Supplementary file 1: Comparison between INLA and JAGS estimations and assessment of the stability of the inference.
1 Descriptive: number of events

| H.Area | N   | F → R | F → D | R → D |
|--------|-----|-------|-------|-------|
|        | Men | Women | Men   | Women | Men | Women |
| 1      | 141 | 442   | 9     | 31    | 77  | 215   | 5    | 20    |
| 2      | 510 | 1478  | 23    | 114   | 301 | 704   | 17   | 58    |
| 3      | 339 | 934   | 21    | 63    | 207 | 417   | 11   | 28    |
| 4      | 353 | 1019  | 19    | 89    | 216 | 511   | 14   | 45    |
| 5      | 550 | 1724  | 36    | 147   | 320 | 769   | 24   | 69    |
| 6      | 489 | 1716  | 31    | 154   | 299 | 821   | 19   | 74    |
| 7      | 349 | 1111  | 26    | 88    | 204 | 523   | 16   | 39    |
| 8      | 111 | 293   | 3     | 19    | 83  | 154   | 3    | 11    |
| 9      | 639 | 2085  | 30    | 173   | 386 | 1029  | 20   | 73    |
| 10     | 578 | 1815  | 31    | 142   | 364 | 870   | 20   | 68    |
| 11     | 406 | 1224  | 25    | 104   | 272 | 674   | 17   | 56    |
| 12     | 374 | 1095  | 30    | 83    | 206 | 500   | 20   | 37    |
| 13     | 335 | 966   | 25    | 96    | 189 | 408   | 10   | 46    |
| 14     | 438 | 1246  | 23    | 88    | 280 | 610   | 18   | 43    |
| 15     | 278 | 908   | 16    | 55    | 167 | 461   | 12   | 26    |
| 16     | 277 | 679   | 12    | 41    | 154 | 304   | 8    | 20    |
| 17     | 385 | 1210  | 19    | 93    | 224 | 602   | 14   | 44    |
| 18     | 386 | 1118  | 26    | 85    | 222 | 571   | 13   | 34    |
| 19     | 358 | 1140  | 29    | 94    | 199 | 487   | 18   | 28    |
| 20     | 281 | 795   | 21    | 57    | 164 | 395   | 14   | 25    |
| 21     | 254 | 732   | 17    | 44    | 138 | 308   | 9    | 19    |
| 22     | 325 | 713   | 19    | 52    | 153 | 278   | 7    | 19    |
| 23     | 322 | 842   | 20    | 66    | 188 | 379   | 13   | 32    |
| 24     | 206 | 522   | 5     | 38    | 120 | 222   | 4    | 13    |
| **Total** | **8684** | **25807** | **516** | **2016** | **5133** | **12212** | **326** | **927** |

Supplementary table 1: Number of patients among transitions by Health Area, and sex.
2 INLA vs JAGS

We compared estimations from both procedures using a reduced case study. We selected 5 neighbouring Health Areas of the 24 in the Valencia Region, and applied an illness-death model with Weibull transition intensities, and with region-specific random effects. Random effects follow a gaussian distribution which precision matrix only includes between-transition correlation. The illness-death part of the model remains unchanged and the only difference appears in the random effects model:

\[
(b_{k}^{FR}, b_{k}^{FD}, b_{k}^{RD})^T \sim N(0, \Sigma_{\text{between}}), \quad k = 1, \ldots, 5,
\]

where \(b_{k}^{ij}\) is the random effect of the Health Area \(k\) in the intensity of the transition \(i \rightarrow j\), and \(\Sigma_{\text{between}}\) is the between-transition correlation matrix defined as:

