

APPENDIX A. SEARCH STRATEGIES

MEDLINE

1	((("Chest Pain"[Mesh] OR "Myocardial Ischemia"[Mesh] OR "Acute Coronary Syndrome"[Mesh] OR "Myocardial Infarction"[Mesh] OR (acute coronary syndrome*[tiab]) OR (preinfarc*[tiab] AND Angina*[tiab]) OR (pre-infarc*[tiab] AND Angina*[tiab]) OR "Unstable angina"*[tiab] OR ((heart*[tiab] OR myocardi*[tiab] OR cardiac[tiab] OR coronary[tiab]) AND (preinfarc*[tiab] OR infarc*[tiab] OR attack*[tiab] OR arrest*[tiab] OR occlusion*[tiab] OR ischemia*[tiab] OR ischaemia[tiab]) OR occlusi*[tiab]) OR MI[tiab] OR ACS[tiab] OR STEMI[tiab] OR NSTEMI[tiab] OR NSTEMI[tiab] OR NSTEMI[tiab] OR AMI[tiab] OR UAP[tiab] OR OMI[tiab] OR ((acute[tiab] OR ischem*[tiab] OR ischaem*[tiab]) AND (coronar*[tiab] OR cardiac*[tiab] OR heart[tiab])) OR ((heart[tiab] OR myocardi*[tiab]) AND infarc*[tiab])))
2	((("troponin T"[Mesh] OR "troponin I"[Mesh] OR troponin[Mesh] OR "trop I"[tiab] OR "trop t"[tiab] OR "troponin I"[tiab] OR "troponin T"[tiab] OR accu-tni[tiab] OR accutni[tiab] OR ctni-hs[tiab] OR ctni-ultra[tiab] OR ctni[tiab] OR ctnihs[tiab] OR cntnt-hs[tiab] OR cntnt[tiab] OR cTnT[tiab] OR cntnths[tiab] OR hs-ctni[tiab] OR hs-cTnT[tiab] OR hs-tni[tiab] OR hs-TnT[tiab] OR hsctni[tiab] OR hscTnT[tiab] OR Hstni[tiab] OR hsTnT[tiab] OR tni[tiab] OR tnt-hs[tiab] OR tnt[tiab] OR tnths[tiab] OR tropI[tiab] OR troponin*[tiab] OR tropT[tiab] OR "Accelerated diagnostic protocol"* OR "HEART Pathway" OR "EDACS-ADP" OR "EDACS" OR ADP)))
3	((("Emergency Service, Hospital"[Mesh] OR emergency room* OR emergency department* OR ED OR ER OR "Triage"[Mesh] OR "Emergencies"[Mesh] OR "Emergency Responders"[Mesh] OR "Emergency Treatment"[Mesh] OR "Emergency Medicine"[Mesh] OR "Emergency Medical Technicians"[Mesh] OR "Emergency Medical Services"[Mesh] OR "Ambulances"[Mesh] OR "Hospital Rapid Response Team"[Mesh] OR triage OR emergenc* OR ambulance* OR EMT OR EMS OR "Cardiology Service, Hospital"[Mesh])))
5	#1 AND #2 AND #3
6	((("2008/01/01"[Date - Entry] : "3000"[Date - Entry])) OR (("2008/01/01"[Date - Publication] : "3000"[Date - Publication])) OR (("2008/01/01"[Date - Create] : "3000"[Date - Create])))
7	AND/5-6

EMBASE

1	Heart muscle ischemia/exp OR heart muscle ischemia
2	Myocardial ischemia
3	Acute coronary syndrome
4	Heart infarction
5	Myocardial infarction
6	Unstable angina pectoris
7	Unstable angina
8	(heart* OR myocardi* OR cardiac OR coronary) AND ((preinfarc* OR infarc* OR attachk* OR arrest*or) AND occlusion* OR ischemia* OR ischaemia* OR occlusi*)
9	mi OR acs OR stemi OR 'nste acs' OR nsteacs. OR nonstemi OR nstemi OR ami OR uap OR omi
10	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9
11	troponin i
12	troponin t
13	trop i OR trop t OR troponin i OR troponin t OR accu tni OR accutni OR ctni hs OR ctni ultra OR ctni OR ctnihs OR cntnt hs OR cntnt OR cntnths OR hs ctni OR hs tni OR hs tnt OR hsctni OR hsctnt

	OR hstni OR hstnt OR tni OR tnt hs OR tnt OR tnths OR tropi OR troponin* OR tropt OR accelerated diagnostic protocol* OR heart pathway OR edacs-adp OR edacs OR adp
14	#11 OR #12 OR #13
15	emergency ward
16	(Emergency AND room* OR emergency) AND department* OR ed OR er OR triage OR emergenc* OR emt OR ems
17	#15 OR #16
18	#10 AND #14 AND #17
19	#10 AND #14 AND #17 AND ([article/lim OR [article in press]/lim) AND [humans]/lim AND [2008-2022-04-15]/py

COCHRANE

1	MeSh descriptor: [Chest Pain] explode all trees
2	MeSh descriptor: [Myocardial Ischemia] explode all trees
3	MeSh descriptor: [Acute Coronary Syndrome] explode all trees
4	MeSh descriptor: [Myocardial Infarction] explode all trees
5	((hear* OR myocardi* OR cardiac OR coronary) AND (preinfarc* OR infarc* OR attack* OR arrest* OR ischemia* OR ischaemia* OR occlusi*))
6	#1 OR #2 OR #3 OR #4 OR #5
7	MeSh descriptor: [Troponin I] explode all trees
8	MeSh descriptor: [Troponin T] explode all trees
9	*trop I OR trop T OR troponin I OR troponin T OR accu-tni OR accutni OR ctni-hs OR ctni-ultra OR ctnihs OR cntn-hs OR cntn OR cTnT OR ctnths OR hs-ctni OR hs-cTnT OR hs-tni OR hs-TnT OR hsctni OR hscTnT OR Hstni OR hsTnT OR tni OR tnt-hs OR tnt OR tnths OR tropI OR troponin* OR tropT OR Accelerated diagnostic protocol* OR HEART Pathway OR EDACS-ADP OR EDACS OR ADP
10	#7 OR #8 OR #9
11	MeSh descriptor: [Emergency Medical Services] explode all trees
12	Triage OR emergenc* OR ambulance* OR EMT OR EMS
13	#11 OR #12
14	#6 AND #10 AND #13

APPENDIX B. EXCLUDED STUDIES

1. Agrawal AVS, Rupesh; Singh, Manbir. Validation of 0 -2 hour algorithm for rule in and rule out myocardial infarction based on highly sensitive troponin I assay. *Indian Heart Journal*. 2018;70:S27-S44. *Abstract, no PDF*.
2. Aloe R, Lippi G, Di Pietro M, et al. Improved efficiency and cost reduction in the emergency department by replacing contemporary sensitive with high-sensitivity cardiac troponin immunoassay. *Acta Biomed*. Dec 23 2019;90(4):614-620. doi:10.23750/abm.v90i4.8769. *No defined ADP*.
3. Aldous SJ, Richards AM, Cullen L, Than MP. Early dynamic change in high-sensitivity cardiac troponin T in the investigation of acute myocardial infarction. *Clin Chem*. Aug 2011;57(8):1154-60. doi:10.1373/clinchem.2010.161166. *No defined ADP*.
4. Aldous S, Pemberton C, Richards AM, Troughton R, Than M. High-sensitivity troponin T for early rule-out of myocardial infarction in recent onset chest pain. *Emerg Med J*. Oct 2012;29(10):805-10. doi:10.1136/emered-2011-200222. *No defined ADP*.
5. Allen BR, Christenson RH, Cohen SA, et al. Diagnostic Performance of High-Sensitivity Cardiac Troponin T Strategies and Clinical Variables in a Multisite US Cohort. *Circulation*. Apr 27 2021;143(17):1659-1672. doi:10.1161/circulationaha.120.049298. *Not prospective*.
6. Allen BR, Simpson GG, Zeinali I, et al. Incorporation of the HEART Score Into a Low-risk Chest Pain Pathway to Safely Decrease Admissions. *Crit Pathw Cardiol*. Dec 2018;17(4):184-190. doi:10.1097/hpc.000000000000155. *Not high-sensitivity Tn*.
7. Ambavane A, Lindahl B, Giannitsis E, et al. Economic evaluation of the one-hour rule-out and rule-in algorithm for acute myocardial infarction using the high-sensitivity cardiac troponin T assay in the emergency department. *PLoS One*. 2017;12(11):e0187662. doi:10.1371/journal.pone.0187662. *Not prospective*.
8. Ambavane A, Lindahl B, Giannitsis E, et al. Correction: Economic evaluation of the one-hour rule-out and rule-in algorithm for acute myocardial infarction using the high-sensitivity cardiac troponin T assay in the emergency department. *PLoS One*. 2018;13(1):e0191348. doi:10.1371/journal.pone.0191348. *Not published/peer reviewed*.
9. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. Dec 23 2014;130(25):2354-94. doi:10.1161/cir.000000000000133. *No defined ADP*.
10. Anand A, Shah ASV, Strachan FE, et al. P3593 Improving the performance of high-sensitivity cardiac troponin for the diagnosis of myocardial infarction. *European Heart Journal*. 2019;40(Supplement_1)doi:10.1093/eurheartj/ehz745.0453. *No defined ADP*.
11. Andersen CF, Bang C, Lauridsen KG, et al. Single troponin measurement to rule-out acute myocardial infarction in early presenters. *Int J Cardiol*. Oct 15 2021;341:15-21. doi:10.1016/j.ijcard.2021.08.005. *Not prospective*.
12. Andruchow JE, Boyne T, Innes G, et al. Low High-Sensitivity Troponin Thresholds Identify Low-Risk Patients With Chest Pain Unlikely to Benefit From Further Risk Stratification. *CJC Open*. Nov 2019;1(6):289-296. doi:10.1016/j.cjco.2019.08.002. *Not prospective*.
13. Andruchow JE, Boyne T, Seiden-Long I, et al. Prospective comparative evaluation of the European Society of Cardiology (ESC) 1-hour and a 2-hour rapid diagnostic algorithm

- for myocardial infarction using high-sensitivity troponin-T. *Cjem*. Sep 2020;22(5):712-720. doi:10.1017/cem.2020.349. *Not prospective*.
14. Arslan M, Dedic A, Boersma E, Dubois EA. Serial high-sensitivity cardiac troponin T measurements to rule out acute myocardial infarction and a single high baseline measurement for swift rule-in: A systematic review and meta-analysis. *Eur Heart J Acute Cardiovasc Care*. Feb 2020;9(1):14-22. doi:10.1177/2048872618819421. *No defined ADP*.
 15. Arslan M, Schaap J, Rood PPM, et al. HEART score improves efficiency of coronary computed tomography angiography in patients suspected of acute coronary syndrome in the emergency department. *European Heart Journal Acute Cardiovascular Care*. 2020;9(1):23-29. doi:10.1177/2048872619882424. *Secondary analysis study*.
 16. Astley CM, Beltrame JF, Zeitz C, et al. Study design of embracing high-sensitivity troponin effectively: the value of more information: a randomized comparison. *Contemp Clin Trials*. Nov 2014;39(2):183-90. doi:10.1016/j.cct.2014.08.012. *This is a study design with no results*.
 17. Aurora L, McCord J, Nowak R, et al. Prognostic Utility of a Modified HEART Score When Different Troponin Cut Points Are Used. *Crit Pathw Cardiol*. Sep 1 2021;20(3):134-139. doi:10.1097/hpc.000000000000262. *Not prospective*.
 18. Avigni N, Ippoliti M, Muccinelli M, et al. Chest pain in the emergency department: benefits of a management model modified from the ANMCO-SIMEU recommendations. *Giornale Italiano di Cardiologia (2006)*. 2011;12(5):365-373. *No PDF found*.
 19. Badertscher P, Boeddinghaus J, Nestelberger T, et al. Effect of Acute Coronary Syndrome Probability on Diagnostic and Prognostic Performance of High-Sensitivity Cardiac Troponin. *Clin Chem*. Mar 2018;64(3):515-525. doi:10.1373/clinchem.2017.279513. *No defined ADP*.
 20. Badertscher P, Boeddinghaus J, Twerenbold R, et al. Direct Comparison of the 0/1h and 0/3h Algorithms for Early Rule-Out of Acute Myocardial Infarction. *Circulation*. Jun 5 2018;137(23):2536-2538. doi:10.1161/circulationaha.118.034260. *Not prospective*.
 21. Bahrman P, Christ M, Bahrman A, et al. A 3-hour diagnostic algorithm for non-ST-elevation myocardial infarction using high-sensitivity cardiac troponin T in unselected older patients presenting to the emergency department. *J Am Med Dir Assoc*. Jun 2013;14(6):409-16. doi:10.1016/j.jamda.2012.12.005. *No defined ADP*.
 22. Bandstein N, Ljung R, Johansson M, Holzmann MJ. Undetectable high-sensitivity cardiac troponin T level in the emergency department and risk of myocardial infarction. *J Am Coll Cardiol*. Jun 17 2014;63(23):2569-2578. doi:10.1016/j.jacc.2014.03.017. *No defined ADP*.
 23. Bang C, Andersen CF, Lauridsen KG, et al. Rapid Rule-Out of Myocardial Infarction After 30 Minutes as an Alternative to 1 Hour: The RACING-MI Cohort Study. *Ann Emerg Med*. Feb 2022;79(2):102-112. doi:10.1016/j.annemergmed.2021.08.024. *Not prospective*.
 24. Bang C, Hansen C, Lauridsen KG, et al. Rapid use of high-sensitive cardiac troponin I for ruling-in and ruling-out of acute myocardial infarction (RACING-MI): study protocol. *Open Heart*. 2019;6(1):e000995. doi:10.1136/openhrt-2018-000995. *Protocol itself has no results, and the results were published in a different study (Bang-2022-34969529)*.
 25. Bank IE, Dekker MS, Hoes AW, et al. Suspected acute coronary syndrome in the emergency room: Limited added value of heart type fatty acid binding protein point of care or ELISA tests: The FAME-ER (Fatty Acid binding protein in Myocardial infarction

- Evaluation in the Emergency Room) study. *Eur Heart J Acute Cardiovasc Care*. Aug 2016;5(4):364-74. doi:10.1177/2048872615584077. *Not prospective*.
26. Baugh CW, Scirica BM, Januzzi JL, et al. Implementation of an Emergency Department High-Sensitivity Troponin Chest Pain Pathway in the United States. *Crit Pathw Cardiol*. Mar 2019;18(1):1-4. doi:10.1097/hpc.000000000000164. *Neither primary study nor SR*.
 27. Beaune G, Yayehd K, Rocher T, et al. [Evaluation of rule out strategy for patients with non-ST-elevation acute coronary syndrome with single measurement of high-sensitivity cardiac troponin I from one sample tested between 3 and 6 hours after chest pain onset]. *Ann Cardiol Angeiol (Paris)*. Nov 2021;70(5):270-274. Évaluation d'une stratégie d'exclusion d'un syndrome coronarien aigu non ST+ basé sur une unique mesure de troponine de haute sensibilité à partir d'un prélèvement effectué entre 3 et 6 heures après le début de la douleur. doi:10.1016/j.ancard.2021.07.006. *Only r/out MI (others excluded)*.
 28. Bellini C, Cinci F, Bova G, et al. Methodology to Evaluate Clinical Impact of 0/3 Hour High-Sensitivity Cardiac Troponin T Protocol on Managing Acute Coronary Syndrome in Daily Emergency Department Practice. *Lab Med*. Sep 1 2021;52(5):452-459. doi:10.1093/labmed/lmaa118. *No defined ADP*.
 29. Bevins NJ, Chae H, Hubbard JA, et al. Emergency Department Management of Chest Pain With a High-Sensitivity Troponin-Enabled 0/1-Hour Rule-Out Algorithm. *Am J Clin Pathol*. May 4 2022;157(5):774-780. doi:10.1093/ajcp/aqab192. *No defined ADP*.
 30. Bhatti Y, Stevenson A, Weerasuriya S, Khan S. Reducing avoidable chest pain admissions and implementing high-sensitivity troponin testing. *BMJ Open Qual*. 2019;8(4):e000629. doi:10.1136/bmjoq-2019-000629. *ADP cannot be replicated*.
 31. Biener M, Mueller M, Vafaie M, et al. Comparison of a 3-hour versus a 6-hour sampling-protocol using high-sensitivity cardiac troponin T for rule-out and rule-in of non-STEMI in an unselected emergency department population. *Int J Cardiol*. Aug 20 2013;167(4):1134-40. doi:10.1016/j.ijcard.2012.09.122. *Not prospective*.
 32. Björkelund A, Ohlsson M, Lundager Forberg J, et al. Machine learning compared with rule-in/rule-out algorithms and logistic regression to predict acute myocardial infarction based on troponin T concentrations. *J Am Coll Emerg Physicians Open*. Apr 2021;2(2):e12363. doi:10.1002/emp2.12363. *Retrospective cross-sectional with no follow-up and ML*.
 33. Bjurman C, Zywczyk M, Zangana S, et al. Patients discharged with elevated baseline high-sensitive cardiac troponin T from the emergency department. *Biomarkers*. Jul 2021;26(5):410-416. doi:10.1080/1354750x.2021.1917662. *No outcomes within 6 weeks reported*.
 34. Body R, Burrows G, Carley S, Lewis PS. The Manchester Acute Coronary Syndromes (MACS) decision rule: validation with a new automated assay for heart-type fatty acid binding protein. *Emerg Med J*. Oct 2015;32(10):769-74. doi:10.1136/emered-2014-204235. *Not high-sensitivity Tn*.
 35. Body R, Carley S, McDowell G, et al. The Manchester Acute Coronary Syndromes (MACS) decision rule for suspected cardiac chest pain: derivation and external validation. *Heart*. Sep 15 2014;100(18):1462-8. doi:10.1136/heartjnl-2014-305564. *Not prospective*.
 36. Body R, Carlton E, Sperrin M, et al. Troponin-only Manchester Acute Coronary Syndromes (T-MACS) decision aid: single biomarker re-derivation and external validation in three cohorts. *Emerg Med J*. Jun 2017;34(6):349-356. doi:10.1136/emered-2016-205983. *Not prospective*.

