] Observational 9 N	Non-cardiac surgery	Total n=3582 Continue DAPT: n=984, (27.4%) Discontinue APT n=1750, (49%)	Indication for DAPT: PCI Time since indication, mean months (SD): not specified Age, years mean (SD): 69 (61-75) Gender, %male: 1282 (70)		HR: Incidence Major bleeding d/c 1-3 days OR, OR LIC, OR UCI: 1.54, 0.85, 2.8 d/c 4-8 days OR, OR LIC, OR UCI: 0.89, 0.55, 1.44 d/c: at least 9 days OR, OR LIC, OR UCI: 1.5, 0.76, 2.97	Continue DAPT MACE: 47 (4.8%)	Discontinue DAPT MACE (events): 36 (4.5%)	multivariate logistic regression model (Note: in an additional model looking at holding >8 days, they reported higher adjusted MACE compared to <8d (adjusted HR, 3.38; 95% CI, 1.36–8.38; P=0.009))	
Heidari 2016[21] Observational 1 N	CABG	100 (66%) Group A: DAPT continued, urgent CABG, experienced surgeon (n=50) Group C: DAPT held > 5d, elective CABG, experienced surgeon (n=50) (*Group B not relevant - does not vary DAPT)	Indication: ACS Time: not specified Age, years mean (SD): A: 59.5 (9.70), C: 57.9 (8.70) Gender, %male: A: 72, C: 66	DAPT continued (Group A) RBC transfusions (units): 0.78 (1.14) Intraop blood loss volume (cc): 987.9 (443) Reoperation: 0	DAPT held >5d (Group C) RBC transfusions (units): 3.14 (1.9) Intraop blood loss volume (cc): 973 (537.5) Reoperation: 0	DAPT continued (Group A) All-cause death: 0 (0%) [in-hospital]	DAPT held >5d (Group C) All-cause death: 0(0%) [in-hospital]	N, all data are unadjusted. (Group B was urgent CABG with DAPT continuation with empiric transfusions given and inexperienced surgeons. Given that the DAPT management did not vary, we determined A and C groups were the comparison of interest, and C was not randomized)	

Notes. Mean (SD) unless otherwise specified; median [IQR].
Abbreviations. ACS=acute coronary syndrome; CV=cardiovascular; d/c=discontinue; MACE=major adverse cardiovascular events; MACCE=all-cause death, myocardial infarction, definite stent thrombosis and stroke; MALE=major adverse limb; MI=myocardial infarction; ns=not significant; OR=odds ratio.

APPENDIX F. PEER REVIEW DISPOSITION

Comment #	Reviewer #	Comment	Author Response
Are the objectives, scope, and methods for this review clearly described?			
1	2	Yes	Thank you.
2	3	Yes	Thank you.
3	5	Yes	Thank you.
4	6	Yes	Thank you.
Is there any indication of bias in our synthesis of the evidence?			
5	2	No	Thank you.
6	3	No	Thank you.
7	5	No	Thank you.
8	6	No	Thank you.
Are there any published or unpublished studies that we may have overlooked?			
9	2	Yes - Grzegorz L. Kaluza MD, PhD, Jane Joseph, Joseph R. Lee MD, Michael E. Raizner MD and Albert E. Raizner MD, Catastrophic outcomes of noncardiac surgery soon after coronary stenting Catastrophic outcomes of noncardiac surgery soon after coronary stenting FACC 2000 25:5 1288-1294.	We reviewed this study and do not think it meets eligibility criteria, as it does not report the details on pre-op DAPT management or present different treatment strategies
10	3	No	Thank you.
11	5	No	Thank you.
12	6	Yes - Douketis JD, Spyropoulos AC, Murad MH, et al. Perioperative Management of Antithrombotic Therapy: An American College of Chest Physicians Clinical Practice Guideline. Chest. 2022;162(5):e207-e243. doi:10.1016/j.chest.2022.07.025 Devereaux PJ, Mrkobrada M, Sessler DI, et al. Aspirin in patients undergoing noncardiac surgery. N Engl J Med. 2014;370(16):1494-1503	We reviewed this study. It is a practice guideline and thus not primary evidence. We do cite it in the discussion. We reviewed this study, it is about ASA therapy and not about DAPT

