

Code used in the video vignette

A short demonstration of the EvidenceSynthesis package

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This vignette contains the code used in a short video on the EvidenceSynthesis package: <https://youtu.be/dho7E97vpgQ>.

Simulate data

Simulate 10 sites:

```
simulationSettings <- createSimulationSettings(  
  nSites = 10,  
  n = 10000,  
  treatedFraction = 0.8,  
  nStrata = 5,  
  hazardRatio = 2,  
  randomEffectSd = 0.5  
)  
set.seed(1)  
populations <- simulatePopulations(simulationSettings)  
  
head(populations[[1]])
```

```
##   rowId stratumId x time y  
## 1     1         5 1   10 0  
## 2     2         2 1  113 0  
## 3     3         4 1  135 0  
## 4     4         2 1   27 0  
## 5     5         2 1  104 0  
## 6     6         3 1  342 0
```

```
table(populations[[1]][, c("x", "y")])
```

```
##      y  
## x      0      1  
## 0 1998      2  
## 1 7981     19
```

Fit a model locally

Assume we are at site 1:

```
library(Cyclops)
```

```

population <- populations[[1]]

cyclopsData <- createCyclopsData(Surv(time, y) ~ x + strata(stratumId),
  data = population,
  modelType = "cox"
)
cyclopsFit <- fitCyclopsModel(cyclopsData)

# Hazard ratio:
exp(coef(cyclopsFit))

##           x
## 2.378318

# 95% confidence interval:
exp(confint(cyclopsFit, parm = "x")[2:3])

## [1] 0.6888127 14.9382268

```

Approximate the likelihood function at one site

Normal approximation

```

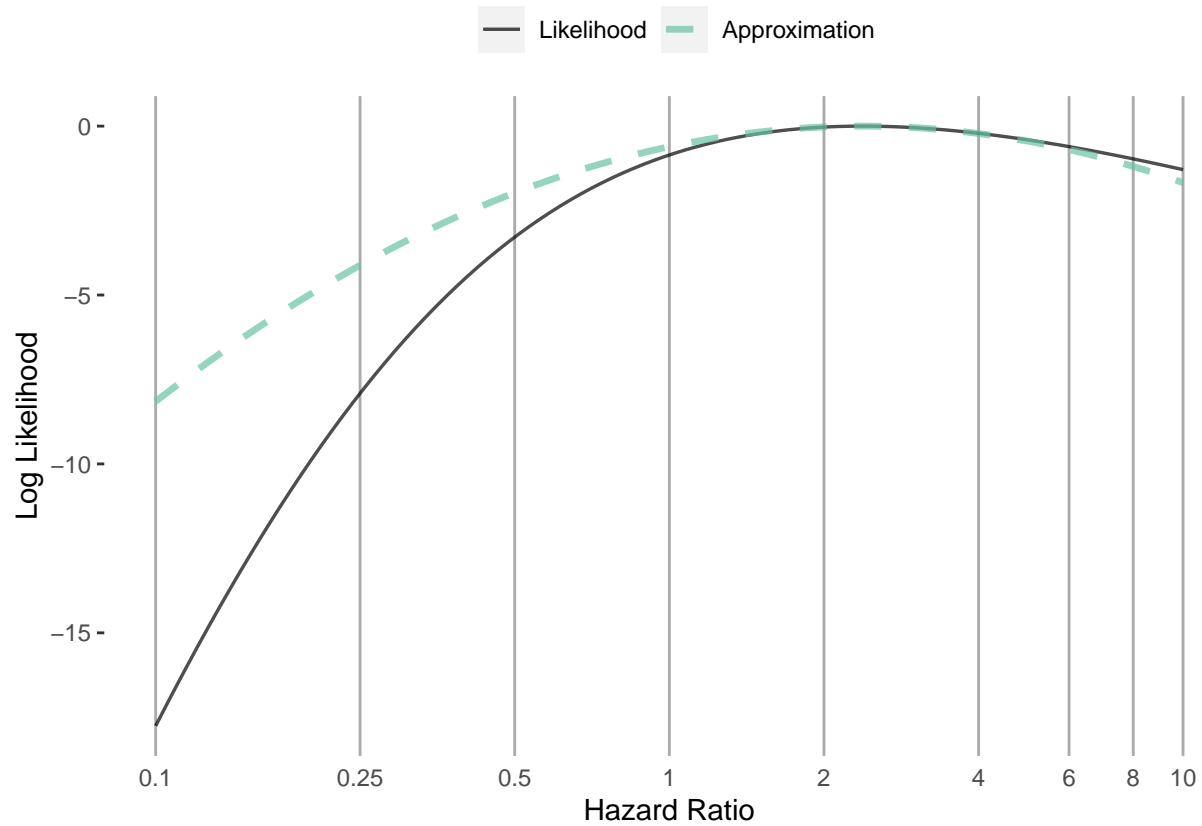
normalApproximation <- approximateLikelihood(
  cyclopsFit = cyclopsFit,
  parameter = "x",
  approximation = "normal"
)
normalApproximation

##           rr      ci95Lb  ci95Ub      logRr  seLogRr
## x 2.378318 0.6888127 14.93823 0.8663934 0.7848893

plotLikelihoodFit(
  approximation = normalApproximation,
  cyclopsFit = cyclopsFit,
  parameter = "x"
)

## Detected data following normal distribution

