## **Appendix 3: Shifts in disease rate (In) (Move) and disease severity levels (Isn) (Grade).**

The objective is to demonstrate what will happen with the overall cost given a shift in disease rate (I*n*) moving to higher numbers in the more aged groups. The disease rate (I*n*) by age group is initiated, as presented in Appendix 2, as an exponential increase in function of age (𝐼𝑛 = 0.0562 ∗ 𝑒0.2353𝐴𝑛) with limits of 59% in the oldest age group and 7% in the youngest age group. The sensitivity analysis ‘*Move’* causes a steeper exponential increase by age defined by the following equation (𝐼𝑛 = 0.0422 ∗ 𝑒0.304𝐴𝑛) with limits of 88% in the oldest age group and 6% in the youngest group (see next Table).

**Table 1:** Changing baseline values for infection rate (I) in Move and severity level (Is) in Grade 1.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Basic | **N** | **1000** |  | | |  |  | **Severity** | | | | | |  | **Cost** | | | | | |
|  | **Age class** | | **verage ag** | **Proportion** | **#** | **rate I** | **Disease** | **rate Isl** | **L** | **rate Ism** | **M** | **rate Ish** | **H** | **Total** | **L** | **M** | **H** | **Total** | **Average** | **Average I** |
|  | 1 | 65-68.5 | 66.75 | 19% | 190 | 7.10% | 13 | 0.65 | 8.71 | 0.25 | 3.37 | 0.1 | 1 | 13.42 | 10 | 20 | 30 | 194.75 | € 1 | € 15 |
|  | 2 | 68.5-72 | 70.25 | 18% | 180 | 9.00% | 16 | 0.59 | 9.64 | 0.25 | 4.11 | 0.16 | 3 | 16.39 | 10 | 20 | 30 | 257.83 | € 1 | € 16 |
|  | 3 | 72-75.5 | 73.75 | 16% | 160 | 11.40% | 19 | 0.53 | 9.78 | 0.25 | 4.66 | 0.22 | 4 | 18.55 | 10 | 20 | 30 | 314.42 | € 2 | € 17 |
|  | 4 | 75.5-79 | 77.25 | 15% | 150 | 14.40% | 21 | 0.47 | 9.63 | 0.25 | 5.19 | 0.28 | 6 | 20.67 | 10 | 20 | 30 | 375.58 | € 3 | € 18 |
|  | 5 | 79-82.5 | 80.75 | 12% | 123 | 18.20% | 22 | 0.41 | 8.94 | 0.25 | 5.54 | 0.34 | 8 | 22.07 | 10 | 20 | 30 | 427.96 | € 3 | € 19 |
|  | 6 | 82.5-86 | 84.25 | 8% | 82 | 23.10% | 21 | 0.34 | 7.39 | 0.25 | 5.39 | 0.41 | 9 | 21.49 | 10 | 20 | 30 | 442.94 | € 5 | € 21 |
|  | 7 | 86-89.5 | 87.75 | 7% | 70 | 29.20% | 18 | 0.28 | 5.08 | 0.25 | 4.51 | 0.47 | 8 | 17.96 | 10 | 20 | 30 | 392.17 | € 6 | € 22 |
|  | 8 | 89.5-93 | 91.25 | 3% | 30 | 36.90% | 12 | 0.22 | 2.6 | 0.25 | 2.94 | 0.53 | 6 | 11.7 | 10 | 20 | 30 | 269.58 | € 9 | € 23 |
