Implementing Probabilitic Sensitivity Analysis for Parametric Survival Model, Age at Onset Distribution for the Autoimmune Disorder

Background

This Jupyter notebook contains scripts to implemnt fitting parametric survival models based on summary statisics from literautre, and probabistic sensitivity analysis (PSA).

In [ ]:
```
# Todo (November 1, 2026):
# 1. Update title and subtitles
# 2. Update imported libraries
# 3. Improve formatting
# 4. Update inline comments
# 5. Refactor functions for better readability
# 6. Add error handling
```

Necessary modules

In [95]:
```
import numpy as np
import pandas as pd
import matplotlib.pyplot as plt
import seaborn as sns
from scipy.stats import lognorm, weibull_min, gamma, genextreme # Importing neces
from scipy.optimize import minimize # Optimization for parameter fitting
from scipy.stats import probplot # Probability plot for visual assessment
from sklearn.metrics import mean_squared_error # Mean Squared Error for goodness-
from scipy.stats import gaussian_kde # Kernel Density Estimation for smooth CDF
```

Fitting Generalized Gamma Model Based on Summary Statistics Derived from Literature

Background

The summary statistics derived from literature informed three parametric survival model, consisting of log normal, weibull and generalized gamma. Of them, generalized gamma has the optimal fit of goodness, with lowest AIC.

For better transparency and reproducibility, this section presents the procedure to achive the fitted generalized gamma, with fitted parameters.

The generalized Gamma distribution has three parameters to fit:

- a: shape parameter
- c: power parameter
- scale: scale parameter

In [ ]:
```
# import numpy as np
# from scipy.stats import gengamma
# from scipy.optimize import minimize
```

Input Data

The summary statistics is derived from literature, which informs the parametric survival models.

In [97]:
```
median = 66
q1 = 61
q3 = 72
min = 19
max = 88
mean = 67
size = 111

empirical_q = [q1, median, q3]
```

Fitting Generalized Gamma Model

Apply quantile matching method to seek for the optimal model with smallest difference between predicted and observed quantiles.

In [98]:
```
# Define the quantile-matching objective function
def gengamma_objective(params):
    a, c, scale = params
    if a <= 0 or scale <= 0:
        return np.inf
    try:
        dist = gengamma(a=a, c=c, scale=scale)
        theo_q = dist.ppf([0.25, 0.5, 0.75])
        return np.sum((np.array(theo_q)- np.array(empirical_q))**2)
    except:
        return np.inf
```

In [99]:
```
# Run the optimization
initial_guess_gengamma = [2.0, 1.0, 10.0]
bounds_gengamma = [(0.01, None), (0.01, None), (0.01, None)]

result_gengamma = minimize(gengamma_objective, x0=initial_guess_gengamma, bounds=
a_fit_gengamma, c_fit_gengamma, scale_fit_gengamma = result_gengamma.x

print(f"Fitted Generalized Gamma parameters:\n a = {a_fit_gengamma:.3f}, c = {c_f
```

```
Fitted Generalized Gamma parameters:
 a = 26.611, c = 1.583, scale_fit_gengamma = 8.409
```

```
/var/folders/b8/9ymtxc2j7rb00xx34s753cwc0000gn/T/ipykernel_51726/1451994867.py:9:
RuntimeWarning: overflow encountered in square
  return np.sum((np.array(theo_q)- np.array(empirical_q))**2)
/opt/anaconda3/lib/python3.12/site-packages/scipy/optimize/_numdiff.py:590: Runti
meWarning: invalid value encountered in subtract
  df = fun(x) - f0
```

Visualization of Empirical and Fitted CDF

In [100…

```
# Simulate and visualize
import matplotlib.pyplot as plt
```

In [101…

```
# Simulate onset ages
sim_ages_gengamma = gengamma(a = a_fit_gengamma, c = c_fit_gengamma, scale = scal
```