Comment #	Reviewer #	Comment	Author Response
		Antolovic D, Reissfelder C, Rakow A, et al. A randomised controlled trial to evaluate and optimize the use of antiplatelet agents in the perioperative management in patients undergoing general and abdominal surgery--the APAP trial (ISRCTN45810007). BMC Surg. 2011;11:7. Published 2011 Mar 3.	We reviewed this study. This is the protocol for a study, and does not contain any study results
		Wang A, Wu A, Wojdyla D, et al. Dual antiplatelet therapy for perioperative myocardial infarction following CABG surgery. Am Heart J. 2018;199:150-155.	We reviewed this study. Not all of these patients are on pre-op DAPT and therefore it does not meet the inclusion criteria
		Burdess A, Nimmo AF, Garden OJ, et al. Randomized controlled trial of dual antiplatelet therapy in patients undergoing surgery for critical limb ischemia. Ann Surg. 2010;252(1):37-42.	We reviewed this study. Not all of these patients are on pre-op DAPT and therefore it does not meet the inclusion criteria.
Additional suggestions or comments can be provided below.			
13	2	Note: I used the page numbers for the PDF not the page numbers on the pages in the PDF. So when I say Page 11 (from the PDF) that is page 8 of the report. Comments: Page 4&5: No anesthesia authors on review panel. Heavy surgical presence. No input from highest risk for DAPT surgical field, neurosurgery.	Lacking an anesthesiologist among our technical experts is a limitation we acknowledge. The lack of a neurosurgeon we don't consider a significant limitation since there were no eligible studies of neurosurgical procedures.
14	2	Page 12: With only 19 studies (1 RCT and 18 Observational Studies) review of literature is unlikely to find a result. I know it is against your charge but epidemiologic analysis of data from the VA CDW is likely to provide superior information to your review of the literature. On the time of NPO to scope ESP, there were no conclusions possible from the literature. Epidemiologic analysis of CDW data provided	Thank you. In our Future Research section, we suggest the VA QUIP database as a potential data source that could provide answers to our clinical questions. If the database has preoperative data on DAPT use and indication in addition to perioperative DAPT management, then analyzing this would benefit from the considerable existing work done to develop risk adjusting models.

Comment #	Reviewer #	Comment	Author Response
		meaningful results that were vastly more informative than the no conclusion possible from literature review.	We included your suggestion to also consider patient data from the CDW as another potential data source for analysis.
15	2	Page 12: CABG and cases that utilize cardiopulmonary bypass are fundamentally different from all non-cardiac surgery and should not be included with analysis from non-cardiac surgery.	In our draft report we did not lump together CABG and non-CABG cases, except for the one publication which did so. To make it more clear that we kept these separate we revised the wording in the Executive Summary to discuss CABG surgery and noncardiac surgery separately. We also present our findings for cardiac surgery separately from noncardiac surgery in the Results section of the Evidence Report.
16	2	Page 13 Line 3 "less blood less" I think you mean "loss". This paragraph is not interpretable for a very simple reason. If you lump cardiac surgery with non-cardiac surgery with neurosurgery, you will get meaningless results. All cardiac surgical cases, that use extracorporeal circulatory support, damage the coagulation system. They must be analyzed separately from surgical cases that do not use bypass. Vascular surgery cases have a lower risk of hemorrhage and a greater benefit from DAPT. They must be analyzed separately. Cases where hemorrhage will be lethal or cause profound neurologic injury such as neurosurgery, must be analyzed separately. You can't lump all these things together and then talk about blood loss, it is non-sensical. Blood loss of 1-2 liters is standard in CABG, a problem in vascular cases but not unexpected, and lethal in intracranial surgery. They must be analyzed separately to have any meaning.	Thank you. Please see the above comment. This paragraph is now referring only to studies involving CABG. The following paragraph discusses results from the single combined cardiac and noncardiac surgery and the remaining studies involving only noncardiac surgery.
17	2	Page 13 Line 22. When we did the ESP for GI NPO, I said and I quote "There is nothing in the literature that will indicate the risk from aspiration pneumonia and the risk of misdiagnosis because the sample sizes are too	We appreciate your insight. Please see Comment #14 above. We included your suggestion to perform an epidemiologic analysis using CDW data in the Future Research section, although if VA-QUIP has the data it would be far easier to do so with its