```



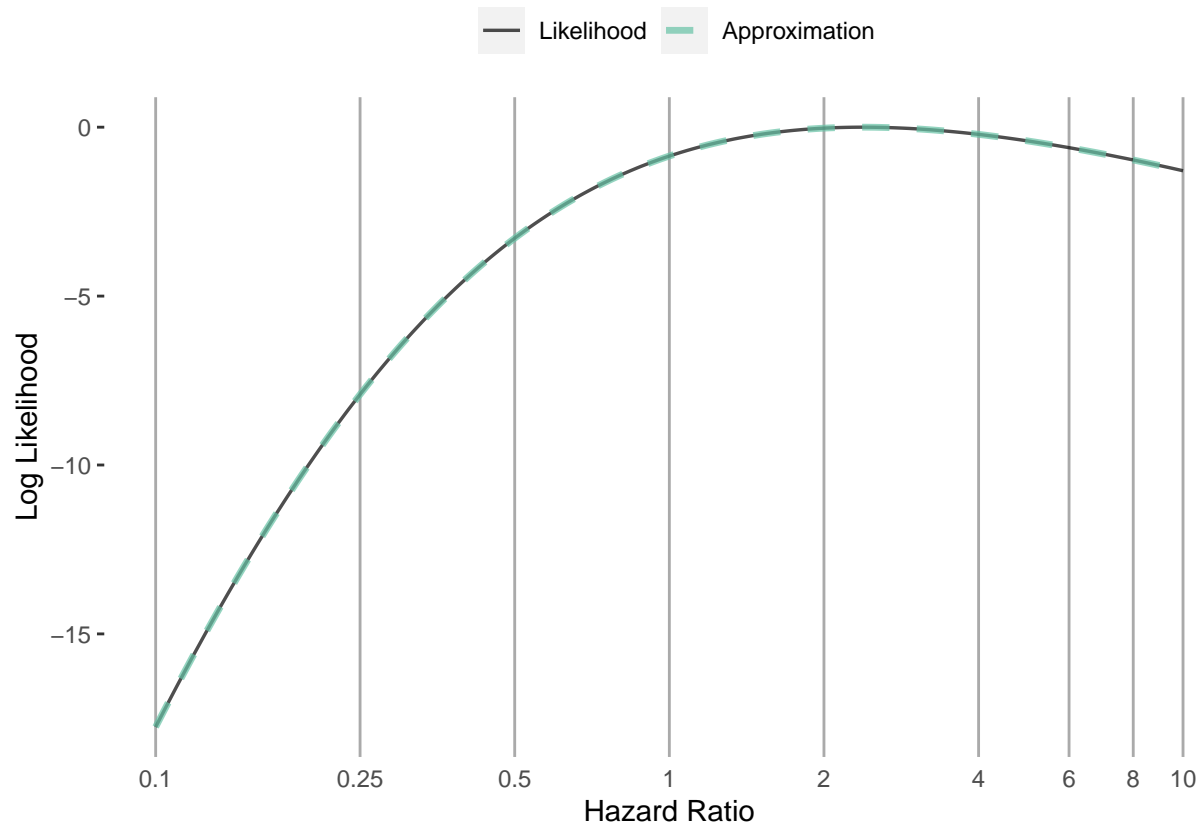
Adaptive approximation

```
approximation <- approximateLikelihood(
  cyclopsFit = cyclopsFit,
  parameter = "x",
  approximation = "adaptive grid",
  bounds = c(log(0.1), log(10))
)
head(approximation)
```

```
## # A tibble: 6 x 2
##   point value
##   <dbl> <dbl>
## 1 -2.30 -156.
## 2 -2.29 -156.
## 3 -2.27 -156.
## 4 -2.25 -155.
## 5 -2.24 -155.
## 6 -2.22 -155.
```

```
plotLikelihoodFit(
  approximation = approximation,
  cyclopsFit = cyclopsFit,
  parameter = "x"
)
```

```
## Detected data following adaptive grid distribution
```