\[
\Sigma_{\text{between}} = \begin{pmatrix}
\frac{1}{\tau_{FR}} & \frac{\rho(\text{FR})(\text{FD})}{\sqrt{\tau_{FR}\tau_{FD}}} & \frac{\rho(\text{FR})(\text{RD})}{\sqrt{\tau_{FR}\tau_{RD}}} \\
\frac{\rho(\text{FR})(\text{FD})}{\sqrt{\tau_{FR}\tau_{FD}}} & \frac{1}{\tau_{FD}} & \frac{\rho(\text{FD})(\text{RD})}{\sqrt{\tau_{FD}\tau_{RD}}} \\
\frac{\rho(\text{FR})(\text{RD})}{\sqrt{\tau_{FR}\tau_{RD}}} & \frac{\rho(\text{FD})(\text{RD})}{\sqrt{\tau_{FD}\tau_{RD}}} & \frac{1}{\tau_{RD}}
\end{pmatrix}.
\]

Non-informative priors were used. In particular, \(\text{Gamma}(0.01, 0.01)\) priors for shape parameters \(\alpha\) and normal distributions, \(N(0, 0.001)\) (in terms of precision) for intercepts and effects of covariates. For the precision matrix, \(\Sigma_{\text{between}}^{-1}\), we assumed a Wishart prior with \(\nu = 7\) degrees of freedom and the identity as the scale matrix.
Supplementary figure 1: Posterior mean of the region-specific random effects for 5 Health Areas of the Valencia Region, from an illness-death model with gaussian random effects considering between-transition correlation, using INLA and MCMC methods via JAGS.

Supplementary figure 2: Absolute differences in the estimated posterior mean of random effects using INLA and MCMC methods via JAGS.

Note that slight differences were observed between random effects obtained from both procedures.
2.1 JAGS diagnostics

Convergence to the posterior distribution was assessed using three chains and 5,000 iterations per chain (each chain with an adapt period of 1000 and burn-in of 500 iterations). A post-sweeping procedure was applied to random effects and intercepts to improve identifiability and reduce the number of iterations needed to reach this convergence.

We assessed convergence and mixing of the Markov chains. We obtained point estimates and upper confidence limits of the Gelman and Rubin’s potential scale reduction factor, for each parameter and latent effect in the model, in order to assess convergence. We show a summary of it.

|            | Min. | 1st Qu. | Median | Mean  | 3rd Qu. | Max.  |
|------------|------|---------|--------|-------|---------|-------|
| Point est. | 1.000| 1.001   | 1.003  | 1.005 | 1.009   | 1.023 |
| Upper C.I. | 1.000| 1.002   | 1.008  | 1.017 | 1.026   | 1.067 |

Supplementary table 2: Summary of the estimated Gelman and Rubin’s potential scale reduction factor for the samples obtained via JAGS. Point estimates and upper confidence limits.

2.2 MCSE of posterior outcomes

We estimated Monte Carlo Standard Errors (MCSE) for the samples of the posterior outcomes. Note that we first simulated values of the parameters from the joint posterior distribution with INLA, and then we obtained samples of cumulative incidences and transition probabilities. We provide the MCSE of those samples, analogously to what should be done when simulating from MCMC or other methods which work with random draws. We calculated it for each Health Area, \( k = 1, \ldots, 24 \), for each \( t = 1, \ldots, 5 \), for each quantity of interest, and for both women and men. It has been summarized in the following table:

| Outcome | Min. | 1st Qu. | Median | Mean  | 3rd Qu. | Max.  | Min. | 1st Qu. | Median | Mean  | 3rd Qu. | Max.  |
|---------|------|---------|--------|-------|---------|-------|------|---------|--------|-------|---------|-------|
| \( F_{12} \) | 1.82 | 2.06    | 2.22   | 2.22  | 2.36    | 2.92  | 1.71 | 2.11    | 2.26   | 2.26  | 2.40    | 3.03  |
| \( p_{FR} \) | 1.86 | 2.11    | 2.26   | 2.26  | 2.36    | 2.99  | 1.46 | 2.17    | 2.31   | 2.30  | 2.45    | 3.16  |
| \( p_{FD} \) | 1.78 | 2.13    | 2.34   | 2.40  | 2.61    | 3.61  | 1.77 | 2.06    | 2.25   | 2.27  | 2.43    | 3.28  |
| \( p_{RD} \) | 1.91 | 2.10    | 2.27   | 2.27  | 2.46    | 2.68  | 1.81 | 2.18    | 2.32   | 2.31  | 2.47    | 2.78  |

Supplementary table 3: Summary of the Monte Carlo standard errors as a percentage of the posterior SD.

