Estimating the future burden of myocardial infarction in France until 2035: an illness-death model-based approach

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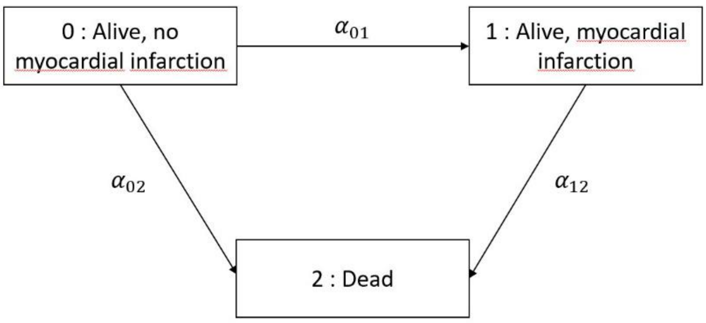
Supplementary methods

Illness-death model

In the *illness-death* model, we denoted as $\alpha_{ij}(a_1)$ the transition intensities while the cumulative transition intensities are denoted as $A_{ij}(a_1)$. Here, α_{01} is the incidence of subjects hospitalized for myocardial infarction, α_{02} the mortality of healthy subjects, and α_{12} the mortality of diseased subjects.

$$A_{ij}(a_1, a_2) = \int_{a_1}^{a_2} \alpha_{ij}(u)\, du$$



The illness-death model

Transition probabilities

For a given individual, the probability of being alive with no disease (state 0) between ages a_1 and a_2 is

$$P_{00}(a_1, a_2) = e^{-A_{01}(a_1,a_2)-A_{02}(a_1,a_2)}$$

The probability of staying alive but having the disease (state 1) between ages a_1 and a_2 is:

$$P_{11}(a_1, a_2) = e^{-\ A_{12}(a_1,a_2)}$$

For an individual in state 0, the probability of transitioning to state 1 between a_1 and a_2 is the probability of remaining in state 0 until age a_1, then transitioning to state 1 between a_1 and a_2, and finally remaining in state 1:

$$P_{01}(a_1, a_2) = \int_{a_1}^{a_2} P_{00}(a_1, u)\ \alpha_{01}(u)\ P_{11}(u, a_2)\ du$$

$$P_{01}(a_1, a_2) = \int_{a_1}^{a_2} e^{-A_{01}(a_1,u)-A_{02}(a_1,u)}\ \alpha_{01}(u) e^{-A_{12}(u,a_2)}\ du$$

Transition intensities

In our study, the incidence of subjects hospitalized for myocardial infarction was modelled with an age-cohort model and therefore depended on both age a and cohort c:

$$\alpha_{01}(a, c)$$

Mortality of healthy subjects is equivalent to the mortality in the general population α_2. Mortality was retrieved from INSEE data and depended on both age and cohort:

$$\alpha_{02}(a, c) = \ \alpha_2(a, c)$$

Mortality of diseased individuals was considered as the mortality of healthy individuals multiplied by a relative risk depending on time since disease onset. Let us denote RR_{d_1} the relative risk associated with the first year following the myocardial infarction event and RR_{d_2} the relative risk thereafter. During the first year after the event mortality is written as:

$$\alpha_{12}(a, c) = \alpha_2(a, c)\ \times RR_{d_1} \quad (1)$$

and in subsequent years as:

$$\alpha_{12}(a, c) = \alpha_2(a, c)\ \times RR_{d_2} \quad (2)$$

Rewriting P_{11} when α_{12} depends on the time since disease onset

We can rewrite P_{11} according to the rewriting of α_{12}. a_d is the age of disease onset.

If we then have (1):

$$P_{11}(a_d, a_2|c) = \exp[-A_{12}(a_d, a_2, c)] \quad if\ a_2 - a_d \le 1$$

$$P_{11}(a_d, a_2|c) = \exp[-\int_{a_d}^{a_2} \alpha_2(u, c) \times RR_{d_1}\, du]$$

If we then have (2):

$$P_{11}(a_d, a_2|c) = \exp[-A_{12}(a_d, a_d + 1, c)] \times \exp[-A_{12}(a_d + 1, a_2, c)] \quad if\ a_2 - a_d > 1$$

$$P_{11}(a_d, a_2|c) = \exp[-\int_{a_d}^{a_d+1} \alpha_2(u, c) \times RR_{d_1}\, du] \times \exp[-\int_{a_d+1}^{a_2} \alpha_2(u, c) \times RR_{d_2}\, du]$$