Approximate at all sites

```
fitModelInDatabase <- function(population, approximation) {  
  cyclopsData <- createCyclopsData(Surv(time, y) ~ x + strata(stratumId),  
    data = population,  
    modelType = "cox"  
  )  
  cyclopsFit <- fitCyclopsModel(cyclopsData)  
  approximation <- approximateLikelihood(cyclopsFit,  
    parameter = "x",  
    approximation = approximation  
  )  
  return(approximation)  
}  
adaptiveGridApproximations <- lapply(  
  X = populations,  
  FUN = fitModelInDatabase,  
  approximation = "adaptive grid"  
)  
normalApproximations <- lapply(  
  X = populations,  
  FUN = fitModelInDatabase,  
  approximation = "normal"
```

```
)  
normalApproximations <- do.call(rbind, (normalApproximations))
```

Synthesize evidence

Fixed-effects

Gold standard (pooling data):

```
fixedFxPooled <- computeFixedEffectMetaAnalysis(populations)  
fixedFxPooled
```

```
##          rr          lb          ub      logRr  seLogRr  
## x 2.432933 1.370034 4.800644 0.8890975 0.319882
```

Normal approximation:

```
fixedFxNormal <- computeFixedEffectMetaAnalysis(normalApproximations)
```

```
## Warning: Estimate(s) with NA seLogRr detected. Removing before computing  
## meta-analysis.
```

```
fixedFxNormal
```

```
##          rr          lb          ub      logRr  seLogRr  
## 1 1.605267 0.8168054 3.154828 0.4732898 0.3447228
```

Adaptive grid approximation:

```
fixedFxAdaptiveGrid <- computeFixedEffectMetaAnalysis(adaptiveGridApproximations)  
fixedFxAdaptiveGrid
```

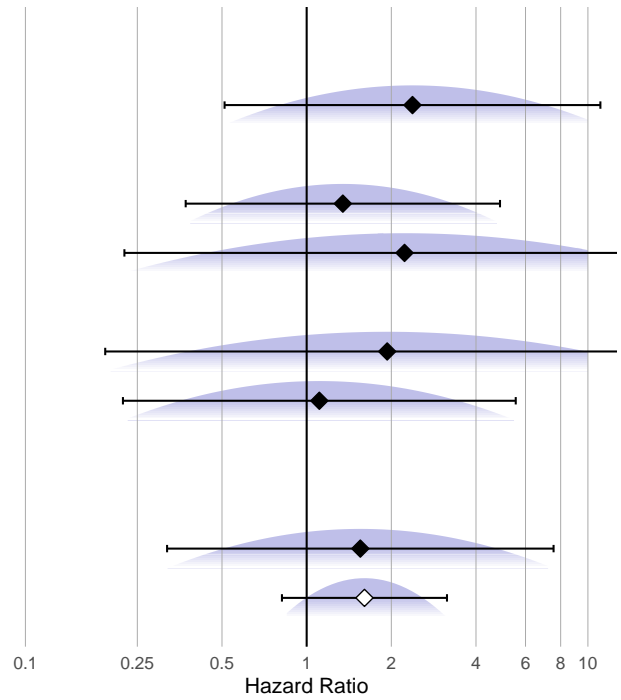
```
##          rr          lb          ub      logRr  seLogRr  
## 1 2.448437 1.376857 4.792428 0.8954498 0.3181777
```

