Process Performance Qualification:

A Bayesian Optimized Sampling Plan for Attributes

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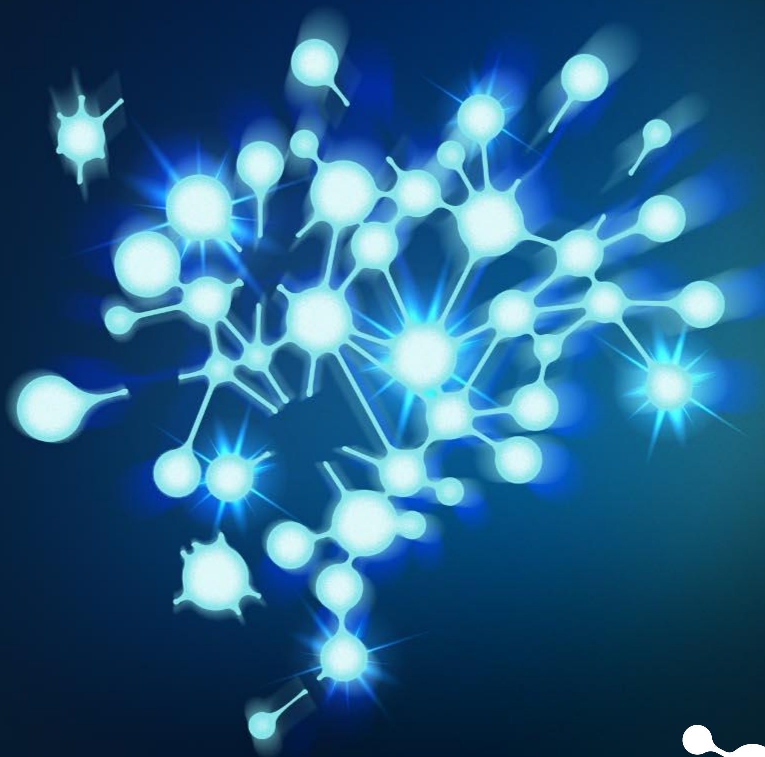
Agenda

- **Introduction**
  - Inspection of supply
- **Acceptance Sampling**
  - Frequentist
  - Bayesian
- **Conclusion**



Introduction

- We receive a huge shipment of *N* widgets/material from a supplier/vendor.

Question:

- Is the shipment good enough to put into our inventory or to use the material?

How to preform the inspection?

How will you decide?

Introduction – Inspection via Sampling

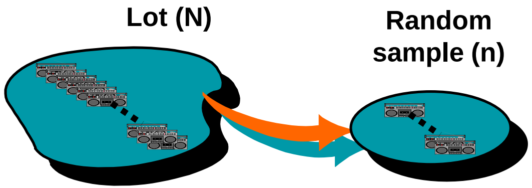
an inspection of supplied material to judge "conformance" to predetermined regulatory standards → **Acceptance Sampling!**

Acceptance Sampling Options

- Look at all *N* widgets (100% inspection)
  - This can take eternity! + $$$$$ + time, etc.

- Don't look at any, send directly to storage (0% inspection)
  - Seriously?

- Look at a sample, *n*, and if "*enough*" of the sample are good, keep the lot
  - Reasonable
  - Be prepared to accept some risks



