Comparing ROBINS-I V2 and Downs & Black for nRCTs in the Context of HTA

HTA84

Yogesh Punekar[1], Ranjith Babu Vagichalra[2], Aditi Agarwal[2], Manne Mithun Chakrawarthy[2], Premsagar Kummari[2], Veeranki Prasanth[2] , Geddamuri Bala Ganesh[2]
[1]*IQVIA, London, United Kingdom*
[2]*IQVIA, India*

Supplementary Table 1: *Comparison of ROBINS-I V2 and Downs & Black checklist in endometrial cancer studies*

Domains	ROBINS-I V2				Downs & Black checklist			
	Oaknin et al., 2020 (1)	O'Malley et al., 2022 (2)	Makker et al., 2022 (3)	Comments	Oaknin et al., 2020 (1)	O'Malley et al., 2022 (2)	Makker et al., 2022 (3)	Comments
Bias due to confounding	Moderate	Moderate	Low	Q1.1–1.5 assess if baseline confounders were reported for (e.g., "Were there important confounding domains not considered or controlled for?").	0	1	1	Item 5: "Are distributions of principal confounders described?" Limited; no structured approach to confounder identification or adjustment is included.
Bias in classification of interventions	Low	Low	Low	Q2.1–2.5 address intervention classification and missclassification (e.g., "Was intervention status accurately classified for all or nearly all participants?").	1	1	1	Item 4: "Were interventions clearly described?" Ensures clarity but does not explore misclassification risk systematically.
Bias in selection of participants	Low	Low	Low	Q3.1–3.10 evaluate if participant inclusion led to bias (e.g., "Were eligible participants representative of the population?").	1	1	1	Item 21: "Were subjects representative of the source population?" Also reflects external validity rather than bias alone.
Bias due to deviations from intended interventions	Low	Low	Low	Q4.1–4.5 assess non-adherence, co-interventions, and whether deviations introduced bias (e.g., "Were deviations balanced or affected outcome?").	1	1	1	Item 6: "Were the main findings of the study clearly described?" Simpler compliance check, lacks causal implications or assessment of deviations.
Bias due to missing data	Low	Low	Low	Q5.1–5.11 examine extent, reasons, and handling of missing data (e.g., "Is it likely that missing data could bias the results?").	0	1	1	Items 9 and 26 cover reporting and justification of attrition and loss to follow-up (e.g., "Were loss to follow-up described or were loss to follow-up taken into account").
Bias in measurement of outcomes	Low	Low	Low	Q6.1–6.4 determine if outcome assessment was blinded or influenced by intervention knowledge (e.g., "Could outcome measurement be influenced by bias?").	1	1	1	Items 7–8: "Were the outcome measures valid and reliable?" and "Were they applied equally to all subjects?" Relates to accuracy and consistency.
Bias in selection of reported result	Moderate	Moderate	Low	Q7.1–7.3 evaluate if prespecified outcomes were all reported (e.g., "Was there evidence of selective reporting of outcomes or timepoints?").	0	1	1	Item 16: "Were all important outcomes considered in analysis?" Implies thoroughness but lacks structure to detect selective reporting.
External validity (generalizability)	Not assessed	Not assessed	Not assessed	Not assessed. ROBINS-I is designed to evaluate internal validity only.	1	1	1	Items 11–13: "Were staff and representative members blinded?" Addresses applicability of findings to real-world populations.
Reporting quality (clarity)	Not assessed	Not assessed	Not assessed	Not covered in ROBINS-I (reporting clarity is not the same as bias).	0	1	1	Items 1–3, 10, 17–20 assess clarity of objectives, methods, variability, and adverse event reporting. Evaluates completeness and transparency of reporting.
Power/sample size estimation	Not assessed	Not assessed	Not assessed	Not included. ROBINS-I does not assess adequacy of power or sample size.	1	0	1	Item 27: "Did the study have sufficient power to detect a clinically important effect?" One item assesses design robustness.
Overall*	Serious to Critical	Low	Serious to Critical		18	24	18	

Abbreviations: ROBINS-I V2, Risk of Bias in Non-randomized Studies of Interventions, Version 2

References:
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2. O'Malley D, Bariani G, Cassier P, Marabelle A, Hansen A, Acosta ADJ, et al. Health-related quality of life with pembrolizumab monotherapy in patients with previously treated advanced microsatellite instability high/mismatch repair deficient endometrial cancer in the KEYNOTE-158 study. Gynecologic oncology. 2022;166(2):245-53.
3. Makker V, Colombo N, Casado Herráez A, Santin AD, Colomba E, Miller DS, et al. Lenvatinib plus pembrolizumab for advanced endometrial cancer. New England Journal of Medicine. 2022;386(5):437-48.

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