Visualization

Normal approximation:

```
plotMetaAnalysisForest(  
  data = normalApproximations,  
  labels = paste("Site", 1:10),  
  estimate = fixedFxNormal,  
  xLabel = "Hazard Ratio"  
)
```

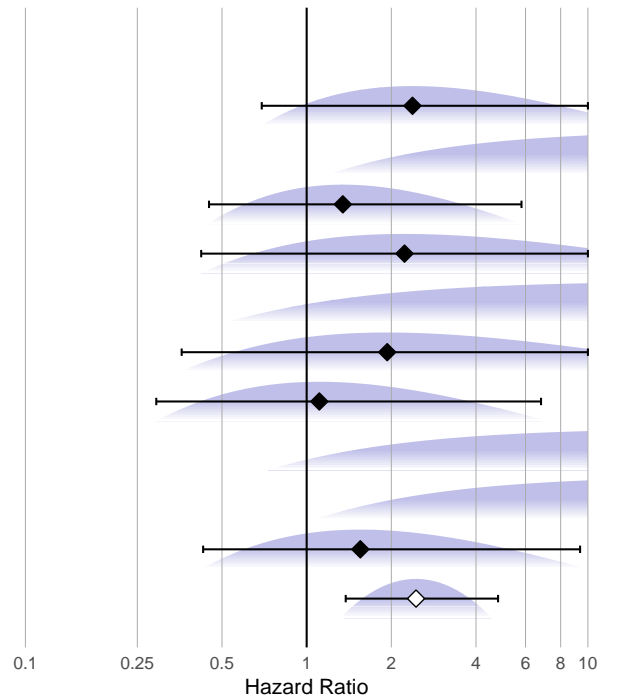
| Source | Hazard Ratio (95% CI) |
|---------|-----------------------|
| Site 1 | 2.38 (0.51 – 11.08) |
| Site 2 | – |
| Site 3 | 1.34 (0.37 – 4.87) |
| Site 4 | 2.23 (0.22 – 22.08) |
| Site 5 | – |
| Site 6 | 1.93 (0.19 – 19.45) |
| Site 7 | 1.11 (0.22 – 5.54) |
| Site 8 | – |
| Site 9 | – |
| Site 10 | 1.55 (0.32 – 7.55) |
| Summary | 1.61 (0.82 – 3.15) |



Adaptive grid approximation:

```
plotMetaAnalysisForest(
  data = adaptiveGridApproximations,
  labels = paste("Site", 1:10),
  estimate = fixedFxAdaptiveGrid,
  xLabel = "Hazard Ratio"
)
```

| Source | Hazard Ratio (95% CI) |
|---------|-----------------------|
| Site 1 | 2.38 (0.69 – 10.00) |
| Site 2 | – |
| Site 3 | 1.34 (0.45 – 5.81) |
| Site 4 | 2.23 (0.42 – 10.00) |
| Site 5 | – |
| Site 6 | 1.93 (0.36 – 10.00) |
| Site 7 | 1.11 (0.29 – 6.81) |
| Site 8 | – |
| Site 9 | – |
| Site 10 | 1.55 (0.43 – 9.38) |
| Summary | 2.45 (1.38 – 4.79) |



Random-effects

Gold standard (pooling data):

```
randomFxPooled <- computeBayesianMetaAnalysis(populations)
exp(randomFxPooled[, 1:3])
```

```
##           mu    mu95Lb    mu95Ub
## 1 2.594023 1.326203 5.272257
```