Acceptance Sampling Plan - Design

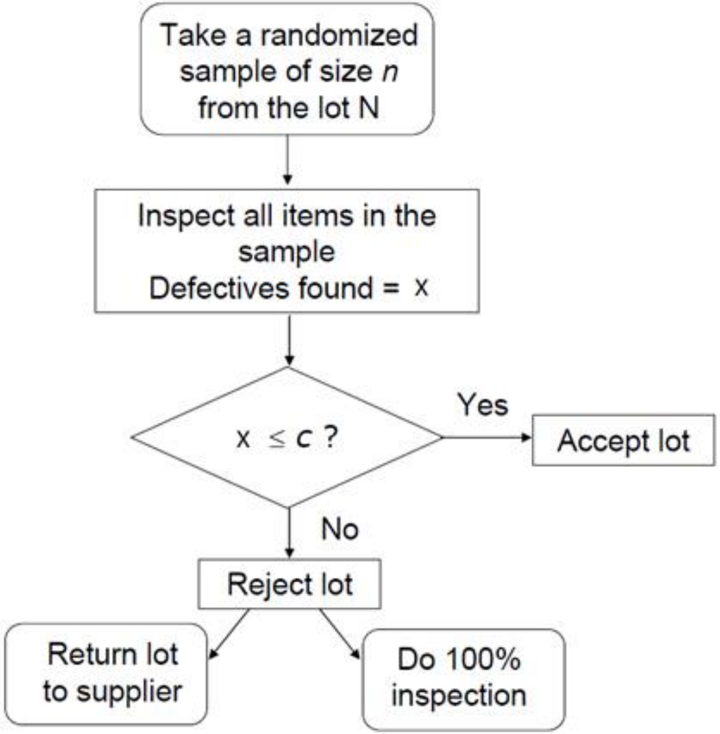
- Sampling Plan specifies the
  - lot size (N)
  - sample size (n)
  - defective found in a sample (x)
  - acceptable number of defectives in a sample (c)

- Types (Single, Double, Multiple and Sequential)

- Each item in the sample is examined and classified as good/defective

- If the number of defective exceeds a cut-off value *c* the whole lot is rejected; otherwise accepted

Acceptance Single Sampling Plan - Flowchart



What is probability of Accepting?

Pr[Accept | p=x/n]

Some important terms

- 100% inspection is impractical (set acceptable levels)

Acceptable Quality Level (AQL)

- maximum % of defects that is acceptable to ship to your customer

Lot Tolerance Percent Defective (LTPD)

- maximum % of defects that a customer is willing to accept

Some terminology

- 100% inspection is impractical (set acceptable levels)

Acceptable Quality Level (AQL)

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Lot Tolerance Percent Defective (LTPD)

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Consumer & Producer Risk

- Producer Risk = Pr(Reject Good Lot)
  - $\alpha = Pr[\mathrm{X} > c|\mathrm{p} = AQL]$

$$= \sum_{x=0}^{c} \binom{n}{x} AQL^{x}(1 - AQL)^{n-x}$$

  - Type I error

- Consumer Risk = Pr(Accept Bad Lot) → Regulatory Concern
  - $\beta = Pr[\mathrm{X} \leq c|\mathrm{p} = LTPD]$

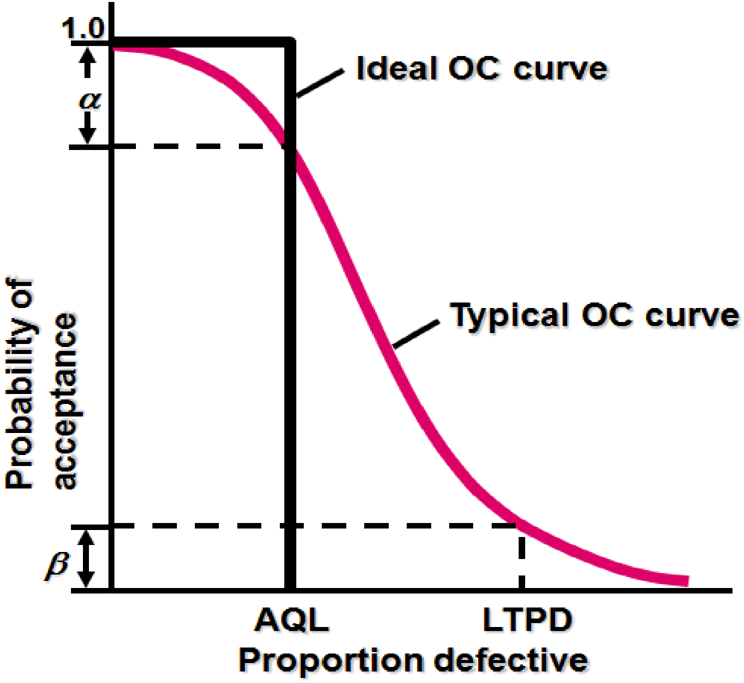
$$= \sum_{x=0}^{c} \binom{n}{x} LTPD^{x}(1 - LTPD)^{n-x}$$

