Reliability of Oncology Value Framework Outputs: Concordance Between Independent Research Groups

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BACKGROUND

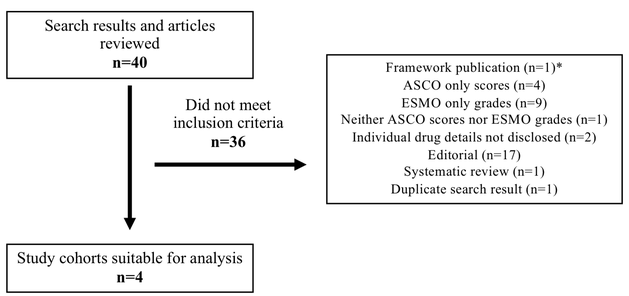
- Little is known of the reliability of modern value frameworks, despite their increasing utilization.

OBJECTIVE

- This study aims to assess the concordance and inter-rater reliability of previously published scores/grades of drugs using the American Society of Clinical Oncology Value Framework (ASCO-VF) and European Society for Medical Oncology Meaningful Clinical Benefit Scale (ESMO-MCBS).

METHODS

- All previously published data sets containing both ASCO-VF scores and ESMO-MCBS grades were identified through a *PubMed* search of studies utilizing value frameworks.
- The final data set included drugs evaluated by both ASCO-VF and ESMO-MCBS grades, independently rated by least two different studies (Figure 1); these scores/grades were abstracted for statistical evaluation.
- Intraclass correlation coefficient (ICC) was used to assess inter-rater reliability.



*ESMO-MCBS framework paper grades were included in the correlative analysis, where applicable.

Figure 1. Identification of randomised controlled trials of systemic therapy in breast cancer, non-small-cell lung cancer, colorectal cancer, and pancreatic cancer published 2011–15

RESULTS

Drug	Indication	PMID(s) for Framework Outputs	Becker et al.[1]		Vivot et al.[2]		Cheng et al.[3]		Del Paggio et al.[4]		ESMO Authorship Grade[5]
			ASCO	ESMO	ASCO	ESMO	ASCO	ESMO	ASCO	ESMO	
Abiraterone acetate	Second-line treatment of prostate cancer	22995653, 21612468	23	4	34.6	4	34.3	4	X	X	4
Ado-trastuzumab emtansine	Second-line treatment of HER2-positive breast cancer	23020162	33.7	5	62.4	5	36.4	5	45	5	5
Afatinib	First-line treatment of non-small cell lung cancer with EGFR mutations	23816960	47.7	4	31.7	4	30.6	4	31	4	4
Bevacizumab	First-line treatment of colorectal cancer	15175435	23.5	1	31	3	X	X	X	X	3
Cabazitaxel	Second-line treatment	20888992	45.2	2	40.5	2	25.2	2	X	X	2

Table 1. Sample abstraction of drugs scores/grades evaluated by ASCO-VF and ESMO-MCBS, respectively, by four independent research publications, as well as grades denoted by the ESMO framework authorship group, where applicable.

Framework	Authorship Concordance	Deviation in Scores/Grades	
		±10 points or ±1 grade	±20 points or ±2 grades
ASCO-VF (v2)	2 (5%)	18 (46%)	29 (74%)
ESMO-MCBS	17 (44%)	31 (80%)	35 (90%)

Table 2. Score/grade concordance and deviation frequencies for 39 evaluated drugs.

Framework	Setting	ICC	95% CI
ASCO	All drugs (n=39)	0.82	0.7 to 0.9
	Only drugs evaluated from single RCT (n=29)	0.85	0.72 to 0.92
ESMO	All drugs (n=39)	0.88	0.8 to 0.93
	Only drugs evaluated from single RCT (n=29)	0.9	0.83 to 0.95

Table 3. Inter-rater reliability of framework outputs between four independent authorship groups.

- Out of 40 eligible studies, 4 contained drugs that were evaluated by both frameworks (Figure 1).
- The final data set contained 36 drugs for 39 indications (Table 1).
- 29 drug indications were evaluated by the authorshop groups using a single RCT; more than one RCT was used to evaluate 10 drug indications.
- Absolute concordance was found to be 5% for ASCO-VF and 44% for ESMO-MCBS, increasing to 74% and 80% when deviations within 20 points and 1 grade were considered, respectively (Table 2).
- ICC was 0.82 (95% CI 0.70 - 0.90) for ASCO-VF and 0.88 (95% CI 0.80 - 0.93) for ESMO-MCBS (Table 3).
- Dichotomizing ESMO-MCBS grades by "substantial clinical benefit" (i.e., grades B, A, 4, or 5) yielded similar ICCs.

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DISCUSSION

- Our results show that despite excellent ICCs, absolute concordance is poor for ASCO-VF and fair for ESMO-MCBS.
- ESMO-MCBS concordance improves substantially with a deviation of 1 grade above and below the output, while ASCO-VF requires a deviation of 20 points in order to achieve comparable concordance.
- The complexity in tabulating framework outputs partially explains the differences in absolute concordance: ASCO-VF involves points that cumulate to 120 or above vs ESMO-MCBS which has discrete grading thresholds (e.g. 1 to 5 for palliative trials, and C to A for curative trails).
- Discrepant scores/grades were also seen due to authorship groups evaluating the same drug indication using a differing RCTs; however, this minimally changed the ICC (Table 3).
- Continued updating of the ASCO-VF and ESMO-MCBS is a major limitation of the data generated in this study.

CONCLUSIONS

- Current value frameworks are remarkably reliable in their outputs.
- Absolute concordance in framework outputs, however, is poor.
- Future iterations of each framework should strongly consider formal measurement studies (e.g. inter-rater reliability) prior to publication in order to adequately evaluate their measurement characteristics and prevent errors in framework utilization.
- These are important considerations for users placing an onus on the absolute grades/scores of these frameworks, particularly if the outputs are used for public policy implementation and patient/doctor decision-making.