The use and validation of oncology endpoint proxies in real-world studies: Targeted literature review mapping 64 retrospective and validation real-world studies

RWD20

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Objective

- Oncology clinical endpoints are not always recorded in real-world (RW) data. Proxy endpoints are increasingly being used in RW studies.[1]
- The objective of this **targeted literature review** was to provide a summary of the use of proxied clinical endpoints in RW oncology studies.

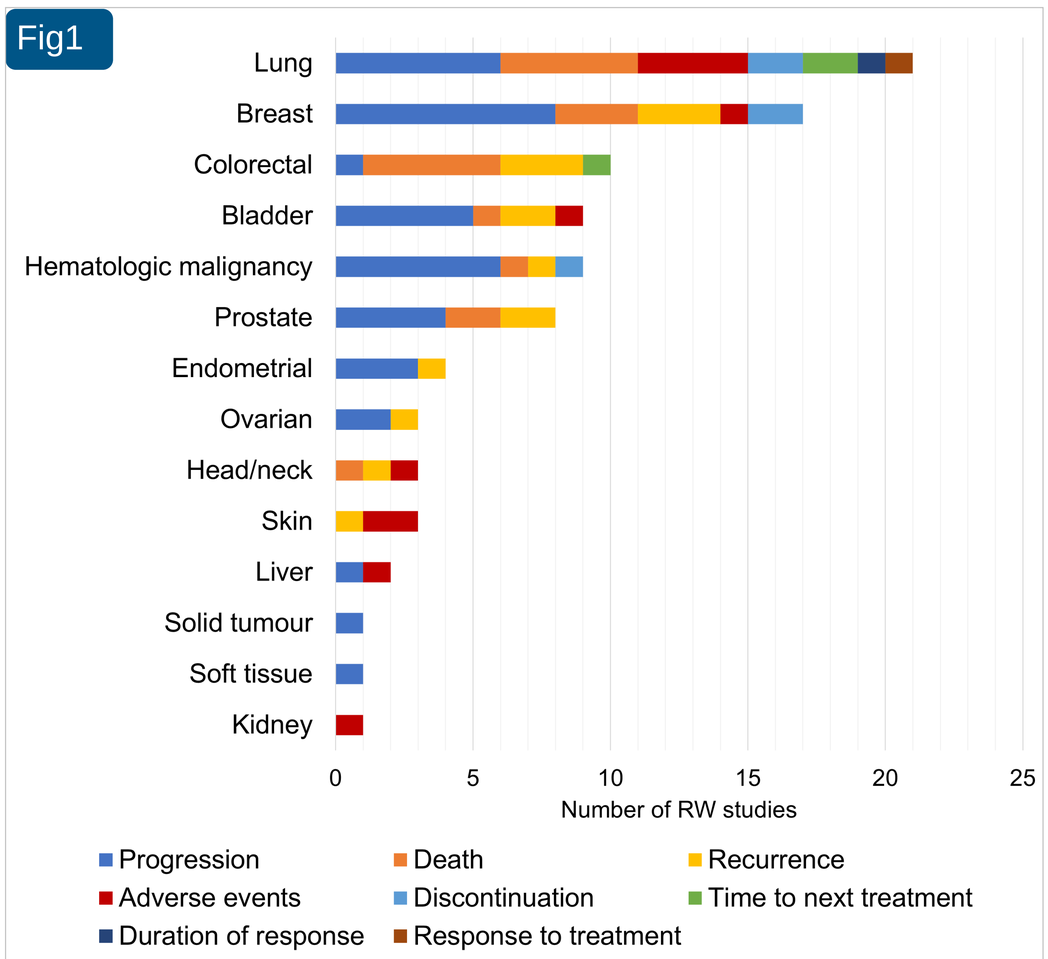
Methods

- Pragmatic literature searches were conducted in EMBASE® via OVID SP® from database inception, on 25th April to 3rd May 2024, by combining free-text terms for cancer and for the concept of proxy endpoints. No publication date limits were used.
- One experienced reviewer performed screening and data extraction of retained records reporting use of proxying in RW oncology studies. Snowball and desktop searches (on Google®) were used to identify additional studies.
- Quality-check was conducted by subject-matter experts.