37. Body R, Morris N, Collinson P. Single test rule-out of acute myocardial infarction using the limit of detection of a new high-sensitivity troponin I assay. *Clin Biochem*. Apr 2020;78:4-9. doi:10.1016/j.clinbiochem.2020.02.014. *Not prospective*.
38. Body R, Morris N, Reynard C, Collinson PO. Comparison of four decision aids for the early diagnosis of acute coronary syndromes in the emergency department. *Emerg Med J*. Jan 2020;37(1):8-13. doi:10.1136/emered-2019-208898. *No defined ADP*.
39. Body R, Mueller C, Giannitsis E, et al. The Use of Very Low Concentrations of High-sensitivity Troponin T to Rule Out Acute Myocardial Infarction Using a Single Blood Test. *Acad Emerg Med*. Sep 2016;23(9):1004-13. doi:10.1111/acem.13012. *No defined ADP*.
40. Body R, Twerenbold R, Austin C, et al. Diagnostic Accuracy of a High-Sensitivity Cardiac Troponin Assay with a Single Serum Test in the Emergency Department. *Clin Chem*. Aug 2019;65(8):1006-1014. doi:10.1373/clinchem.2018.294272. *Not prospective*.
41. Boeddinghaus J, Lopez-Ayala P, Nestelberger T, et al. Prospective Validation of the ESC 0/1h-Algorithm Using High-Sensitivity Cardiac Troponin I. *Am J Cardiol*. Nov 1 2021;158:152-153. doi:10.1016/j.amjcard.2021.08.007. *Not prospective*.
42. Boeddinghaus J, Nestelberger T, Badertscher P, et al. Predicting Acute Myocardial Infarction with a Single Blood Draw. *Clin Chem*. Mar 2019;65(3):437-450. doi:10.1373/clinchem.2018.294124. *No defined ADP*.
43. Boeddinghaus J, Nestelberger T, Koechlin L, et al. Early Diagnosis of Myocardial Infarction With Point-of-Care High-Sensitivity Cardiac Troponin I. *J Am Coll Cardiol*. Mar 17 2020;75(10):1111-1124. doi:10.1016/j.jacc.2019.12.065. *Not prospective*.
44. Boeddinghaus J, Nestelberger T, Twerenbold R, et al. High-Sensitivity Cardiac Troponin I Assay for Early Diagnosis of Acute Myocardial Infarction. *Clin Chem*. Jul 2019;65(7):893-904. doi:10.1373/clinchem.2018.300061. *Not prospective*.
45. Boeddinghaus J, Nestelberger T, Twerenbold R, et al. Impact of age on the performance of the ESC 0/1h-algorithms for early diagnosis of myocardial infarction. *Eur Heart J*. Nov 7 2018;39(42):3780-3794. doi:10.1093/eurheartj/ehy514. *Not prospective*.
46. Boeddinghaus J, Nestelberger T, Twerenbold R, et al. Direct Comparison of 4 Very Early Rule-Out Strategies for Acute Myocardial Infarction Using High-Sensitivity Cardiac Troponin I. *Circulation*. Apr 25 2017;135(17):1597-1611. doi:10.1161/circulationaha.116.025661. *Retrospective applied cutoffs to compare 4 strategies*.
47. Boeddinghaus J, Reichlin T, Cullen L, et al. Two-Hour Algorithm for Triage toward Rule-Out and Rule-In of Acute Myocardial Infarction by Use of High-Sensitivity Cardiac Troponin I. *Clin Chem*. Mar 2016;62(3):494-504. doi:10.1373/clinchem.2015.249508. *Not prospective*.
48. Boeddinghaus J, Twerenbold R, Nestelberger T, et al. Clinical Validation of a Novel High-Sensitivity Cardiac Troponin I Assay for Early Diagnosis of Acute Myocardial Infarction. *Clin Chem*. Sep 2018;64(9):1347-1360. doi:10.1373/clinchem.2018.286906. *Not prospective*.
49. Boeddinghaus J, Twerenbold R, Nestelberger T, et al. Clinical Use of a New High-Sensitivity Cardiac Troponin I Assay in Patients with Suspected Myocardial Infarction. *Clin Chem*. Nov 2019;65(11):1426-1436. doi:10.1373/clinchem.2019.304725. *Validating hs-cTnI-VITROS*.
50. Bohyn E, Dubie E, Lebrun C, et al. Expeditious exclusion of acute coronary syndrome diagnosis by combined measurements of copeptin, high-sensitivity troponin, and GRACE

- score. *Am J Emerg Med*. Apr 2014;32(4):293-6. doi:10.1016/j.ajem.2013.11.043. *Not prospective*.
51. Borna C, Frostred KL, Ekelund U. Predictive role of high sensitivity troponin T within four hours from presentation of acute coronary syndrome in elderly patients. *BMC Emerg Med*. Jan 4 2016;16:1. doi:10.1186/s12873-015-0064-z. *Retrospective applied cutoffs to compare 4 strategies*.
 52. Borna C, Kollberg K, Larsson D, Mokhtari A, Ekelund U. The objective CORE score allows early rule out in acute chest pain patients. *Scand Cardiovasc J*. Dec 2018;52(6):308-314. doi:10.1080/14017431.2018.1546891. *Retrospective applied cutoffs to compare 4 strategies*.
 53. Boyle RSJ, Body R. The Diagnostic Accuracy of the Emergency Department Assessment of Chest Pain (EDACS) Score: A Systematic Review and Meta-analysis. *Ann Emerg Med*. Apr 2021;77(4):433-441. doi:10.1016/j.annemergmed.2020.10.020. *SR, not primary study*.
 54. Bozdereli Berikol G, Aydın H, Doğan H. Early discharging patients with chest pain using EDACS-ADP and COMPASS-MI risk predictors. *Heart Vessels*. Feb 8 2022:1-10. doi:10.1007/s00380-022-02036-9. *Not prospective*.
 55. Braga F, Dolci A, Cavallero A, Ghezzi A, Infusino I, Milano M, Rubino M, Marenzi G, Panteghini M. Evaluation of the sensitivity of two highly sensitive troponin assays for early detection of non ST-elevation myocardial infarction (NSTEMI). *Biochimica Clinica*. 35(3):186-189. *Not English*.
 56. Brophy J. In adults with chest pain, a troponin limit of detection strategy did not increase early discharge rate. *Ann Intern Med*. Oct 20 2020;173(8):Jc45. doi:10.7326/acpj202010200-045. *Neither primary study nor SR*.
 57. Buccelletti F, Galiuto L, Marsiliani D, et al. Comparison of diagnostic accuracy between three different rules of interpreting high sensitivity troponin T results. *Intern Emerg Med*. Aug 2012;7(4):365-70. doi:10.1007/s11739-012-0787-8. *Not prospective*.
 58. Bularga A, Lee KK, Stewart S, et al. High-Sensitivity Troponin and the Application of Risk Stratification Thresholds in Patients With Suspected Acute Coronary Syndrome. *Circulation*. Nov 5 2019;140(19):1557-1568. doi:10.1161/circulationaha.119.042866. *Not prospective*.
 59. Burgio MA, Marino G, Di Maria D. Troponin cTnT-hs: a matter of gender and age? Evaluation of differentiated cut-offs by gender and age in an Emergency Department population. *La Rivista Italiana della Medicina di Laboratorio - Italian Journal of Laboratory Medicine*. 2018/03/01 2018;14(1):41-49. doi:10.1007/s13631-018-0184-z. *Not Prospective*.
 60. Burgos LM, Trivi M, Costabel JP. Performance of the European Society of Cardiology 0/1-hour algorithm in the diagnosis of myocardial infarction with high-sensitivity cardiac troponin: Systematic review and meta-analysis. *Eur Heart J Acute Cardiovasc Care*. Jun 29 2020;doi:10.1177/2048872620935399. *Systematic Review*.
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 62. CADTH Optimal Use Reports. *High-Sensitivity Cardiac Troponin for the Rapid Diagnosis of Acute Coronary Syndrome in the Emergency Department: A Clinical and Cost-Effectiveness Evaluation*. Canadian Agency for Drugs and Technologies in Health. Copyright © 2013 Canadian Agency for Drugs and Technologies in Health.; 2013. *Systematic Review*.

63. Cappellini F, Falbo R, Saltafossi D, et al. Development of an algorithm for ruling-out non-ST elevation myocardial infarction in the emergency department using high sensitivity troponin T assay. *Clin Chim Acta*. Aug 2019;495:1-7. doi:10.1016/j.cca.2019.03.1625. *Not prospective*.
64. Carlton E, Body R, Greaves K. External Validation of the Manchester Acute Coronary Syndromes Decision Rule. *Acad Emerg Med*. Feb 2016;23(2):136-43. doi:10.1111/acem.12860. *Not prospective*.
65. Carlton E, Campbell S, Ingram J, et al. Randomised controlled trial of the Limit of Detection of Troponin and ECG Discharge (LoDED) strategy versus usual care in adult patients with chest pain attending the emergency department: study protocol. *BMJ Open*. Oct 2 2018;8(10):e025339. doi:10.1136/bmjopen-2018-025339. *No data were included in the main paper*.
66. Carlton EW, Cullen L, Than M, Gamble J, Khattab A, Greaves K. A novel diagnostic protocol to identify patients suitable for discharge after a single high-sensitivity troponin. *Heart*. Jul 2015;101(13):1041-6. doi:10.1136/heartjnl-2014-307288. *Not prospective*.
67. Carlton EW, Ingram J, Taylor H, et al. Limit of detection of troponin discharge strategy versus usual care: randomised controlled trial. *Heart*. Oct 2020;106(20):1586-1594. doi:10.1136/heartjnl-2020-316692. *No defined ADP*.
68. Carlton EW, Khattab A, Greaves K. Identifying Patients Suitable for Discharge After a Single-Presentation High-Sensitivity Troponin Result: A Comparison of Five Established Risk Scores and Two High-Sensitivity Assays. *Ann Emerg Med*. Dec 2015;66(6):635-645.e1. doi:10.1016/j.annemergmed.2015.07.006. *Not prospective*.
69. Carlton EW, Khattab A, Greaves K. Beyond triage: the diagnostic accuracy of emergency department nursing staff risk assessment in patients with suspected acute coronary syndromes. *Emerg Med J*. Feb 2016;33(2):99-104. doi:10.1136/emered-2015-204780. *Not prospective*.
70. Carlton EW, Pickering JW, Greenslade J, et al. Assessment of the 2016 National Institute for Health and Care Excellence high-sensitivity troponin rule-out strategy. *Heart*. Apr 2018;104(8):665-672. doi:10.1136/heartjnl-2017-311983. *Not prospective*.
71. Chacón-Díaz M, Salinas J, Doig R. Stratification of thoracic pain with modified HEART score and its relationship to short term cardiovascular events. *Archivos de cardiología de México*. 2018;88(5):333-338. *Unclear how modified HEART used by physician in ED to stratify patients. Not English language*.
72. Chapman AR, Adamson PD, Shah ASV, et al. High-Sensitivity Cardiac Troponin and the Universal Definition of Myocardial Infarction. *Circulation*. Jan 21 2020;141(3):161-171. doi:10.1161/circulationaha.119.042960. *No defined ADP*.
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APPENDIX C. CRITERIA USED IN QUALITY ASSESSMENT

Question	Yes	No	Unclear
1. Design			
a. Randomized control trial			
b. Nonrandomized comparison of interventions			
c. Single group			
2. Was the article free of discrepancies (eg, between text and tables)? Add note if No (High concern)?			
3. Were patient eligibility criteria sufficiently clear? Add note if No (High concern).			
4. Were the ADP (and comparator) sufficiently clear? Add note if No (High concern)			
5. Were outcomes adequately defined without problem? Add note if No (High concern). Not every outcome requires an explicit definition (eg, duration of ED stay).			
6. Was the setting sufficiently clearly defined? (eg,, do we know the hospital (and ED) type?) Add note if No (High concern).			
7. Were there missing results data for ANY patients for outcomes that occurred in ED or hospital? Were there missing results data for >20% of patients (or imbalance between study groups) for outcomes that occurred after ED/hospital discharge? Add Note if Yes			
8. Outcome assessment			
a. No (or inadequate) description of how final determination of MI was diagnosed [Unclear RoB]			
b. Independent or blind adjudication of MI for each patient by reference to secure medical records [Low RoB]			
c. Record linkage (eg identified through ICD codes on database records) [Moderate RoB]			
d. Self report (by patient or family) with no reference to original structured injury data or imaging [High RoB]			
9. If RCT, was there inadequate randomization method or allocation concealment? Whether randomization was done at the level of the ED or the patient, answer No (low RoB), unless there’s an obvious flaw.			
10. If observational study, eligible patients having ADP were all selected or a random selection was selected. No concerns about biased selection of ADP patients. Add note if No (high RoB)			
11. If observational study, comparator group (or ED) was sufficiently similar (and selected patients were all included or a random sample were included). Add note if No (high RoB)			
12. If observational study, Adjustment for confounders.			
a. Crude analysis (unadjusted comparison between ADP and no ADP) [High RoB]			
b. Regression adjustment or patient-matching (accounting for at least age, sex, and symptom duration OR a risk score) [Low RoB]			
c. Regression adjustment or patient-matching (not accounting at least one of for age, sex, symptom duration, or risk score) [Moderate RoB]			
d. Propensity score analysis (or equivalent) [Low RoB]			

APPENDIX D. QUALITY RATINGS FOR ALL ELIGIBLE STUDIES

Appendix Table D-1. Quality Rating for Comparative Studies

Author, Year, PMID	Free of Discrepancies	Eligibility Clear	ADP Clear	Outcomes Adequately Defined	Setting Clearly Defined	Missing Results	Outcome Assessment Blind / Independent	RCT		Observational study			Effect on Clinical Measures Overall	Effect on Health Service Use Measures Overall
								Adequate Randomization and Allocation Concealment	Patients Selected at Random	Comparator Group Similar	Adjustment for Confounders			
<i>RCT</i>														
Anand 2021 33752439 RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low RoB)	Yes (low RoB)	Yes (low RoB)					Low RoB (RCT)	Low RoB (RCT)
Than 2016 26947800 RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (high RoB)	Yes (low RoB)	Yes (low RoB)					Low RoB (RCT)	Low RoB (RCT)
<i>NRCS</i>														
Barnes 2021 33436490 NRCS	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low RoB)	No or inadequate description (unclear RoB)		Yes (low RoB)	Yes (low RoB)	Yes regression adjustment (low RoB)		Medium RoB (NRCS)	Low RoB (NRCS)
Hyams 2018 29478861 NRCS	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low RoB)	No (moderate RoB)		Yes (low RoB)	Yes (low RoB)	Yes regression adjustment (low RoB)		Medium RoB (NRCS)	Low RoB (NRCS)
Sandeman 2021 34824100 NRCS	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low RoB)	Record linkage (moderate RoB)		Yes (low RoB)	Yes (low RoB)	Yes regression adjustment (low RoB)		Medium RoB (NRCS)	Low RoB (NRCS)
Stoyanov 2020 31298551 NRCS	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low RoB)	Yes (low RoB)		Yes (low RoB)	No (high RoB)	Yes regression adjustment (low RoB)		Medium RoB (NRCS)	Low RoB (NRCS)
Than 2021 33753972 NRCS	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low RoB)	No or inadequate description (unclear RoB)		Yes (low RoB)	No or inadequate description (unclear RoB)	Crude analysis (high RoB)		High RoB (NRCS)	High RoB (NRCS)