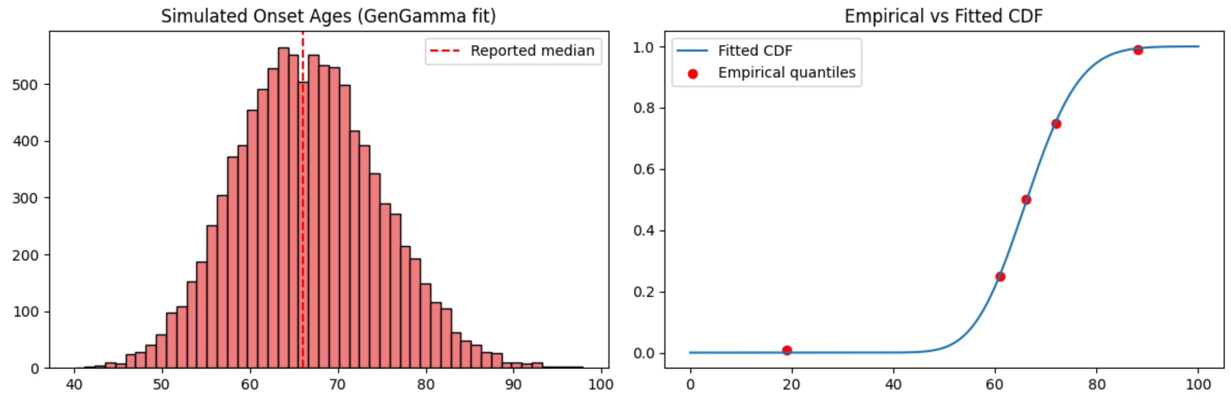
In [102…

```
# Plot histogram and CDF
fig, ax = plt.subplots(1, 2, figsize = (12, 4))

# Histogram
ax[0].hist(sim_ages_gengamma, bins=50, color='lightcoral', edgecolor='black')
ax[0].axvline(x=median, color='red', linestyle='--', label='Reported median')
ax[0].set_title('Simulated Onset Ages (GenGamma fit)')
ax[0].legend()

# CDF
x_gengamma = np.linspace(0, 100, 300)
model_cdf_gengamma = gengamma(a=a_fit_gengamma, c=c_fit_gengamma, scale=scale_fit
ax[1].plot(x_gengamma, model_cdf_gengamma, label='Fitted CDF')
ax[1].scatter([min, q1, median, q3, max], [0.01, 0.25, 0.5, 0.75, 0.99], color='r
ax[1].set_title('Empirical vs Fitted CDF')
ax[1].legend()

plt.tight_layout()
plt.show()
```



In this case, the Generalized Gamma distribution shows the smallest squared difference, indicating the best fit among the three candidate distributions.

Sensitivity analysis with Monte Carlo simulation

Purpose

Monte Carlo simulation using fitted distribution parameters offers three key advantages:

- Continuous uncertainty representation rather than relying on only low, central, and high values.
- Faster and smoother calculations through the cumulative distribution function (CDF), without the need for inner resampling.
- More stable confidence intervals and compatibility with tornado analysis for identifying key drivers.

Code for implementation

In [103…

```python
import numpy as np
import pandas as pd
from scipy.stats import gengamma, norm
```

In [ ]:

```python
# The fitted model object from previous analysis
result_gengamma
```

Out[ ]:

```
  message: CONVERGENCE: REL_REDUCTION_OF_F_<=_FACTR*EPSMCH
  success: True
   status: 0
      fun: 0.10243077858152738
        x: [ 2.661e+01  1.583e+00  8.409e+00]
      nit: 88
      jac: [-1.463e-02  1.069e+00 -8.571e-02]
     nfev: 456
     njev: 114
 hess_inv: <3x3 LbfgsInvHessProduct with dtype=float64>
```

Getting Fitted Parameter

In [106…

```python
# Get the MLE
theta_hat = result_gengamma.x

print(theta_hat)
```

```
[26.61103626  1.58349596  8.40915197]
```

Getting Covariance Matrix

Compute the Hessian numerically at the optimum

In [107…

```python
import numpy as np
from statsmodels.tools.numdiff import approx_hess

H = approx_hess(theta_hat, gengamma_objective)  # by default, central differences
```

In [108…

```python
# Invert the Hessian to get the variance-covariance matrix
vcov_matrix = np.linalg.inv(H)

print(vcov_matrix)
```

```
[[ 5.95129550e+02 -1.77608293e+01 -3.15062237e+02]
 [-1.77608293e+01  5.51055889e-01  9.63377691e+00]
 [-3.15062237e+02  9.63377691e+00  1.69340808e+02]]
```