|  | 9 | 93-96.5 | 94.75 | 1% | 10 | 46.70% | 5 | 0.16 | 0.79 | 0.25 | 1.24 | 0.59 | 3 | 4.93 | 10 | 20 | 30 | 119.66 | € 12 | € 24 |
|  | 10 | 96.5-100 | 98.25 | 1% | 5 | 59.10% | 3 | 0.1 | 0.28 | 0.25 | 0.71 | 0.65 | 2 | 2.84 | 10 | 20 | 30 | 72.29 | € 14 | € 25 |
|  | **Total** |  |  |  | **1000** |  | **150** |  | **63** |  | **38** |  | **50** | **150** |  |  |  | **€ 2,867** | **€ 3** | **€ 19** |
|  |  |  |  |  |  | **Linest** | **0.0073** | **-0.1699** | **1.3538** | **-4.9368** | **10.6257** | **6.5414** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | **Belgian (X2)** | | | | | | | | | | | | | | | | | | | |
|  | **N** | **1000** |  | | |  |  | **Severity** | | | | | |  | **Cost** | | | | | |
|  | **Age class** | | **verage ag** | **Proportion** | **#** | **rate I** | **Disease** | **rate Isl** | **L** | **rate Ism** | **M** | **rate Ish** | **H** | **Total** | **L** | **M** | **H** | **Total** | **Average** | **Average I** |
| Move | 1 | 65-68.5 | 66.75 | 19% | 190 | 5.70% | 10 | 0.65 | 7 | 0.251 | 3 | 0.1 | 1 | 10 | € 10 | € 20 | € 30 | € 147 | € 1 | € 15 |
|  | 2 | 68.5-72 | 70.25 | 18% | 180 | 7.80% | 14 | 0.59 | 8 | 0.251 | 3 | 0.161 | 2 | 14 | € 10 | € 20 | € 30 | € 214 | € 1 | € 16 |
|  | 3 | 72-75.5 | 73.75 | 16% | 160 | 10.50% | 16 | 0.53 | 8 | 0.251 | 4 | 0.222 | 4 | 16 | € 10 | € 20 | € 30 | € 273 | € 2 | € 17 |
|  | 4 | 75.5-79 | 77.25 | 15% | 150 | 14.20% | 19 | 0.47 | 9 | 0.251 | 5 | 0.283 | 5 | 19 | € 10 | € 20 | € 30 | € 349 | € 2 | € 18 |
|  | 5 | 79-82.5 | 80.75 | 12% | 123 | 19.30% | 22 | 0.41 | 9 | 0.251 | 6 | 0.344 | 8 | 22 | € 10 | € 20 | € 30 | € 430 | € 3 | € 19 |
|  | 6 | 82.5-86 | 84.25 | 8% | 82 | 26.20% | 23 | 0.34 | 8 | 0.251 | 6 | 0.405 | 9 | 23 | € 10 | € 20 | € 30 | € 479 | € 6 | € 21 |
|  | 7 | 86-89.5 | 87.75 | 7% | 70 | 35.40% | 21 | 0.28 | 6 | 0.251 | 5 | 0.466 | 10 | 21 | € 10 | € 20 | € 30 | € 451 | € 6 | € 22 |
|  | 8 | 89.5-93 | 91.25 | 3% | 30 | 48.00% | 14 | 0.22 | 3 | 0.251 | 4 | 0.527 | 8 | 14 | € 10 | € 20 | € 30 | € 329 | € 11 | € 23 |
|  | 9 | 93-96.5 | 94.75 | 1% | 10 | 65.10% | 7 | 0.16 | 1 | 0.251 | 2 | 0.588 | 4 | 7 | € 10 | € 20 | € 30 | € 159 | € 16 | € 24 |
|  | 10 | 96.5-100 | 98.25 | 1% | 5 | 88.20% | 4 | 0.1 | 0 | 0.251 | 1 | 0.649 | 3 | 4 | € 10 | € 20 | € 30 | € 102 | € 20 | € 25 |
