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A Practical Guide to Applying RECIST 1.1 in Clinical Trial Data Programming

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Abstract: ***RECIST 1.1 provides standardized rules for measuring solid tumors and assigning response categories in clinical trials. Accurate programming requires more than applying percentage cutoffs: teams must preserve lesion identity, distinguish target from non-target disease, use the correct measurement axis, compare tumor sums with the correct reference, account for new lesions, and derive time-point and best overall response according to the protocol. This tutorial translates the principal RECIST 1.1 concepts into a programming-oriented workflow and relates them to the CDISC Study Data Tabulation Model (SDTM) Tumor Identification (TU), Tumor Results (TR), and Disease Response (RS) domains. A synthetic example illustrates why progressive disease for target lesions requires both a relative increase of at least 20% from the smallest on-study sum and an absolute increase of at least 5 mm, while a qualifying new lesion may establish progression independently. The article is a narrative educational synthesis, not a systematic review, clinical study, or validation of a programming implementation. It emphasizes traceability from protocol and source assessments through standardized datasets to analysis endpoints.***

Keywords: RECIST 1.1; oncology; clinical trials; SDTM; statistical programming

1. Introduction

Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 standardizes anatomic tumor assessment in solid-tumor clinical trials. The criteria support consistent measurement of disease over time and inform endpoints such as objective response and progression-free survival. RECIST 1.1 reduces the number of target lesions compared with RECIST 1.0, clarifies lymph-node assessment, and defines progression using a change from the smallest on-study target-lesion sum together with an absolute increase threshold [1].

For statistical programmers, the challenge is to translate protocol-specified assessments into reproducible records and analysis variables without losing the clinical meaning of each observation. A tumor diameter, a lesion-level response, a time-point response, and a patient's best overall response are related but distinct concepts. This tutorial presents the criteria as a data flow from baseline lesion selection through longitudinal assessment and response derivation, with reference to CDISC SDTM oncology domains.

2. Literature Survey

The RECIST Working Group published RECIST 1.1 in 2009 after examining data from more than 6,500 patients and over 18,000 target lesions. The revision retained unidimensional anatomic measurement and introduced a maximum of five target lesions overall and two per organ. It also specified short-axis measurement for lymph nodes, a 5 mm absolute increase condition for target-lesion progression, and separate response rules for target and non-target disease [1]. Later clarifications from the RECIST Committee address implementation questions that arise in clinical trials [2].

CDISC provides a complementary representation layer for study data. Tumor identification and lesion classification are represented in TU, quantitative or qualitative lesion assessments in TR, and disease-level response in RS. The RECIST 1.1 oncology response supplement includes guidance for supporting domains and relationships among records, including PR, TU, TR, RS, and RELREC as applicable [3,4]. These standards describe tabulation structure; the protocol, imaging charter, and analysis plan remain controlling sources for study-specific collection and analysis decisions.

3. Problem Definition

A slide-based summary can make RECIST appear to be a set of independent thresholds. Programming errors arise when those thresholds are applied without their context. Common examples include measuring a lymph node by its long axis, treating every measurable lesion as a target lesion, comparing progression with baseline instead of the smallest on-study sum, omitting the 5 mm absolute increase, or assigning progression without considering non-target disease and new lesions. A separate risk occurs when a derived response is confused with a site-reported assessment or when a subject-level endpoint is derived from an incomplete assessment history.

The programming objective is therefore to preserve the lineage of each response: protocol-defined criteria and schedule; source lesion assessments; standardized lesion records; lesion and time-point response rules; and the final analysis endpoint. Decisions about assessment windows, missing or unevaluable data, confirmation, censoring, and analysis populations must be documented in the protocol and statistical analysis plan rather than inferred from a general teaching example.

4. Methodology and Approach

This article reorganizes an educational presentation into a narrative tutorial. The principal rules were checked against the published RECIST 1.1 guideline and CDISC SDTM oncology materials [1,3,4]. No systematic literature search, patient-level analysis, software validation, or empirical comparison was performed. The examples below are synthetic and serve only to explain the logic.

