

# Do the American Society of Clinical Oncology (ASCO) Value Framework Version 2 and the European Society of Medical Oncology (ESMO) Magnitude of Clinical Benefit Scale measure the same construct of clinical benefit?

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## Introduction

- ASCO and ESMO both aim to measure clinical benefit.<sup>1,2</sup>
- ASCO version 1 (v1) Value Framework published August 2015<sup>1</sup>, ASCO version 2 (v2) published May 2016<sup>3</sup>, ESMO Magnitude of Clinical Benefit Scale (ESMO-MCBS) published May 2015.<sup>2</sup>
- Many definitions of “clinical benefit” exist –quality-adjusted life-years (QALYs) often treated as an established standard.<sup>4,5</sup>
- Unclear whether ASCOV2 and ESMO-MCBS measure similar constructs of clinical benefit, and whether scores relate to QALYs and funding recommendations in UK and Canada.

## Methods

### Selection of Studies

- Randomized clinical trials (RCTs) of oncology drug approvals (Jan 2006–Aug 2015) by the Food and Drug Administration (FDA), European Medicines Agency (EMA), Health Canada.
- Inclusion criteria: phase III, double/triple-arm RCTs, primary endpoint of overall survival (OS), progression-free survival (PFS), time to progression (TTP), response rate (RR).