Appendix Table D-2. Quality Rating for Single Group Studies

Author, Year, PMID	Free of Discrepancies	Eligibility Clear	ADP Clear	Outcomes Adequately Defined	Setting Clearly Defined	Missing Results	Outcome Assessment Blind / Independent	RCT	Observational study			Measurement of Clinical Measures Overall	Measurement of Health Service Use Measures Overall	
								Adequate Randomization and Allocation Concealment	Patients Selected at Random	Comparator Group Similar	Adjustment for Confounders			
Single Group														
Chew 2019 31478763 Lambrakis 2021 33998255 RCT (analyzed as single group)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low RoB)	Yes (low RoB)			Yes (low RoB)			Low RoB (single)	Low RoB (single)
Conde 2013 23810070 NRCS (analyzed as single group)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low RoB)	No or inadequate description (unclear RoB)			Yes (low RoB)			Medium RoB (single)	Low RoB (single)
Costable 2014 NA Single group	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low RoB)	No or inadequate description (unclear RoB)			Yes (low RoB)			Medium RoB (single)	Low RoB (single)
Crowder 2015 26387473 NRCS (analyzed as single group)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low RoB)	No or inadequate description (unclear RoB)			Yes (low RoB)			Low RoB (single)	Low RoB (single)
Ford 2021 33662739 NRCS (analyzed as single group)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low RoB)	Record linkage (moderate RoB)			Yes (low RoB)			Medium RoB (single)	Low RoB (single)
Ljung 2019 30661856 NRCS (analyzed as single group)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low RoB)	Yes (low RoB)			Yes (low RoB)			Low RoB (single)	Low RoB (single)

Author, Year, PMID	Free of Discrepancies	Eligibility Clear	ADP Clear	Outcomes Adequately Defined	Setting Clearly Defined	Missing Results	Outcome Assessment Blind / Independent	Observational study			Measurement of Clinical Measures Overall	Measurement of Health Service Use Measures Overall	
								RCT	Adequate Randomization and Allocation Concealment	Patients Selected at Random			Comparator Group Similar
Suh 2022 35571147 NRCS (analyzed as single group)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (Low concern)	No (low RoB)	Yes (low RoB)			Yes (low RoB)		Low RoB (single)	Low RoB (single)
Sweeney 2020 32104767 NRCS (analyzed as single group)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low RoB)	No or inadequate description (unclear RoB)			Yes (low RoB)		n/a	Low RoB (single)
Twerenbold 2019 31345421 Single group	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low RoB)	Yes (low RoB)			Yes (low RoB)		Low RoB (single)	Low RoB (single)
Vigen 2020 32320036 NRCS (analyzed as single group)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low RoB)	Record linkage (Moderate RoB)			Yes (low RoB)		Medium RoB (single)	Medium RoB (single)

APPENDIX E. PEER REVIEW DISPOSITION

Comment #	Reviewer #	Comment	Author Response
<i>Are the objectives, scope, and methods for this review clearly described?</i>			
1	1	Yes	Thank you.
2	2	Yes	Thank you.
3	3	Yes	Thank you.
4	5	Yes	Thank you.
5	6	Yes	Thank you.
6	11	Yes	Thank you.
<i>Is there any indication of bias in our synthesis of the evidence?</i>			
7	1	No	Thank you.
8	2	No	Thank you.
9	3	No	Thank you.
10	5	No	Thank you.
11	6	No	Thank you.
12	11	No	Thank you.
<i>Are there any published or unpublished studies that we may have overlooked?</i>			
13	1	Yes - references to consider are included in comments	Thank you. Please see our response to Comment #19.
14	2	No	Thank you.
15	3	No	Thank you.
16	5	No	Thank you.
17	6	No	Thank you.
18	11	No	Thank you.
<i>Additional suggestions or comments can be provided below.</i>			
19	1	This report from the ESP seeks to summarize current available knowledge on the topic of using high-sensitivity troponin (HSTN) assays in combination with accelerated diagnostic protocols. A variety of important clinical	Thank you.

Comment #	Reviewer #	Comment	Author Response
		<p>comparisons are made with appropriate notation on the confidence of each comparison. The implications of adopting the findings to clinical practices could result in fewer hospital admissions without any appreciable increase in adverse cardiovascular events.</p> <p>The executive summary provides concise, understandable statements of key findings that should be easy for clinicians in the field to understand and adopt.</p> <p>The Key Questions are well reasoned and applicable to clinical care in the ED.</p> <p>The methods are thoroughly described and readily reproducible. Inclusion/exclusion criteria are appropriate for the intended analysis. ROBINS-I, PROSPERO, and appropriate online software options were applied. Studies are organized in a thoughtful manner based on the clinical importance of the reported outcomes.</p> <p>The tables supplement the text by providing greater detail in a format that is digestible to the reader, the tables also help demonstrate the heterogeneity of the literature.</p> <p>The limitations section adequately reflects the fact that most of the work on hstn, ADPs, and implementation has been done internationally and very little in the VA. As noted, the international work, often done in countries with integrated health care systems, may actually have good overlap with the VA due to similar infrastructures.</p> <p>The authors identify one of the more important gaps in the literature as being the documentation of best practices for implementation. The authors express optimism in what the widespread adoption of HSTN/ADP could mean for the VA, but acknowledge that local practices groups are often difficult to convince into a change in practice.</p>	

Comment #	Reviewer #	Comment	Author Response
		<p>If the authors wish to expand on the discussion about implementation, some references to consider are (PMIDs): 36328155, 35604774, 34224384. And the following description of implementation in a VAMC: https://vpjournal.net/article/view/3867</p>	<p>Thank you. The Discussion now comments on the potential implementation challenges associated with hs-cTn in the US and VA. Per the suggested references, we highlight the experience of one large VA’s transition to hs-cTn.</p>
20	2	<p>Thorough</p>	<p>Thank you.</p>
21	3	<p>I appreciate the authors’ thoroughness and skill in navigating a challenging set of evidence on an important topic that is highly relevant to an emergency department clinical scenario that is common, costly, and will benefit from this synthesis. I think the manuscript could be improved in a few areas, primarily around the framing of some of the discussion points.</p> <p>Major</p> <ul style="list-style-type: none"> - Title: Need to include some reference to “emergency department” in the title given the focus of the literature review was restricted to that care setting. - Discussion: Generally agree with statement that given the state of available evidence regarding ADPs that individual EDs should have freedom to create their own approach (page 5, line 8; page 38, line 9). However, I think it is important to caveat that this should still be based on the available evidence. The way this is currently worded, it implies that there are no limits, when, in fact, it should be about adopting and adapting what is supported by the evidence (risk tools, troponin timing, etc) to their local requirements. I think this should be the overall message and main take-home points from the evidence review: (1) importance of standardizing practice to avoid overuse of health services and testing; but, (2) no clear and obvious best in choice from the evidence; with (3) support for a variety of approaches; therefore, (4) importance of factoring in local structural needs and preferences in adopting a tailored but still standardized approach. 	<p>Thank you.</p> <p>We revised the title to reference the Emergency Department.</p> <p>We agree that EDs should implement evidence-based ADPs, and we do not want to give the impression that there are no limits. We revised the Discussion and Conclusion to note the importance of adopting evidence-based interventions and EDs may need to tailor an evidence-based ADP to fit within their local context.</p> <p>We also revised the Discussion and Conclusions to highlight the helpful key messages proposed by the reviewer.</p>

Comment #	Reviewer #	Comment	Author Response
		<p>- Discussion: Really liked the last paragraph under “Implications for VA Policy” (page 6, lines 6-16). These are excellent points and describes many of the features of an integrated health system that could be leveraged and are ripe for adopting and standardizing into routine practice. This approach seems like a natural and obvious next step in implementing this evidence synthesis. Recognize the focus of this review was not on implementation, but still wondering if there is a way to elevate this point within the manuscript?—could it even go in the Executive Summary?</p>	<p>We revised the Discussion to provide additional context on potential implementation challenges (see response to Comment 19, Reviewer 1). The Discussion now highlights the experience of one large VA during their transition to hs-cTn. We also revised the Executive Summary to elevate the importance of implementation.</p>
		<p>Minor - Introduction: In general, probably better to use a more general term than “ED physicians” when referencing providers who may be drawing on this evidence for incorporation in ED care (page 2, line 18). For example, there are increasingly advance practice providers (PAs, NPs) being used in this role. Options could include “ED provider” or “ED clinicians”—I tend to lean toward the latter in my work.</p>	<p>Thank you. We revised the text to be more inclusive in our definition of individuals who provide care in an ED setting.</p>
		<p>- Results: When introducing ADPs, I think worth referencing the table on clinical risk tools (Appendix C, page 93) that summarizes those evaluated in this evidence review (page 3, lines 12). Given ADPs are the major focus of this review, readers will quickly want to understand which chest pain risk scores (beyond just the abbreviations) were being evaluated and the references for these.</p>	<p>The text referenced by the reviewer is in the Executive Summary. Per ESP style, we do reference appendices in the Executive Summary.</p>
		<p>- Discussion: “administers” should be “administrators” (page 5, line 6)</p>	<p>Thank you.</p>
		<p>- Discussion: Definitely a minor point, but I don’t agree with this statement: “Studies, and by extension ADPs,</p>	<p>The intent of our comment was for the need for standardized language in the literature. We clarified the</p>

Comment #	Reviewer #	Comment	Author Response
		<p>should categorize patients as rule-in, rule-out, grey zone rule-out and grey zone rule-in and avoid terms that do not correspond to clinical diagnosis (e.g., low risk, discharge) which only muddy interpretation of results” (page 6, lines 33-36). Agree with need to approach with a standard language, but disagree with need to correspond these to categories of clinical diagnoses. That later approach is not consistent with how emergency providers approach these clinical scenario—their heuristic is more consistent with the process of stratifying patients into categories of risk rather than arriving at definitive diagnoses. Even if a patient is “ruled-out” for acute MI in that moment, most emergency providers would still consider that patient to be in a low risk category because their heuristic is simultaneously both excluding MI and also assessing the patient’s risk for having MACE within the short term (studies usually assess this to be a 4-6 week horizon).</p>	<p>text to note terms like low or high risk should be clearly defined.</p>
		<p>- Limitations: Agree with the point regarding effect rather than implementation. Also seems this section should reinforce some of the limitations noted throughout the rest of the manuscript: heterogeneity of studies with respect to populations, locations, methods, outcomes, etc.</p>	<p>The objective of the Limitations section is to describe the limitations of the review (e.g., methods or focus) and not the limitations identified literature. As noted, we describe in other sections the limitations of the scientific literature.</p>
22	5	<p>Congratulations on an amazing job of organizing this complicated report in a clinically meaningful way. Despite the lack of clarity within the literature on defining ADP’s the criteria used in the quality assessment distilled the studies to a more manageable number for the readers to digest. There is enough confidence in the ADPs to answer meaningful questions as well as highlight area where further studies are needed.</p> <p>Although no “best protocol” for ADP plus hs-TN with low MACE risk stood out, this report provides a foundation which will help subsequent pilots and research to narrow the scope of questions that will provide meaningful clinical answers for the VA. This work will save a lot of time for groups that wish to use this report for future meta-analysis</p>	<p>Thank you.</p>

Comment #	Reviewer #	Comment	Author Response
		<p>when more studies are completed. I appreciate the complexity and the challenge that it took to create, distill, and synthesize this data. The information is descriptive which adds to its length which appears to be necessary to provide adequate understanding of the protocols as medical definitions and terminology variability was notable. The inconsistent descriptions proved to be difficult to combine studies in a typical meta-analytic approach.</p>	
		<p>It provides information on which source trials are most informative. A reader can find relevant information pertinent to their interest in the tables (Table 3. Description of Accelerated Diagnostic Protocol on pg 22) that categorize the accelerated diagnostic protocol with the more descriptive information in the body of the report. The prioritization presents the more important data of MACE, LOS, admit status and ED revisits as well as cardiac testing and revascularization.</p>	
		<p>Overall, the report does not have enough comparable data to support new VA protocols and highlights the need for further investigation to attempt to single out an ADP + hs TN with low risk for the VA emergency Departments. As there are not uniformity in terms and uniformity in ADPs to supply comparable data, the report supplies the data needed for the additional work required. If future studies present similar metrics and comparable ADPs, even underpowered studies could be combined though the cumulative reporting to gain power across studies. As noted in the Research Gaps/Future Research on page 6, it will continue to be important to understand whether hs-cTN ADPs can be successfully and safely implemented in US EDs that may not be part of large integrated health systems.</p>	
		<p>On page 3, last paragraph is meaningful as direct comparisons of shorter vs longer duration ADPS as noted with a moderate confidence, the studies reported “no</p>	

Comment #	Reviewer #	Comment	Author Response
		<p>evidence of difference between shorter and longer duration ADPs in 30 day MACE (RD – 0.1%, 95% CI – 0.2 – 0.03) or 30 day MI (RD – 0.1%, 95% CI – 0.2 to 0.01), but shorter ADPs probably reduce ED length of stay (by 2 to 4 hours in each study, mostly reporting as statistically significant and probably increase discharge to the community from the ED (in two studies, by either 3% or 21% both statistically significant)”. Summarizing across different ADPs studies using common risk scores adds meaningful information that the 01 vs 03 vs 06 appears not to make a difference in outcomes. This supports the metric concerns of ED LOS does not impact negatively on quality of care and may actually improve quality by reducing crowding and provides supports to narrow future studies to use ADPs with 02 or possibly 01 analysis.</p>	
		<p>Page 15 Synthesis and Certainty of evidence fourth paragraph, it would be important to comment that CIs can be used in place of P values to test hypotheses, so studies using CIs in place of p values is using statistics correctly. In Appendix Table J-5 in Appendix F, if a confidence interval (CI) is reported statistical significance can be inferred.</p>	<p>Thank you. We edited for clarity and revised the text that describes the method for conducting synthesis & certainty of evidence. Edits also included removing language around the specific GRADE domains (e.g., precision and the role of p-values / 95% CI) and instead we reference the interested reader to the relevant GRADE publication (ref 22).</p>
		<p>This sentence in the last paragraph is unclear: “In both studies, the novel ADP was associated with a significantly shorter length of stay (mean [SD] High-STEACS 0/3 ADP 6.8 [4.1] vs. 0/6/12 ADP 10 [4.1]; p<0.001;21 and median [inter quartile range] 0/3/6 ADP 6.5 [6.3 to 19.8] vs. 0/6/12 GRACE ADP 8.9 [3.7 to 38]; p<0.001); Appendix Table K-1).” The p values suggest the medians are different in the two groups, but when you look at the IQR they do not seem that different. So maybe the p values are testing each median? Perhaps comment on the lack of clarity? How were these p values interpreted?</p>	<p>We revised the sentence to clarify the findings.</p>
		<p>In Appendix Table K-6 pg 102, I’m not sure what the p values are testing. What is the “Beta” parameter in the MD</p>	<p>We revised the Appendix table to clarify the interpretation of the beta coefficient. Specifically, the coefficient is the</p>



Comment #	Reviewer #	Comment	Author Response
		(95% CI) column. In appendix table K-6 should it note what the parameters are for column MD (95% CI) and what is the P value testing in the column Reported P value?	association of the novel ADP compared to standard ADP and the outcome is log-transformed duration of stay. The coefficient is adjusted by age, sex, diabetes, creatinine, and history of MI, heart failure or cerebrovascular disease. For example, the coefficient -0.0135 is interpreted as the novel ADP results in a -1.34% reduction in ED length of stay.
		Page 36 minor spelling error on mortality as “morality” in paragraph three and disposition as “disposotion” in paragraph four.	Thank you.
23	6	This was a very much needed report, at the least to describe the current state of literature and evidence for clinical use of hs-cTn in risk-stratifying chest pain.	Thank you.
24	11	This is an excellent synthesis of review on the topic of use of HsTn in the clinical evaluation of patients. It fairly summarizes the literature on this topic, which is indeed a bit over-interpreted by the field. The suggestions for further study and for VA implications are fair and in line with what is actually published on the subject.	Thank you.
		My only suggestion is to add one element in the Discussion sections. There is little to no discussion in the review on the natural variation between hsTroponin I and hsTroponin T. TnT is only marketed by Roche, but we have a lot of Roche labs in the VA system (and thus will have both markers in use in VA longitudinally). The two troponin markers are not exactly the same and cannot necessarily be protocolized interchangeably. A note to this effect in the discussion is likely sufficient at this juncture, as I'm not aware of any literature that addresses the impact of marker variation on the specifics of protocol synthesis and validation. Bottom-line: Any VA-wide protocols or studies will need to account for the inherent differences between these two markers.	Thank you. We revised the Discussion to comment that troponin I and T are not interchangeable. Any ED that aims to implement a protocol will need to account for these inherent differences.

