Summary of Authoritative Material on Intermittent Rapamycin as Gerosuppressant (>65 years, weekly low-dose regimens ~5-10 mg)

Preclinical (mice): Multiple replicated studies (e.g., Apelo 2016, Bitto 2016, Baghdadi 2024) show intermittent rapamycin (e.g., every 5 days or weekly) extends lifespan and healthspan even when started late in life (equivalent to human 60-70+). Benefits include delayed age-related decline, fewer side effects than daily dosing.

Human evidence (focused on older adults):

- **PEARL trial (2025, Aging journal, n=114, ages 50-85, 48 weeks)**: 5 mg or 10 mg compounded rapamycin weekly (intermittent). Safe (adverse events similar to placebo; mild GI discomfort most common). Benefits: women on 10 mg gained lean tissue mass and reported less pain; 5 mg improved emotional well-being/general health. No change in primary visceral fat endpoint.
- Mannick et al. (2014/2021, elderly cohorts >65): Low-dose rapalogs (intermittent/weekly equivalents) improved immune function (better flu vaccine response, fewer infections) without major immunosuppression.
- Kraig et al. (2018, ages 70-95): Low daily (continuous but low) safe short-term; mixed but overall tolerable metabolic/hematologic shifts.
- Systematic review (Lancet Healthy Longevity 2024): Rapamycin/derivatives improved immune, some cardiovascular, and skin parameters in adults; no serious adverse events in healthy older groups. Common self-reported/off-label regimen: 6 mg weekly.
- Other pilots/ongoing (e.g., periodontal, cardiac signals): Positive or neutral surrogates; no large long-term mortality data yet.
- Fora (rapamycin.news, related discussions): Older users (>65) report good tolerance with monitoring (lipids/glucose); anecdotal gains in energy/recovery; minor reversible sides (mouth sores, GI) far less than transplant dosing. Physician-supervised common.

Overall: Strong mechanistic/preclinical support; human data (short/intermediate-term) shows good safety and modest healthspan signals (immune rejuvenation, muscle/pain/well-being) at intermittent low doses. Risks (metabolic, infection) minimal/reversible vs. high/chronic dosing; not zero but low in healthy elderly. Evidence tilts toward moderate effectiveness with high uncertainty on "very" long-term magnitude

due to trial size/duration. Neutral possible if benefits prove surrogate-only; negative unsupported at this regimen.

Dempster-Shafer Theory Imprecise Probabilities

Frame of discernment Θ = {Very effective (V), Moderately effective (M), Neutral (N), Negative (G due to risks)}.

Basic probability assignment (bpa) derived from evidence weighting:

- m({V,M}) = 0.45 (preclinical strength + human signals)
- m({M}) = 0.25 (PEARL/Mannick modest benefits)
- m({N}) = 0.12 (limited long-term human proof)
- m({G}) = 0.03 (rare/minor risks observed)
- m({N,G}) = 0.05 (possible no net gain or minor downsides)
- m(Θ) = 0.10 (translational/long-term gaps)

Results (rounded to 2 decimals):

Scenario	Belief (Bel)	Plausibility (Pl)	Pignistic Belief (BetP)	Imprecise Probability Range
1 Very effective	0.00	0.55	0.25	[0.00, 0.55]
2 Moderately effective	0.25	0.80	0.50	[0.25, 0.80]
3 Neutral	0.12	0.27	0.17	[0.12, 0.27]
4 Negative (risks)	0.03	0.18	0.08	[0.03, 0.18]

Plot of Imprecise Probability Ranges (0% to 100% scale; each "=" ≈5%; "|" marks Bel start / Pl end; "X" marks pignistic point)

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0%    10%   20%   30%   40%   50%   60%   70%   80%   90%  100%
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
1 Very:     |==================X==========|               [0-55%, X=25%]
2 Mod:  |============X=========================|       [25-80%, X=50%]
3 Neut:     |======X====|                                [12-27%, X=17%]
4 Neg:      |==X=======|                                 [3-18%, X=8%]
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Belief is lower-bound support directly assigned; Plausibility is upper-bound (1 - belief in complement); pignistic is "betting" probability distributing ignorance/mass proportionally. Highest support for moderate effectiveness; negative least plausible. These are evidence-derived estimates reflecting current limited but promising human data + strong preclinical. Larger/long-term trials would narrow ranges.