In broad terms, MC standard errors are low compared to standard deviation, which implies that we have good estimations of the posterior mean of the outcomes depicted in Figures 6-9 in the manuscript.
3 Stability of the inference

3.1 Fixing spatial-correlation parameter, $\gamma$

Note that few differences were observed by fixing $\gamma$ parameter, comparing to an unknown value of $\gamma$ which is estimated from the model and data (mean of 0.841). The model considering no spatial correlation at all, $\gamma = 0$, differed the most.

Supplementary figure 3: Absolute differences in the estimated posterior mean of random effects for fixed values of $\gamma = 0, 0.5, 0.99$ compared to a variable value of $\gamma$ (posterior mean of 0.841 estimated according to the main analysis), approximated via INLA.
| Parameter       | $\gamma = 0$ |          | $\gamma = 0.5$ |          | Unknown $\gamma$ |          | $\gamma = 0.99$ |          |
|-----------------|--------------|----------|----------------|----------|-----------------|----------|----------------|----------|
| $\beta_{FR}$    | -3.603 (-3.739, -3.468) | 3.598    | -3.603 (-3.739, -3.468) | 3.598    | -3.596 (-4.764, -2.430) | 3.596    | -3.596 (-4.764, -2.430) | 3.596    |
| $\beta_{FD}$    | -1.104 (-1.196, -1.013) | 0.999    | -1.104 (-1.196, -1.013) | 0.999    | 1.105 (-2.094, -0.115) | 1.105    | 1.105 (-2.094, -0.115) | 1.105    |
| $\beta_{RD}$    | -0.537 (-0.694, -0.381) | 0.371    | -0.537 (-0.694, -0.381) | 0.371    | 0.545 (-0.984, -0.107) | 0.545    | 0.545 (-0.984, -0.107) | 0.545    |
| $\beta_{FR, Woman}$ | 0.021 (-0.076, 0.119) | 0.021    | 0.021 (-0.076, 0.119) | 0.021    | 0.021 (-0.076, 0.119) | 0.021    | 0.021 (-0.076, 0.119) | 0.021    |
| $\beta_{FD, Woman}$ | -0.510 (-0.542, -0.477) | -0.510   | -0.510 (-0.542, -0.477) | -0.510   | -0.510 (-0.542, -0.477) | -0.510   | -0.510 (-0.542, -0.477) | -0.510   |
| $\beta_{RD, Woman}$ | -0.633 (-0.760, -0.504) | -0.634   | -0.633 (-0.760, -0.504) | -0.634   | -0.634 (-0.760, -0.504) | -0.634   | -0.634 (-0.760, -0.504) | -0.634   |
| $\beta_{FR, Age}$ | 0.024 (0.018, 0.030) | 0.024    | 0.024 (0.018, 0.030) | 0.024    | 0.024 (0.018, 0.030) | 0.024    | 0.024 (0.018, 0.030) | 0.024    |
| $\beta_{FD, Age}$ | 0.070 (0.068, 0.073) | 0.070    | 0.070 (0.068, 0.073) | 0.070    | 0.070 (0.068, 0.073) | 0.070    | 0.070 (0.068, 0.073) | 0.070    |
| $\beta_{RD, Age}$ | 0.050 (0.040, 0.059) | 0.050    | 0.050 (0.040, 0.059) | 0.050    | 0.049 (0.040, 0.059) | 0.049    | 0.049 (0.040, 0.059) | 0.049    |

Supplementary table 4: Posterior estimates from different spatial illness-death models with fixed values of the spatial correlation parameter $\gamma = 0, 0.5, 0.99$, and with an unknown $\gamma$ estimated from the model, via INLA.
3.2 Varying degrees of freedom, $\nu$

Note that few differences were observed by varying $\nu$ parameter, comparing to estimations for $\nu = 7$. Transition from refracture to death showed the highest differences, but probably due to the lower sample size (See Supplementary Table 1).