APPENDIX F. DESIGN DETAILS

Author, Year, PMID, Cohort Name, Protocol Number, Country, Funder	Study Design	Study Dates	Study Location Details	Inclusion Criteria	Exclusion Criteria
Anand 2021 33752439 <i>HiSTORIC</i> NCT03005158 Scotland Non-industry	RCT	2014-16	Multiple EDs	Sites able to implement rule-out pathway and submitted data to national registry. ED or acute medical patients with suspected ACS and a hs-cTnI < sex-specific 99th percentile url	STEMI, out-of-hospital cardiac arrest, admitted previously during the trial
Barnes 2021 33436490 <i>STAT-Chest Pain</i> ACTRN12618000797279 Australia Non-industry	Pre-Post comparison	2018-19	Single ED	ED patients with potential ACS, ≥18 yo	STEMI, myocardial revascularization within the preceding 6 mo, admission to hospital for other reasons, a clear non-cardiac cause of the symptoms, or prior enrolment in the study
Chew 2019 31478763 Lambrakis 2021 33998255 <i>RAPID-TnT</i> ACTRN12615001379505 Australia Industry and non-industry	RCT [analyzed as single group]	2015-2019	Multiple EDs	Chest pain or suspected ACS as the principal cause for investigation and a baseline ECG interpreted as not definitive for coronary ischemia, ≥18 yo, intention to undertake troponin testing, willing to give written consent	STEMI, comorbidity that precludes completing the clinical history questionnaire, non-cardiac chest pain, transfer from another hospital, presented for suspected ACS within 30 days of last presentation, required permanent dialysis
Conde 2013 23810070 NA Argentina NR	Pre-post comparison [analyzed as single group]	2011-2012	Single ED	ED patients with probable ACS, >18 yo	Unstable angina or MI without STEMI, angina equivalent.

Author, Year, PMID, Cohort Name, Protocol Number, Country, Funder	Study Design	Study Dates	Study Location Details	Inclusion Criteria	Exclusion Criteria
Costable 2014 NA Argentina NR	Single group	2013	Single ED	ED patients with suspected ACS and who were evaluated according to the chest pain unit protocol, > 18 yo.	STEMI, non-cardiac chest pain, admission indicated by another physician, transfer of patient due to lack of beds, patient refusal to stay for observation, impossibility of follow-up
Crowder 2015 26387473 NR NR Canada NR	Pre-post comparison [analyzed as single group]	2011-2012	Multiple EDs	Patients with chest pain or potential ACS and who had a troponin assay performed during the study periods.	STEMI
Ford 2021 33662739 NR NR US None	Pre-post comparison [analyzed as single group]	2017-2018	Single ED	ED patients with a chief complaint of chest pain, ≥ 18 yo.	NR
Hyams 2018 29478861 NR NR US NR	Pre-post comparison	2014-2016	Single ED	ED patients with a chief complaint of “chest pain,” “chest tightness,” or “chest pressure, >18 yo	STEMI, patients with nonpainful ACS presentations such as shortness of breath unless accompanied by symptoms related to chest discomfort. Patients without a documented follow-up at least 6 wks after the ED visit, without adequate information (such as ECG or troponin) documented in their electronic medical record to calculate a HEART score

Author, Year, PMID, Cohort Name, Protocol Number, Country, Funder	Study Design	Study Dates	Study Location Details	Inclusion Criteria	Exclusion Criteria
Ljung 2019 30661856 <i>FASTEST</i> NR Sweden Industry and non-industry	Pre-post comparison [analyzed as single group]	2013-2016	Multiple EDs	Chest pain suggestive of ACS with a duration ≥ 10 minutes and an onset of last episode ≤ 12 hours. ≥ 18 yo, willing to have blood samples taken according to the study protocol, a signed written informed consent in Swedish	STEMI, new left bundle branch block on ECG at presentation or previous participation in the study
Sandeman 2021 34824100 NR NR Scotland Industry and non-industry	Pre-post comparison	2014-2017	Single ED	Patients with suspected ACS presenting to a secondary care hospital, all patients who had an hs-cTnT measurement on presentation to hospital since the introduction of the assay	STEMI, patient were not residents in Scotland, had a previous presentation during the study period
Stoyanov 2020 31298551 <i>RAPID-CPU</i> NCT03111862 Germany Industry	Pre-post comparison	2016-2017	Single ED	Initial presentation of clinically suspected ACS (based on a broad spectrum of symptoms including atypical symptoms and dyspnea)	STEMI, patients on chronic haemodialysis, repeated presentations beyond the index admission ('frequent flyer'); patients referred from other hospitals for early or primary PCI without receiving a standard diagnostic work-up; diagnostic set of hsTnT samples not available (eg, missing initial or consecutive blood sample). Patients with atrioventricular nodal re-entrant tachycardia. Inappropriate command of the English/German language or permanent residence in a foreign country.
Suh 2022 35571147 NR NCT03590535 US Industry	Pre-post comparison [analyzed as single group]	2018-2020	Single ED	Patients with ACS and received troponin testing as part of their evaluation, ≥ 19 yo	STEMI, pre-heart transplant, without capacity to consent, left ventricular assist device, who were presenting after a cardiac arrest, lacked fluency in either English or Spanish, or were

Author, Year, PMID, Cohort Name, Protocol Number, Country, Funder	Study Design	Study Dates	Study Location Details	Inclusion Criteria	Exclusion Criteria
					otherwise unable to participate in telephone follow-up
Sweeney 2020 32104767 NR NR UK NR	Pre-post comparison [analyzed as single group]	2015-2018	Multiple EDs	ED patients with a triage diagnosis of chest pain	NR
Than 2021 33753972 NR NR New Zealand NR	QIP and Pre-post comparison	2020-2020	Single ED	Patients presenting with symptoms of chest pain and symptoms of MI, ≥18 yo	STEMI, <18 yo, a clear cause of symptoms other than MI; transfer from another hospital; pregnancy; unable to be followed-up; or staff considered recruitment inappropriate (eg, receiving palliative care), unable or unwilling to consent
Than 2016 26947800 NR ACTRN126130007457 41 New Zealand Non-industry	RCT	2013-2014	Single ED	Possible cardiac symptoms suggestive of MI and for which serial cTn analysis were performed, ≥18 yo	STEMI, noncoronary pathology of symptoms; transfer from another hospital; pregnancy; unable to be followed-up; or staff considered recruitment inappropriate (eg, receiving palliative care); need for admission because of other medical conditions regardless of a negative cTn result; previously enrolled in this study; unable to consent.
Twerenbold 2019 31345421 NR NR Switzerland, Argentina Industry and non-industry	Single group	2015-2017	Multiple EDs	Adult ED patients with symptoms suggestive of MI	STEMI

Author, Year, PMID, Cohort Name, Protocol Number, Country, Funder	Study Design	Study Dates	Study Location Details	Inclusion Criteria	Exclusion Criteria
Vigen 2020 32320036 NR NR US Non-industry	Pre-post comparison, [analyzed as single group]	2017-2018	Single ED	Patients had both ECG and troponin testing obtained within 3 hr of arrival and prior to the disposition decision, did not undergo hemodialysis in the ED.	Patients undergoing emergent hemodialysis, testing was done on an outpatient basis or in day surgery, missing values for time from cTn draw to disposition time, disposition decision time was recorded prior to a cTn draw time, redundant encounters.

APPENDIX G. SUMMARY OF RISK SCORES

Risk Score [Key Reference]	Items
HEART (History, Electrocardiogram, Age, Risk factors, Troponin), [Hyams 2018 29478861]	<ul style="list-style-type: none"> • History • Electrocardiogram • Age • Risk factors • Troponin
<p>Each item is scored 0, 1, or 2. High risk = 7-10; Medium risk = 4-6; Low risk = 0-3</p>	
TIMI (Thrombolysis in Myocardial Infarction), [Than 2016 26947800]	<ul style="list-style-type: none"> • Age ≥65 y • Coronary artery disease (CAD) risk factor ≥3 (family history of premature coronary artery disease (CAD), dyslipidemia, diabetes, hypertension, current smoker) • Known coronary artery disease (CAD) (stenosis ≥50%) • Acetylsalicylic acid/ aspirin use in the last 7 days • Recent severe angina (eg, ≥2 events in last 24 h)
<p>Each item is score 0 or 1. Not low risk ≥1; Low risk = 0</p>	
EDACS (the Emergency Department Assessment of Chest Pain Score), [Than 2016 26947800]	<ul style="list-style-type: none"> • Age (classified by predefined age ranges: ≤30, 30-39, 40-49, 50-59, 60-69, 70-79, 80-89, ≥90); scored 2-20 [even numbers only]; • If age 18-50 ys then coronary artery disease event (CAD) or coronary artery disease risk factors; scored 3, 4 or 5 • Symptoms (diaphoresis, pain radiates to arm or shoulder, pain occurs or worsened with inspiration, pain reproduced by palpation); scored 3, 5, -4, or -6. • Male; scored 6
<p>Not low risk ≥16; Low risk <16</p>	
GRACE (Global Registry of Acute Coronary Events), [Fox 2006 17032691]	<ul style="list-style-type: none"> • Killip class (4 classes: I, II, III, IV); scored 0, 20, 39, or 59 • SBP mm Hg; scored 58, 53, 43, 34, 24, 10, 0 • Heart rate beats/min; scored 0, 3, 9, 15, 24, 38, or 46 • Age; scored 0, 8, 25, 41, 58, 75, 91, or 100 • Creatinine level mg/dL; scored 1, 4, 7, 10, 13, 21, or 28 • Cardiac arrest at admission; scored 39 • ST-segment deviation; scored 28

-
- Elevated cardiac enzyme levels; scored 14
High risk >140; intermediate risk 109-140; low risk <109.
-

APPENDIX H. SUMMARY OF HS-CTN

Author, Year, PMID	Arm	Test Manufacturer & Name	Troponin Var (I or T)	Limit of Detection	99 th Percentile
Anand 2021 33752439	Early rule-out pathway (High-STEACS): High-STEACS ADP 0/3	Abbott Architect STAT	hs-cTnI	NR	Women; 16 ng/L; Men; 34 ng/L
	Standard rule-out pathway: ADP 0/6/12			Same	
Barnes 2021 33436490	Single Troponin Accelerated Triage (STAT)-Chest Pain: STAT ADP 0/2/6 HEART	Abbott Architect	hs-cTnI	1.2 ng/L (reported as <2 ng/L)	Women upper limit of normal; <16 ng/L; Men upper limit of normal; <26 ng/L
	Standard pathway: ADP 0/(2 or 3)/6 TIMI			Same	
Chew 2019 31478763	ADP 0/1	5 th generation Roche Elecys	hs-cTnT	5 ng/L	14 ng/L
Lambrakis 2021 33998255	ADP 0/3 [arm excluded from analysis due to hs-cTnT being blinded]			Same	
Conde 2013 23810070	Post-implementation: ADP 0/3	NR	hs-cTnT	NR	NR
	Pre-implementation [arm excluded from analysis due to standard troponin]	4 th generation troponin	cTnT	NR	NR
Costable 2014	hs-cTn Chest Pain Protocol: ADP 0/3	NR	hs-cTnT	NR	NR
Crowder 2015 26387473	Post-implementation: ADP 0/2-4	Roche	hs-cTnT	NR	14 ng/L
	Pre-implementation [arm excluded from analysis due to standard troponin]	4 th generation Roche	cTnT	NR	NR
	Historical control [arm excluded from analysis due to standard troponin]	NA	NA	NA	NA
Ford 2021 33662739	Post-implementation: ADP 0/1/3 HEART	5 th generation Roche	hs-cTnT	NR	19 ng/L
	Pre-implementation [arm excluded from analysis due to standard troponin]	TnI-Ultra Siemens	cTnI	NR	40 ng/L

Author, Year, PMID	Arm	Test Manufacturer & Name	Troponin Var (I or T)	Limit of Detection	99 th Percentile
Hyams 2018 29478861	HEART Pathway Post-implementation: ADP 0/3 HEART	Roche	hs-TnT	NR	NR
	Pre-implementation hs-cTn alone			Same	
Ljung 2019 30661856	Post-implementation: ADP 0/1 HEART	Roche and Abbott	hs-cTnT, hs-cTnI	Roche; 5 ng/L; Abbott; 1.2-1.9 ng/L	Roche; 14 ng/L; Abbott; Women; 15.6 ng/L; Abbott; Men; 34.2 ng/L
	Pre-implementation [arm excluded from analysis due to standard troponin]	Roche, Abbott, Siemens-Stratus	hs-cTnT, hs-cTnI, cTn	Roche; 5 ng/L; Abbott; 1.2-1.9 ng/L; Siemens-Stratus; 30 ng/L	Roche; 14 ng/L; Abbott; Women; 15.6 ng/L; Abbott; Men; 34.2 ng/L; Stratus; 70 ng/L
Sandeman 2021 34824100	Post-implementation: ADP 0/3/6	Roche Cobas e602 platform	hs-TnT	3 ng/L	14 ng/L
	Pre-implementation: ADP 0/6/12 GRACE			Same	
Stoyanov 2020 31298551	ESC 0/1 Post-implementation: ADP ESC 0/1	Roche Cobas e411	hs-TnT	5 ng/L	NR
	ESC 0/3 Pre-implementation: ADP ESC 0//3			Same	
Suh 2022 35571147	Post-implementation: ADP 0/1 mHEART	5 th generation Roche Elecsys	hs-TnT	6 ng/L	Women; 14 ng/L; Men; 22 ng/L (the US (FDA)-approved sex-specific 99th percentile values)
	Pre-implementation [arm excluded from analysis due to standard troponin]	Abbott i-STAT and 4 th generation Roche	POC cTnI or cTnT	NR	NR
Sweeney 2020 32104767	Post-implementation chest pain algorithm: ADP 0/3 TIMI & GRACE	Abbott Architect STAT cTnI	hs-cTnI	NR	NR
	Pre-implementation [arm excluded from analysis due to standard troponin]	NR	cTn	NR	NR
Than 2021 33753972	COVID-ADP: COVID-ADP 0/2 EDACS	Abbott Architect i2000	hs-TnI	1.9 ng/L	Women; 16 ng/L; Men; 34 ng/L; Overall; 26 ng/L
	EDACS: ADP 0/2/6 EDACS			Same	
	EDACS-ADP: ADP 0/2 EDACS	Abbot Architect	hs-cTnI	NR	Women; 16 ng/L; Men; 34 ng/L

Author, Year, PMID	Arm	Test Manufacturer & Name	Troponin Var (I or T)	Limit of Detection	99 th Percentile
Than 2016 26947800	ADAPT-ADP: ADP 0/2 TIMI			Same	
Twerenbold 2019 31345421	ADP ESC 0/1	Roche Elecsys 2010	hs-cTnT	5 ng/L	14 ng/L
Vigen 2020 32320036	Post-implementation: ADP 0/1/3 mHEART	NR	hs-cTnT	NR	NR
	Pre-implementation [arm excluded from analysis due to standard troponin]	4 th generation Roche	cTnT	0.01 ng/L	NR