In [109…

```
# Multivariate normal sampling on fitted scale

from numpy.random import default_rng
rng = default_rng(123)
N = 5000

m = theta_hat  # MLE parameter vector
L = np.linalg.cholesky(vcov_matrix)  # Cholesky decomposition of variance-covaria
Z = rng.standard_normal((N, len(m)))  # Standard normal samples

theta_draws = m + Z @ L.T  # MVN samples of parameters
mu_draws, log_sigma_draws, Q_draws = theta_draws.T
```

In [110…

```
np.mean(log_sigma_draws)
```

Out[110…

```
1.5637918813315672
```

In [111…

```
# Age bands (inclusive of lower, exclusive of upper)
age_bands = [(0, 12), (12, 18), (18, 100)]
```

Calculating cumulative probability specific to predefined age bands

In [112…

```
# Compute band probabilities for each parameter set via CDF
def band_probs_for_draw(a, c, s):
    F = gengamma(a=a, c=c, scale=s).cdf
    p0_12 = F(12.0) - F(0.0)
    p12_18 = F(18.0) - F(12.0)
    p18_100 = F(100.0) - F(18.0)
    return p0_12, p12_18, p18_100
```

gengamma(a=a, c=c, scale=s) constructs a "frozen" SciPy generalized Gamma distribution with given parameters. Appending .cdf returns that distribution's cumulative distribution function as a callable (i.e., can be called like a function).

What F is: a function F(x) that returns P(x <= x) for X ~ GenGamma(a,c,scale=s). It accepts acalars or numpy arrays and returns probabities in [0,1].

In [113…

```
P = np.array([band_probs_for_draw(a, c, s) for a, c, s in zip(mu_draws, log_sigma
```

In [114…

```
print(P[:10])
```

```
[[1.20059387e-02 7.33904212e-02 9.14603640e-01]
 [1.08145832e-25 8.45280534e-18 9.99985839e-01]
 [1.92092384e-12 1.54251855e-08 9.99999974e-01]
 [1.20756676e-18 5.23993223e-13 9.99994565e-01]
 [           nan            nan            nan]
 [1.70337946e-27 3.55365476e-19 9.99994112e-01]
 [3.04377245e-19 1.99256162e-13 9.99996554e-01]
 [1.00000000e+00 2.01283434e-13 0.00000000e+00]
 [           nan            nan            nan]
 [           nan            nan            nan]]
```

In [115…
```
# Filter out NaNs in all three columns
P = P[~np.isnan(P).any(axis=1)]
```

In [116…
```
print(P[:10])
```

```
[[1.20059387e-02 7.33904212e-02 9.14603640e-01]
 [1.08145832e-25 8.45280534e-18 9.99985839e-01]
 [1.92092384e-12 1.54251855e-08 9.99999974e-01]
 [1.20756676e-18 5.23993223e-13 9.99994565e-01]
 [1.70337946e-27 3.55365476e-19 9.99994112e-01]
 [3.04377245e-19 1.99256162e-13 9.99996554e-01]
 [1.00000000e+00 2.01283434e-13 0.00000000e+00]
 [8.17154984e-16 4.93084700e-11 9.99937577e-01]
 [1.00000000e+00 0.00000000e+00 0.00000000e+00]
 [2.02810919e-20 2.75611355e-14 9.99997395e-01]]
```