  - Type II error

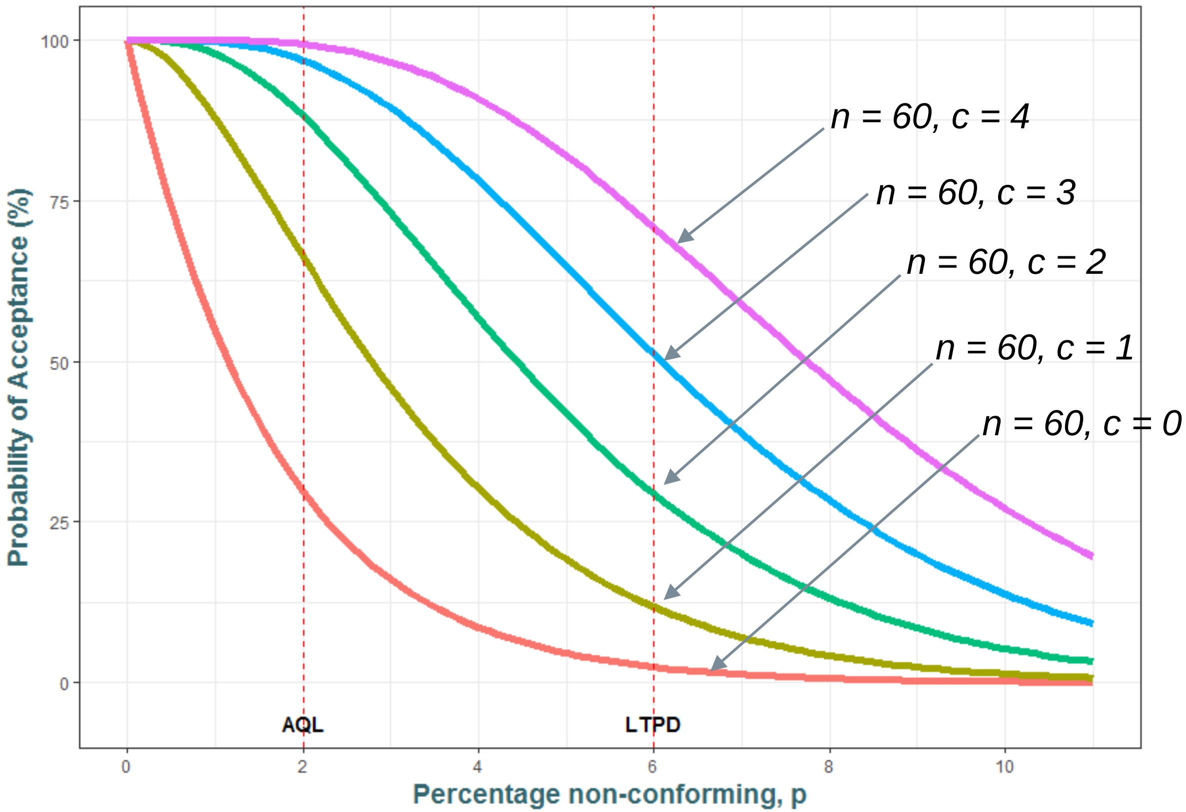
Acceptance Sampling Plan – Operating Characteristic Curve (OCC)

➤ Curve showing probabilities of accepting versus % defects.

