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Supplemental Online Content

Hansford HJ, Cashin AG, Jones MD, et al. Reporting of observational studies explicitly emulating randomized trials: a systematic review. *JAMA Netw Open*. 2023;6(9):e2336023. doi:10.1001/jamanetworkopen.2023.36023

- Supplement 1. Appendix 1.** Methodological Differences to the Protocol
- Appendix 2.** Complete Search Strategies for All Databases
- Appendix 3.** List of Phrases Deemed to Indicate Explicit Emulation of a Target Trial
- Appendix 4.** Operational Definitions for Items of the Emulation of the Target Trial
- Appendix 5.** Items Extracted That Are Not Included in Commonly Used Reporting Guidelines (STROBE, RECORD, ISPOR)
- Appendix 6.** Reasons for Study Exclusion at Level of Full Text
- Appendix 7.** Subgroup Analysis of Reporting of Target Trial Protocol and How It Was Emulated, by Reporting Guideline Use

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

22 **Appendix 1. Methodological Differences to the Protocol**

23

24 We initially set out to identify ‘implicit’ emulations of a target trial as well as studies which
25 explicitly state the study as an attempt to emulate a target trial. However, there are many ways
26 by which a study could emulate a target trial without doing so explicitly. Therefore, to contain
27 the scope of this study, we made a post-hoc decision to exclude studies from our analysis which
28 we initially identified as implicitly emulating a target trial. The studies excluded at this stage
29 are listed in Appendix 5.

30

31

32 **Appendix 2. Complete Search Strategies for All Databases**

33

34 Medline

35 1 (emulat* adj5 trial?).mp. 177

36 2 (target adj (trial? or experiment?)).mp. 668

37 3. (observational adj (stud* or research or data)).mp. 217117

38 4. ((real world or rwd) adj2 (stud* or research or data)).mp. 11627

39 5. (routine* adj2 data).mp. 8107

40 6. (comparative effectiveness adj2 (stud* or research or data)).mp. 5817

41 7. (emulat* or propensity score? or (causal adj2 (inference? or analys?s or effect*))).mp.

42 51359

43 8. 3 or 4 or 5 or 6 or 7 284549

44 9. 2 and 8 89

45 10. (target adj (trial? or experiment?)).ti. 95

46 11. 1 or 9 or 10 254

47 Filtered for time (2012-2022) manually after search

48

49 Embase

50 1. (emulat* adj5 trial?).mp.

51 2. (target adj (trial? or experiment?)).mp.

52 3. (observational adj (stud* or research or data)).mp.

53 4. ((real world or rwd) adj2 (stud* or research or data)).mp.

54 5. (routine* adj2 data).mp.

55 6. (comparative effectiveness adj2 (stud* or research or data)).mp.

56 7. (emulat* or propensity score? or (causal adj2 (inference? or analys?s or effect*))).mp.

57 8. 3 or 4 or 5 or 6 or 7

58 9. 2 and 8

59 10. (target adj (trial? or experiment?)).ti.

60 11. 1 or 9 or 10

61

62 psycINFO

63 noft(target trial emulat*) OR ((noft(real world data) OR (noft(emulat* trial)) OR

64 noft(observational) OR noft(routine* data)) AND noft(comparative effective*) AND

65 noft(causal infer*))

66

67 Web of Science
68 (TI=(emulat* trial)) OR (TI=(real world data) OR TI=(routine* data) OR
69 TI=(comparative effectiveness study comparative effectiveness research or
70 comparative effectiveness data) OR (TI=(emulat* or propensity score?) AND
71 TI=(causal inference or causal analysis or causal effect*))) AND ALL=(target trial or
72 emulat* or target trial emulation)

73

74 note: '?' is used as a wildcard symbol to capture different spellings

75

76

77 **Appendix 3. List of Phrases Deemed to Indicate Explicit Emulation of a Target Trial**
78 Target trial emulation, emulate* *near* target trial, emulat* trial, emulat* *near* randomi?ed trial,
79 trial emulation, randomi?ed trial emulation, hypothetical trial emulation, trial replication.
80
81 note: '?' is used as a wildcard symbol to capture different spellings
82
83

84 **Appendix 4. Operational Definitions for Items of the Emulation of the Target Trial**

85

Protocol element	Requirements to be deemed reported
Eligibility criteria	Stated all characteristics that define inclusion in the target trial
Treatment strategies	Stated the treatment strategies under comparison
Treatment assignment	Stated that randomization was assumed conditional on baseline covariates
Outcome(s)	Stated the outcome(s) of interest
Follow-up	Described the observation period of participants, including when follow up starts and ends
Causal contrast(s) of interest	Stated the estimand(s) of interest: e.g., intention-to-treat effect, per-protocol effect
Analysis plan	Described the statistical analyses, including methods by which covariates were adjusted to emulate randomization, e.g., matching, standardization, inverse-probability weighting

86

87

88 **Appendix 5.:** Items Extracted That Are Not Included in Commonly Used Reporting
89 Guidelines (STROBE, RECORD, ISPOR)