|  | **Total** |  |  |  | **1000** |  | **150** |  | **59** |  | **38** |  | **53** | **150** |  |  |  | **€ 2,934** | **€ 3** | **€ 20** |
|  |  |  |  |  |  | Linest | 0.010603 | -0.257614 | 2.156397 | -7.941296 | 15.71779 | 0.467057 |  |  |  |  |  | € 67 |  | € 6,308 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 2.20% |  |  |
|  | **Belgian (X2)** | | | | | | | | | | | | | | | | | | | |
| Grade 1 | **N** | **1000** |  | | |  |  | **Severity** | | | | | |  | **Cost** | | | | | |
|  | **Age class** | | **verage ag** | **Proportion** | **#** | **rate I** | **Disease** | **rate Isl** | **L** | **rate Ism** | **M** | **rate Ish** | **H** | **Total** | **L** | **M** | **H** | **Total** | **Average** | **Average I** |
|  | 1 | 65-68.5 | 66.75 | 19% | 190 | 5.70% | 10 | 0.7498 | 8 | 0.1502 | 2 | 0.1 | 1 | 10.15 | € 10 | € 20 | € 30 | € 137 | € 1 | € 14 |
|  | 2 | 68.5-72 | 70.25 | 18% | 180 | 7.80% | 14 | 0.6776 | 9 | 0.1502 | 2 | 0.1722 | 2 | 13.61 | € 10 | € 20 | € 30 | € 203 | € 1 | € 15 |
|  | 3 | 72-75.5 | 73.75 | 16% | 160 | 10.50% | 16 | 0.6054 | 10 | 0.1502 | 2 | 0.2444 | 4 | 16.08 | € 10 | € 20 | € 30 | € 264 | € 2 | € 16 |
|  | 4 | 75.5-79 | 77.25 | 15% | 150 | 14.20% | 19 | 0.5332 | 10 | 0.1502 | 3 | 0.3166 | 6 | 19.19 | € 10 | € 20 | € 30 | € 342 | € 2 | € 18 |
|  | 5 | 79-82.5 | 80.75 | 12% | 123 | 19.30% | 22 | 0.461 | 10 | 0.1502 | 3 | 0.3888 | 9 | 22.2 | € 10 | € 20 | € 30 | € 428 | € 3 | € 19 |
|  | 6 | 82.5-86 | 84.25 | 8% | 82 | 26.20% | 23 | 0.3888 | 9 | 0.1502 | 3 | 0.461 | 11 | 23.25 | € 10 | € 20 | € 30 | € 482 | € 6 | € 21 |
|  | 7 | 86-89.5 | 87.75 | 7% | 70 | 35.40% | 21 | 0.3166 | 7 | 0.1502 | 3 | 0.5332 | 11 | 20.68 | € 10 | € 20 | € 30 | € 458 | € 7 | € 22 |
|  | 8 | 89.5-93 | 91.25 | 3% | 30 | 48.00% | 14 | 0.2444 | 3 | 0.1502 | 2 | 0.6054 | 9 | 14.28 | € 10 | € 20 | € 30 | € 337 | € 11 | € 24 |
|  | 9 | 93-96.5 | 94.75 | 1% | 10 | 65.10% | 7 | 0.1722 | 1 | 0.1502 | 1 | 0.6776 | 4 | 6.55 | € 10 | € 20 | € 30 | € 164 | € 16 | € 25 |
|  | 10 | 96.5-100 | 98.25 | 1% | 5 | 88.20% | 4 | 0.1 | 0 | 0.1502 | 1 | 0.7498 | 3 | 4.02 | € 10 | € 20 | € 30 | € 106 | € 21 | € 26 |
|  | **Total** |  |  |  | **1000** |  | **150** |  | **68** |  | **23** |  | **60** | **150** |  |  |  | **€ 2,922** | **€ 3** | **€ 19** |