$$Pr[Accept|p] = \sum_{x=0}^{c} \binom{n}{x} p^x (1-p)^{n-x}$$

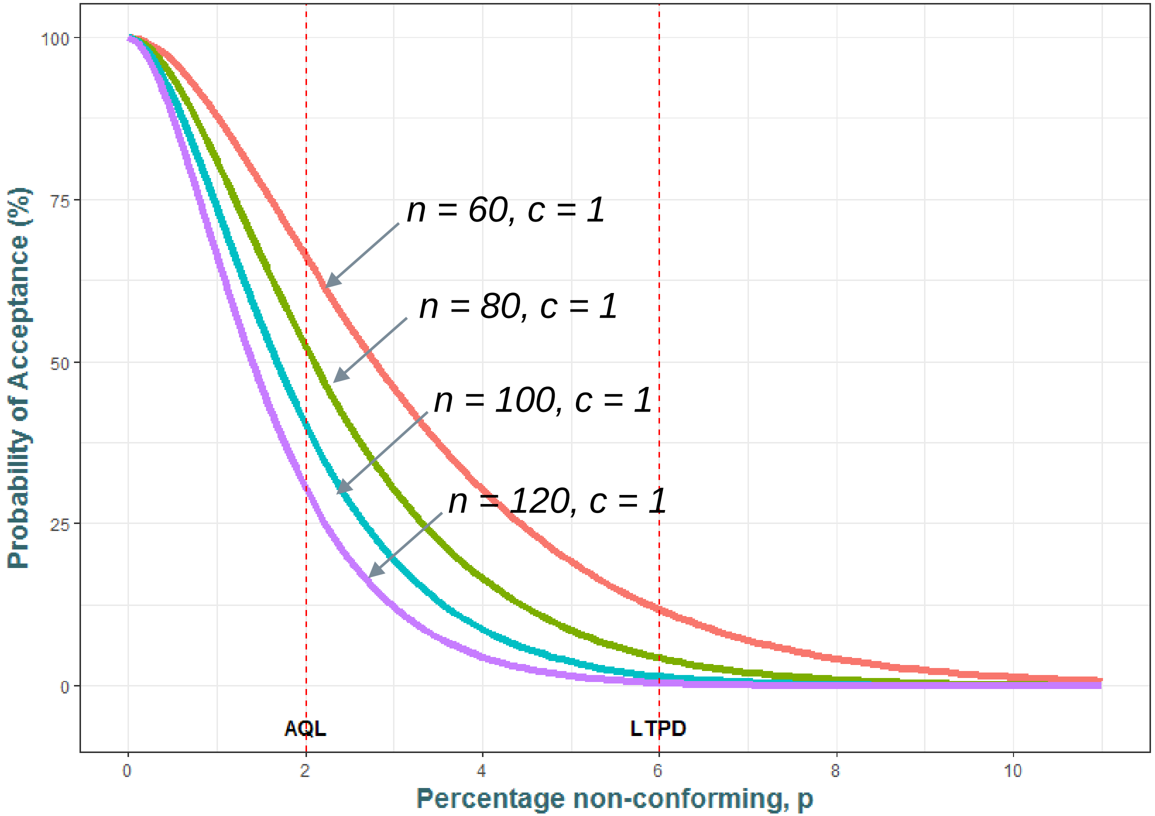


Acceptance Sampling Plan – % Defect effect



- *Increasing c while holding n constant decreases the producer's risk and increases the consumer's risk.*

Acceptance Sampling Plan – Sample size effect



- *Increasing n while holding c constant increases the producer's risk and reduces the consumer's risk*
- *As the sample size n increases, the OC curve becomes more like idealized OC curve* → more discriminatory power

Binary Attribute - Statistical formulation

- **Problem:**
  - assumed that lots come from a stable production process, i.e. p treated as constant → far from reality
- Uncertainty of p can't be ignored
- Bayesian becomes natural choice
- Assume Beta prior on p, i.e. $f(p \mid \alpha, \beta) \sim Beta(\alpha, \beta)$
- Note: Posterior given data x and p is $Beta(\alpha + x, \beta + n - x)$

