d. Conditionality principal: If

  i. data arises from random mixture of experiments

  - Here indexed by d_+

  ii. mixing distribution does not depend on unknown parameter

  iii. Then perform inference based on experiment we see

e. p-value $2 \times \min(\mathsf{P}\left[d_0 \geq \text{observed}\right], \mathsf{P}\left[d_0 \leq \text{observed}\right])$

  i. $= 2\Phi(-\left|\text{observed} - \text{observed}\pi\right| / \sqrt{d_+\pi(1-\pi)})$.

  ii. To properly account for probability at observed, add $\pm\frac{1}{2}$ to numerator to make absolute value smaller. See Figure 3.

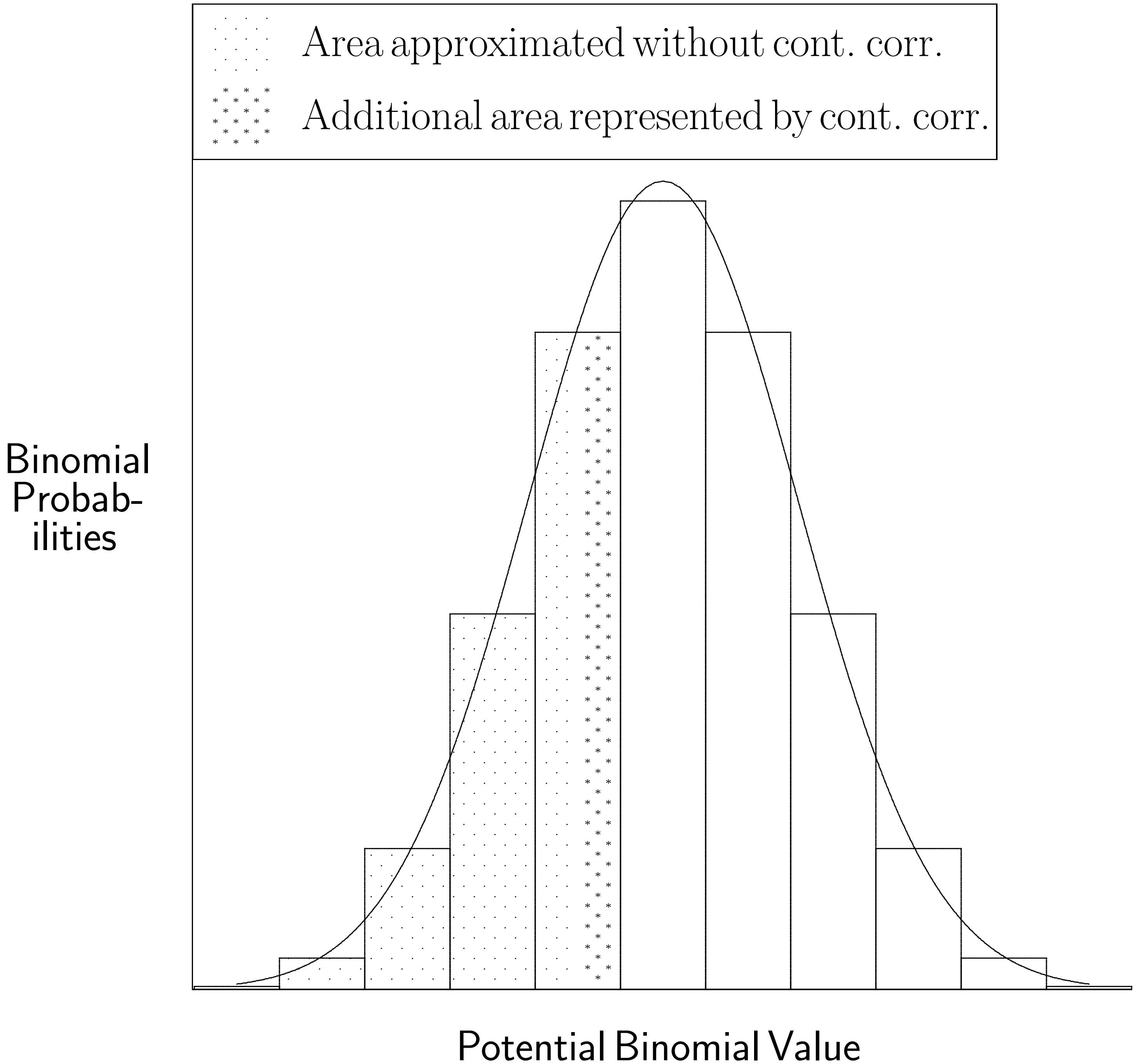
f. Get CI for π using

  i. Normal approx. $\pi \in d_1/d_+ \pm 1.96\sqrt{\frac{d_0 d_1}{(d_1+d_0)^3}}$

  - Problem if $d_0 = 0$
  - Less obvious problem for small $d_1 + d_0$

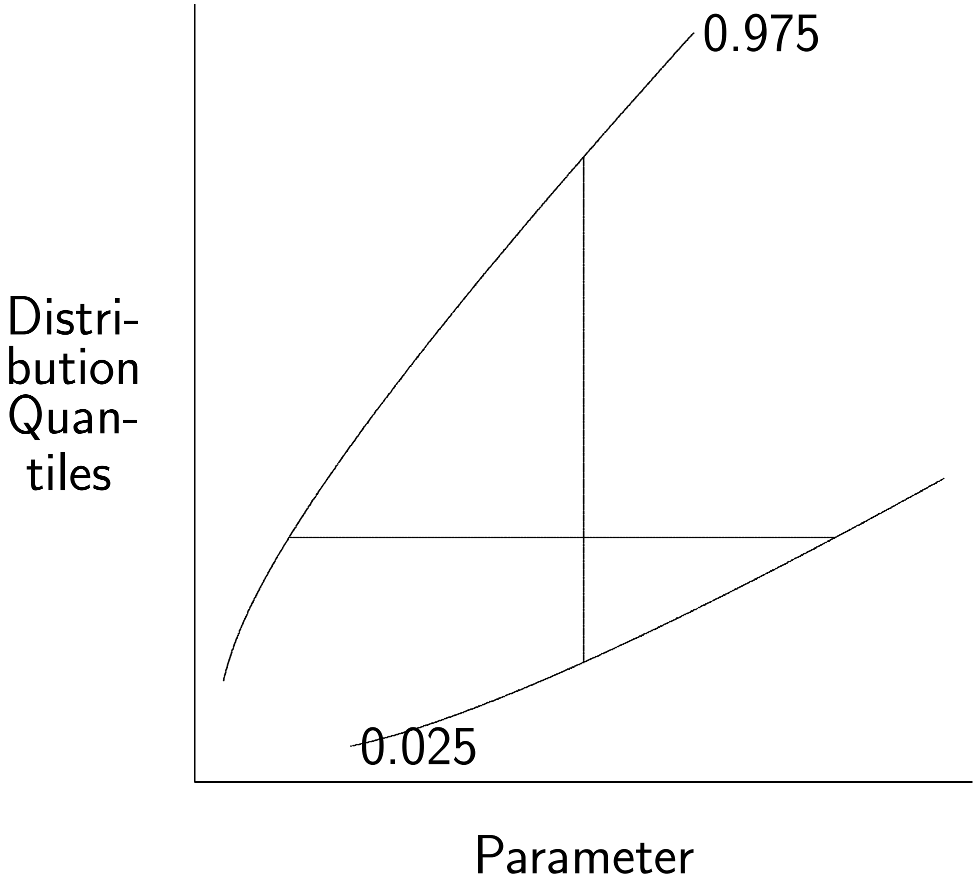
  ii. Fix problem by working exactly:

  - Lower bound π_L satisfies $\mathsf{P}_\pi\left[d_0 \geq \text{observed}\right] = .025$
  - Upper bound π_U satisfies $\mathsf{P}_\pi\left[d_0 \leq \text{observed}\right] = .025$
  - Vertical line has probability .95 for any value of parameter
  - Hence horizontal line has same coverage
  - Lower confidence bound is generated by upper quantile and



vice versa

- See Figure 4.
- Can be expressed in terms of F distribution upper tail:



$$\left(\frac{d_0}{d_0+(d_1+1)F_{\alpha/2}(2d_1+2,2d_0)},\frac{(d_0+1)F_{\alpha/2}(2d_0+2,2d_1)}{d_1+(d_0+1)F_{\alpha/2}(2d_0+2,2d_1)}\right)$$

iii. Are intermediate policies between these extremes.

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g. Get CI for q using $q = e_0\pi/[e_1(1-\pi)]$ evaluated at upper and lower CI of π_1

i. Works since relationship between π_1 and q is strictly increasing.

h. Special Case: one age group

i. Then population SMR=relative risk for exposure group re standard population