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Baseline Lesion Selection

Only lesions documented at baseline can be selected as target lesions. A patient can have measurable disease without every measurable lesion becoming a target. Select no more than five target lesions in total and no more than two in any one organ, prioritizing lesions that can be measured reproducibly. For non-nodal lesions, use the longest diameter. For lymph nodes, use the short axis. A non-nodal lesion generally meets the measurable threshold at 10 mm or more on CT or MRI when image slice thickness is appropriate; a pathological lymph node is measurable at a short axis of 15 mm or more. Nodes measuring 10 mm to less than 15 mm in short axis are pathological but non-target, while nodes under 10 mm are considered non-pathological for RECIST measurement [1].

Record all other disease sites as non-target lesions, including measurable lesions that were not selected as targets and lesions that do not meet measurability requirements. Follow non-target lesions qualitatively, commonly as present, absent, or unequivocal progression. Record new lesions as new findings rather than adding them to the baseline target-lesion set. The protocol should define imaging modalities, assessment schedules, and any disease-specific adaptations.

Longitudinal Target-Lesion Response

At each scheduled assessment, calculate the sum of diameters using the longest diameter for each non-nodal target lesion and the short axis for each target lymph node. Compare the current sum with the baseline sum for partial response and with the smallest sum recorded on study (the nadir, including baseline when it is the smallest) for progressive disease. A node may shrink below 10 mm and still contribute its actual short-axis value to the sum; complete response additionally requires all pathological nodes to have a short axis below 10 mm [1].

Category	Target-lesion rule	Programming reference
Complete response (CR)	Disappearance of all target lesions; pathological lymph nodes must be <10 mm short axis.	Current lesion status and nodal short axes.
Partial response (PR)	At least a 30% decrease in the target-lesion sum from baseline.	Baseline sum.
Progressive disease (PD)	At least a 20% increase from the smallest on-study sum and an absolute increase of at least 5 mm; a qualifying new lesion also indicates progression.	Nadir plus absolute-change check; new-lesion assessment.
Stable disease (SD)	Neither PR nor PD.	Baseline and nadir; protocol-defined timing requirements.

For example, assume a synthetic baseline sum of 100 mm, a smallest on-study sum of 70 mm, and a current sum of 84 mm. The increase from nadir is 14 mm, or 20%. Both the relative threshold and the absolute increase of at least 5 mm are met, so the target-lesion category is PD. If the current sum were 72 mm, the relative increase would be less than 20%; the PD threshold would not be met on the sum alone. This calculation illustrates why a percent-only rule is insufficient [1].

Non-target disease, new lesions, and time-point response

Non-target lesions are assessed as a group. Complete response requires disappearance of all non-target lesions and normalization of tumor-marker levels when relevant; pathological lymph nodes must be below 10 mm short axis. Non-CR/non-PD applies when non-target disease persists without unequivocal progression. Unequivocal progression means a substantial overall increase in non-target tumor burden sufficient to warrant discontinuing therapy, not a minor change in one lesion. A new malignant lesion generally establishes progression, subject to confirmation of equivocal findings under the trial's imaging procedures [1].

Time-point overall response combines target-lesion status, non-target status, and new-lesion status. Thus, target-lesion PR does not produce an overall PR when unequivocal non-target progression or a qualifying new lesion is present. Conversely, a patient may have stable target disease with non-target disease that remains present and no new lesion, resulting in an overall SD classification when the applicable rules are met. The exact combination logic should be programmed from the RECIST tables and study conventions, not from a simplified slide diagram.

Best overall response and trial endpoints

Best overall response summarizes the sequence of overall responses across protocol-defined post-baseline assessments. The ordering of response categories alone is not enough: response confirmation may be required in some non-randomized trials where response is the primary endpoint, while it is not routinely required in randomized trials or trials with other primary endpoints under RECIST 1.1. When required, confirmation intervals and the handling of missing assessments must follow the guideline and study analysis plan [1]. Stable disease also depends on meeting the protocol-specified minimum duration.

