The Art of Medicine

Chelsea D. Gawryletz, DO
Breast Cancer Medical Oncology
University of Colorado UCHealth Fort Collins
October 20, 2024

Official Health Care Partner

Official Hospital of the U.S. Olympic and Paralympic Training Center, Colorado Springs

uchealth

6th Annual Breast Cancer Symposium Hudson, NY
Yesterday, Today and Tomorrow

The Art of

Adjuvant Endocrine Therapy

Patients Questions at diagnosis:
Q: The studies demonstrate benefit in a population, but will this medication will help ME?
Q: The studies demonstrate side effects with the percentages and AE grades you explain.
Will I get the side effects you mention? How bad will it be for me?
Q: How long should I endure these side effects?
Q: Will the side effects of the intervention possibly worsen my overall survival?
Q: How do we decide when toxicity is greater than benefit? So many variables!

The Art of Medicine: A Case weighing dynamic balance of risk versus benefits in continuity of time while on systemic therapy… and beyond

- 55 y/o post-menopausal Latina woman, G4P4, with invasive ductal carcinoma, ER 99%, PR 99%, HER2/neu 2+ / DISH negative with ratio 1.1, cT1c,cN0,cM0, G2 (3,2,2), clinical prognostic stage IA, s/p lumpectomy and SLNBx: pT1c,pN0(sn),cM0, G2 (3,2,1), pathologic prognostic stage IB, 21 gene panel RS 8, adjuvant chemotherapy not indicated, 70-gene panel Ultra Low Risk Luminal A, randomized to no radiotherapy on DEBRA / NRG-BR007 clinical trial, initiated on adjuvant endocrine therapy with aromatase inhibitor.

- After 2 years, increasing intolerance to 2nd generation daily aromatase inhibitor: tenosynovitis, decreased mobility limited by arthralgia's, trigger finger requiring release, fatigue, depression / generalized decline in sense of wellbeing, ennui, insomnia, patient reported feeling “edgy”. Discontinued and took a few week “drug holiday” while journaling symptom burden.