Number of prevalent cases

The number of prevalent cases for a year t is the number of subjects with MI over all ages at year t. Let a_0 be the minimum age and a_{max} the maximum age of all the individuals (35 and 95 years, respectively), $\nu(a_0, t)$ the size of the population for age a_0 and year t. The number of prevalent cases is then:

$$N_{prev}(t) = \sum_{k=a_0}^{a_{max}} \nu(a_0, t - a_{max} + k) \times P_{01}(a_0, a_{max} - k + a_0|c)$$

with $P_{01}(a_0, a_{max} - k + a_0|c)$ the probability of being in state 1 in $a_{max} - k + a_0$ knowing that the individual was in state 0 (healthy) in a_0 according to the cohort c and c can be written as $c = t - a_{max} + (k - a_0)$.

The probability $P_{01}(a_0, a_{max}|c)$ is defined as:

$$P_{01}(a_0, a_{\max}|c) = \int_{a_0}^{a_{max}} e^{-A_{01}(a_0,u,c) - A_{02}(a_0,u,c)}\ a_{01}(u, c)\ e^{-A_{12}(u,a_{max},c)}\ du$$

If we want to compute the number of prevalent cases in 2015 for example, we start by first computing the number of prevalent cases aged 95 years old in 2015:

$$\nu(35{,}2015 - 95 + 35) \times P_{01}(35{,}95 - 35 + 35|2015 - 95 + (35 - 35))$$

$$= \nu(35{,}1955) \times P_{01}(35{,}95|1920)$$

Effectively, this is the number of people aged 35 in 1955 (born in 1920) multiplied by the probability of being diseased between 35 and 95 for people born in 1920 (aged 35 in 1955) and still alive.

For the number of prevalent cases aged 94 in 2015 we have:

$$\nu(35{,}1956) \times P_{01}(35{,}94|1921)$$

and so on for each age and each year.

Mean age of incident cases

The mean age of incident cases is defined as:

$$\overline{age_{(inci)}}(t) = \frac{\sum_{a_0}^{a_{max}} a \ \times P_{00}(a_0, a|c) \times \alpha_{01}(a, c) \times \nu(a_0, c)}{\sum_{a_0}^{a_{max}} P_{00}(a_0, a|c) \ \times \ \alpha_{01}(a, c) \ \times \ \nu(a_0, c)}$$

with $\nu(a_0, c)$ the population of age a_0 for a cohort c and $P_{00}(a_0, a|c)$ the probability of remaining in state 0 (healthy) between ages a_0 and a according to the cohort c.

And $P_{00}(a_0, a|c)$ is defined as:

$$P_{00}(a_0, a|c) = e^{-A_{01}(a_0,a,c) - A_{02}(a_0,a,c)}$$

Supplementary tables and figures

Table S1. Different assumptions for the three INSEE scenarios[1]

Variables	Low scenario	Central scenario	High scenario
Life expectancy	90.0 years old in 2070	93.0 years old in 2070	96.0 years old in 2070
Fecundity	1.95 between 2013 and 2019 1.80 from 2020 onward	1.95 between 2013 and 2070	1.95 between 2013 and 2019 2.10 from 2020 onward
Net migration	+20 000 each year between 2013 and 2070	+70 000 each year between 2013 and 2070	+120 000 each year between 2013 and 2070

Table S2. Placement and value of the knots for the natural splines to model $\boldsymbol{\alpha_{01}}(\boldsymbol{a},\boldsymbol{c})$

	Number of knots		Value of the knots	
	Age	Cohort	Age	Cohort
Men	11	7	35,41,47,53,59,65, 71,77,83,89,95	1912,1923,1934,1945, 1956,1967,1980
Women	11	7	35,41,47,53,59,65, 71,77,83,89,95	1912,1922,1932,1942, 1952,1962,1980

Table S3. Description of the sample of the French population from SNDS used to estimate $\boldsymbol{RR_{d_1}}$ and $\boldsymbol{RR_{d_2}}$

	Men	Women
Total	449 046	547 345
Sex ratio	45.1	54.9
Events of MI	10 451	5299
Events of death	93 966	98 162
Events of death after MI	3672	2765
Mean age of MI (SD)	65.6 (13.2)	74.73 (14.0)
Estimation of RR_{d_1}	5.62 [5.32-5.93]	7.19 [6.78-7.62]
Estimation of RR_{d_2}	1.46 [1.41-1.52]	1.72 [1.64-1.81]

