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

**Simulate data**

Simulate 10 sites:
```r
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:
```r
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**

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

head(approximation)
```

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

```r
plotLikelihoodFit(
  approximation = approximation,
  cyclopsFit = cyclopsFit,
  parameter = "x"
)
```
## Detected data following adaptive grid distribution

![Graph showing hazard ratio vs. log likelihood for adaptive grid approximation.](image)

### Approximate at all sites

```r
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):

```r
fixedFxPooled <- computeFixedEffectMetaAnalysis(populations)
fixedFxPooled
## rr  lb   ub  logRr  seLogRr
## x 2.432933 1.370034 4.800644 0.8890975 0.319882
```

Normal approximation:

```r
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:

```r
fixedFxAdaptiveGrid <- computeFixedEffectMetaAnalysis(adaptiveGridApproximations)
fixedFxAdaptiveGrid
## rr  lb   ub  logRr  seLogRr
## 1 2.448437 1.376857 4.792428 0.8954498 0.3181777
```

Visualization

Normal approximation:

```r
plotMetaAnalysisForest(
  data = normalApproximations,
  labels = paste("Site", 1:10),
  estimate = fixedFxNormal,
  xLabel = "Hazard Ratio"
)
```
<table>
<thead>
<tr>
<th>Source</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site 1</td>
<td>2.38 (0.51 – 11.08)</td>
</tr>
<tr>
<td>Site 2</td>
<td>–</td>
</tr>
<tr>
<td>Site 3</td>
<td>1.34 (0.37 – 4.87)</td>
</tr>
<tr>
<td>Site 4</td>
<td>2.23 (0.22 – 22.08)</td>
</tr>
<tr>
<td>Site 5</td>
<td>–</td>
</tr>
<tr>
<td>Site 6</td>
<td>1.93 (0.19 – 19.45)</td>
</tr>
<tr>
<td>Site 7</td>
<td>1.11 (0.22 – 5.54)</td>
</tr>
<tr>
<td>Site 8</td>
<td>–</td>
</tr>
<tr>
<td>Site 9</td>
<td>–</td>
</tr>
<tr>
<td>Site 10</td>
<td>1.55 (0.32 – 7.55)</td>
</tr>
<tr>
<td>Summary</td>
<td>1.61 (0.82 – 3.15)</td>
</tr>
</tbody>
</table>

Adaptive grid approximation:

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

Gold standard (pooling data):

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

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

Normal approximation:

```r
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:

```r
randomFxAdaptiveGrid <- computeBayesianMetaAnalysis(adaptiveGridApproximations)

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

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

Visualization

Normal approximation:

```r
plotMetaAnalysisForest(
  data = normalApproximations,
  labels = paste("Site", 1:10),
  estimate = randomFxNormal,
  xLabel = "Hazard Ratio"
)
```
<table>
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</tr>
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</tr>
<tr>
<td>Site 9</td>
<td>–</td>
</tr>
<tr>
<td>Site 10</td>
<td>1.55 (0.32 − 7.55)</td>
</tr>
<tr>
<td>Summary (tau = 0.25)</td>
<td>1.55 (0.77 − 3.25)</td>
</tr>
</tbody>
</table>

Adaptive grid approximation:

```r
plotMetaAnalysisForest(
  data = adaptiveGridApproximations,
  labels = paste("Site", 1:10),
  estimate = randomFxAdaptiveGrid,
  xLabel = "Hazard Ratio"
)
```
<table>
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<td>Site 1</td>
<td>2.38 (0.69 – 10.00)</td>
</tr>
<tr>
<td>Site 2</td>
<td>–</td>
</tr>
<tr>
<td>Site 3</td>
<td>1.34 (0.45 – 5.81)</td>
</tr>
<tr>
<td>Site 4</td>
<td>2.23 (0.42 – 10.00)</td>
</tr>
<tr>
<td>Site 5</td>
<td>–</td>
</tr>
<tr>
<td>Site 6</td>
<td>1.93 (0.36 – 10.00)</td>
</tr>
<tr>
<td>Site 7</td>
<td>1.11 (0.29 – 6.81)</td>
</tr>
<tr>
<td>Site 8</td>
<td>–</td>
</tr>
<tr>
<td>Site 9</td>
<td>–</td>
</tr>
<tr>
<td>Site 10</td>
<td>1.55 (0.43 – 9.38)</td>
</tr>
<tr>
<td>Summary (tau = 0.28)</td>
<td>2.67 (1.33 – 5.26)</td>
</tr>
</tbody>
</table>

![Graph showing hazard ratios and 95% confidence intervals for different sources.](image-url)