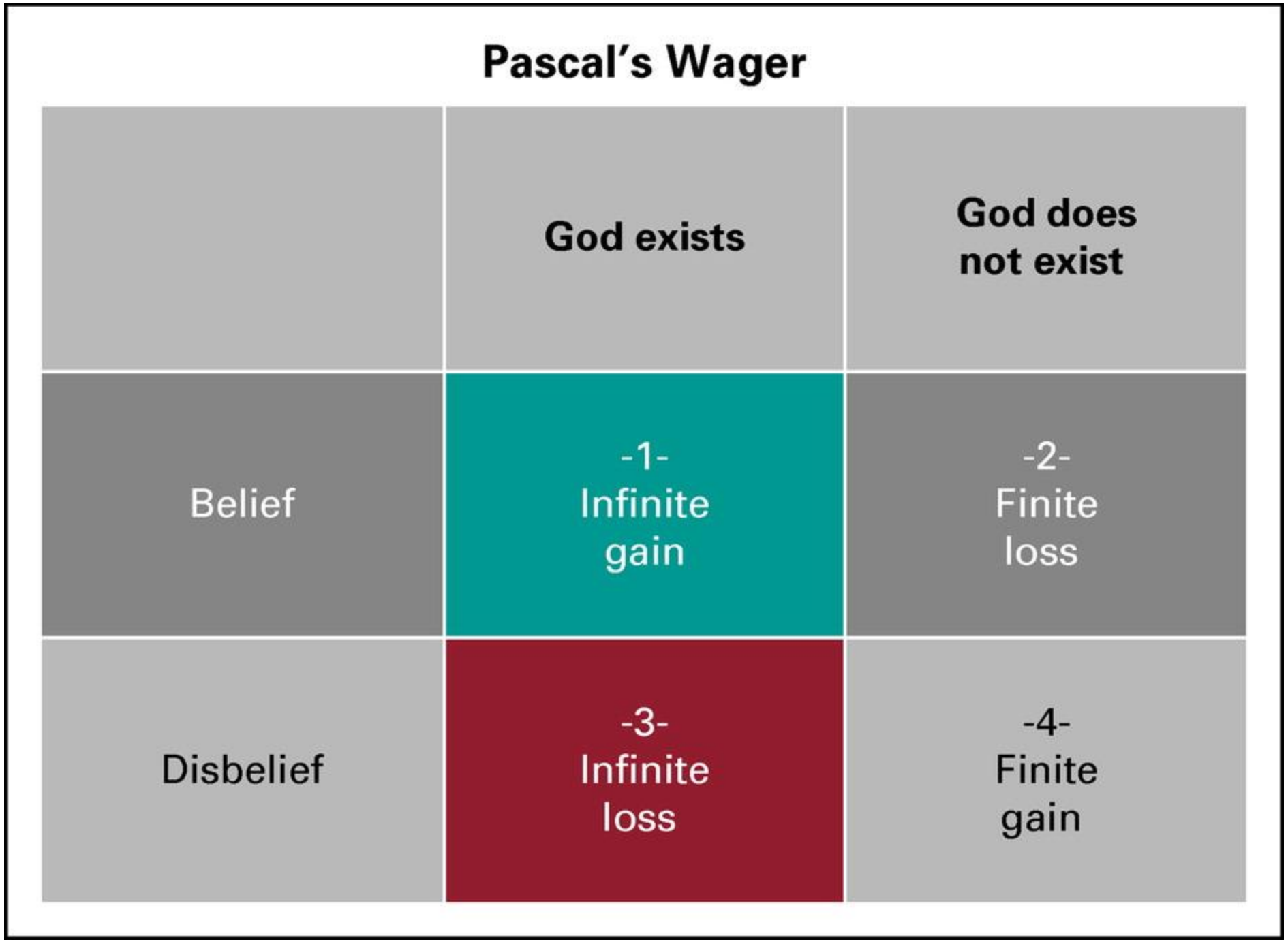
- Symptoms attenuated and attempted 3rd generation daily aromatase inhibitor. Similar intolerance, slowly escalating, ultimately discontinued after a few months.

- Attempted 3rd generation aromatase inhibitor 3x/week dosing. Tolerating OK, but how do the attenuated (but still present) toxicities affect her survival? Do some of the toxicities from aromatase inhibitor contribute to worsened overall survival, ie how do we quantify that risk?

- BCSS at 10 and 20 years with and without endocrine therapy
- HoxB13/IL17BR (H/I) ratio predicts not likely to benefit from extended endocrine therapy
- DECISION MAKING: Pascal’s Wager and Oncologist Wager, are heuristic flaws made in the process of decision making?

NRG-BR007: The DEBRA Trial (nrgoncology.org)

Efficacy of Alternative Dose Regimens of Exemestane in Postmenopausal Women With Stage 0 to II Estrogen Receptor-Positive Breast Cancer: A Randomized Clinical Trial - PubMed (nih.gov)



Hájek A. *Pascal's Wager* (ed 2018). The Stanford Encyclopedia of Philosophy 2018, https://plato.stanford.edu/archives/sum2018/entries/pascal-wager/