ii. Then ratio of population SMR=relative risk for exposure groups

5. Multiple (K) Exposure Categories

a. How do exposure groups differ?

i. Choose one group as baseline

- Usually the one with no exposure, if there is one
- Be careful what you lump in here

ii. Calculate relative risks with respect to this group

b. Wrong answer:

i. Calculate hypothesis tests

- for each pair
- or against a baseline

ii. Claim heterogeneity if any of these shows up different

iii. Problem of multiple comparisons

c. To avoid multiple comparisons, need one test for all groups

d. Choose a measure of disagreement with null answer

i. Calculate Expected value

- Expected value in light of all coming from this non–standard cohort
- Hence don't expect each rate to be associated expectation
- Expect each rate to be $\propto$ associated expectation
- $E_k = d_+ Q_k / \sum_j Q_j$

ii. Use as test statistic sum distances from expectation

- squared
- weighted by estimated variance
- $\sum_k (d_k - E_k)^2 / E_k$
- Distribution is that of sum of K squared $\mathcal{N}(0,1)$
  - ▷ Not independent
  - ▷ Equivalent to $K-1$ independent $\mathcal{N}(0,1)^2$
  - ▷ Distribution called χ^2 on $K-1$ *degrees of freedom*

e. Why not CI?

i. CI can give test when we have one parameter to test

ii. Here we need $K-1$ parameters

iii. CI becomes confidence region: more complicated.

f. Exact methods?

i. Same test statistic

ii. Distribution in cells is given by sequence of binomials

iii. Hard to calculate

g. When $K = 2$:

i. $d_1 = d_+ - d_0$ and $E_1 = d_+ - E_0$.

ii. $E_1 = d_+\pi$

iii. $T = (d_0 - E_0)^2/E_0 + (d_1 - E_1)^2/E_1 = (d_0 - E_0)^2[1/E_0 + 1/E_1] = (d_0 - E_0)^2 d_+^{-1}[1/\pi + 1/(1-\pi)] = (d_0 - E_0)^2 d_+^{-1}/(\pi(1-\pi))$

iv. Hence χ^2 statistic is square of Z statistic

v. Hence inference is the same.