Comment #	Reviewer #	Comment	Author Response
		small, you must do epidemiologic analysis of data from the CDW." The published literature can't answer these questions. You must recognize this fault prior to doing an ESP, and do epidemiologic analysis of CDW data which will likely give you insight. This is the third ESP I have seen (two for DAPT and one for GI NPO) with no result that likely would have a result if you changed your mission statement to do epidemiologic analysis of VA CDW data when the literature has no chance to answering the question.	standardized data collection and risk-adjusting models already created.
18	2	Page 13 Line 40 Future Research: Absolutely, this can and should be done. ESP with no chance of success are a waste of time.	Thank you. Please see above.
19	2	Page 20 Line 21. The Turkish study is a comparison of four approaches to managing emergency patients all of whom are on DAPT (TXA, TXA+Desmopressin, Desmopressin, Nothing). This will only tell you if TXA or Desmopressin reduce risk of bleeding in patients on DAPT. It won't tell you what the effect of taking DAPT is versus not. What does this RCT, the only RCT in your ESP have to do with the risk of DAPT? There is no control group off DAPT.	Thank you; while we initially included this study because it tested a perioperative management strategy to mitigate the effect of DAPT, upon further review, we agree that it is outside the scope of our key questions since it did not vary or alter the DAPT itself. Thus, we excluded the article with subsequent alterations made in the report text.
20	2	Page 22 Line 43. How much less blood loss. 250 ml less blood loss, in the face of an average of 1-2 liters, is interesting but not clinically significant. A liter difference would be clinically significant difference. You need to know the difference that was detected to make this paragraph contributory. My guess from the graph is the average of all the studies is 125 ml, which is something you can write a paper about but is clinically not significant in CABG surgery.	We added information about the quantity of blood loss from the relevant studies. The question of whether or not this is clinically significant is raised in the Discussion section.

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21	2	Page 23 Line 38 Transfusion differences are clinically significant results. 4 of 9 fewer patients needing transfusion is interesting but 5 of 9 with no difference is consistent with the guess of 125 ml average additional blood loss.	Agreed. Thank you.
22	2	Page 24 Line 37 The requirement for surgical re-exploration after CABG for bleeding increases perioperative risk. Avoiding re-exploration requirements is important. Can you conclude there is less need for re-exploration if DAPT is discontinued more than 2 days before surgery? That would be an important conclusion. Figure 3 shows one study concluded a 20% reduction in the need for re-exploration,1 out of 5 at 20% reduction, likely isn't meaningful.	The data are not conclusive as 2 of the 5 studies comparing DAP withdrawal strategies prior to surgery were not significant. However, 3 of the studies do show statistically significant differences in reoperation risk and there is an overall trend in all these studies favoring withdrawal >2 days. We believe that this is clinically meaningful but acknowledge the limitations of the data in future sections of the report.
23	2	Page 26 Figure 4. My guess is a large epidemiologic analysis of CDW data would show an increase in mortality from DAPT. In the McSPI dataset, there was a 10 fold increased risk in patients who were on coumadin within 7 days of CABG. There is likely some additional risk from DAPT but you need to do a large epidemiologic analysis of CDW data to show it.	Thank you. We included your suggestion to perform an epidemiologic analysis using CDW data in the Future Research section.
24	2	Page 27 Line 30 Some discussion of how long the DAPT was discontinued would help make this section more interpretable. I would exclude all ophthalmic cases. Most of these are intraocular lens which doesn't cut through any blood vessels. The chance of bleeding is zero. Adding IOL cases into general surgery just confuses the results. Is this a week of discontinuation or 2 days? When did they restart the DAPT?	This study reports the ophthalmic cases grouped with all the other surgeries, so it cannot be excluded from analysis. However, we adjusted the paragraph to more clearly explain the study's findings. Information was added about how long DAPT was held preop, surgery types in which antiplatelet therapy was continued vs held, and DAPT duration.
25	2	Page 27 Line 35 This may be the most important study so far. There are two effects here. The first is the mortality effect of delaying	Thank you for the comment. We agree that they may be measuring increased risk from two phenomenon: the surgical delay after hip fracture and the impact of