APPENDIX I. BASELINES

Author, Year, PMID	N Enrolled	Race/Ethnicity, %	Age, Mean (SD) or %	Male, %	History of CVD, %	CVD Risk Factors, %
Anand 2021 33752439	31492	NR	59 (17)	55%	Prior MI; 8% Prior revascularization; 10.4% History CVD; NR Stroke/TIA; NR PAD; NR MI 30 days: 0.3%	Hypertension; NR Diabetes; 6% Smoking; NR BMI; NR FHx; NR Hyperlipidemia; NR
Barnes 2021 33436490	2255	NR	54 (17)	53%	Prior MI; 10% Prior revascularization; 10% History CVD; NR Stroke/TIA; 4% PAD; 2% MI 30 days: 0.0%	Hypertension; 35% Diabetes; 14% Smoker, current; 19% BMI; 13% FHx CAD; 9% Hyperlipidemia; 29%
Chew 2019 31478763 Lambrakis 2021 33998255	1646	NR	Median (IQR) 58.7 (48.6,69.4)	53.2%	Prior MI; 10.3% Prior revascularization; 10.4% Stroke/TIA; 3.2% History CVD; 27.8% PAD; NR MI 30 days: 1%	Hypertension; 19.7% Diabetes; 15.8% Smoking; 34.6% BMI; NR FHx; 61.2% Hyperlipidemia; 43.3%
Conde 2013 23810070	300	NR	65	51%	Prior MI; 1% Prior revascularization; 23% History CVD; 3% Stroke/TIA; NR PAD; NR MI 30 days: NR	Hypertension; 58% Diabetes; 15% Smoking; 50% BMI; NR FHx; NR Hyperlipidemia; 64%
Costable 2014	528	NR	58 (13)	58%	Prior MI; 8% Prior revascularization; 16.8% History CVD; 3.6% Stroke/TIA; NR PAD; NR MI 30 days: 6.3%	Hypertension; 38% Diabetes; 12% Smoking; 39% BMI; NR FHx; NR Hyperlipidemia; 45%

Author, Year, PMID	N Enrolled	Race/Ethnicity, %	Age, Mean (SD) or %	Male, %	History of CVD, %	CVD Risk Factors, %
Crowder 2015 26387473	5754	NR	61.4	49.9%	Prior MI; NR Prior revascularization; NR History CVD; NR Stroke/TIA; NR PAD; NR MI 30 days: NR	Hypertension; NR Diabetes; NR Smoking; NR BMI; NR FHx; NR Hyperlipidemia; NR
Ford 2021 33662739	1616	NR	Median (IQR) 55 (41, 66)	51%	Prior MI; NR Prior revascularization; NR History CVD; NR Stroke/TIA; NR PAD; NR MI 30 days: NR	Hypertension; NR Diabetes; NR Smoking; NR BMI; NR FHx; NR Hyperlipidemia; NR
Hyams 2018 29478861	866	NR	54.7	50.1%	Prior MI; 11.8% Prior revascularization; 15.4% History CVD; NR Stroke/TIA; 2.2% PAD; NR MI 6 weeks: 4.8%	Hypertension; 50.5% Diabetes; 22.5% Smoking; 22.6% BMI; 46.4% FHx; 31.3% Hyperlipidemia; 32%
Ljung 2019 30661856	621	NR	63 (53, 71)	54%	Prior MI; 19% Prior revascularization; 19% History CVD; 21% Stroke/TIA; 8% PAD; 2% MI 30 days: 0.5%	Hypertension; 43% Diabetes; 12% Smoking; 52% BMI (≥ 30 kg/m ²); 19% FHx; 29% Hyperlipidemia; NR
Sandeman 2021 34824100	10315	NR	63.6 (16.4)	54%	Prior MI; 6.4% Prior revascularization; NR History CVD; 4.2% Stroke/TIA; NR PAD; NR MI 30 days: NR	Hypertension; NR Diabetes; 17.7% Smoking; NR BMI; NR FHx; NR Hyperlipidemia; NR
Stoyanov 2020 31298551	2525	NR	62 (18)	58%	Prior MI; 17% Prior revascularization; 6.6% History CVD; NR	Hypertension; 65.4% Diabetes; 21.2% Smoking; 21.8%

Author, Year, PMID	N Enrolled	Race/Ethnicity, %	Age, Mean (SD) or %	Male, %	History of CVD, %	CVD Risk Factors, %
					Stroke/TIA; NR PAD; NR MI 30 days: NR	BMI; NR FHx; 26.3% Hyperlipidemia; 44.9%
Suh 2022 35571147	821	White (Non-Hispanic) 13.4% Black 25.5% Hispanic/Latino 60.4% Asian (Any) 2.6% Other1 53.7% Other2 1.1%	60.4 (15.9)	45.6%	Prior MI; NR Prior revascularization; NR History CVD; 25.9% Stroke/TIA; NR PAD; 32.9% MI 30 days: 2.6%	Hypertension; 68.6% Diabetes; 36.2% Smoking; 11.2% BMI; 41.2% FHx; 15.4% Hyperlipidemia; 44.7%
Sweeney 2020 32104767	15882	NR	49.9 (14.2)	NR	Prior MI; NR Prior revascularization; NR History CVD; NR Stroke/TIA; NR PAD; NR MI 30 days: NR	Hypertension; NR Diabetes; NR Smoking; NR BMI; NR FHx; NR Hyperlipidemia; NR
Than 2021 33753972	2416	White 72.2% Other1 Pacific 0.9% Other2 New Zealand Maori 3.5% Other3 11.1%	63 (13)	61.8%	Prior MI; NR Prior revascularization; NR History CVD; 35.3% Stroke/TIA; NR PAD; NR MI 30 days: NR	Hypertension; 55% Diabetes; 15% Smoking; 15.2% BMI; NR FHx; 54.3% Hyperlipidemia; 55.6%
Than 2016 26947800	558	Asian (Any) 2.5% Other1 Maori; 3.8% Other2 Pacific Islander; 1.6% Other3 (New Zealand European +	58.7 (11.9)	60.9%	Prior MI; 23.3% Prior revascularization; 27.4% History CVD; NR Stroke/TIA; 5.9% PAD; 5.7% MI 30 days: NR	Hypertension; 52% Diabetes; 14% Smoking; 15.1% BMI; NR FHx; 35.7% Hyperlipidemia; 50.9%

Author, Year, PMID	N Enrolled	Race/Ethnicity, %	Age, Mean (SD) or %	Male, %	History of CVD, %	CVD Risk Factors, %
		Other European); 84.0%				
Twerenbold 2019 31345421	2296	NR	Median 60	64%	Prior MI; 17% Prior revascularization; 30% History CVD; 29% Stroke/TIA; 2% PAD; 3% MI 30 days: 9.9%	Hypertension; 51% Diabetes; 13% Smoking; 19% BMI; NR FHx; 16% Hyperlipidemia; 41%
Vigen 2020 32320036	14552	White 55% Black 41.9% Hispanic/Latino 38.2% Non-Hispanic 61.8% Other 1 3%	54.2 (14.6)	53%	Prior MI; NR Prior revascularization; NR History CVD; NR Stroke/TIA; NR PAD; NR MI 30 days: NR	Hypertension; NR Diabetes; NR Smoking; NR BMI; NR FHx; NR Hyperlipidemia; NR

Abbreviations. BMI=body mass index; CVD=cardiovascular disease; FHx=family history; IQR=interquartile range; MI=myocardial infarction; N=sample size; NR=not reported; PAD=peripheral arterial disease; PMID=PubMed identifier; SD=standard deviation; TIA=transient ischemic attack.



APPENDIX J. MACE OUTCOMES

Appendix Table J-1. MACE Comparative Studies

Study PMID, Study	Follow-up Time (days)	Outcome Definition	Subgroup	Arm	n/N (%)	OR (95% CI)*	Reported P value
<i>Overall Comparison: ADP vs hs-cTn without ADP</i>							
Hyams 2018 29478861	6 wk	Mortality, nonfatal MI, revascularization		ADP 0/3 HEART	25/449 (5.6)	0.73 (0.42, 1.24) RD -1.8 (-5.1, 1.5)*	NR
				Hs-cTn	31/417 (7.4)		
<i>Overall Comparison: ADP vs ADP</i>							
Anand 2021 33752439	30	MI (type 1/4b/4c) or cardiac death		High-STEACS ADP 0/3	56/16792 (0.3)	0.86 (0.59, 1.24) RD -0.1 (-0.2, 0.03)*	0.068
				ADP 0/6/12	57/14700 (0.4)		
Anand 2021 33752439	30	MI (type 1/2/4b/4c) or cardiac death		High-STEACS ADP 0/3	68/16792 (0.4)	0.84 (0.60, 1.17)* RD -0.1 (-0.2, 0.05)*	NR
				ADP 0/6/12	71/14700 (0.5)		
Than 2016 26947800	30	Death, cardiac arrest, emergency revascularization, cardiogenic shock, ventricular arrhythmia needing intervention, high-degree atrioventricular block needing intervention, and MI		ADP 0/2 EDACS	2/279 (0.7) (all events occurred in non-low risk patients)	RD 0.3 (-0.9, 1.5)*	NR
				ADPAT ADP 0/2 TIMI	1/279 (0.4) (all events occurred in non-low risk patients)		
<i>Subgroup Comparison</i>							
Hyams 2018 29478861	6 wk	Mortality, nonfatal MI, revascularization	HEART score ≤3	ADP 0/3 HEART	0/denominator (0)	NR	NR
				Hs-cTn	0/denominator (0)		

Study PMID, Study	Follow-up Time (days)	Outcome Definition	Subgroup	Arm	n/N (%)	OR (95% CI)*	Reported P value
Than 2016 26947800	30	Death, cardiac arrest, emergency revascularization, cardiogenic shock, ventricular arrhythmia needing intervention, high-degree atrioventricular block needing intervention, and MI	Low risk patients	ADP 0/2 EDACS	0/116 (0)		NR
				ADAPT ADP 0/2 TIMI	0/85 (0)		
Twerenbold 2019 31345421	30	Cardiovascular death and MI	CP ≤3h and rule-out group	ADP ESC 0/1	0/655 (0.0)	RD -0.3 (-0.6, 0.04)*	0.171
			CP >3h and rule-out group	ADP ESC 0/1	3/1063 (0.3)		
Twerenbold 2019 31345421	30	Cardiovascular death and MI	Female and rule-out group	ADP ESC 0/1	2/663 (0.3)	RD 0.2 (-0.3, 0.7)*	0.372
Twerenbold 2019 31345421	30	Cardiovascular death and MI	Male and rule-out group	ADP ESC 0/1	1/1049 (0.1)		
Twerenbold 2019 31345421	30	Cardiovascular death and MI	Age >65 years and rule-out group	ADP ESC 0/1	2/500 (0.3)	RD 0.1 (-0.4, 0.6)*	0.688
Twerenbold 2019 31345421	30	Cardiovascular death and MI	Age ≤65 years and rule-out group	ADP ESC 0/1	3/1219 (0.2)		
Twerenbold 2019 31345421	30	Cardiovascular death and MI	CP ≤3h and discharge	ADP ESC 0/1	0/614 (0)	RD -0.1 (-0.3, 0.1)*	0.435
Twerenbold 2019 31345421	30	Cardiovascular death and MI	CP >3h and discharge	ADP ESC 0/1	1/1004 (0.1)		
Twerenbold 2019	30	Cardiovascular death and MI	Female and discharge	ADP ESC 0/1	1/614 (0.2)	RD 0.2 (-0.2, 0.5)*	0.202

Study PMID, Study	Follow-up Time (days)	Outcome Definition	Subgroup	Arm	n/N (%)	OR (95% CI)*	Reported P value
31345421							
Twerenbold 2019 31345421	30	Cardiovascular death and MI	Male and discharge	ADP ESC 0/1	0/1004 (0)		
Twerenbold 2019 31345421	30	Cardiovascular death and MI	Age >65 years and discharge	ADP ESC 0/1	0/509 (0)	RD -0.1 (- 0.3, 0.1)*	0.501
Twerenbold 2019 31345421	30	Cardiovascular death and MI	Age ≤65 years and discharge	ADP ESC 0/1	1/1120 (0.1)		

Notes. * Calculated by research team.

Abbreviations. ADP=accelerated diagnostic protocol; CI=confidence interval; CP=chest pain; EDACS=Emergency Department Assessment of Chest Pain Score; ESC=European Society of Cardiology; HEART=History, Electrocardiogram, Age, Risk factors, Troponin; High-STEACS=High-Sensitivity Troponin in the Evaluation of Patients With Suspected Acute Coronary Syndrome; hs-cTn=high-sensitivity cardiac troponin; MACE=major adverse cardiac events; MI= myocardial infarction, n/N%=(number of events/sample size)%; NR=not reported; OR=odds ratio; PMID=PubMed identifier; RD=risk difference; TIMI=Thrombolysis in Myocardial Infarction; wk=week.



Appendix Table J-2. MACE: Rule Out, Low Risk Not Described as Rule Out, Discharge or Grey Zone, and Rule In or High Risk

Study, Year, PMID	ADP	Follow-up Time (days)	Outcome Definition	n/N (%)
<i>Rule Out</i>				
Chew 2019 31478763	ADP 0/1	30	Death and MI	6/1187 (0.5)
			Death, MI, and unstable angina	10/1187 (0.8)
Twerenbold 2019 31345421	ADP ESC 0/1	30	Cardiovascular death and MI	3/1420 (0.2)
<i>Low Risk Not Described as Rule Out</i>				
Than 2016 26947800	ADP 0/2 EDACS	30	Death, cardiac arrest, emergency revascularization, cardiogenic shock, ventricular arrhythmia needing intervention, high-degree atrioventricular block needing intervention, and MI	0/116 (0)
	ADAPT ADP 0/2 TIMI	30	Death, cardiac arrest, emergency revascularization, cardiogenic shock, ventricular arrhythmia needing intervention, high-degree atrioventricular block needing intervention, and MI	0/85 (0)
Hyams 2018 29478861	ADP 0/3 HEART	6 wk	Death, nonfatal MI, revascularization (based on HEART score ≤ 3)	0/denominator NR (0)
<i>Discharge</i>				
Suh 2022 35571147	ADP 0/1 mHEART	30	MI, revascularization, ventricular arrhythmia, high degree atrioventricular block requiring intervention, cardiogenic shock requiring mechanical support, cardiac arrest with return of spontaneous circulation, and death	4/381 (1)
Twerenbold 2019 31345421	ADP ESC 0/1	30	Cardiovascular death and MI	1/1619 (0.06)
<i>Observe / Grey Zone</i>				
Chew 2019 31478763	ADP 0/1	30	Death and MI	7/308 (2.3)
			Death, MI, and unstable angina	9 /308 (2.9)
			MI with or without revascularization	3/308 (1)
Twerenbold 2019 31345421	ADP ESC 0/1	30	Cardiovascular death and MI	31/581 (5.3)
<i>Rule In</i>				
Chew 2019 31478763	ADP 0/1	30	Death and MI	5/136 (3.7)

Study, Year, PMID	ADP	Follow-up Time (days)	Outcome Definition	n/N (%)
Twerenbold 2019 1345421	ADP ESC 0/1	30	Cardiovascular death and MI	197/295 (66.8)
<i>High Risk Not Described as Rule In</i>				
Suh 2022 35571147	ADP 0/1 mHEART	30	MI, revascularization, ventricular arrhythmia, high degree atrioventricular block requiring intervention, cardiogenic shock requiring mechanical support, cardiac arrest with return of spontaneous circulation, and death	35/395 (8.9)
Twerenbold 2019 1345421	ADP ESC 0/1	30	Cardiovascular death and MI (Based on admitted)	230/677 (34)
Than 2016 26947800	ADP 0/2 EDACS	30	Death, cardiac arrest, emergency revascularization, cardiogenic shock, ventricular arrhythmia needing intervention, high-degree atrioventricular block needing intervention, and MI	2/279 (0.7)
	ADAPT ADP 0/2 TIMI	30	Death, cardiac arrest, emergency revascularization, cardiogenic shock, ventricular arrhythmia needing intervention, high-degree atrioventricular block needing intervention, and MI	1 /279 (0.4)

Abbreviations. ADP=accelerated diagnostic protocol; EDACS=Emergency Department Assessment of Chest Pain Score; ESC=European Society of Cardiology; HEART=History, Electrocardiogram, Age, Risk factors, Troponin; MACE=major adverse cardiac events; mHEART=modified HEART; MI=myocardial infarction; n/N%=(number of events/sample size)%; NR=not reported; PMID=PubMed identifier; TIMI=Thrombolysis in Myocardial Infarction; wk=week.

