**Problem Set 2: Vitamin A Supplementation to Prevent Children's Mortality in Nepal**

**Scientific Background**

Xerophthalmia, due to vitamin A deficiency, was long known to be a leading cause of childhood blindness in the developing world. Hopkins investigators showed in large trials in Indonesia and Nepal that dosing young children every 4-6 months with high-potency vitamin A could reduce child mortality by approximately 30%. This analysis examines data from the original community trial carried out in Nepal.

**i. Contingency Table Analysis**

**R Code:**

CT <- table(nepal621$trt, nepal621$status)

addmargins(CT)

prop.table(CT, margin=1)

**Results:**

**Contingency Table:**

Alive Died Sum

Placebo 13099 290 13389

Vit A 13499 233 13732

Sum 26598 523 27121

**Mortality Rates:**

* Placebo group: 0.0217 (2.17%)
* Vitamin A group: 0.0170 (1.70%)
* Relative reduction: 21.7%

**Journal Summary:**

Vitamin A supplementation reduced child mortality from 2.17% in the placebo group to 1.70% in the treatment group, representing a 21.7% relative reduction in mortality risk.

**ii.a) Probability Calculations**

**R Code:**

n <- sum(CT)

pr\_vita <- sum(CT["Vit A", ]) / n

pr\_died <- sum(CT[, "Died"]) / n

pr\_died\_vita <- CT["Vit A", "Died"] / n

pr\_died\_placebo <- CT["Placebo", "Died"] / n

pr\_died\_given\_vita <- CT["Vit A", "Died"] / sum(CT["Vit A", ])

pr\_died\_given\_placebo <- CT["Placebo", "Died"] / sum(CT["Placebo", ])

**Results:**

**Marginal Probabilities:**

* Pr(VitA) = 0.5063
* Pr(Died) = 0.0193

**Joint Probabilities:**

* Pr(Died and VitA) = 0.0086
* Pr(Died and Placebo) = 0.0107

**Conditional Probabilities:**

* Pr(Died | VitA) = 0.0170
* Pr(Died | Placebo) = 0.0217

**ii.b) Bayes' Theorem Calculation**

**Hand Calculation:**

Using Bayes' Theorem: **Pr(VitA | Died) = [Pr(Died | VitA) × Pr(VitA)] / Pr(Died)**

**Step-by-step calculation:**

* Numerator: Pr(Died | VitA) × Pr(VitA) = 0.0170 × 0.5063 = 0.0086
* Denominator: Pr(Died) = 0.0193
* Result: Pr(VitA | Died) = 0.0086 / 0.0193 = **0.4455**

**Interpretation:**

The probability that a child who died received Vitamin A is 0.4455 (44.55%).

**iii. Sex as Effect Modifier Analysis**

**R Code:**

nepal\_plac <- filter(nepal621, trt == "Placebo")

nepal\_vit <- filter(nepal621, trt == "Vit A")

CT\_plac <- table(nepal\_plac$sex, nepal\_plac$status)

CT\_vit <- table(nepal\_vit$sex, nepal\_vit$status)

**Results:**

**Placebo Group:**

Alive Died Sum

Female 6376 166 6542

Male 6723 124 6847

* Female mortality: 0.0254 (2.54%)
* Male mortality: 0.0181 (1.81%)

**Vitamin A Group:**

Alive Died Sum

Female 6544 121 6665

Male 6955 112 7067

* Female mortality: 0.0182 (1.82%)
* Male mortality: 0.0158 (1.58%)

**Treatment Effects:**

* Males: 0.0181 - 0.0158 = **0.0023** (0.23 percentage points)
* Females: 0.0254 - 0.0182 = **0.0072** (0.72 percentage points)
* Difference: |0.0023 - 0.0072| = **0.0049**

**Journal Summary:**

Vitamin A supplementation reduced mortality in both sexes, with a greater effect observed in females. The treatment effect in females (0.72 percentage points) was approximately three times larger than in males (0.23 percentage points), suggesting effect modification by sex, with females showing greater benefit from vitamin A supplementation.