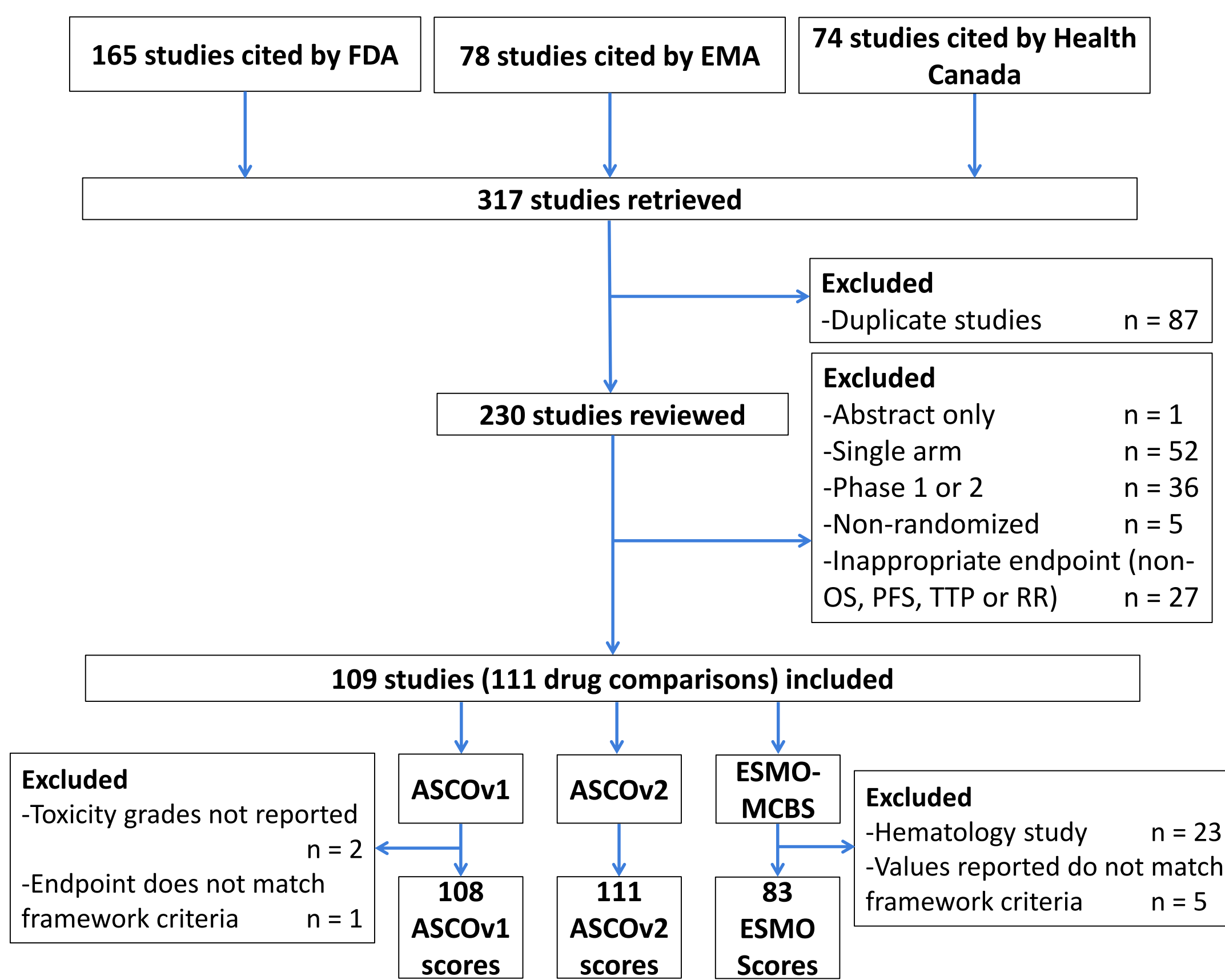
### Study Scoring

- Studies scored by multiple independent reviewers (2-3 reviewers) with each framework.
- Disagreements resolved by consensus to yield accepted scores.
  - Preliminary score:** scores prior to applying adjustments (i.e. toxicity/bonus points).
  - Final score:** scores after applying adjustments.

### Statistical Analyses

- Spearman correlation coefficients: construct convergent validity (between frameworks) and criterion validity against incremental QALYs from the National Institute of Clinical Excellence (NICE) and the pan-Canadian Oncology Drug Review (pCODR).
- Logistic regression: associations between scores and NICE/pCODR recommendations.
- Inter-rater reliability: intra-class correlation coefficients (ICCs), absolute degree of concordance.

## Results



**Table 1. Characteristics of evaluated studies**

	ASCOv1	ASCOv2	ESMO
Median Score (IQR)	24 (16-34)	22 (8.3-34.9)	3 (2-4)
<b>Indications</b>			
Lung Cancer	12	12	12
Colorectal Cancer	12	12	11
Breast Cancer	10	10	10
Myeloma	10	10	NA
Melanoma	9	9	9
Renal Cell Carcinoma	8	8	8
Prostate Cancer	7	8	7
Chronic Lymphocytic Leukemia	8	8	NA
Other	32	34	26
<b>Primary endpoints</b>			
OS	36	36	36
PFS	54	56	41
RR	4	4	2
Other	21	22	12

**Table 2. Inter-rater reliability of the frameworks**

	SCORE	ICC (95% CI)	ABSOLUTE CONCORDANCE
ASCOV1	Preliminary	0.90 (0.86 – 0.93)	55.9%
	Final	0.93 (0.91 – 0.95)	63.9%
ASCOV2	Preliminary	0.90 (0.85 – 0.93)	69.4%
	Final	0.86 (0.76 – 0.89)	18.0%
ESMO-MCBS	Preliminary	0.94 (0.91 – 0.96)	67.0%
	Final	0.94 (0.91 – 0.96)	64.8%

- Good inter-rater reliability for all frameworks.
- Absolute concordance rate of ASCOV2 final scores was low due to difficult toxicity scoring guidelines.

**Table 3. Criterion validity - logistic regression**

	FRAMEWORK	ODDS RATIO (95% CI)	P-VALUE
NICE	ASCOv1	1.02 (0.98 - 1.07)	0.29
	ASCOv2	1.02 (0.98 - 1.05)	0.37
	ESMO	1.73 (0.73 - 4.13)	0.22
pCODR	ASCOv1	1.04 (0.99 - 1.10)	0.12
	ASCOv2	1.03 (0.96 - 1.08)	0.086
	ESMO	2.47 (0.88 - 6.96)	0.087

- Funding recommendations made by NICE or pCODR were not significantly associated with ASCOV1, ASCOV2 or ESMO scores (all p > 0.05).

