

CHAPTER 4

How the grades work — the A-E system and the evidence ladder

If you only read one line:

Read the letter with the claim, the study setting and the outcome; a strong biomarker grade is not a human-lifespan grade.

A letter is quick to find—and easy to detach from its claim. A B beside an ingredient can then look stronger than the evidence it summarizes.

- A** strong and directly relevant
- B** supportive with meaningful limits
- C** uncertain, mixed or modest
- D** little reliable support
- E** no meaningful benefit, or an unfavorable proposition

SPECIES IS A SEPARATE QUESTION

Humans / named animals / cells

OUTCOME IS A SEPARATE QUESTION

Mortality / function / biomarker / mechanism

The grades in this book belong to specific assessments. They do not grade people, brands or whole categories of treatment. Each one keeps the intervention, form, route, research exposure, outcome and studied population attached. Change one of those details and the assessment may need to change too.

The five meanings

These are the Decoded Press definitions used throughout the series. They are editorial judgments under this rubric, not conversions of another organization's grading scale.

Badge	Meaning
A	strong and directly relevant
B	supportive with meaningful limits
C	uncertain, mixed or modest
D	little reliable support
E	no meaningful benefit, or an unfavorable proposition

The sentence beside a grade explains why it was assigned. A large randomized trial does not automatically receive A. It may test the wrong outcome for the advertised claim, have important limitations, or show no benefit. A strong study can be the reason a proposition receives E.

A small study may support a narrow finding without settling the larger question. Grade the strength and relevance of the evidence, not the study’s name.

The evidence ladder has more than one axis

The ladder asks about confidence in a particular answer. Sound evidence in cells need not answer a question about human function.

Random assignment helps test causation; observation tracks patterns over time. Both require scrutiny of measurement, missing data, comparisons and uncertainty, regardless of sample size.

The two prominent lines on each card prevent the ladder from hiding the question:

Tested in: names the setting for this claim, such as a human randomized trial, an animal experiment with its species named, or cells only.

What it's been shown to do: names the outcome and the finding. The main groups are all-cause mortality, healthspan/function, a biomarker only, and a mechanism only. They do not imply that every study showed a benefit.

An observational mortality result can say “association only.” A null result can say “**Not demonstrated for this claim.**” A specific clinical endpoint keeps its actual name. Disease-free survival, for example, must not be recast as a blood marker or quietly substituted for overall survival. [\[E01\]](#) [\[E03\]](#)

These lines can be read before the rest of the card. They should tell you immediately whether the letter concerns people and whether the outcome matches the thing you hope to achieve.

One compound, two different answers

The following two cards are worked examples from Chapter 14. They retain their own assessment identities. They are not combined into a single grade for NR, NAD or longevity supplements.

As assessed in Chapter 14 — the same assessment, not a new grade.

NR chloride and whole-blood NAD

B

Tested in: Humans · randomized placebo-controlled trial

What it's been shown to do: A biomarker only · whole-blood NAD increased; clinical benefit was not established by this result.

Evidence: The tested oral NR chloride exposure raised blood NAD in an eight-week study. Other human work supports a blood-NAD response, but this grade belongs to that marker, not slower aging. [\[N04\]](#) [\[N05\]](#)

Value: Clearer for proving a biological effect than for justifying spending on longevity.

Best fit: Otherwise healthy adults with overweight interpreting the studied formulation and exposure.

Safety, without the small print

The study did not find significant adverse-event differences from placebo over eight weeks. Its duration and selected population cannot establish long-term safety. [\[N04\]](#)

The B applies to a blood effect in the tested setting. It does not say that raising that measure is worth paying for, that it improves every tissue, or that it extends life. The Value line makes that practical gap visible.

Now change the population and the question. Instead of asking whether NAD rises in blood, ask whether thinking and memory improve in adults with amnesic mild cognitive impairment.

As assessed in Chapter 14 — the same assessment, not a new grade.

NR and cognition in mild cognitive impairment

D

Tested in: Humans · randomized twelve-week pilot trial

What it's been shown to do: Not demonstrated for this claim · cognition did not improve; higher blood NAD was a separate result.

Evidence: Forty-two participants completed the study. The primary cognitive outcome did not improve over placebo despite a rise in NAD. The small, short trial leaves uncertainty about longer-term effects. [N07]

Value: No established cognitive benefit to purchase on the strength of this study.

Best fit: Understanding this clinical pilot; it neither proves dementia prevention nor settles every possible cognitive use.