SD = Standard Deviation, values of the estimations of RR are HR [95% CI]

Table S4. Distribution and parameters used to compute 95% uncertainty intervals with Monte Carlo method

Variable	Distribution	Value of the estimated parameters
RR_{d_1}	Log-normal distribution	$\hat{\mu}_M = 1.735$
		$\hat{\sigma}_M = 0.0278$
		$\hat{\mu}_W = 1.981$
		$\hat{\sigma}_W = 0.0298$
RR_{d_2}	Log-normal distribution	$\hat{\mu}_M = 0.394$
		$\hat{\sigma}_M = 0.0209$
		$\hat{\mu}_W = 0.556$
		$\hat{\sigma}_W = 0.0251$
α_{01}	Multivariate normal distribution	$\mu = \hat{\phi}_M, \sigma = \hat{V}_{\hat{\phi}_M}$
		$\mu = \hat{\phi}_W, \sigma = \hat{V}_{\hat{\phi}_W}$

M = Men, W = Women

$\hat{\phi}_M$ and $\hat{\phi}_F$ are vectors containing the estimated parameters for the knots (age and cohort), $\hat{V}_{\hat{\phi}_M}$ and $\hat{V}_{\hat{\phi}_W}$ are the associated estimated variance-covariance matrix for the age-cohort model.