APPENDIX K. ED LENGTH OF STAY OUTCOMES

Appendix Table K-1. ED Length of Stay (Continuous) Comparative Studies

Study, Year, PMID	Outcome Definition	Subgroup	Arm*	N	Mean (SD)	MD (95% CI)	Reported P Value
<i>Overall Comparison: ADP vs ADP</i>							
Anand 2021 33752439	LOS		High-STEACS ADP 0/3	16792	6.8 (4.1)	Geometric Mean 0.78 (0.73, 0.83)	<0.001
			ADP 0/6/12	14700	10 (4.1)		
Barnes 2021 33436490	LOS		STAT ADP 0/2/6 HEART	1124	Median (IQR) 3.6 (2.6, 5.4)	IRR 0.71 (0.65, 0.77)	<0.001
			ADP 0/(2 or 3)/6 TIMI	1131	Median (IQR) 4.3 (3.3, 7.1)		
Sandeman 2021 34824100	LOS		ADP 0/3/6	3673	Median (IQR) 6.5 (6.3,19.8)	1.34% (-2.21%, -0.26%) reduction in LOS associated with early rule-out	<0.001
			ADP 0/6/12 GRACE	6642	Median (IQR) 8.9 (3.7,38.0)		
Stoyanov 2020 31298551	LOS		ADP ESC 0/1	1282	Median (IQR) 3.2 (2.7,4.4)	Difference in median hours: -2.1*	<0.001
			ADP ESC 0/3	1243	Median (IQR) 5.3 (4.7,6.5)		
Than 2021 33753972	LOS		COVID-ADP 0/2 EDACS	1343	Median (IQR) 3.4 (2.6,4.6)	Difference in median hours: -0.4*	<0.001
			ADP 0/2/6 EDACS	1073	Median (IQR) 3.8 (2.8,4.9)		
<i>Subgroup Comparisons</i>							
Costable 2014	LOS	CP >6h	ADP 0/3	264	2.9 (2)		0.352
		CP ≤6h	ADP 0/3	264	5.1 (2.8)		
Sandeman 2021 34824100	LOS	Patients with troponin <5 ng/L	ADP 0/3/6	945	Median (IQR) 3.7 (170,329)	2.99% (-4.32, -1.64) reduction in LOS associated with early rule-out pathway	NR
			ADP 0/6/12 GRACE	2188	Median (IQR) 3.9 (3,8.1)		

Study, Year, PMID	Outcome Definition	Subgroup	Arm*	N	Mean (SD)	MD (95% CI)	Reported P Value
Sandeman 2021 34824100	LOS	Patients with troponin 5–14 ng/L	ADP 0/3/6	1380	Median (IQR) 5.2 (3.6,14.0)	3.61% (-5.30%, -1.90%) reduction in LOS associated with early rule-out pathway with	NR
			ADP 0/6/12 GRACE	1885	Median (IQR) 7 (3.6,20.2)		
Sandeman 2021 34824100	LOS	Patients with troponin >14 ng/L	ADP 0/3/6	1348	Median (IQR) 42.8 (11.3,103.1)	0.99% (-0.95%, 2.98%) reduction in LOS associated with early rule-out pathway with duration of stay	NR
			ADP 0/6/12 GRACE	2569	Median (IQR) 37.7 (11.1,100.1)		
Than 2021 33753972	LOS	Discharged from ED	COVID-ADP 0/2 EDACS	NR	Mean 3.4 Median (IQR) 3.1 (2.4,4.1)	Difference in median hours: -0.5 hours*	NR
			ADP 0/2/6 EDACS	NR	Mean 3.9 Median (IQR) 3.7 (2.7,4.6)		

Notes. * Calculated by research team.

Abbreviations. ADP=accelerated diagnostic protocol; CI=confidence interval; CP=chest pain; ED=emergency department; EDACS=Emergency Department Assessment of Chest Pain Score; ESC=European Society of Cardiology; GRACE=Global Registry of Acute Coronary Events; h=hour; HEART=History, Electrocardiogram, Age, Risk factors, Troponin; High-STEACS=High-Sensitivity Troponin in the Evaluation of Patients With Suspected Acute Coronary Syndrome; IQR=interquartile range; IRR=incidence rate ratio; LOS=length of stay; MD=mean difference; N=sample size; NR=not reported; PMID=PubMed identifier; SD=standard deviation; STAT=single troponin accelerated triage; TIMI=Thrombolysis in Myocardial Infarction.



Appendix Table K-2. ED Length of Stay (Categorical) Comparative Studies

Study PMID, Study Design	Follow-up Time (days)	Outcome Definition	Subgroup	Arm	n/N (%)	OR (95% CI)	Reported P value
<i>Overall Comparison: ADP vs. ADP</i>							
Barnes 2021 33436490	ED visit	Discharge <3h		STAT ADP 0/2/6 HEART	425/1124 (37.8)	aOR 2.1 (1.73,2.55)	<0.001
				ADP 0/(2 or 3)/6 TIMI	241/1131 (21.3)	RD 16.5 (12.8, 20.2)*	
Sandeman 2021 34824100	ED visit	Discharge ≤4h		ADP 0/3/6	1281/3650 (34.9)	RD 2.3 (0.4, 4.2)*	NR
				ADP 0/6/12 GRACE	2150/6597 (32.6)		
Than 2016 26947800	ED visit	Discharge <6h ^a		ADP 0/2 EDACS	90 /279 (32.3)	RD -2.1 (-10.3, 6)	0.65
				ADAPT ADP 0/2 TIMI	96/279 (34.4)		
Than 2021 33753972	ED visit	Discharge <2h		COVID-ADP 0/2 EDACS	109/1343 (8.1)	44.6% increase	NR
				ADP 0/2/6 EDACS	60/1073 (5.6)		
Than 2021 33753972	ED Visit	Discharge <3h		COVID-ADP 0/2 EDACS	594/1343 (44.2)	35.2% increase	NR
				ADP 0/2/6 EDACS	351/1073 (32.7)		
<i>Subgroup Comparison</i>							
Sandeman 2021 34824100	30	Discharge ≤4h	Patients with troponin <5 ng/L	ADP 0/3/6	604/945 (63.9)	RD 11.4 (7.7, 15.1)*	NR
				ADP 0/6/12 GRACE	1149/2188 (52.5)		
Sandeman 2021 34824100	30	Discharge ≤4h	Patients with troponin 5–14 ng/L	ADP 0/3/6	512/1380 (37.1)	RD 2 (-1.3, 5.3)*	NR
				ADP 0/6/12 GRACE	661/1885 (35.1)		



Study PMID, Study Design	Follow-up Time (days)	Outcome Definition	Subgroup	Arm	n/N (%)	OR (95% CI)	Reported P value
Sandeman 2021 34824100	30	Discharge ≤4h	Patients with troponin >14 ng/L	ADP 0/3/6	165/1348 (12.2)	RD* -1 (-3.2, 1.2)	NR
				ADP 0/6/12 GRACE	340/2569 (13.2)		
Than 2016 26947800	ED visit	Discharge <6h ^a	Low-risk patients	ADP 0/2 EDACS	73/279 (26.2)	RD 3.2 (-4.3,10.7)	NR
				ADAPT ADP 0/2 TIMI	64/279 (22.9)		

Notes. ^a Discharge <6h and no MACE defined as death, cardiac arrest, emergency revascularization, cardiogenic shock, ventricular arrhythmia needing intervention, high-degree atrioventricular block needing intervention, and MI.

Abbreviations. ADP=accelerated diagnostic protocol; aOR=adjusted odds ratio; CI=confidence interval; ED=emergency department; EDACS=Emergency Department Assessment of Chest Pain Score; GRACE=Global Registry of Acute Coronary Events; h=hour; HEART=History, Electrocardiogram, Age, Risk factors, Troponin; n/N%=(number of events/sample size)%; NR=not reported; OR=odds ratio; PMID=PubMed identifier; RD=risk difference; STAT=single troponin accelerated triage; TIMI=Thrombolysis in Myocardial Infarction.

Appendix Table K-3. ED Length of Stay (Continuous): Rule Out, Low Risk Not Described as Rule Out, Discharge or Grey Zone, and Rule In or High-Risk

Study, Year, PMID	ADP	N	Median (IQR) Length of Stay
<i>Rule Out</i>			
Chew 2019 31478763	ADP 0/1	1187	4.6 (3.5, 7.5)
Twerenbold 2019 31345421	ADP ESC 0/1	1420	2.5 (2.2, 3.6)
<i>Low Risk Not Described as Rule Out</i>			
Ljung 2019 30661856	ADP 0/1 HEART	308	4.05 (3.3,5.4)
Costable 2014	ADP 0/3	264	Mean (SD) 2.9 (2)
Sandeman 2021 34824100	ADP 0/3/6	945	3.65 (2.8, 5.5)
	ADP 0/6/12 GRACE	2188	3.9 (3, 8.1)
<i>Discharge</i>			
Lambrakis 2021 33998255 Chew 2019 31478763	ADP 0/1	737	3.8 (3.1,4.7)
Ljung 2019 30661856	ADP 0/1 HEART	419	3.8 (3.1,4.9)
Twerenbold 2019 31345421	ADP ESC 0/1	1619	2.5 (2.2,3.4)
Than 2021 33753972	COVID-ADP 0/2 EDACS	NR	3.1 (2.4, 4.1)
	ADP 0/2/6 EDACS	NR	3.7 (2.7, 4.6)
<i>Observe / Grey Zone</i>			
Chew 2019 31478763	ADP 0/1	308	12.0 (5.1,34.4)
Twerenbold 2019 31345421	ADP ESC 0/1	581	2.6 (2.4, 4.6)
<i>Rule In</i>			
Chew 2019 31478763	ADP 0/1	270	51 (27.6, 77.6)
Twerenbold 2019 31345421	ADP ESC 0/1	295	2.5 (2.3, 4.4)
<i>High Risk Not Described as Rule In</i>			
Ljung 2019 30661856	ADP 0/1 HEART (based on admitted)	202	46.7 (24.4,73.6)
	ADP 0/1 HEART (based on HEART score ≥ 4)	139	4.53 (3.4,24.7)
	ADP 0/1 HEART (based on hs-TnT >14 ng/L hs-cTnI ≥ 35 ng/L (♂) hs-cTnI ≥ 16 ng/L (♀))	130	45.2 (5.1,74.1)

Study, Year, PMID	ADP	N	Median (IQR) Length of Stay
Twerenbold 2019 31345421	ADP ESC 0/1 (based on admitted)	677	3 (2.3,5.3)
Sandeman 2021 34824100	ADP 0/3/6 (based on hs-TnT >14 ng/L)	1384	42.8 (11.3,103.1)
	ADP 0/6/12 GRACE (based on hs-TnT >14 ng/L)	2569	37.6 (11.2,100.9)

Abbreviations. ADP=accelerated diagnostic protocol; ED=emergency department; EDACS=Emergency Department Assessment of Chest Pain Score; ESC=European Society of Cardiology; GRACE=Global Registry of Acute Coronary Events; HEART=History, Electrocardiogram, Age, Risk factors, Troponin; hs-cTnI/T=highly-sensitive cardiac troponin I/T; IQR=interquartile range; N=sample size; NR=not reported; PMID=PubMed identifier; SD=standard deviation.

Appendix Table K-4. ED Length of Stay (Categorical): Rule Out, Low Risk Not Described as Rule Out, Discharge or Grey Zone, and Rule In or High Risk

Study, Year, PMID	ADP	Outcome Definition	n/N (%)
<i>Low Risk Not Described as Rule Out</i>			
Than 2016 26947800	ADP 0/2 EDACS	Discharge <6h and no MACE within 30 days ^a	73/279 (26.2)
	ADAPT ADP 0/2 TIMI	Discharge <6h and no MACE within 30 days ^a	64/279 (22.9)
Sandeman 202134824100	ADP 0/3/6	Discharge ≤4h (based on hs-TnT <5 ng/L)	604/945 (63.9)
	ADP 0/6/12 GRACE	Discharge ≤4h (based on hs-TnT <5 ng/L)	1149/2188 (52.5)
<i>High Risk Not Described as Rule In</i>			
Sandeman 2021 34824100	ADP 0/3/6	Discharge ≤4h (based on hs-TnT >14 ng/L)	165/1348 (12.2)
	ADP 0/6/12 GRACE	Discharge ≤4h (based on hs-TnT >14 ng/L)	340/2569 (13.2)

Notes. ^a Discharge <6h and no MACE defined as death, cardiac arrest, emergency revascularization, cardiogenic shock, ventricular arrhythmia needing intervention, high-degree atrioventricular block needing intervention, and MI.

Abbreviations. ADP=accelerated diagnostic protocol; ED=emergency department; EDACS=Emergency Department Assessment of Chest Pain Score; GRACE=Global Registry of Acute Coronary Events; h=hour; hs-cTnT=high-sensitivity cardiac troponin T; MACE=major adverse cardiac events; n/N %=(number of events/sample size) %; PMID=PubMed identifier; TIMI=Thrombolysis in Myocardial Infarction.

APPENDIX L. DISCHARGE OUTCOMES

Appendix Table L-1. ED Discharge to Community versus Hospital Admission Comparative Studies

Study PMID, Study Design	Follow-up Time (days)	Outcome Definition	Subgroup	Arm	n/N (%)	OR (95% CI)*	Reported P Value
<i>Overall Comparison: ADP vs hs-cTn without ADP</i>							
Hyams 2018 29478861	ED Visit	ED discharge*		ADP 0/3 HEART	232/449 (51.7)*	RD 15.2 (8.7, 21.7)*	<0.001
				Hs-cTn	152/417 (36.5)*		
<i>Overall Comparison: ADP vs ADP</i>							
Anand 2021 33752439	ED Visit	ED discharge		High-STEACS ADP 0/3	11842/16792 (71)	aOR 1.59 (1.45, 1.75) RD 21 (20.0, 22.0)*	<0.001
				ADP 0/6/12	7407/14700 (50)		
Barnes 2021 33436490	ED Visit	ED discharge		STAT ADP 0/2/6 HEART	709/1124 (63)	aOR 2.75 (2.29, 3.29) RD 25 (21.0, 29.0)*	<0.001
				ADP 0/2 or 3/6 TIMI	430/1131 (38)		
Than 2021 33753972	ED visit	ED discharge for patients with chest pain presentation*		COVID-ADP 0/2 EDACS	90.7%*	RD 3 (0.5, 5.5)*	NR
				ADP 0/2/6 EDACS	87.7%*		

Notes. * Calculated by research team.

Abbreviations. ADP=accelerated diagnostic protocol; aOR=adjusted odds ratio; CI=confidence interval; ED=emergency department; EDACS=Emergency Department Assessment of Chest Pain Score; High-STEACS=High-sensitivity Troponin in the Evaluation of Patients With Suspected Acute Coronary Syndrome; HEART=History, Electrocardiogram, Age, Risk factors, Troponin; hs-cTn=high-sensitivity cardiac troponin; n/N %=(number of events/sample size) %; NR=not reported; OR=odds ratio; PMID=PubMed identifier; RD=risk difference; STAT=single troponin accelerated triage; TIMI=Thrombolysis in Myocardial Infarction.

Appendix Table L-2. ED Discharge to Community versus Hospital Admission: Rule Out, Low Risk Not Described as Rule Out, Discharge or Grey Zone, and Rule In or High Risk

Study, Year, PMID	ADP	Outcome Definition	n/N (%)
<i>Rule Out</i>			
Chew 2019 31478763	ADP 0/1	ED discharge to home	589/1187 (49.6)
Twerenbold 2019 31345421	ADP ESC 0/1	ED discharge to home	1243/1420 (88)
<i>Low Risk Not Described as Rule Out</i>			
Ljung 2019 30661856	ADP 0/1 HEART	ED discharge to home (based on HEART score ≤ 3)	269/308 (87.3)
<i>Observe / Grey Zone</i>			
Chew 2019 31478763	ADP 0/1	ED discharge to home	84/308 (27.3)
Twerenbold 2019 31345421	ADP ESC 0/1	ED discharge to home	352/581 (61)
<i>Rule In</i>			
Chew 2019 31478763	ADP 0/1	ED discharge to home	12/136 (8.8)
Twerenbold 2019 31345421	ADP ESC 0/1	ED discharge to home	2/295 (8)
<i>High Risk Not Described as Rule In</i>			
Ljung 2019 30661856	ADP 0/1 HEART	ED discharge (based on HEART score ≥ 4)	87/139 (62.6)
		ED discharge (based on hs-cTnT >14 ng/L hs-cTnI ≥ 35 ng/L (δ) hs-cTnI ≥ 16 ng/L (η))	41/130 (31.5)

Abbreviations. ADP=accelerated diagnostic protocol; ED=emergency department; ESC=European Society of Cardiology; HEART=History, Electrocardiogram, Age, Risk factors, Troponin; hs-cTnI/T=high-sensitivity cardiac troponin I/T; n/N %=(number of events/sample size) %; PMID=PubMed identifier.