Oncologist's Wager

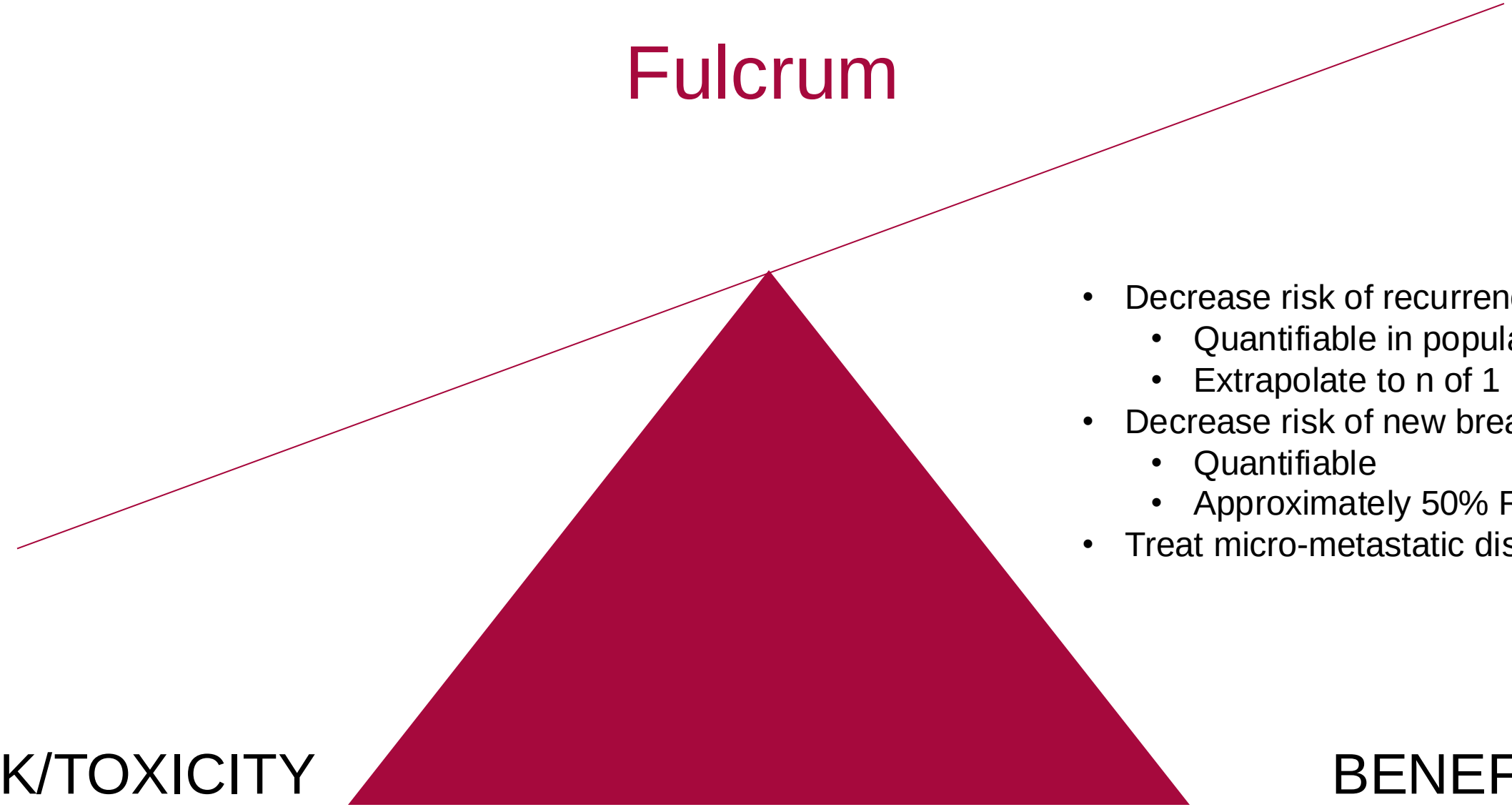
	Cancer free	Recurrent cancer
Treat	-A- Risk, no loss	-B- Risk, loss
Don't treat	-C- No risk, no loss	-D- No risk, loss

Claudius Galenus

- Physician to the gladiators
- Roman Empire
- 2,000 years ago (129 CE – 216 CE)
- Born Pergamon (modern day Turkey)
- Development of clinical trials: importance of systematically gathered objective evidence > anecdotes.
- Ancient conflict: theory vs practice, Galen strove for best of both worlds.
- Challenged his own beliefs: “I will trust no statements until I have tested them for myself,” concluding: “the surest judge of all will be experience alone.”

Thorndike L. A History of Magic and Experimental Science During the First Thirteen Centuries of Our Era. Columbia University Press, New York 1923.