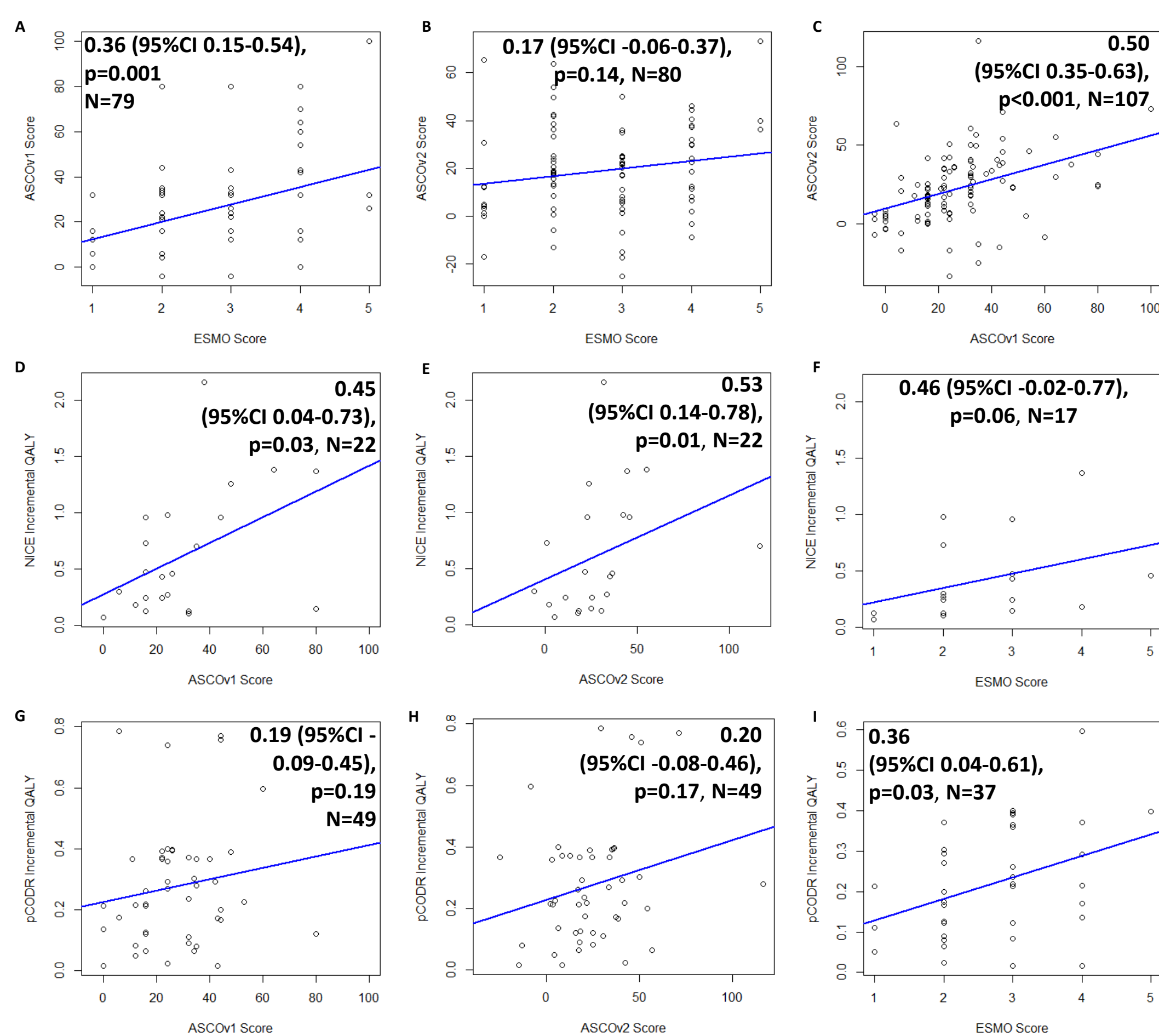
## Conclusions

- The weak-to-moderate correlations between the ASCO frameworks and ESMO-MCBS, with QALYs, and with NICE/pCODR funding recommendations suggest different constructs of clinical benefit measured.
- Construct convergent validity with the ESMO-MCBS in fact did not increase with the updated ASCO framework.

## References

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**Figure 1. Study selection for analysis and scoring**



**Figure 2. Spearman correlation coefficient plots for final scores of A) ASCOV1 vs. ESMO, B) ASCOV2 vs. ESMO, C) ASCOV2 vs. ASCOV1, D) NICE Incremental QALY vs. ASCOV1, E) NICE Incremental QALY vs. ASCOV2, F) NICE Incremental QALY vs. ESMO, G) pCODR Incremental QALY vs. ASCOV1, H) pCODR Incremental QALY vs. ASCOV2, and I) pCODR Incremental QALY vs. ESMO**

- Poor-to-moderate correlations between frameworks, and between each framework and NICE or pCODR incremental QALYs.
- Construct convergent validity of the ASCO framework with the ESMO-MCBS did not increase with the updated ASCOV2 framework (coefficients: 0.17 vs 0.36).