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		ORIF in hip fractures. Each day of delay has an effect on mortality. The second effect is the increased risk from holding DAPT. These two risks are combined to get the OR 7.91 at one week. There are two risks here that are hard to separate.	holding DAPT. Since these factors were dependent on one another, we agree that they are hard to separate and added text to acknowledge this limitation.
26	2	Page 27 Line 51 This is an important study as it contradicts Grzegorz L. Kaluza MD, PhD, Jane Joseph, Joseph R. Lee MD, Michael E. Raizner MD and Albert E. Raizner MD, Catastrophic outcomes of noncardiac surgery soon after coronary stenting Catastrophic outcomes of noncardiac surgery soon after coronary stenting FACC 2000 25:5 1288-1294. I am surprised that they were really able to discontinue clopidogrel for 5-7 days. These must not be cadaveric transplants because there is rarely a 5-7 preoperative warning on a cadaveric transplant. Were these donor related transplants? If not, the results should be looked at carefully to see how they got a 5-7 preoperative time to hold DAPT for a cadaveric transplant.	Thank you for this interesting observation. We think there are several potential explanations as to why the Dogan study included in our analysis seems to contradict the article by Grzegorz et al. All patients in this study underwent renal transplant from living donors. Importantly, the Grzegorz study was published in the early PCI era, when only BMS or first-generation DES were available. The Dogan study is a more contemporary analysis that includes only second-generation DES and newer BMS, which have shown to be protective of cardiac ischemic complications. Finally, the average time from stent placement to surgery in the Gzregorz study was 13 days compared to 3 months in the early DES discontinuation group and 1 month in the BMS group in the Dogan study.
27	2	Page 31 Line 6 We need a large epidemiologic study of the VA CDW data to answer this question. I said this after the 2016 ESP concluded with a similar limitation.	Thank you. We have added this suggestion to the Future Research section.
28	2	Page 31 Line 32 You have an extra period. "Bias. .Further"	This has been corrected, thank you.
29	2	Page 31 Line 55 There are a number of clinical questions we face every day. 1. Patient for CABG, with prior PCI, on DAPT, how long do you discontinue the DAPT? 2. Patient for vascular surgery, like a AAA, with prior PCI, on DAPT, how long do you discontinue DAPT? 3. Same vascular surgery patient for Fem Distal. 4. Patient for general surgery, prior PCI, on DAPT, for exploratory laparotomy. Can we give	Please see additional comments which include your suggestion to consider the CDW as a potential source for an epidemiologic analysis.

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		ASA? Do we continue the clopidogrel? What is risk of MACE? We need an analysis of the CDW data to see the answers to these questions, ESP won't give us the answer.	
30	2	Page 32 Line 20. I guarantee the data is in the VA CDW to answer this question.	Thank you for this suggestion. We include this as a possible avenue for future research.
31	3	Balanced, thoughtful, and clear evaluation of available literature and clearly stated limitations. Did any studies look at continuing one agent rather than holding both agents? There is increasing interest/use of P2Y12i monotherapy in practice. Understand using >/< 2 days timeframe for DAPT DC, but noted some studies looked at significantly longer DC periods (e.g., 7 days) which could be expected to have different outcomes than shorter timeframes. Should this be evalauted or mentioned as a limitation? Suggest recognizing/addressing the 2021 ACC/AHA/SCAI revasc guideline recs for holding APT around CABG surgery (the most common setting studied) and how those fit with your findings. Suggest recognizing potential for differences in the PK/PD profiles of individual P2Y12i and possible need for different hold guidance rather than generic "class" guidance - e.g., how was this issue evaluated in the literature and what are future research needs. Last, the renal transplant study would not be generalizable or extrapolated to other settings - should this be stated?	Thank you. The majority of the studies compared dual antiplatelet therapy with single antiplatelet therapy given that current guidelines recommend continuing aspirin through the perioperative period when possible. In our analysis we considered holding either or both ASA or a P2Y12 inhibitor as discontinuing or withholding DAPT. This was clarified in our Methods section. We appreciate your point about prolonged DAPT withholding duration influencing the aggregate results. We added this as a limitation of our analysis. We added a reference to the 2021 ACC/AHA/SCAI revascularization guidelines and compare these to our results in the Discussion section. We also included the limitation you mention in grouping P2Y12 inhibitors together despite differences in PK/PD profiles. The generalizability of all studies is open to question, as surgical protocols and post-operative care may differ among hospitals, even for procedures given the same name, like “cholecystectomy”. We don’t think we need to call out this one study in specific for generalizability.
32	3	p19-l42 - typo and suggested reword - "point estimate favored less blood loss"	Thank you; this has been reworded.
33	3	p55-L19 - 2019 Irie study - is ticlopidine correct or is it ticagrelor?	Yes, Ticlopidine is correct.