Acceptance Sampling Plan - Bayesian

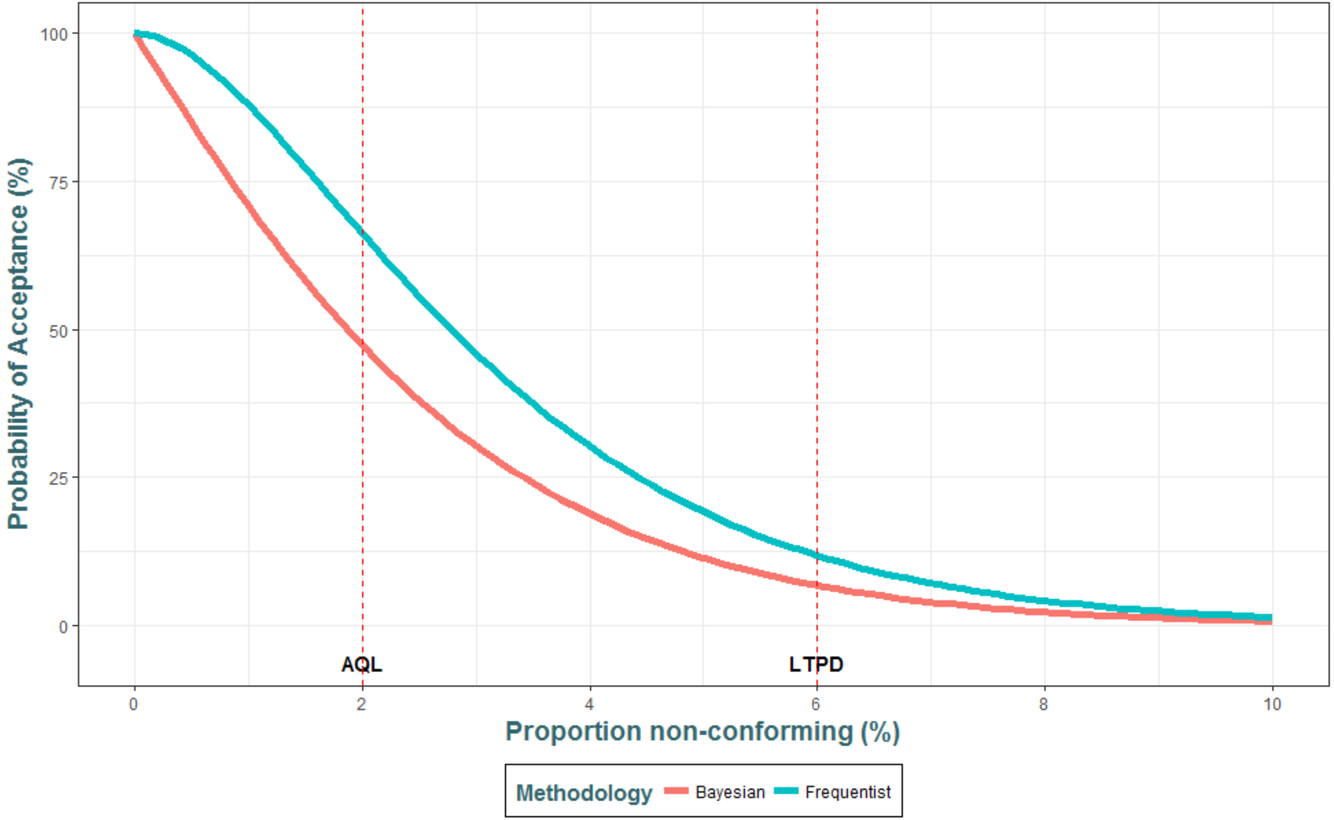
- When *p* has a Beta distribution the Posterior pdf of accepting is:

$$Pr[p|Accepted] = \frac{f(p)\,Pr(Accepted|p)}{\int_0^1 f(p)\,Pr(Accepted|p)\,dp}$$

$$= \frac{\sum_{x=0}^{c}\binom{n}{x}p^{x+a-1}q^{n-x+b-1}}{\sum_{x=0}^{c} B(a+x, n+b-x)}$$

- Can be done even in Excel ☺ → analytical

Acceptance Sampling Plan – Bayesian



$p \sim Beta(1,1)$
$n = 60,$
$c = 1$

Bayesian Consumer Risk

- $\beta = \Pr[p \geq LTPD | X \leq c]$ → Posterior distribution given data & prior **Beta(α, β)**

$$= \sum_{x=0}^{c} \Pr[X = x | X \leq c] \times \Pr[p \geq LTPD | X = x]$$

$$Pr(X = x | X \leq c) = \frac{Pr(X \leq c | X = x) . Pr(X = x)}{Pr(X \leq c)}$$

$$= \frac{\frac{\binom{n}{x}}{B(a,b)} B(a + x, n + b - x)}{\sum_{x=0}^{c} Pr(X = x)}$$

1 - Beta(LTPD, $\alpha + x, \beta + n - x$)

Bayesian Producer Risk

- $\alpha = \Pr[p \leq AQL | X > c]$ → Posterior distribution given data & prior **Beta(α, β)**

$$= \sum_{x=0}^{c} \Pr[X = x | X > c] \times \Pr[p \leq AQL | X = x]$$

$$Pr(X = x | X > c) = \frac{Pr(X > c | X = x) \, . \, Pr(X = x)}{Pr(X > c)}$$

$$= \frac{\frac{\binom{n}{x}}{B(a,b)} B(a + x, n + b - x)}{\sum_{x=c+1}^{c} Pr(X = x)}$$