Fulcrum



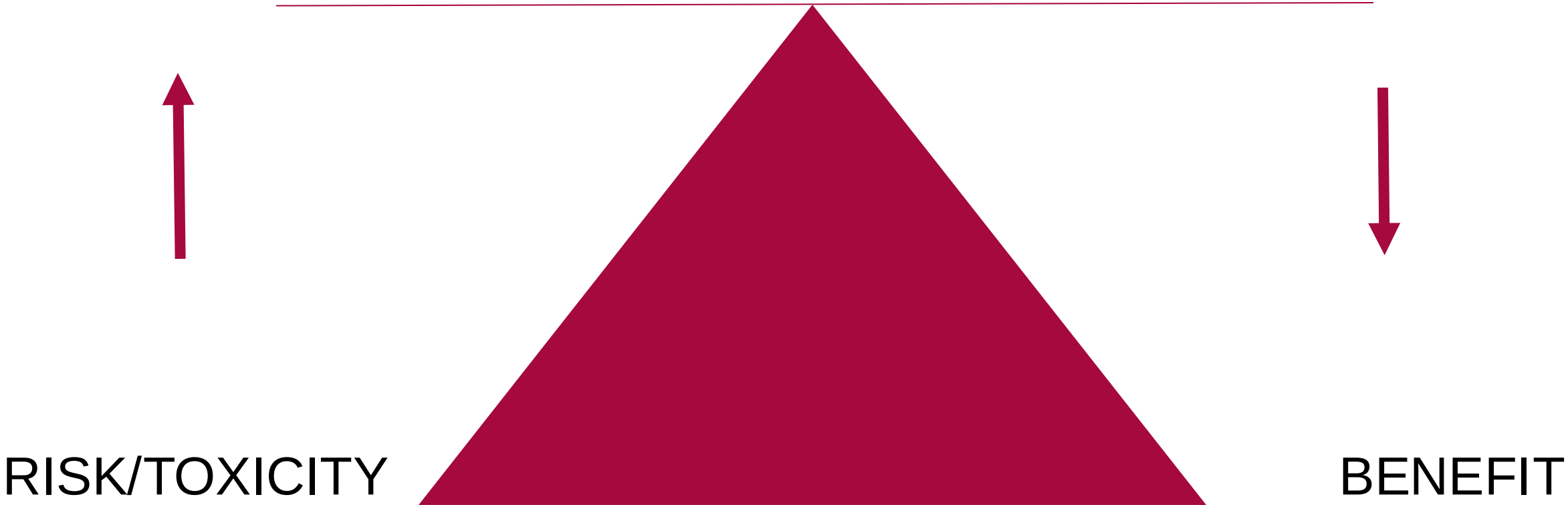
- Decrease risk of recurrence
  - Quantifiable in population
  - Extrapolate to n of 1
- Decrease risk of new breast cancer
  - Quantifiable
  - Approximately 50% RRR
- Treat micro-metastatic disease