Normal approximation:

```
randomFxNormal <- computeBayesianMetaAnalysis(normalApproximations)
```

```
## Warning: Estimate(s) with NA seLogRr detected. Removing before computing
## meta-analysis.
```

```
exp(randomFxNormal[, 1:3])
```

```
##           mu    mu95Lb    mu95Ub
## 1 1.55483 0.7732428 3.254443
```

Adaptive grid approximation:

```
randomFxAdaptiveGrid <- computeBayesianMetaAnalysis(adaptiveGridApproximations)
exp(randomFxAdaptiveGrid[, 1:3])
```

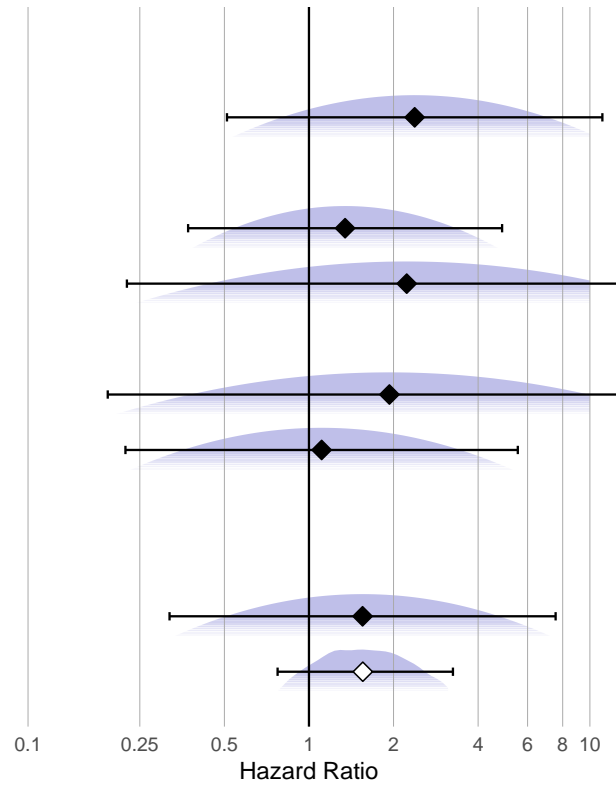
```
##           mu    mu95Lb    mu95Ub
## 1 2.66668 1.329153 5.255041
```

Visualization

Normal approximation:

```
plotMetaAnalysisForest(
  data = normalApproximations,
  labels = paste("Site", 1:10),
  estimate = randomFxNormal,
  xLabel = "Hazard Ratio"
)
```

| Source | Hazard Ratio (95% CI) |
|----------------------|-----------------------|
| Site 1 | 2.38 (0.51 – 11.08) |
| Site 2 | – |
| Site 3 | 1.34 (0.37 – 4.87) |
| Site 4 | 2.23 (0.22 – 22.08) |
| Site 5 | – |
| Site 6 | 1.93 (0.19 – 19.45) |
| Site 7 | 1.11 (0.22 – 5.54) |
| Site 8 | – |
| Site 9 | – |
| Site 10 | 1.55 (0.32 – 7.55) |
| Summary (tau = 0.25) | 1.55 (0.77 – 3.25) |



Adaptive grid approximation:

```
plotMetaAnalysisForest(
  data = adaptiveGridApproximations,
  labels = paste("Site", 1:10),
  estimate = randomFxAdaptiveGrid,
  xLabel = "Hazard Ratio"
)
```


| Source | Hazard Ratio (95% CI) |
|----------------------|-----------------------|
| Site 1 | 2.38 (0.69 – 10.00) |
| Site 2 | – |
| Site 3 | 1.34 (0.45 – 5.81) |
| Site 4 | 2.23 (0.42 – 10.00) |
| Site 5 | – |
| Site 6 | 1.93 (0.36 – 10.00) |
| Site 7 | 1.11 (0.29 – 6.81) |
| Site 8 | – |
| Site 9 | – |
| Site 10 | 1.55 (0.43 – 9.38) |
| Summary (tau = 0.28) | 2.67 (1.33 – 5.26) |