Beta(AQL, $\alpha + x, \beta + n - x$)

Quick Assessment with R Shiny App

PHARMALEX
CONFIDENCE BEYOND COMPLIANCE

PPQ Sample Size for Attributes

Set-Up

Producer Risk: 0.05

Consumer Risk: 0.1

AQL: 0.1

LTPD: 0.1

Sample size: 0 – 100 – 600

0 60 120 180 240 300 360 420 480 540 600

Sample size (optional):

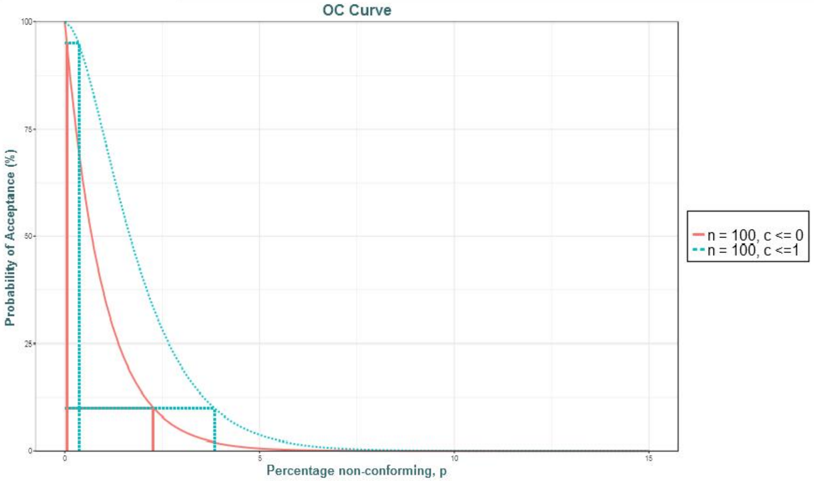
Modeling Approaches

Approach: Frequentist

Acceptable # of defects 1: 0

Acceptable # of defects 2: 1

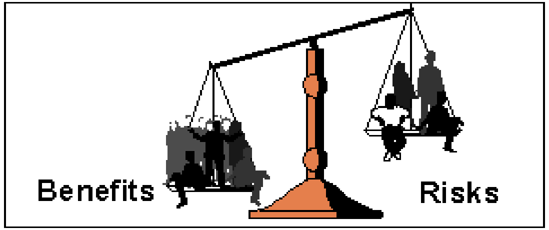
Acceptance Sampling Results



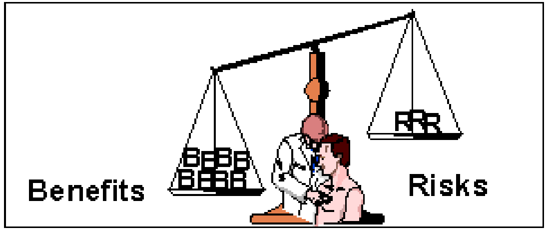
Risk	Value	% Non-conforming	Acceptable Defects	Sample Size
Consumer Risk	0.10	2.2800	0	100
Consumer Risk	0.10	3.8400	1	100
Producer Risk	0.05	0.0504	0	100

Remember

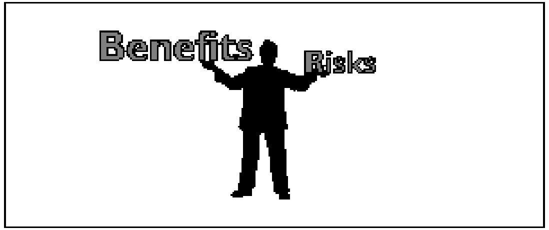
FDA
evaluates
benefits/risks
for the population



Provider
evaluates
benefits/risks
for a patient



Patient
evaluates
benefits/risks
in terms of
personal values



Conclusion

- Traditional way of Sampling Plan design
  - Specify Producer/Consumer Risk/AQL/LTPD
  - Choose n and c to obtain desired OC

- Proportion of defects vary from lot to lot
  - Treat p as a random variable
  - Beta prior distribution easier to work with

- Bayesian formulation reflects reality
  - Analytical solutions to everything given Beta prior
  - Uncertainty is appropriately propagated
  - Historical data available → reduce costs

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