We also like to see what is happening with the overall costs if, in addition to the increase in disease rate (Move), the disease severity level increases (Grade) in addition to a higher frequency in the older age groups. This is a likely scenario happening over time: not only more cases in the most ageing adult ones but also more severe ones. Because the disease severity level was simulated with linear regression equations, we performed two types of sensitivity analyses, reported as Grade 1 and Grade 2.

In Grade 1, we changed the gradient of the linear function to induce a steeper decline for the low severity group starting at a higher frequency of 75% instead of 65% but ending at approximately the same level of 10%. The inverse gradient change is introduced for the high severity level, and the medium severity level remains as a complement to the low and high severity levels.

In Grade 2, we adjusted the linearity of the function to a parallel function changing the constant value. It therefore induced a lower overall frequency of the low severity cases, while the high severity cases were increased (see next Table).

**Table 2:** Adjusting the severity level to the Grade 2 approach

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Garde 2 | **N** | **1000** |  | | |  |  | **Severity** | | | | | |  | **Cost** | | | | | |
|  | **Age class** | | **verage ag** | **Proportion** | **#** | **rate I** | **Disease** | **rate Isl** | **L** | **rate Ism** | **M** | **rate Ish** | **H** | **Total** | **L** | **M** | **H** | **Total** | **Average** | **Average I** |
|  | 1 | 65-68.5 | 66.75 | 19% | 190 | 7% | 14 | 0.55 | 7 | 0.251 | 3 | 0.1998 | 3 | 13.51 | € 10 | € 20 | € 30 | € 223 | € 1 | € 17 |
|  | 2 | 68.5-72 | 70.25 | 18% | 180 | 9% | 16 | 0.4882 | 8 | 0.251 | 4 | 0.2608 | 4 | 16.2 | € 10 | € 20 | € 30 | € 287 | € 2 | € 18 |
|  | 3 | 72-75.5 | 73.75 | 16% | 160 | 11% | 18 | 0.4272 | 8 | 0.251 | 5 | 0.3218 | 6 | 18.22 | € 10 | € 20 | € 30 | € 345 | € 2 | € 19 |
|  | 4 | 75.5-79 | 77.25 | 15% | 150 | 14% | 22 | 0.3662 | 8 | 0.251 | 5 | 0.3828 | 8 | 21.61 | € 10 | € 20 | € 30 | € 436 | € 3 | € 20 |
|  | 5 | 79-82.5 | 80.75 | 12% | 123 | 18% | 22 | 0.3052 | 7 | 0.251 | 6 | 0.4438 | 10 | 22.42 | € 10 | € 20 | € 30 | € 480 | € 4 | € 21 |
|  | 6 | 82.5-86 | 84.25 | 8% | 82 | 23% | 19 | 0.2442 | 5 | 0.251 | 5 | 0.5048 | 10 | 18.91 | € 10 | € 20 | € 30 | € 428 | € 5 | € 23 |
|  | 7 | 86-89.5 | 87.75 | 7% | 70 | 29% | 20 | 0.1832 | 4 | 0.251 | 5 | 0.5658 | 12 | 20.43 | € 10 | € 20 | € 30 | € 487 | € 7 | € 24 |
|  | 8 | 89.5-93 | 91.25 | 3% | 30 | 37% | 11 | 0.1222 | 1 | 0.251 | 3 | 0.6268 | 7 | 11.08 | € 10 | € 20 | € 30 | € 277 | € 9 | € 25 |
|  | 9 | 93-96.5 | 94.75 | 1% | 10 | 47% | 5 | 0.0612 | 0 | 0.251 | 1 | 0.6878 | 3 | 4.67 | € 10 | € 20 | € 30 | € 123 | € 12 | € 26 |
|  | 10 | 96.5-100 | 98.25 | 1% | 5 | 59% | 3 | 0.0002 | 0 | 0.251 | 1 | 0.7488 | 2 | 2.96 | € 10 | € 20 | € 30 | € 81 | € 16 | € 27 |
|  | **Total** |  |  |  | **1000** |  | **150** |  | **48** |  | **38** |  | **64** | **150** |  |  |  | **€ 3,167** | **€ 3** | **€ 21** |

# **Abbreviations:** €: Euro; An: Age Groups; CT: Cost of treatment; CTm: Cost per severity level ESAP: Extended sensitivity plan; In: Rate of infection in each age group Is: Levels of disease severity; Isn: severity level by age group MF: multiplication factor; MTH: multiplication factor high severity MTM: multiplication factor medium severity N: Population number; QALY: Quality adjusted Life Year; VITAL: Vaccines and infectious diseases in the aging population X1: basic homogenous model; X1a: fully homogeneous model X1b: partial homogeneous model; X2: non-homogenous model; X2a: non-homogeneous, no demographic model; X2b: non-homogenous demographic increase of the model