APPENDIX M. RETURN TO ED OR HOSPITAL OUTCOMES

Appendix Table M-1. Return to ED or Hospital Comparisons

Study PMID, Study	Follow-up Time (days)	Outcome Definition	Subgroup	Arm	n/N (%)	RD (95% CI)*	Reported P Value
<i>ADP Comparison</i>							
Barnes 2021 33436490	30	All cause		STAT ADP 0/2/6	107/1124	RD 1.1 (-1.3, 3.4)*	NR
				HEART	(9.5)		
				ADP 0/(2 or 3)/6 TIMI	95/1131 (8.4)		
<i>Subgroup Comparison</i>							
Barnes 2021 33436490	30	Chest pain	Patients who returned to ED	STAT ADP 0/2/6	33/107 (31.0)	RD -2 (-14.9, 10.9)*	NR
				HEART			
				ADP 0/2 or 3/6 TIMI	31/95 (33.0)		

Notes. * Calculated by research team.

Abbreviations. ADP=accelerated diagnostic protocol; CI=confidence interval; ED=emergency department; HEART=History, Electrocardiogram, Age, Risk factors, Troponin; n/N %=(number of events/sample size) %; OR=odds ratio; PMID=PubMed identifier; RD=risk difference; STAT=single troponin accelerated triage; TIMI=Thrombolysis in Myocardial Infarction.

Appendix Table M-2. Return to ED or Hospital Comparisons: Rule Out, Low Risk Not Described as Rule Out, Discharge or Grey Zone, and Rule In or High Risk

Study, Year, PMID	ADP	Follow-up Time (Days)	Outcome Definition	n/N (%)
<i>Rule Out</i>				
Chew 2019 31478763	ADP 0/1	30	Chest pain related	41/1187 (3.5)
<i>Low Risk Not Described as Rule Out</i>				
Ljung 2019 30661856	ADP 0/1 HEART	30	All-cause (Based on HEART score ≤3)	16/308 (5.2)
<i>Discharge</i>				
Ljung 2019 30661856	ADP 0/1 HEART	30	All-cause	45/419 (10.7)
<i>Observe / Grey Zone</i>				
Chew 2019 31478763	ADP 0/1	30	Myocardial injury related	11/308 (3.6)
			Chest pain related	22/308 (7.1)
<i>Rule In</i>				
Chew 2019 31478763	ADP 0/1	30	Chest pain related	7/136 (5.1)
<i>High Risk Not Described as Rule In</i>				
Ljung 2019 30661856	ADP 0/1 HEART	30	All-cause (Based on admitted)	36/202 (17.8)
			All-cause (Based on HEART score ≥4)	27 /139 (19.4)
			All-cause (Based on hs-TnT >14 ng/L hs-cTnI ≥35 ng/L (♂) hs-cTnI ≥16 ng/L (♀))	29/130 (22.3)

Abbreviations. ADP=accelerated diagnostic protocol; ED=emergency department; HEART=History, Electrocardiogram, Age, Risk factors, Troponin; hs-cTnI/T=high-sensitivity cardiac troponin I/T; n/N %=(number of events/sample size) %; PMID = PubMed identifier.



APPENDIX N. MI OUTCOMES

Appendix Table N-1. MI Comparative Studies

Study PMID, Study Design	Follow-up Time (days)	Outcome Definition	Subgroup	Arm	n/N (%)	OR (95% CI)	Reported P Value
<i>Overall Comparison: ADP vs hs-cTn without ADP</i>							
Hyams 2018 29478861	6 wk	MI		ADP 0/3 HEART	21/449 (4.7)	0.96 (0.52,1.81) RD -0.1 (-2.9, 2.7)*	NR
				hs-cTn	20/417 (4.8)		
<i>Overall Comparison: ADP vs ADP</i>							
Anand 2021 33752439	30	Type 1/4b/4c		High-STEACS ADP 0/3	38/16792 (0.2)	0.76 (0.49, 1.17)* RD -0.1 (-0.2, 0.01)*	NR
				ADP 0/6/12	44/14700 (0.3)		
Anand 2021 33752439	30	Type 1/2/4b/4c		High-STEACS ADP 0/3	50/16792 (0.3)	0.75 (0.52, 1.10)* RD -0.1 (-0.2,0.03)*	NR
				ADP 0/6/12	58/14700 (0.4)		
Barnes 2021 33436490	30	MI		STAT ADP 0/2/6 HEART	0/1124 (0)		NR
				ADP 0/(2 or 3)NR/6 TIMI	0/1131 (0.0)		
Than 2016 26947800	30	NSTEMI		ADP 0/2 EDACS	2/279 (0.7)	RD 0.7 (-2.1,0.6)	NR
				ADAPT ADP 0/2 TIMI	0/279 (0)		
Than 2016 26947800	30	STEMI		ADP 0/2 EDACS	0/279 (0)	RD -0.4 (-0.7,1.4)	NR
				ADAPT ADP 0/2 TIMI	1/279 (0.4) all in non-low-risk patients		

Study PMID, Study Design	Follow-up Time (days)	Outcome Definition	Subgroup	Arm	n/N (%)	OR (95% CI)	Reported P Value
Than 2016 26947800	ED visit	STEMI		ADP 0/2 EDACS	2/279 (0.7)	RD -0.4 (-1.6,2.3)	NR
				ADAPT ADP 0/2 TIMI	3 /279 (1.1)		
Than 2016 26947800	ED visit	NSTEMI		ADP 0/2 EDACS	34/279 (12.2) all in non-low-risk patients	RD 2.9 (-8.4,2.6)	NR
				ADAPT ADP 0/2 TIMI	26 /279 (9.3) all in non-low-risk patients		
Subgroup Comparison							
Than 2016 26947800	30	NSTEMI	Low-risk patients	ADP 0/2 EDACS	0/116 (0)		NR
				ADAPT ADP 0/2 TIMI	0/85 (0)		
Than 2016 26947800	30	STEMI	Low-risk patients	ADP 0/2 EDACS	0/116 (0)		NR
				ADAPT ADP 0/2 TIMI	0/85 (0)		

Notes. * Calculated by research team.

Abbreviations. ADP=accelerated diagnostic protocol; CI=confidence interval; ED=emergency department; EDACS=Emergency Department Assessment of Chest Pain Score; HEART=History, Electrocardiogram, Age, Risk factors, Troponin; High-STEACS=High-Sensitivity Troponin in the Evaluation of Patients With Suspected Acute Coronary Syndrome; hs-cTn=high-sensitivity cardiac troponin; MI=myocardial infarction; n/N %=(number of events/sample size) %; NR=not reported; NSTEMI=non ST-elevation myocardial infarction; OR=odds ratio; PMID=PubMed identifier; RD=risk difference; STAT=single troponin accelerated triage; STEMI=ST-elevation myocardial infarction; TIMI=Thrombolysis in Myocardial Infarction; wk=week.



Appendix Table N-2. MI: Rule Out, Low Risk Not Described as Rule Out, Discharge or Grey Zone, and Rule In or High Risk

Study, Year, PMID	ADP	Follow-up Time (days)	Outcome Definition	n/N (%)
<i>Rule Out</i>				
Chew 2019 31478763	ADP 0/1	30	Type 1/2/4a/5	5/1187 (0.4)
			MI or myocardial injury	9/1187 (0.8)
Twerenbold 2019 31345421	ADP ESC 0/1	30	MI	2/1420 (0.1)
<i>Low Risk Not Described as Rule Out</i>				
Ljung 2019 30661856	ADP 0/1 HEART	30	MI (Based on HEART score ≤3)	0/308 (0)
Than 2016 26947800	ADP 0/2 EDACS	30	NSTEMI	0/116 (0)
			STEMI	0/116 (0)
	ADAPT ADP 0/2 TIMI	30	NSTEMI	0/85 (0)
			STEMI	0/85 (0)
<i>Discharge</i>				
Ljung 2019 30661856	ADP 0/1 HEART	30	MI	2/419 (0.5)
Twerenbold 2019 31345421	ADP ESC 0/1	30	MI	0 /1619 (0)
Costable 2014	ADP 0/3	30	MI	0/479 (0)
<i>Observe / Grey Zone</i>				
Chew 2019 31478763	ADP 0/1	30	Type 1/2/4a/5	6/308 (1.9)
			MI or myocardial injury	9/308 (2.9)
Twerenbold 2019 31345421	ADP ESC 0/1	30	MI	30/581 (5.2)
<i>Rule In</i>				
Chew 2019 31478763	ADP 0/1	30	Type 1/2/4a/5	5/136 (3.7)
			MI or myocardial injury	8/136 (5.9)
Twerenbold 2019 31345421	ADP ESC 0/1	30	MI	195/295 (66.1)



Study, Year, PMID	ADP	Follow-up Time (days)	Outcome Definition	n/N (%)
<i>High Risk Not Described as Rule In</i>				
Ljung 2019 30661856	ADP 0/1 HEART	30	MI after discharge (among those who admitted)	1/202 (0.5)
			MI (patients with HEART ≥ 4)	0/139 (0)
			MI (patients with hs-cTnT >14 ng/L hs-cTnI ≥ 35 ng/L (♂) hs-cTnI ≥ 16 ng/L (♀))	1/130 (0.8)
	ADP 0/1 HEART	In-hospital stay	MI (among those who admitted)	44/202 (21.8)
Twerenbold 2019 31345421	ADP ESC 0/1	30	MI (based on admitted)	227/677 (33.5)
Than 2016 26947800	ADP 0/2 EDACS	30	NSTEMI	2/279 (0.7)
			STEMI	0/279 (0)
Than 2016 26947800	ADAPT ADP 0/2 TIMI	30	NSTEMI	0/279 (0)
			STEMI	1/279 (0.4)
Costable 2014	ADP 0/3	30	MI (based on admitted)	33/49 (67.3)

Abbreviations. ADP=accelerated diagnostic protocol; EDACS=Emergency Department Assessment of Chest Pain Score; ESC=European Society of Cardiology; HEART=History, Electrocardiogram, Age, Risk factors, Troponin; hs-cTnI/T=high-sensitivity cardiac troponin I/T; MI=myocardial infarction; n/N %=(number of events/sample size) %; NSTEMI=non ST-elevation myocardial infarction; PMID=PubMed identifier; STEMI=ST-elevation myocardial infarction; TIMI=Thrombolysis in Myocardial Infarction.

APPENDIX O. DEATH OUTCOMES

Appendix Table O-1. Death Comparative Studies

Study PMID, Study Design	Follow-up Time (Days)	Outcome Definition	Subgroup	Arm	n/N (%)	OR (95% CI)*	Reported P Value
<i>Overall Comparison: ADP vs hs-cTn without ADP</i>							
Hyams 2018 29478861	6 wk	All-cause		ADP 0/3 HEART	1/449 (0.2)	0.23 (0.03,2.08) RD -0.8 (-1.8, 0.2)*	NR
				hs-cTn	4/417 (1.0)		
<i>Overall Comparison: ADP vs ADP</i>							
Barnes 2021 33436490	30	All-cause		STAT ADP 0/2/6 HEART	0/1124 (0)		NR
				ADP 0/(2 or 3)/6 TIMI	0/1131 (0)		
Sandeman 2021 34824100	30	All-cause		ADP 0/3/6	141/3673 (3.8)	RD 0.1 (-0.7, 0.9)*	NR
				ADP 0/6/12 GRACE	245/6642 (3.7)		
Sandeman 2021 34824100	30	Cardiovascular		ADP 0/3/6	82/3673 (2.2)	RD 0.1 (-0.5, 0.7)*	NR
				ADP 0/6/12 GRACE	139/6642 (2.1)		
Than 2016 26947800	ED Visit	All-cause		ADP 0/2 EDACS	0/279 (0)	RD -0.4 (-0.7, 1.4)*	NR
				ADAPT ADP 0/2 TIMI	1/279 (0.4) occurred in non-low risk patients		
<i>Subgroup Comparison</i>							
Sandeman 2021 34824100	30	All-cause	Patients with troponin <5 ng/L	ADP 0/3/6	1/945 (0.1)	RD 0 (- 0.2, 0.2)*	NR
				ADP 0/6/12 GRACE	1/2188 (0.1)		
Sandeman 2021 34824100	30	All-cause	Patients with troponin 5–14 ng/L	ADP 0/3/6	12/1380 (0.9)	RD 0.2 (- 0.4, 0.8)*	NR
				ADP 0/6/12 GRACE	14/1885 (0.7)		
Sandeman 2021	30	All-cause		ADP 0/3/6	128/1348 (9.5)		NR

Study PMID, Study Design	Follow-up Time (Days)	Outcome Definition	Subgroup	Arm	n/N (%)	OR (95% CI)*	Reported P Value
34824100			Patients with troponin >14 ng/L	ADP 0/6/12 GRACE	230/2569 (9)	RD 0.5 (- 1.4, 2.4)*	
Sandeman 2021 34824100	30	Cardiovascular	Patients with troponin <5 ng/L	ADP 0/3/6	1/945 (0.1)	RD 0 (- 0.2, 0.2)*	NR
				ADP 0/6/12 GRACE	1/2188 (0.1)		
Sandeman 2021 34824100	30	Cardiovascular	Patients with troponin 5–14 ng/L	ADP 0/3/6	8/1380 (0.6)	RD 0.4 (-0.1, 0.9)*	NR
				ADP 0/6/12 GRACE	4/1885 (0.2)		
Sandeman 2021 34824100	30	Cardiovascular	Patients with troponin >14 ng/L	ADP 0/3/6	73/1348 (5.4)	RD 0.2 (-1.3, 1.7)*	NR
				ADP 0/6/12 GRACE	134/2569 (5.2)		

Notes. * Calculated by research team.

Abbreviations. ADP=accelerated diagnostic protocol; CI=confidence interval; ED=emergency department; EDACS=Emergency Department Assessment of Chest Pain Score; GRACE=Global Registry of Acute Coronary Events; HEART=History, Electrocardiogram, Age, Risk factors, Troponin; hs-cTn=high-sensitivity cardiac troponin; n/N %=(number of events/sample size) %; NR=not reported; OR=odds ratio; PMID=PubMed identifier; RD=risk difference; STAT=single troponin accelerated triage; TIMI=Thrombolysis in Myocardial Infarction; wk=week.