Results

- We included 64 RW studies, of which 14 (22%) were methodological studies (i.e. the authors explicitly aimed to assess proxy performance) and 50 (78%) were retrospective natural history or effectiveness RW studies using proxies.
- The most frequently assessed cancers were lung (n=21 studies) and breast (n=17), and progression proxies were most commonly used (n=38) (**Fig 1**)
- Potential bias from use of proxy endpoints was acknowledged in less than half of the studies (n=25), within which a range of methods were used to assess potential bias (**Fig 3**)

Fig1

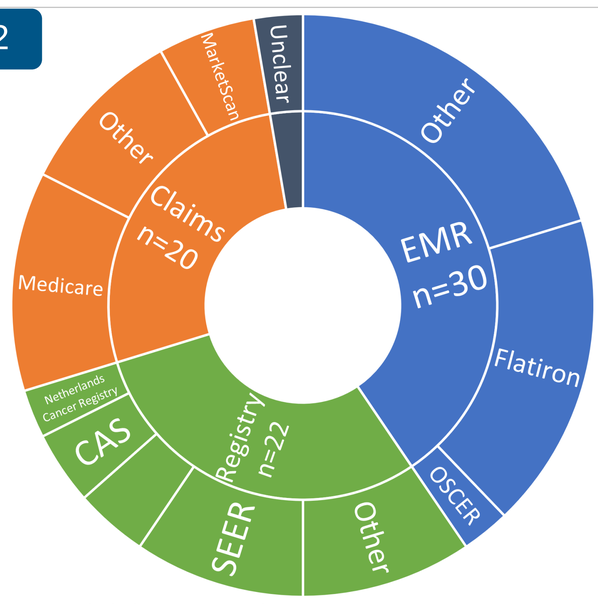


RW studies assessing cancer of the lung and breast were most commonly using endpoint proxies, particularly endpoints of progression, survival and recurrence.

Concluding remarks

- Proxy use in RW oncology studies mainly focuses on **progression in lung and breast cancer**.
- Potential bias was only acknowledged in 25 of 64 studies, of which **concerns of misclassification** prevailed.
- Consistency in assessing bias in studies using proxied endpoints is needed; methods such as **quantitative bias analysis**[2] should be applied more commonly.