Supplementary figure 4: Absolute differences in the estimated posterior mean of random effects for $\nu = 6, 8, 9, 10$ compared to $\nu = 7$ (reference value used in the main analysis), approximated via INLA.
| Parameter | $v = 6$ | Median | $v = 7$ | Median | $v = 8$ | Median | $v = 9$ | Median | $v = 10$ | Median |
|-----------|---------|--------|---------|--------|---------|--------|---------|--------|---------|--------|
| $\beta^{IR}$ | -3.598 (-3.954, -3.243) | -3.570 | -3.598 (-3.993, -3.204) | -3.597 | -3.598 (-3.913, -3.284) | -3.597 | -3.598 (-3.945, -3.251) | -3.597 | -3.597 (-3.878, -3.319) | -3.597 |
| $\beta^{ID}$ | -1.105 (-1.402, -0.809) | -1.105 | -1.105 (-1.436, -0.775) | -1.105 | -1.105 (-1.358, -0.854) | -1.105 | -1.105 (-1.394, -0.818) | -1.105 | -1.105 (-1.332, -0.879) | -1.105 |
| $\beta^{RD}$ | -0.544 (-0.946, -0.142) | -0.544 | -0.545 (-0.984, -0.107) | -0.545 | -0.545 (-0.891, -0.199) | -0.545 | -0.545 (-0.924, -0.166) | -0.545 | -0.546 (-0.852, -0.237) | -0.546 |
| $\beta_{FR, Woman}$ | 0.021 (-0.076, 0.119) | 0.021 | 0.021 (-0.076, 0.119) | 0.020 | 0.021 (-0.076, 0.119) | 0.020 | 0.021 (-0.076, 0.119) | 0.020 | 0.021 (-0.076, 0.119) | 0.020 |
| $\beta_{FD, Woman}$ | -0.510 (-0.543, -0.477) | -0.510 | -0.510 (-0.543, -0.477) | -0.510 | -0.510 (-0.543, -0.477) | -0.510 | -0.510 (-0.543, -0.477) | -0.510 | -0.510 (-0.542, -0.477) | -0.510 |
| $\beta_{RD, Woman}$ | -0.634 (-0.761, -0.505) | -0.634 | -0.634 (-0.761, -0.505) | -0.634 | -0.634 (-0.760, -0.504) | -0.634 | -0.634 (-0.760, -0.504) | -0.633 | -0.633 (-0.759, -0.504) | -0.633 |
| $\beta_{FR, Age}$ | 0.024 (0.018, 0.030) | 0.024 | 0.024 (0.018, 0.030) | 0.024 | 0.024 (0.018, 0.030) | 0.024 | 0.024 (0.018, 0.030) | 0.024 | 0.024 (0.018, 0.030) | 0.024 |
| $\beta_{FD, Age}$ | 0.070 (0.068, 0.073) | 0.070 | 0.070 (0.068, 0.073) | 0.070 | 0.070 (0.068, 0.073) | 0.070 | 0.070 (0.068, 0.073) | 0.070 | 0.070 (0.068, 0.073) | 0.070 |
| $\beta_{RD, Age}$ | 0.049 (0.040, 0.059) | 0.049 | 0.049 (0.040, 0.059) | 0.049 | 0.049 (0.040, 0.059) | 0.049 | 0.049 (0.040, 0.059) | 0.049 | 0.049 (0.040, 0.059) | 0.049 |

Supplementary table 5: Posterior estimates from different spatial illness-death models with fixed values $v = 6, 7, 8, 9, 10$, via INLA. 
A reference value $v = 7$ is used in the main analysis.