**iv. Hypothesis Testing with Statistical Tests**

**R Code:**

*# Test H1: Overall treatment effect*

chi\_test\_overall <- chisq.test(CT)

fisher\_test\_overall <- fisher.test(CT)

*# Test H2: Interaction/effect modification*

combined\_data <- rbind(

data.frame(Treatment = "Placebo", Sex = nepal\_plac$sex, Status = nepal\_plac$status),

data.frame(Treatment = "Vit A", Sex = nepal\_vit$sex, Status = nepal\_vit$status)

)

glm\_model <- glm(Status == "Died" ~ Treatment + Sex + Treatment:Sex,

data = combined\_data, family = binomial)

**Hypothesis 1: Vitamin A supplementation has no effect on mortality**

**H₀:** Vitamin A supplementation has no effect on mortality (OR = 1)  
**H₁:** Vitamin A supplementation affects mortality (OR ≠ 1)

**Statistical Tests:**

* **Chi-square test:** χ² = 7.6449, df = 1, **p = 0.00569**
* **Fisher's exact test:** **p = 0.00536** (more appropriate for rare events)
* **Odds Ratio:** 0.7797 (95% CI: 0.6522 to 0.9312)

**Conclusion:** **Reject H₀** (p < 0.05). There is statistically significant evidence that vitamin A supplementation reduces child mortality.

**Hypothesis 2: Treatment effect is the same for boys and girls**

**H₀:** Treatment effect is the same for boys and girls (no interaction)  
**H₁:** Treatment effect differs by sex (interaction exists)

**Statistical Tests:**

* **Logistic regression interaction term:** **p = 0.247**
* **Odds Ratios by sex:**
  + Males: OR = 0.8731
  + Females: OR = 0.7102
  + Ratio of ORs = 0.8134

**Conclusion:** **Fail to reject H₀** (p > 0.05). Despite the observed difference in treatment effects between sexes, there is insufficient statistical evidence to conclude that sex significantly modifies the treatment effect.

**Summary Table:**

| **Group** | **Placebo Mortality** | **VitA Mortality** | **Treatment Effect** | **Odds Ratio** | **p-value** |
| --- | --- | --- | --- | --- | --- |
| Overall | 0.0217 | 0.0170 | 0.0047 | 0.7797 | 0.00536 |
| Males | 0.0181 | 0.0158 | 0.0023 | 0.8731 | - |
| Females | 0.0254 | 0.0182 | 0.0072 | 0.7102 | - |
| Interaction | - | - | - | - | 0.247 |

**Statistical Interpretation:**

1. **Strong evidence for overall treatment efficacy** (p = 0.00536)
2. **Insufficient evidence for effect modification by sex** (p = 0.247)
3. **Clinical significance:** 22% reduction in odds of death (OR = 0.78)

**v. Binomial Probabilities for Family with 3 Boys on Placebo**

**Parameters:**

* n = 3 boys
* p = 0.0181 (male mortality rate on placebo)