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34	5	page iii - line 27, add 'the' before Surgical Quality Improvement Program	This has been corrected, thank you.
35	5	page 10, line 43 and page 29 line 9 - unclear wording of #1 - perhaps change to "to have a very large sample" or change first part of sentence to "The attributes of such an observational study would include:"	Thank you. We changed the wording here.
36	5	Figure 1 - please explain "Exclude:all else" or just label as "other reasons'	Thank you, this has been changed to “other reasons”.
37	5	page 48, citation of Nardi is cut off, so unable to see what Group C was. Consider reformatting table.	This appears to be fixed in our current version.
38	6	The manuscript sets out to discuss Dual Antiplatelet Management in the Perioperative Period but does not mention relevant clinical trials (presented in the comment box above), contemporary recommendations made by professional guidelines, or manufacturers. Please consider adding the following pertinent information:	We have added where relevant any published studies meeting the inclusion criteria, and in the Discussion have now mentioned the various guidelines and manufacturers information.
39	6	When possible, interrupt therapy with ticagrelor for five days prior to surgery that has a major risk of bleeding. Brilinta. Prescribing information. AstraZeneca; 2022.	Thank you. This has been added to the Discussion section.
40	6	When possible, discontinue prasugrel at least 7 days prior to any surgery. Effient. Prescribing information. Eli Lilly and Company; 2020. Discontinue [clopidogrel] 5 days prior to elective surgery that has a major risk of bleeding. Plavix. Prescribing information. Sanofi-Aventis; 2022. Stopping aspirin 3 or more days prior to surgery has been investigated in the POISE-2 trial <Devereaux PJ, Mrkobrada M, Sessler DI, et al. Aspirin in patients undergoing noncardiac surgery. N Engl J Med. 2014;370(16):1494-1503.>	Thank you. This has been added to the Discussion section.

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41	6	CHEST guideline recommendations for P2y12 antagonists: Stop ticagrelor 3 to 5 days instead of 7 to 10 days before the surgery. Stop prasugrel 7 days instead of 7 to 10 days before the surgery. Stop clopidogrel 5 days instead of 7 to10 days before the surgery. <Douketis JD, Spyropoulos AC, Murad MH, et al. Perioperative Management of Antithrombotic Therapy: An American College of Chest Physicians Clinical Practice Guideline. Chest. 2022;162(5):e207-e243. doi:10.1016/j.chest.2022.07.025>	Thank you. This has been added to the Discussion section.
42	6	In patients receiving aspirin who are undergoing elective non-cardiac surgery, CHEST guidelines suggest aspirin continuation over aspirin interruption. In those who require aspirin interruption, CHEST guidelines suggest stopping ASA 7 or less days instead of 7 to 10 days before the surgery. <Douketis JD, Spyropoulos AC, Murad MH, et al. Perioperative Management of Antithrombotic Therapy: An American College of Chest Physicians Clinical Practice Guideline. Chest. 2022;162(5):e207-e243. doi:10.1016/j.chest.2022.07.025>	This is now cited in the Discussion.
43	6	DATA Sources page 13 lines 27-35: Other search term should include "Perioperative" Furthermore, search term should be Dual "antiplatelet" instead of "anti-platelet" as the former is widely recognized as the preferred spelling. For example, a PUBMED search using ((antiplatelet) AND (dual)) AND (perioperative) will yield significantly more results than if "antiplatelet" is replaced with "anti-platelet"	The spelling of “antiplatelet” is not an issue since in the search strategy both spellings are used, linked with an “OR”, meaning the search will identify either spelling. We added “peri-operative” and “perioperative” to our search and it only found 16 additional titles, none of which met eligibility criteria, and thus it is not a limitation of the original search to have not included these terms.

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44	6	Page 10; Lines 3-4 - please clarify sentence "The preponderance of point estimated favor less blood less with longer duration of suspension of DAPT therapy for at least 2 days." Did the authors intend to state "point estimates favor less blood loss"?	Yes, we meant to state “less blood loss.” This has been corrected.