What does your biomarker actually measure?

FICTIONAL EXAMPLE | [^{18}F]CAE and SENY are invented teaching constructs, not products or discoveries.

01 THE SCIENTIFIC QUESTION

A fictional team proposes using [^{18}F]CAE PET to measure the availability of an invented molecular target, SENY, and infer neuronal health. **Which quantity does the method estimate, and what evidence would justify that biological interpretation?**

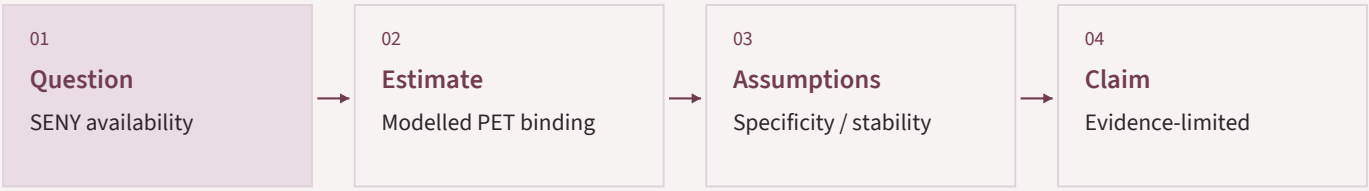


Figure 1. An illustrative claim ladder. Each step needs its own supporting evidence.

02 ASSUMPTIONS TO EXAMINE

The construct. Available binding sites, target engagement, neuronal integrity and future clinical change are different claims. Define the intended use. [1]
The measurement. PET records radioactivity over time. A model-derived binding estimate depends on tracer properties and modelling assumptions; it is not a direct neuron count. [2]
Alternative explanations. Examine delivery, metabolites, off-target binding, competition at SENY sites and reference-tissue behaviour. Specificity and repeatability answer different questions.
The decision. Dose selection, group comparison and progression tracking require different evidence in a defined population and time window.

03 IMPLICATIONS FOR INTERPRETATION

Suppose fictional [^{18}F]CAE binding falls after an intervention. Fewer available sites, including occupancy by a competing compound, could be compatible with that observation. It does not by itself show neuronal loss, recovery or clinical benefit.

04 RECOMMENDED NEXT STEPS

1. Review selectivity, kinetics, metabolites, reference assumptions and test-retest uncertainty.
2. Seek independent evidence for the proposed SENY biology.
3. Pair PET with relevant structural, fluid, digital or clinical measures and state the conclusion each can support.

Define the biological question, then make the measured quantity and assumptions explicit.

SELECTED EVIDENCE | Sources support principles, not the fictional scenarios.

[1] FDA-NIH BEST: biomarker terminology
[2] Innis et al. PET binding nomenclature (2007)