**Hand Calculation using Binomial Formula:**

**P(X = k) = C(n,k) × p^k × (1-p)^(n-k)**

**P(0 boys die):**  
P(X = 0) = C(3,0) × (0.0181)⁰ × (0.9819)³ = 1 × 1 × 0.946648 = **0.946648**

**P(1 boy dies):**  
P(X = 1) = C(3,1) × (0.0181)¹ × (0.9819)² = 3 × 0.0181 × 0.964151 = **0.052380**

**P(2 boys die):**  
P(X = 2) = C(3,2) × (0.0181)² × (0.9819)¹ = 3 × 0.000328 × 0.9819 = **0.000966**

**P(3 boys die):**  
P(X = 3) = C(3,3) × (0.0181)³ × (0.9819)⁰ = 1 × 0.000006 × 1 = **0.000006**

**R Code Verification:**

n\_boys <- 3

boys\_placebo\_mortality <- 0.0181

prob\_0\_bin <- dbinom(0, n\_boys, boys\_placebo\_mortality) *# 0.946648*

prob\_1\_bin <- dbinom(1, n\_boys, boys\_placebo\_mortality) *# 0.052380*

prob\_2\_bin <- dbinom(2, n\_boys, boys\_placebo\_mortality) *# 0.000966*

prob\_3\_bin <- dbinom(3, n\_boys, boys\_placebo\_mortality) *# 0.000006*

**vi. Poisson Approximation**

**Parameters:**

* λ = n × p = 3 × 0.0181 = **0.0543**

**Hand Calculation using Poisson Formula:**

**P(X = k) = (e^(-λ) × λ^k) / k!**

**P(0 boys die):**  
P(X = 0) = (e^(-0.0543) × 0.0543⁰) / 0! = 0.947119 × 1 / 1 = **0.947119**

**P(1 boy dies):**  
P(X = 1) = (e^(-0.0543) × 0.0543¹) / 1! = 0.947119 × 0.0543 / 1 = **0.051457**

**P(2 boys die):**  
P(X = 2) = (e^(-0.0543) × 0.0543²) / 2! = 0.947119 × 0.002946 / 2 = **0.001398**

**P(3 boys die):**  
P(X = 3) = (e^(-0.0543) × 0.0543³) / 3! = 0.947119 × 0.000160 / 6 = **0.000025**

**R Code Verification:**

lambda <- 3 \* 0.0181 *# 0.0543*

pois\_0 <- dpois(0, lambda) *# 0.947119*

pois\_1 <- dpois(1, lambda) *# 0.051457*

pois\_2 <- dpois(2, lambda) *# 0.001398*

pois\_3 <- dpois(3, lambda) *# 0.000025*

**Comparison:**

The Poisson approximation closely matches the binomial probabilities, with slight differences due to the approximation (np = 0.0543 is small, making the approximation appropriate).

**vii. Age Analysis and Triplet Probabilities**

**Age-Specific Mortality Rates:**

**Placebo Group:**

Alive Died Sum

<1 2495 120 2615 (Mortality: 4.59%)

1-2 5385 119 5504 (Mortality: 2.16%)

3-4 5219 51 5270 (Mortality: 0.97%)

**Vitamin A Group:**

Alive Died Sum

<1 2657 114 2771 (Mortality: 4.11%)

1-2 5561 92 5653 (Mortality: 1.63%)

3-4 5281 27 5308 (Mortality: 0.51%)

**Triplet Analysis (18 months old, on Vitamin A treatment):**

**Parameters:**

* Age group: 1-2 years (18 months falls in this category)
* Treatment: Vitamin A
* Mortality rate (p): 0.0163

**R Code:**

age\_1\_2\_mortality <- 0.0163

prob\_jk\_live\_l\_dies <- (1 - age\_1\_2\_mortality)^2 \* age\_1\_2\_mortality

prob\_exactly\_one\_dies <- dbinom(1, 3, age\_1\_2\_mortality)

**a) Probability that J and K live and L dies:**

**Hand Calculation:**  
P(J lives) × P(K lives) × P(L dies) = (1 - 0.0163) × (1 - 0.0163) × 0.0163  
= 0.9837 × 0.9837 × 0.0163 = **0.015749**

**b) Probability that exactly one of the three children dies:**

**Hand Calculation using Binomial:**  
P(X = 1) = C(3,1) × p¹ × (1-p)² = 3 × 0.0163 × (0.9837)²  
= 3 × 0.0163 × 0.968169 = **0.047247**

**Comparison:**

* P(J and K live, L dies) = **0.015749**
* P(exactly one of three dies) = **0.047247**

**Are they the same? No.**

**Why not?** The probability that exactly one child dies includes three different scenarios:

1. J dies, K and L live
2. K dies, J and L live
3. L dies, J and K live

Each scenario has the same probability (0.015749), so the total probability is 3 × 0.015749 = 0.047247. The first calculation only considers one specific scenario (L dies, J and K live), while the second considers all possible ways exactly one child can die.