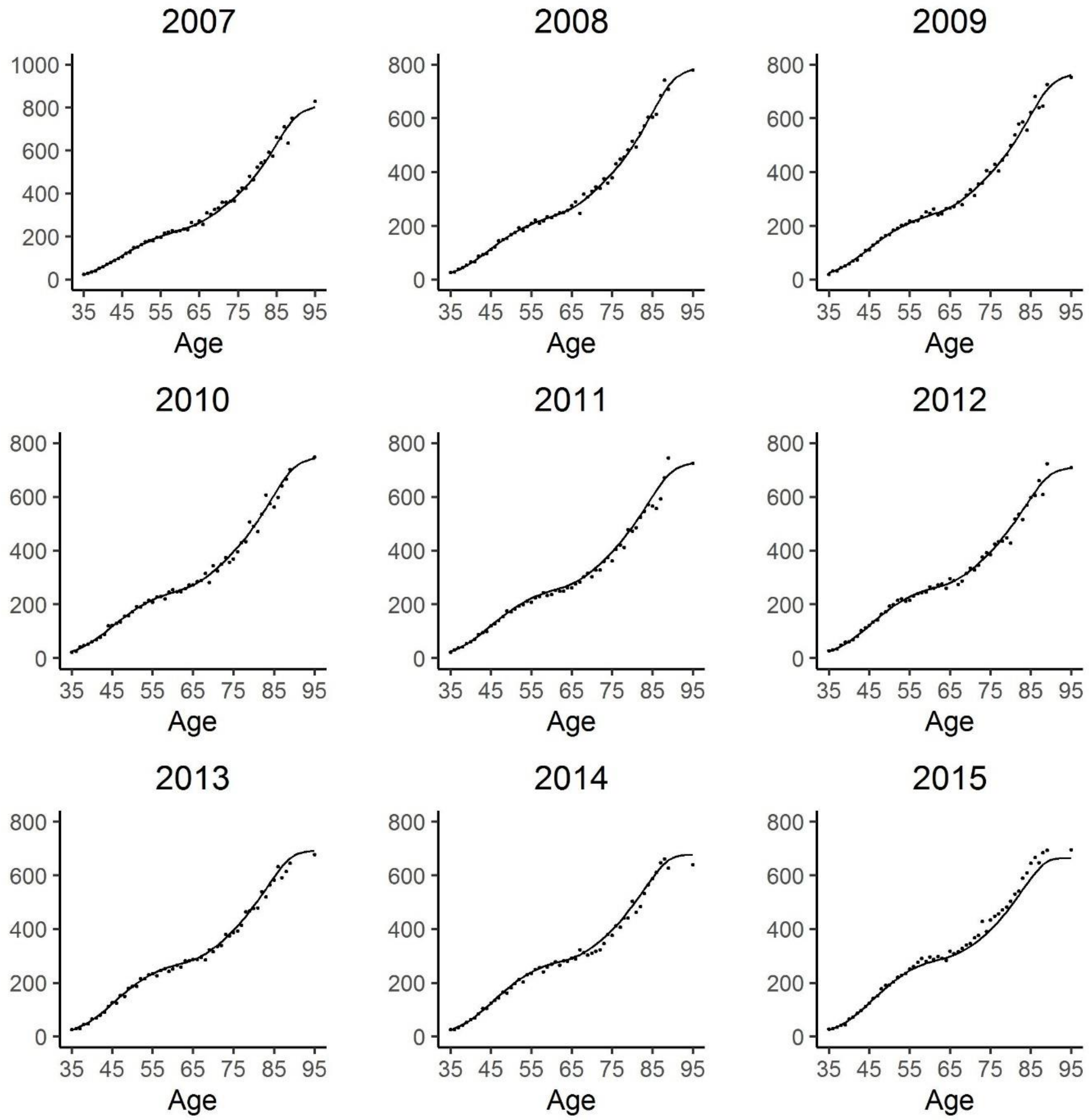


Figure S1. Incidence rate of hospitalizations of men for myocardial infarction $\boldsymbol{\alpha_{01}}$ (per 100 000) by age for several periods between 2007 and 2015. Points represent observed data, and solid lines represent the estimated incidences with the age-cohort model.