90

- 91 • Does it state whether the study was preregistered?
- 92 • Is a reason given that an RCT was not possible?
- 93 • Does the study describe itself as a target trial emulation?
- 94 • In regard to the definition of treatment strategy, which of the following do the study
95 report: duration, type, frequency, dose, other, none)
- 96 • In what form does the study present the target trial / emulated protocol?
- 97 • **Assignment procedures:** Stated that treatment strategies were assigned based upon the
98 assumption that randomization is being adequately emulated, or that baseline
99 variables were adjusted for, given the baseline covariates are reported.
- 100 • **Time zero:** Does the study explicitly report how time zero was defined?
- 101 • **Causal contrast(s):** Does the study explicitly report the causal contrasts / estimands of
102 interest?
- 103 • Does the study report if there are any potential unmeasured confounders?
- 104 • Does the study report how confounders were selected?
- 105 • Which casual assumptions are reported in the paper?
- 106 • Does the study describe similarities / differences between the ideal hypothetical
107 randomized trial and emulation?
- 108 • Is a table comparing characteristics of participants between the two (or more)
109 treatment groups presented?

110

111

112 **Appendix 6. Reasons for Study Exclusion at Level of Full Text**

113

114 **Not in English language (1)**

115

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117 Making the Best of It!]. *Gesundheitswesen*. Nov 2021;83(S 02):S69-s76. Nutzung von
118 Sekundärdaten für die pharmakoepidemiologische Forschung – machen wir das Beste draus!
119 doi:10.1055/a-1633-3827

120

121 **Not in humans (1)**

122

123 2. Van Cuong NK, B. T.: Phu, D. H.: Van, N. T. B.: Hien, V. B.: Thwaites, G.: Carrique-Mas, J.:
124 Choisy, M. Effects of prophylactic and therapeutic antimicrobial uses in small-scale chicken
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126

127 **Not in field of medicine (1)**

128

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132

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134

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208 M. W.: Hernan, M. A.: Mueller, A. L.: Wang, W.: Leaf, D. E.: Walther, C. P.: Anumudu, S. J.:
209 Kopecky, K. F.: Milligan, G. P.: McCullough, P. A.: Nguyen, T. D.: Shaefi, S.: Baskin, S. M.:
210 Shankar, S.: Valencia, J. D.: Pannu, A.: Hayes, M. M.: Grandin, E. W.: Waikar, S. S.: Kibbelaar, Z.
211 A.: Athavale, A. M.: Hart, P.: Upadhyay, S.: Vohra, I.: Oyintayo, A.: Rachoin, J. S.: Schorr, C. A.:
212 Shea, L.: Edmonston, D. L.: Mosher, C. L.: Shehata, A. M.: Cohen, Z.: Allusson, V.: Bambrick-
213 Santoyo, G.: Bhatti, N.: Mehta, B.: Williams, A.: Walters, P.: Go, R. C.: Rose, K. M.: Lisk, R.: Chan,
214 L.: Coca, S. G.: Altman, D. R.: Saha, A.: Soh, H.: Wen, H. H.: Bose, S.: Leven, E. A.: Wang, J. G.:
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216 Kapoor, R.: Meshberger, C.: Kelly, K. J.: Parikh, C. R.: Garibaldi, B. T.: Corona-Villalobos, C. P.:
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221 Kumar, P. N.: Lazarous, D. G.: Kassaye, S. G.: Melamed, M. L.: Mocerino, T. S. J. R.: Prudhvi, K.:
222 Zhu, D.: Levy, R. V.: Azzi, Y.: Fisher, M.: Yunes, M.: Sedaliu, K.: Golestaneh, L.: Brogan, M.:
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224 S. J.: Plataki, M.: Alvarez-Mulett, S. L.: Gomez-Escobar, L. G.: Pan, D.: Lee, S.: Krishnan, J.:
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226 Kruser, J. M.: Wunderink, R. G.: Hodakowski, A. J.: Velez, J. C. Q.: Price-Haywood, E. G.: Matute-
227 Trochez, L. A.: Hasty, A. E.: Mohamed, M. M. B.: Avasare, R. S.: Zonies, D.: Sise, M. E.: Newman,
228 E. T.: Omar, S. A.: Pokharel, K. K.: Correa, S.: Kamal, O.: Yang, H.: Boateng, J. O.: Lee, M.:
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1133

1134 **Appendix 7.** Subgroup Analysis of Reporting of Target Trial Protocol and How It Was Emulated,
 1135 by Reporting Guideline Use

	Value	Count (N (%))	
	Used reporting guideline?	No (n=157)	Yes (n=43)
<i>How the protocol of the emulated target trial was reported</i>	Not fully described	54 (34)	15 (35)
	Only in text	50 (32)	19 (44)
	Table	54 (34)	9 (21)
<i>Both target trial protocol and its emulation described explicitly as such?</i>	Yes	73 (46)	13 (30)
Description of how the target trial was emulated ^a			
<i>Eligibility criteria</i>	Yes	151 (96)	42 (98)
<i>Treatment strategies</i>	Yes	149 (96)	42 (98)
<i>Assignment procedures</i>	Yes	142 (90)	31 (72)
<i>Outcome(s)</i>	Yes	152 (97)	42 (98)
<i>Follow-up</i>	Yes	146 (93)	40 (93)
<i>Causal contrast(s)</i>	Yes	112 (71)	34 (79)
<i>Analysis plan</i>	Yes	153 (97)	41 (95)
<i>Specification of time zero (i.e., baseline)</i>	Yes	128 (82)	37 (86)

1136 ^a. Operational definitions of target trial protocol items are described in Appendix 5.
 1137