Safety, without the small print

No serious adverse effects were reported during the trial. That does not establish long-term safety. Memory symptoms warrant appropriate assessment rather than reliance on a supplement. [N07]

The D does not contradict the B. These are different claims. A product can change a marker without delivering the clinical benefit that a reader wants. It can also remain worth studying after a small trial fails to demonstrate that benefit.

Which claim was tested?

Pair of assessments	What stays the same	What changes the interpretation
Daily steps and mortality: B; NR and blood NAD: B	The rubric's meaning of B	An observational mortality association versus a randomized biomarker finding [E01] [N04]
NR and blood NAD: B; NR and cognition: D	The broad ingredient family	Different populations, outcomes, durations and results [N04] [N07]

Pair of assessments	What stays the same	What changes the interpretation
NR alone versus NR with resveratrol for walking	The outcome measured in the same PAD trial	The combination needs its own comparison; component evidence is not an inherited grade [N06]

This is why a shelf of “A-grade ingredients” is not an A-grade protocol. Mixing the ingredients changes the proposition. The package may have different effects, burdens or risks, and it needs evidence of its own.

For a combination, the wording is explicit: **This stack is assessed on its own evidence. It does not inherit the grades of its individual components.** Chapter 22 applies that rule to the stacks sold as complete longevity plans.

Unknown, unhelpful and harmful are different judgments

A lack of useful research leaves uncertainty. It does not establish that an intervention can never work. Nor does uncertainty justify selling a benefit as if the missing study had already been successful.

For an untested claim, “Tested in” can read “No qualifying direct study identified for this claim.” “What it's been shown to do” then reads “Not demonstrated for this claim.” This is a display example, not an assessment of a named intervention. Missing evidence must not be filled with an invented species or a borrowed result.

A null study also needs interpretation. Was the sample large enough and the follow-up long enough for the question? Did the estimate leave room for a useful effect? Was the comparison appropriate? The answer can be “not demonstrated here” without pretending that all future research is settled.

E is not a substitute for “we do not know.” The niacin assessment in Chapter 14 concerns a defined add-on treatment in a large cardiovascular trial. Improved lipid markers did not translate into the added clinical benefit being tested. That directly informs the proposition on the card. It is not an E for every form of vitamin B3 or for treating deficiency. [\[N09\]](#)

Harm is another question again. Evidence against a benefit does not automatically prove harm, and evidence for a benefit does not guarantee safety. The safety block remains beside the verdict because a reader should not have to search elsewhere for the qualification that changes the decision.

Evidence, Value and Best fit

Evidence describes the support for the claim and its main limits. It should make clear whether an effect was primary or secondary, observational or randomized, precise or uncertain. It should not turn a promising explanation into a finding.

Value considers likely benefit alongside cost, effort and burden. A technically convincing laboratory result can have poor value for someone paying for longer life. A supported functional benefit can have real value while still requiring time, access and clinical support.

Best fit identifies circumstances in which the evidence is more relevant. It is not a personal prescription. Being the same age as trial participants does not establish the same health context, and meeting some entry criteria does not mean a treatment is suitable for you.

Check an assessment whose grade exceeds its Evidence line or whose Value line exceeds its measured outcome. The badge summarizes the explanation; it cannot overrule it.

Safety, without the small print: No letter clears an intervention for your personal use. A benefit grade does not cancel an interaction, an exclusion, a monitoring need or a reason to avoid treatment. Short-term tolerability is limited information about long-term use. Keep the safety question open even when the efficacy finding is strong.

A grade should leave a trail

Each assessment links to a register record with the precise claim, study details, source identifiers, limitations and evidence date. That trail makes disagreement useful: a reader can inspect the evidence and the reasoning rather than guess what the letter meant.

New evidence can change an assessment. A refresh should explain which claim changed and why, while preserving the earlier record. A new biomarker study should not silently upgrade a lifespan claim. A corrected paper should not leave an old headline untouched.

The levers come next so their evidence receives full attention, not because every claim deserves the same letter.

Plain Lane

A grade describes the evidence for a particular claim. Read it with the two lines beneath it: who or what was tested, and what the study showed. A better blood result does not prove a longer life.

The same ingredient can have different grades for different outcomes, and a stack needs its own evidence. A benefit that was not shown is still uncertain; it is not a promise waiting to be claimed. Read the safety information even when the grade is strong. The source record should explain how the assessment was reached and what would change it.