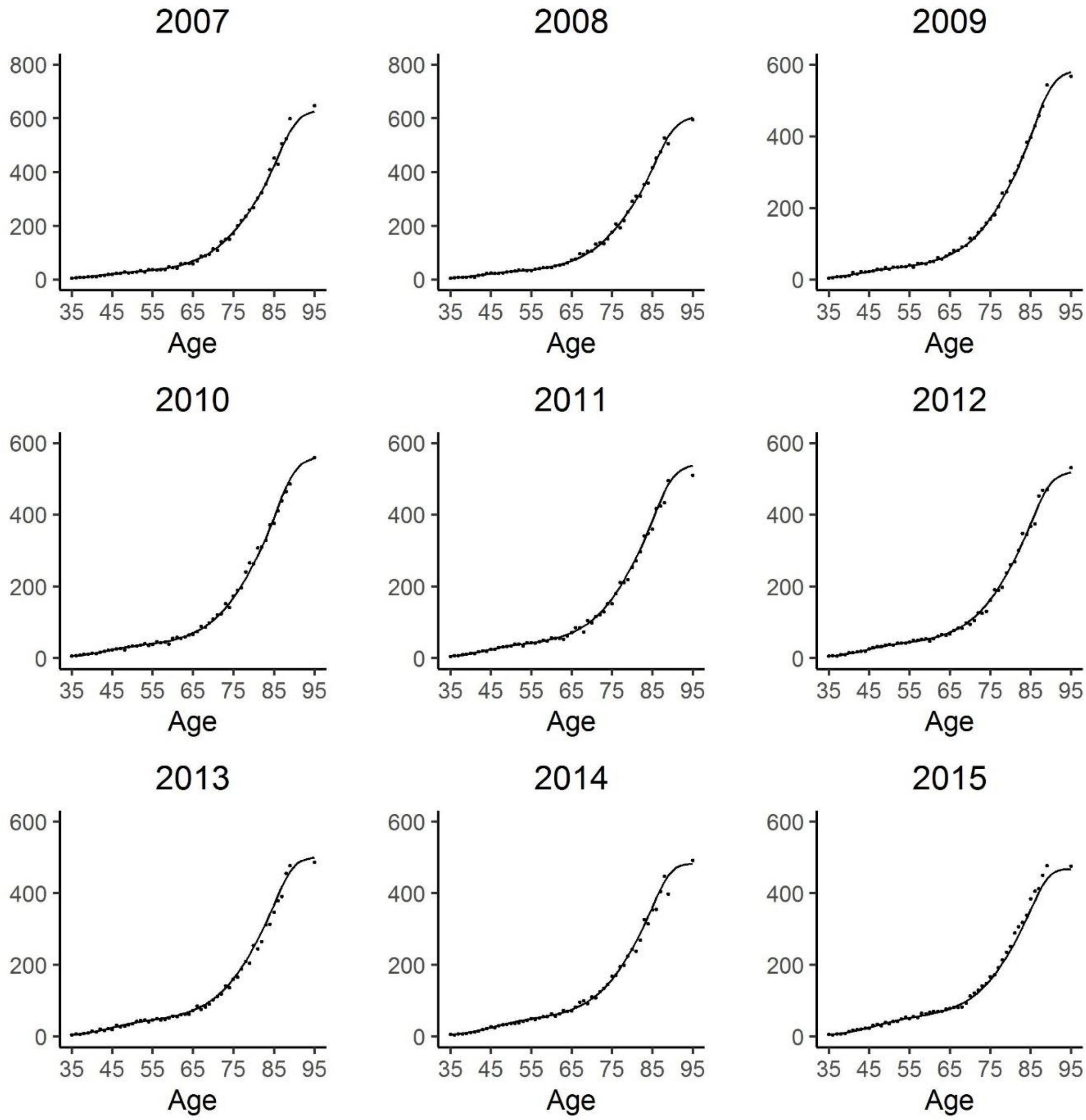


Figure S2. Incidence rate of hospitalizations of women for myocardial infarction $\boldsymbol{\alpha_{01}}$ (per 100 000) by age for several periods between 2007 and 2015. Points represent observed data, and solid lines represent the estimated incidences with the age-cohort model.

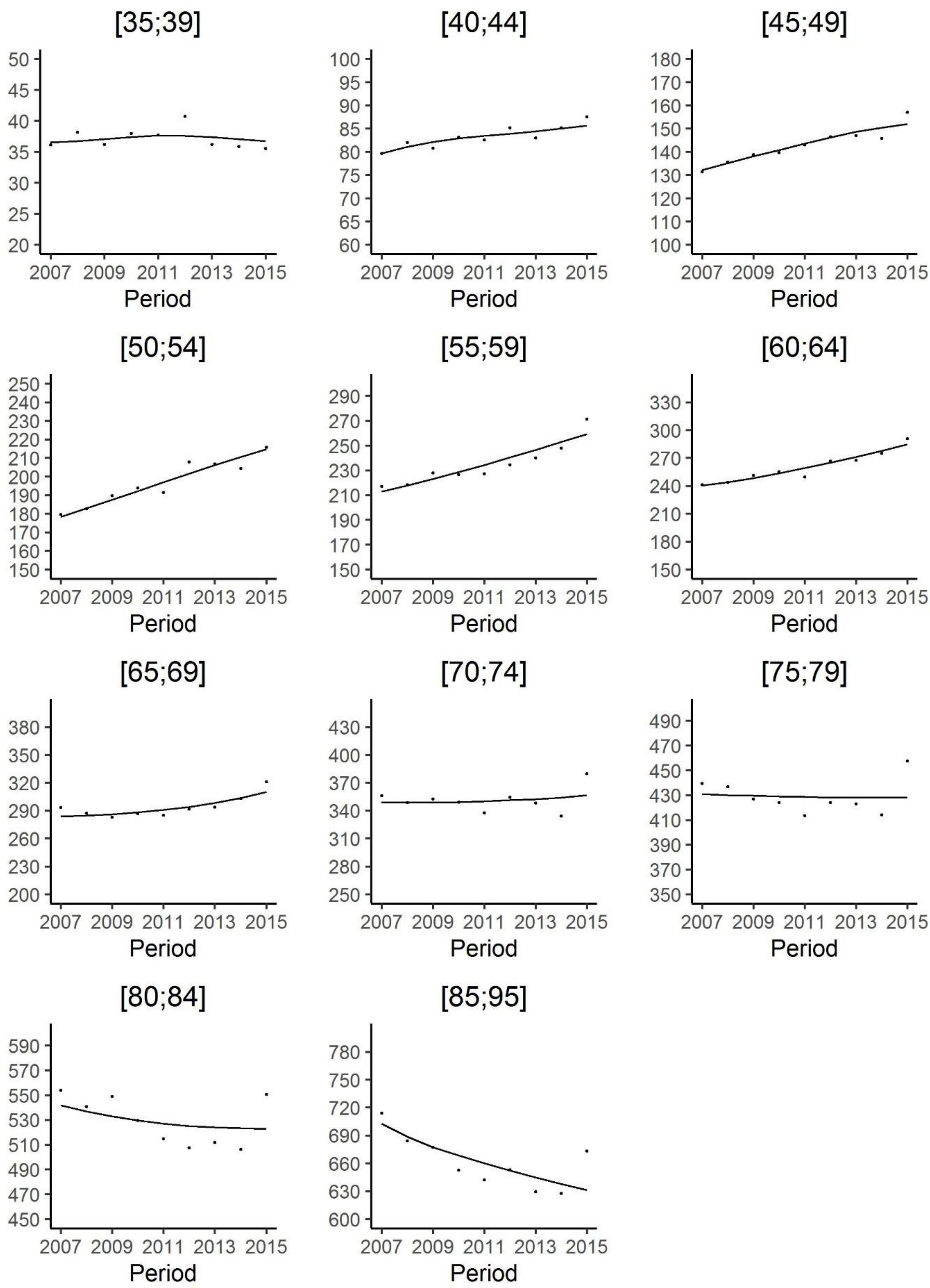


Figure S3. Incidence rate of hospitalizations of men for myocardial infarction $\boldsymbol{\alpha_{01}}$ (per 100 000) by period for several five-year age groups. Points represent observed data and solid lines represent the estimated incidences with the age-cohort model.