Results

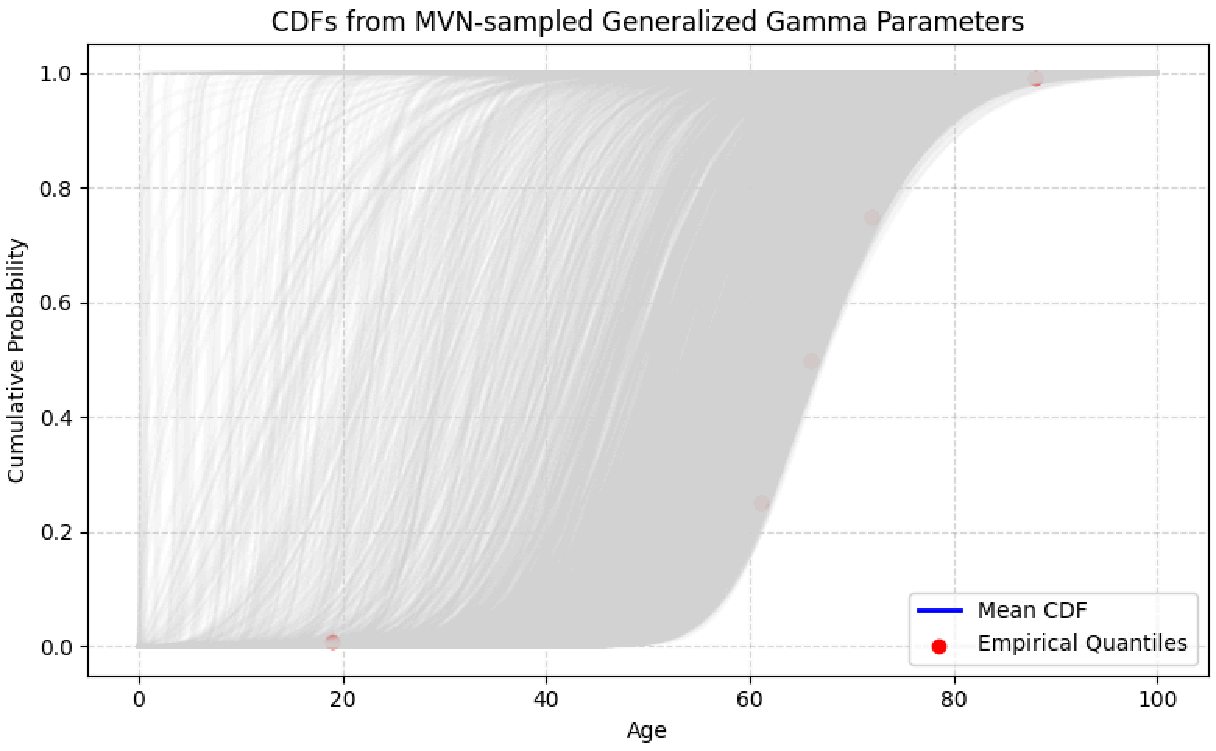
In [117…
```
# Summarize reults
summary = pd.DataFrame({
    'Age Band': ['0-12', '12-18', '18+'],
    'Mean': np.char.mod('%.2f%%', P.mean(axis=0)*100),
    "SD": np.char.mod('%.2f%%', P.std(axis=0)*100),
    "Median": np.char.mod('%.2f%%', np.median(P, axis=0)*100),
    "CI Lower (2.5%)": np.char.mod('%.2f%%', np.percentile(P, 2.5, axis=0)*100),
    "CI Upper (97.5%)": np.char.mod('%.2f%%', np.percentile(P, 97.5, axis=0)*100)
})

print(summary)
```

```
  Age Band    Mean      SD   Median CI Lower (2.5%) CI Upper (97.5%)
0     0-12   2.67%  14.00%    0.00%           0.00%           44.47%
1    12-18   1.95%   9.41%    0.00%           0.00%           23.81%
2      18+  95.38%  18.45%  100.00%           9.54%          100.00%
```

Visualization of multivariate normal sampling

In [118…
```
# Draw CDF for sampled parameters
x = np.linspace(0, 100, 300)
cdf_samples = [gengamma(a=a, c=c, scale=s).cdf(x) for a, c, s in zip(mu_draws, lo
import matplotlib.pyplot as plt
# Plot sampled CDFs
plt.figure(figsize=(8, 5))
for cdf in cdf_samples:
    plt.plot(x, cdf, color='lightgray', alpha=0.1)
# Plot mean CDF
mean_cdf = np.mean(cdf_samples, axis=0)
plt.plot(x, mean_cdf, color='blue', label='Mean CDF', linewidth=2)
# Plot empirical quantiles
plt.scatter([min, q1, median, q3, max], [0.01, 0.25, 0.5, 0.75, 0.99], color='rec
# Format plot
plt.title('CDFs from MVN-sampled Generalized Gamma Parameters')
plt.xlabel('Age')
plt.ylabel('Cumulative Probability')
plt.legend()
plt.grid(linestyle='--', alpha=0.5)
plt.tight_layout()
plt.show()
```


CDFs from MVN-sampled Generalized Gamma Parameters
Cumulative Probability
Age
Mean CDF
Empirical Quantiles