Fig2



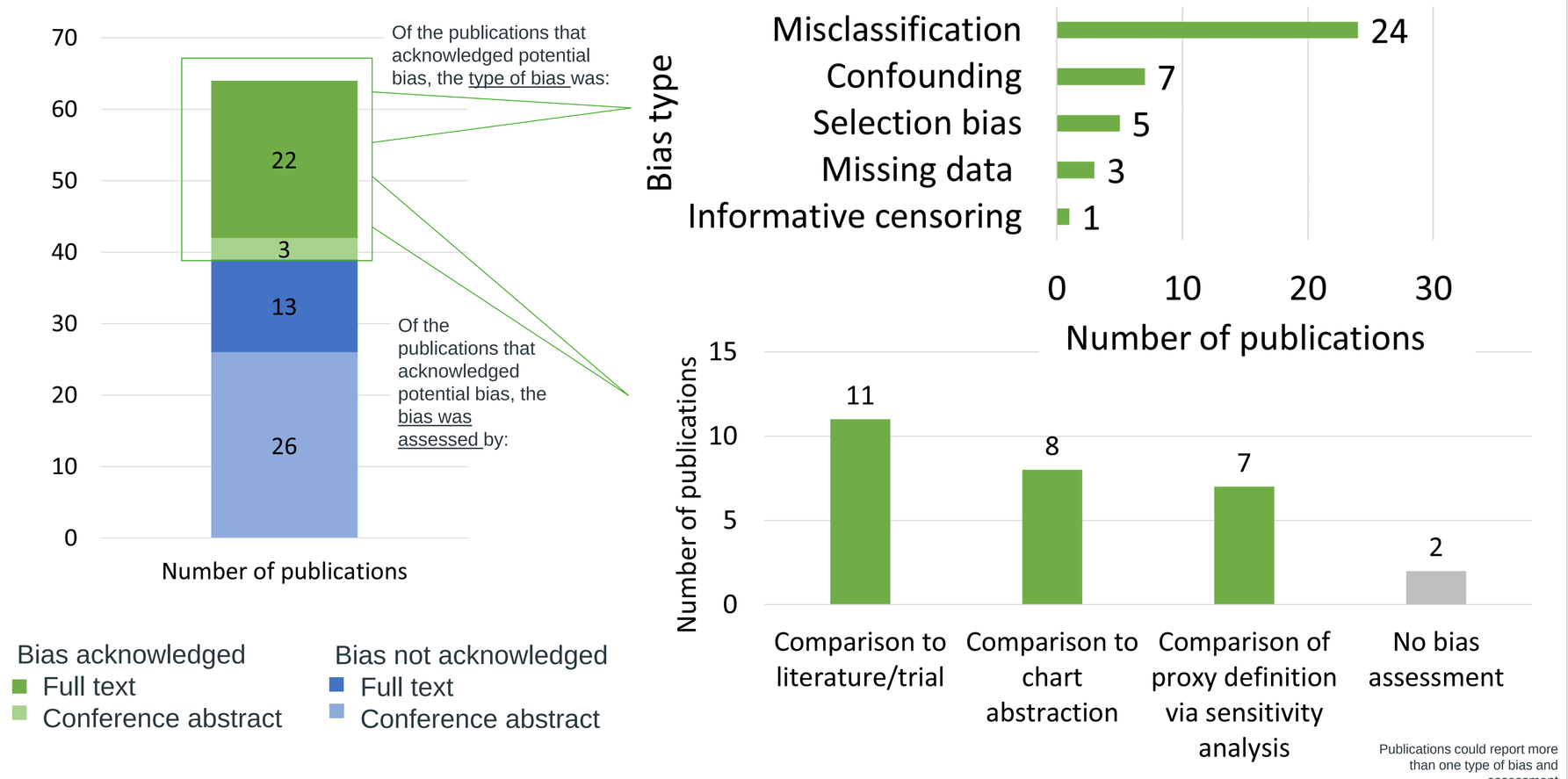
RW studies with proxy endpoints mostly used Electronic Medical Records (EMR), national or state registries and claims data.

Abbreviations: CAS, Cancer Analysis System (England's cancer registry); EMR, Electronic Medical Records; OSCER, Oncology Services Comprehensive Electronic Records (US data); SEER, Surveillance, Epidemiology, and End Results (US data).

Fig3

Potential bias was acknowledged in 25/64 RW studies, of which almost all recognised possible misclassification.

The potential bias induced by proxied endpoints were assessed via comparisons with the literature/trials, chart abstractions or altering proxy definitions in sensitivity analyses.



Publications could report more than one type of bias and assessment

1. Li Q, Zhang H, Chen Z, Guo Y, George TJ Jr, Chen Y, Wang F, Bian J. Validation of Real-World Data-based Endpoint Measures of Cancer Treatment Outcomes. AMIA Annu Symp Proc. 2022 Feb 21;2021:716-725. PMID: 35308944; PMCID: PMC8861715.
2. Gray, C., Ralphs, E., Fox, M.P., Lash, T.L., Liu, G., Kou, T.D., Rivera, D.R., Bosco, J., Braun, K.V.N., Grimson, F. and Layton, D., 2024. Use of quantitative bias analysis to evaluate single-arm trials with real-world data external controls. *Pharmacoepidemiology and Drug Safety*, *33*(5), p.e5796.

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