Appendix Table O-2. Death: Rule Out, Low Risk Not Described as Rule-Out, Discharge or Grey Zone, and Rule In or High Risk

Study, Year, PMID	ADP	Follow-up Time (Days)	Outcome Definition	n/N (%)
<i>Rule Out</i>				
Chew 2019 31478763	ADP 0/1	30	All-cause	1/1187 (0.1)
			Cardiovascular	1/1187 (0.1)
Twerenbold 2019 31345421	ADP ESC 0/1	30	All-cause	2/1420 (0.1)
			Cardiovascular	1/1420 (0.1)
<i>Low-Risk Not Described as Rule Out</i>				
Ljung 2019 30661856	ADP 0/1 HEART	30	All-cause after discharge (based on HEART score ≤ 3)	0/308 (0)
Sandeman 202134824100	ADP 0/3/6	30	All-cause (based on hs-TnT < 5 ng/L)	1/945 (0.1)
			Cardiovascular (based on hs-TnT < 5 ng/L)	1/945 (0.1)
Sandeman 2021 34824100	ADP 0/6/12 GRACE	30	All-cause (based on hs-TnT < 5 ng/L)	1/2188 (0.1)
			Cardiovascular (based on hs-TnT < 5 ng/L)	1/2188 (0.1)
<i>Discharge</i>				
Ljung 2019 30661856	ADP 0/1 HEART	30	All-cause	0/419 (0)
Twerenbold 2019 31345421	ADP ESC 0/1	30	All-cause	1/1619 (0.1)
			Cardiovascular	1/1619 (0.1)
Costable 2014	ADP 0/3	30	All-cause	0/479 (0)
<i>Observe / Grey Zone</i>				
Chew 2019 31478763	ADP 0/1	30	All-cause	1/308 (0.3)
			Cardiovascular	1/308 (0.3)
Twerenbold 2019 31345421	ADP ESC 0/1	30	All-cause	1/581 (0.2)
			Cardiovascular	1/581 (0.2)

Study, Year, PMID	ADP	Follow-up Time (Days)	Outcome Definition	n/N (%)
<i>Rule In</i>				
Chew 2019 31478763	ADP 0/1	30	All-cause	0/136 (0.0)
			Cardiovascular	0/136 (0.0)
Twerenbold 2019 31345421	ADP ESC 0/1	30	All-cause	5/295 (1.7)
			Cardiovascular	3/295 (1)
<i>High Risk Not Described as Rule In</i>				
Ljung 2019 30661856	ADP 0/1 HEART	30	All-cause after discharge (based on admitted)	0/202 (0)
Ljung 2019 30661856	ADP 0/1 HEART	30	All-cause after discharge (based on HEART score ≥ 4)	0/139 (0)
Ljung 2019 30661856	ADP 0/1 HEART	30	All-cause after discharge (based on hs-TnT >14 ng/L hs-cTnI ≥ 35 ng/L (♂) hs-cTnI ≥ 16 ng/L (♀))	0/130 (0)
Twerenbold 2019 31345421	ADP ESC 0/1	30	All-cause (based on admitted)	7/677 (1)
			Cardiovascular (based on admitted)	4/677 (0.6)
Costable 2014	ADP 0/3	30	All-cause (based on admitted)	0/49 (0)
Sandeman 2021 34824100	ADP 0/3/6	30	All-cause (based on hs-TnT >14 ng/L)	128/1348 (9.5)
			Cardiovascular (based on hs-TnT >14 ng/L)	73/1348 (5.4)
Sandeman 2021 34824100	ADP 0/6/12 GRACE	30	All-cause (based on hs-TnT >14 ng/L)	230/2569 (9)
			Cardiovascular (based on hs-TnT >14 ng/L)	134/2569 (5.2)

Abbreviations. ADP=accelerated diagnostic protocol; ESC=European Society of Cardiology; GRACE=Global Registry of Acute Coronary Events; HEART=History, Electrocardiogram, Age, Risk factors, Troponin); hs-TnI/T=high-sensitivity cardiac troponin I/T; n/N %=(number of events/sample size) %; PMID=PubMed identifier.

APPENDIX P. CARDIAC TESTING OUTCOMES

Appendix Table P-1. Cardiac Testing Comparative Studies

Study, Year, PMID	Test Category	Test	Subgroup	ADP	n/N (%)	OR (95% CI)*		
<i>Overall Comparison: ADP vs ADP</i>								
Barnes 2021 33436490	Stress test, ECG	Stress ECG	-	STAT ADP 0/2/6 HEART	90/1124 (8.0)	1.2 (0.85, 1.57)*		
				ADP 0/(2 or 3)/6 TIMI	79 /1131 (7.0)	RD 1 (-1.2, 3.2)*		
	Stress test, imaging	Myocardial perfusion scan	-	STAT ADP 0/2/6 HEART	23/1124 (2.0)	0.50 (0.30, 0.83)*		
				ADP 0/(2 or 3)/6 TIMI	45/1131 (4.0)	RD -2 (-3.4, -0.6)*		
	Angiogram, standard	Angiogram	-	STAT ADP 0/2/6 HEART	10/1124 (0.9)	0.77 (0.34, 1.77)*		
				ADP 0/(2 or 3)/6 TIMI	13/1131 (1.1)	RD -0.2 (-1.0, 0.6)*		
	Angiogram, imaging	CT angiogram	-	STAT ADP 0/2/6 HEART	52/1124 (4.6)	1.6 (1.04, 2.5)*		
				ADP 0/(2 or 3)/6 TIMI	33/1131 (2.9)	RD 1.7 (0.1, 3.3)*		
Stoyanov 2020 31298551	Stress test, ECG	Stress ECG	Rule out and direct discharge	ADP ESC 0/1	89/806 (11)	1.1 (0.77,1.49)*		
				ADP ESC 0/3	70/672 (10.4)	RD 0.6 (-2.6, 3.8)*		
	Stress test, imaging	Myocardial perfusion scan	-	-	-	-		
				Stress echocardiogram	Rule out and direct discharge	ADP ESC 0/1	5/806 (0.6)	0.69 (0.21, 2.28)*
						ADP ESC 0/3	6/672 (0.9)	RD -0.3 (-1.2, 0.6)*
	Cardiac MRI stress test	Rule out and direct discharge	ADP ESC 0/1	7/806 (0.9)	1.9 (0.50, 7.6)*			
	Angiogram, standard	Angiogram	-	ADP ESC 0/1	328/1282 (25.6)	0.85 (0.73, 0.99)*		
				ADP ESC 0/3	358/1243 (28.8)	RD -3.2 (-6.7, 0.3)*		
	Angiogram, imaging	CT angiogram	Rule out and direct discharge	ADP ESC 0/1	9/806 (1.1)	1.5 (0.50, 4.5)*		
				ADP ESC 0/3	5/672 (0.7)	RD 0.4 (-0.6, 1.4)*		

Notes. * Calculated by research team.

Abbreviations. ADP=accelerated diagnostic protocol; CI=confidence interval; CT=computerized tomography scan; ECG=electrocardiogram; ESC=European Society of Cardiology; HEART=History, Electrocardiogram, Age, Risk factors, Troponin; MRI=magnetic resonance imaging; n/N %=(number of events/sample size) %; OR=odds ratio; PMID=PubMed identifier; RD=risk difference; STAT=single troponin accelerated triage; TIMI=Thrombolysis in Myocardial Infarction.



Appendix Table P-2. Cardiac Testing: Rule Out, Low Risk Not Described as Rule Out, Discharge or Grey Zone, and Rule In or High Risk

Outcome (Test)	Diagnosis Category	Study, Year, PMID	ADP	n/N	%	
Stress test, any	Rule out	Chew 2019 31478763	ADP 0/1	61/1187	5.1	
		Twerenbold 2019 31345421	ADP ESC 0/1	125/1420	8.8	
	Low risk	Ljung 2019 30661856	ADP 0/1 HEART	31/308	10.1	
	Discharge	Twerenbold 2019 31345421	ADP ESC 0/1	104/1619	6.4	
	Observe/grey zone	Chew 2019 31478763	ADP 0/1	41/308	13.2	
		Twerenbold 2019 31345421	ADP ESC 0/1	58/581	10.0	
	Rule in	Chew 2019 31478763	ADP 0/1	19/136	14.0	
		Twerenbold 2019 31345421	ADP ESC 0/1	92/677	13.6	
	High risk	Ljung 2019 30661856 ^a	ADP 0/1 HEART	21/139	15.1	
		Ljung 2019 30661856 ^b	ADP 0/1 HEART	12/130	9.2	
	Stress test, ECG	Rule out	Chew 2019 31478763	ADP 0/1	17/1187	1.4
			Twerenbold 2019 31345421	ADP ESC 0/1	81/1420	5.7
Stoyanov 2020 31298551 ^c			ADP ESC 0/1	89/806	11	
Stoyanov 2020 31298551 ^c			ADP ESC 0/3	70/672	10.4	
Discharge		Twerenbold 2019 31345421	ADP ESC 0/1	61/1619	3.8	
Observe/grey zone		Chew 2019 31478763	ADP 0/1	15/308	4.9	
		Twerenbold 2019 31345421	ADP ESC 0/1	39/581	6.7	
Rule in		Chew 2019 31478763	ADP 0/1	3/136	2.2	
		Twerenbold 2019 31345421 ^d	ADP ESC 0/1	11/295	3.7	
		Twerenbold 2019 31345421 ^e	ADP ESC 0/1	70/677	10.3	
High risk		-	-	-	-	
Stress test, imaging		Rule out	Chew 2019 31478763 ^f	ADP 0/1	40/1187	3.4
	Chew 2019 31478763 ^g		ADP 0/1	4/1187	0.3	
	Stoyanov 2020 31298551 ^h		ADP ESC 0/1	5/806	0.6	
	Stoyanov 2020 31298551 ^h		ADP ESC 0/3	6/672	0.9	

Outcome (Test)	Diagnosis Category	Study, Year, PMID	ADP	n/N	%	
		Stoyanov 2020 31298551 ¹	ADP ESC 0/1	7/806	0.9	
		Stoyanov 2020 31298551 ¹	ADP ESC 0/3	3/672	0.4	
	Discharge	-	-	-	-	
	Observe/grey zone	Chew 2019 31478763 ^f	ADP 0/1	25/308	8.1	
		Chew 2019 31478763 ^g	ADP 0/1	3/308	1.0	
	Rule in	Chew 2019 31478763	ADP 0/1	7/136	5.1	
	High risk	-	-	-	-	
Angiogram, Standard	Rule out	Chew 2019 31478763	ADP 0/1	59/1187	5.0	
		Twerenbold 2019 31345421	ADP ESC 0/1	82/1420	5.8	
		Stoyanov 2020 31298551	ADP ESC 0/1	328/1282	25.6	
		Stoyanov 2020 31298551	ADP ESC 0/3	358/1243	28.8	
	Discharge	Twerenbold 2019 31345421	ADP ESC 0/1	14/1619	0.9	
	Observe/grey zone	Chew 2019 31478763	ADP 0/1	43/308	14.0	
		Twerenbold 2019 31345421	ADP ESC 0/1	109/581	18.8	
	Rule in	Chew 2019 31478763	ADP 0/1	69/136	50.7	
		Twerenbold 2019 31345421 ^d	ADP ESC 0/1	211/295	71.5	
		Twerenbold 2019 31345421 ^e	ADP ESC 0/1	388/677	57.3	
	High risk	-	-	-	-	
	Angiogram, imaging	Rule out	Stoyanov 2020 31298551 ^c	ADP ESC 0/1	9/806	1.1
			Stoyanov 2020 31298551 ^c	ADP ESC 0/3	5/672	0.7
Discharge		-	-	-	-	
Observe/grey zone		-	-	-	-	
Rule in		Chew 2019 31478763	ADP 0/1	0/136	0.0	
High risk		-	-	-	-	

Notes. ^a High risk based on HEART score ≥ 4 ; ^b High risk based on hs-TnT > 14 ng/L hs-cTnI ≥ 35 ng/L (δ) hs-cTnI ≥ 16 ng/L (δ); ^c Rule out and discharge subgroup; ^d Rule in subgroup; ^e Admitted subgroup; ^f Stress echocardiogram; ^g Cardiac MRI stress test; ^h Stress echocardiogram in rule out and direct discharge group; ⁱ Stress MRI in rule out and direct discharge group.

Abbreviations. ADP=accelerated diagnostic protocol; ECG=electrocardiograph; ESC=European Society of Cardiology; HEART=History, Electrocardiogram, Age, Risk factors, Troponin; n/N=number of events/sample size; PMID=PubMed identifier.

APPENDIX Q. REVASCULARIZATION OUTCOMES

Appendix Table Q-1. Revascularization Comparative Studies

Study PMID, Study Design	Follow-up Time (days)	Outcome Definition	Subgroup	Arm	n/N (%)	OR (95% CI)*	Reported P Value
<i>Overall Comparison: ADP vs hs-cTn without ADP</i>							
Hyams 2018 29478861	6 wk	CABG		ADP 0/3 HEART	5/449 (1.1)	0.3 (0.11,0.84)	NR
				hs-cTn	15/417 (3.6)		
Hyams 2018 29478861	6 wk	PCI		ADP 0/3 HEART	13/449 (2.9)	1.33 (0.53,3.84)	NR
				hs-cTn	9/417 (2.2)		
Hyams 2018 29478861	6 wk	Any revascularization		ADP 0/3 HEART	18/449 (4.0)	RD -1.7 (-4.6, 1.1)*	NR
				hs-cTn	24/417 (5.8)		
<i>Subgroup Comparison</i>							
Stoyanov 2020 31298551	30	PCI	Patients who received coronary angiography	ADP ESC 0/1	140/328 (42.7)	RD 0.2 (-7.2, 7.6)*	NR
				ADP ESC 0/3	152/358 (42.5)		

Notes. * Calculated by research team.

Abbreviations. ADP=accelerated diagnostic protocol; CABG=coronary artery bypass graft; CI=confidence interval; ESC=European Society of Cardiology; HEART=History, Electrocardiogram, Age, Risk factors, Troponin; hs-cTn=high-sensitivity cardiac troponin; n/N %=(number of events/sample size) %; NR=not reported; OR=odds ratio; PCI=percutaneous coronary intervention; PMID=PubMed identifier; RD=risk difference; wk=week.

Appendix Table Q-2. Revascularization: Rule Out, Low Risk Not Described as Rule Out, Discharge or Grey Zone, and Rule In or High Risk

Study, Year, PMID	ADP	Follow-up Time (Days)	Outcome Definition	n/N (%)
<i>Rule Out</i>				
Chew 2019 31478763	ADP 0/1	30	PCI	11/1187 (0.9)
			CABG	4/1187 (0.3)
			Any revascularization	15/1187 (1.3)
Twerenbold 2019 31345421	ADP ESC 0/1	30	PCI	49/1420 (3.5)
			CABG	1/1420 (0.1)
			Any revascularization	62/1420 (4.4)
<i>Discharge</i>				
Twerenbold 2019 31345421	ADP ESC 0/1	30	PCI	1/1619 (0.1)
			CABG	0/1619 (0)
			Any revascularization	10/1619 (0.6)
<i>Observe / Grey Zone</i>				
Chew 2019 31478763	ADP 0/1	30	PCI	15/308 (4.9)
			CABG	3/308 (1.0)
			Any revascularization	18/308 (5.8)
Twerenbold 2019 31345421	ADP ESC 0/1	30	PCI	53/581 (9.1)
			CABG	17/581 (2.9)
			Any Revascularization	69/581 (11.9)
<i>Rule In</i>				
Chew 2019 31478763	ADP 0/1	30	PCI	27/136 (19.9)
			CABG	6/136 (4.4)
			Any revascularization	33/136 (24.3)

Study, Year, PMID	ADP	Follow-up Time (Days)	Outcome Definition	n/N (%)
Twerenbold 2019 31345421	ADP ESC 0/1	30	PCI	116/295 (39.3)
			CABG	36/295 (12.2)
			Any revascularization	151/295 (51.2)
<i>High Risk Not Described as Rule In</i>				
Twerenbold 2019 31345421	ADP ESC 0/1	30	CABG (based on admitted)	54/677 (8)
			PCI (based on admitted)	217/677 (32.1)
			Any revascularization (based on admitted)	272/677 (40.2)

Abbreviations. ADP=accelerated diagnostic protocol; CABG=coronary artery bypass graft; ESC=European Society of Cardiology; n/N %=(number of events/sample size) %; PCI=percutaneous coronary intervention; PMID=PubMed identifier.Appendix R. Hospital length of Stay outcomes

APPENDIX R. HOSPITAL LENGTH OF STAY OUTCOMES

Appendix Table R-1. Hospital Length of Stay: Rule Out, Low Risk Not Described as Rule Out, Discharge or Grey Zone, and Rule In or High Risk

Study, Year, PMID	ADP	Follow-up Time (Days)	Outcome Definition	N	Median (IQR)
<i>Rule Out</i>					
Twerenbold 2019 1345421	ADP 0/1	30	Nights	1420	0 (0,0)
<i>Discharge</i>					
Twerenbold 2019 1345421	ADP 0/1	30	Nights	1619	0 (0,0)
<i>Observe / Grey Zone</i>					
Twerenbold 2019 31345421	ADP 0/1	30	Nights	581	1 (0,5)
<i>Rule In</i>					
Twerenbold 2019 31345421	ADP 0/1	30	Nights	295	5 (3,9)
<i>High Risk Not Described as Rule In</i>					
Twerenbold 2019 31345421	ADP 0/1	30	Nights	677	5 (2,8)

Abbreviations. ADP=accelerated diagnostic protocol; ESC=European Society of Cardiology; IQR=interquartile range; N=sample size; PMID=PubMed identifier.