Objective response rate is generally the proportion of the defined analysis population whose best overall response is CR or PR. Progression-free survival is measured from randomization or another protocol-defined origin to documented progression or death, with event, censoring, and analysis-set rules specified in the protocol and statistical analysis plan. The slide deck's simple endpoint descriptions should not be treated as complete estimand or programming specifications; treatment of missing assessments, censoring, stratification, and intercurrent events requires study-specific documentation.

Mapping concepts to SDTM

A useful programming model keeps identity, measurement, and response in separate layers. TU identifies tumors or lesions and captures classification needed to track them. TR contains the lesion-level results, including measurements or qualitative findings. RS contains disease-level response assessments. The RECIST 1.1 CDISC supplement also addresses procedures and record relationships, so the mapping should follow the selected SDTMIG and supplement version rather than rely on domain names alone [3,4].

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Concept	Typical SDTM role	Programming check
Lesion identity and class	TU	Keep tumor identifiers stable across visits; distinguish target, non-target, and new lesions.
Measurements and lesion findings	TR	Retain units, assessment date, method, anatomic location, and the correct diameter axis.
Disease-level response	RS	Distinguish collected response from derived response and preserve assessment timing.
Relationships and procedures	RELREC and PR as applicable	Use the chosen CDISC supplement and study metadata to link supporting records.

Before programming, confirm the version of RECIST and SDTM standards, controlled terminology, source of each assessment, lesion identifier conventions, measurement units, visit windows, and derivation ownership. Create traceable intermediate variables for baseline sum, nadir, current sum, percent change, absolute change, lesion-level status, time-point response, and best overall response. Unit tests should include boundary cases such as exactly 30% decrease, exactly 20% increase with and without a 5 mm absolute increase, lymph-node response around 10 mm, new lesions, non-target progression, and missing or unevaluable visits. These checks support reproducibility; they do not replace clinical review or sponsor validation.

5. Results and Discussion

The tutorial yields a practical distinction among three programming decisions: whether a lesion is measurable, whether it is selected as a target, and how the patient's disease is classified at an assessment. Keeping these decisions, separate helps prevent thresholds from migrating into the wrong stage of derivation. It also makes review easier because a reviewer can trace the subject-level response back to lesion measurements and the source assessment.

The synthetic calculation shows the importance of the dual PD threshold. The SDTM discussion shows that data standardization is not itself response derivation: TU, TR, and RS organize different observations, while protocol-specific rules govern analysis variables. A robust implementation should retain both source-reported and derived assessments when both are collected, identify the method and criteria used, and document discrepancies for medical review. Statistical programmers should not silently overwrite investigator-assessed results with independently derived results.

This narrative is educational and has important limits. It does not provide a complete catalog of RECIST exceptions, imaging rules, special tumor types, or immune-response criteria. RECIST 1.1 should not be substituted for iRECIST in immunotherapy analyses when the protocol specifies iRECIST, which distinguishes unconfirmed from confirmed progression [5]. The examples are not clinical advice and have not been validated against a production dataset or program.

6. Conclusion

Reliable RECIST 1.1 programming depends on applying the full sequence of rules: select and classify baseline lesions, preserve lesion identity, measure the correct axis, compare target sums with the correct reference, evaluate non-target disease and new lesions, and derive time-point and best overall response under protocol-defined conventions. Mapping those records to SDTM TU, TR, and RS can improve traceability when programmers preserve the distinctions among lesion findings, disease response, and analysis endpoints. Every final derivation should be checked against the study protocol, imaging charter, statistical analysis plan, and applicable CDISC implementation materials.

7. Future Scope

The next step is to test the workflow against a de-identified or synthetic dataset with prespecified edge cases and independent medical review. Further work could document a reproducible derivation specification, controlled terminology map, and validation suite for RECIST 1.1 and the applicable CDISC supplement. Any evaluation of accuracy or efficiency would require a defined dataset, comparator, and prespecified outcomes; this tutorial makes no such performance claim.

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