RISK/TOXICITY

BENEFIT

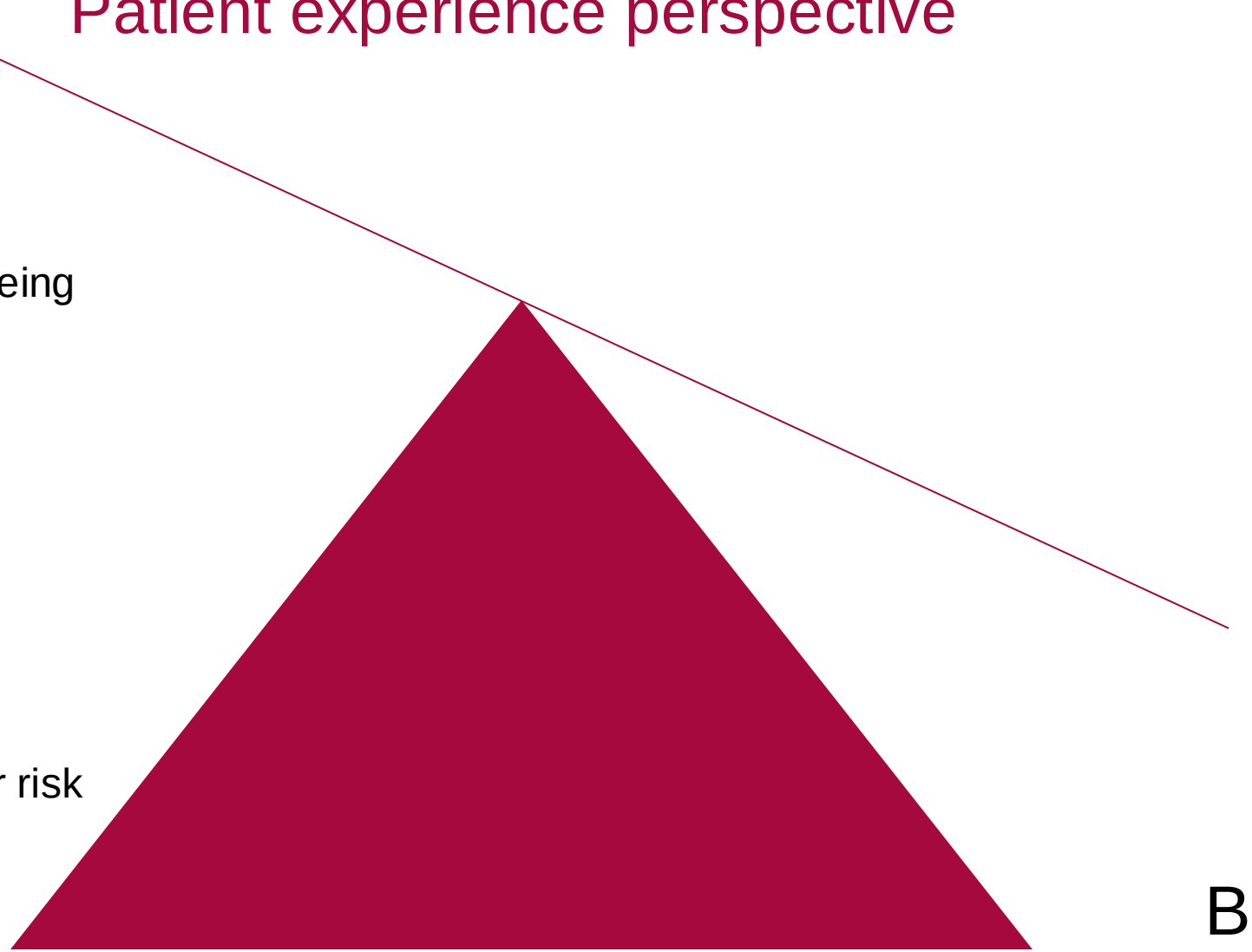
At time of diagnosis

Fulcrum
Relative risk/benefit analysis



Fulcrum:
Patient experience perspective

- Arthralgia's
- Less mobile
- Dyspareunia
- Insomnia
- Hot flashes
- Decrease sense of wellbeing
- Labile emotions
  - Depression
  - Anger
  - Edgy
  - Anxiety
  - Suicidal ideation
- Weight gain
- Increase UTI
- Dyslipidemia
- Increased cardiovascular risk
- Bone density loss



RISK/TOXICITY

BENEFIT

Feelings Wheel

uchealth

The Art of Adjuvant Endocrine therapy

- How do we quantify toxicities like “emotional lability”?
- Would that data be meaningful to guide in risk/benefit decision making at diagnosis and in continuity?
- Can we predict toxicity at time of diagnosis in an individual based on individual factors? Genetics? Genomics? Tumor biology? BMI? History of trauma? Past and/or ongoing environmental exposures?
- Longitudinal Multivariate analysis c Patient Reported Outcomes
- How to harness Artificial intelligence to help understand risk, to best inform dialogue of risk/benefit for an individual. Can we further individualize medicine to answer patients questions at diagnosis?

Thank you