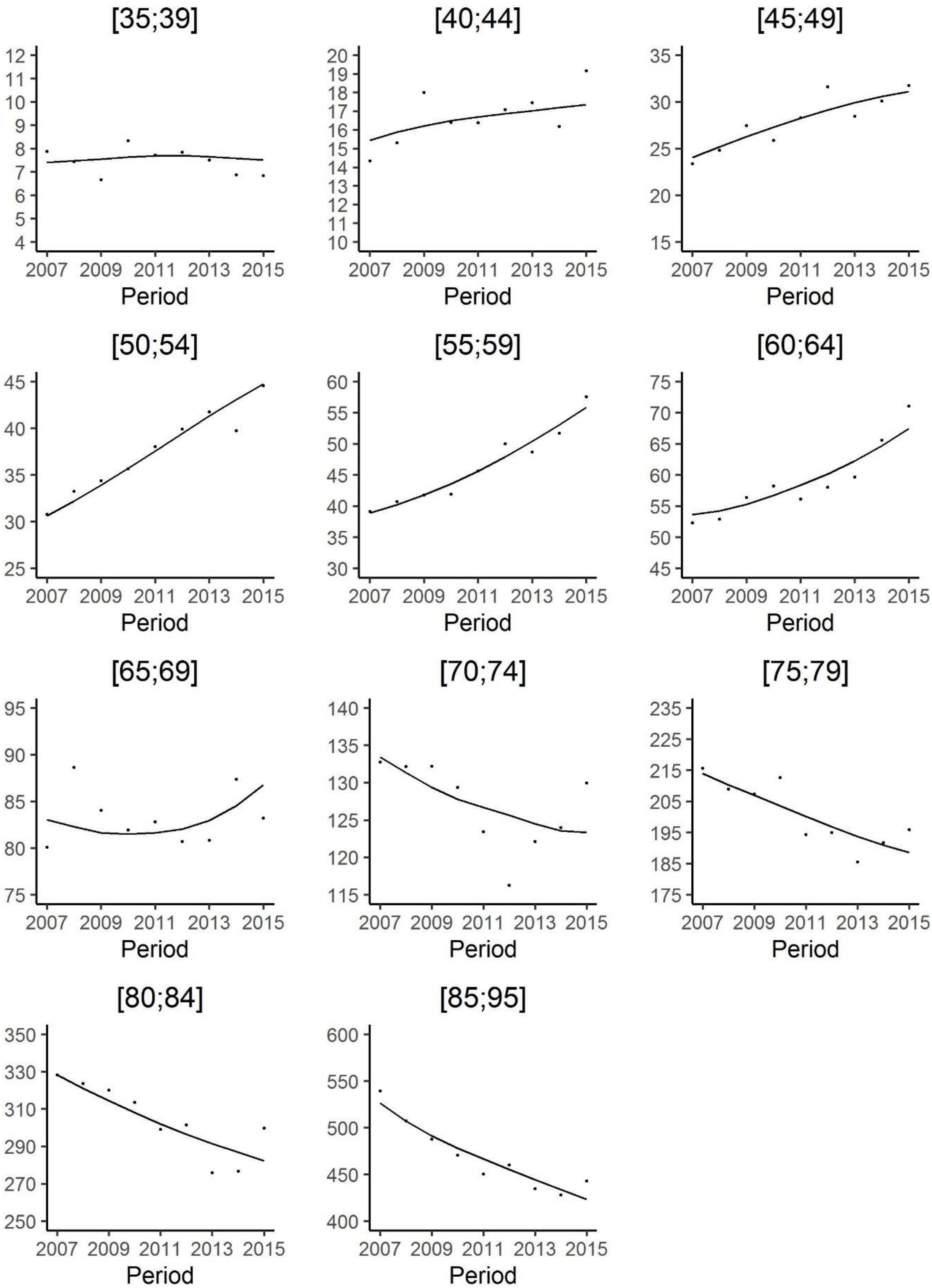


Figure S4. Incidence rate of hospitalizations of women for myocardial infarction $\boldsymbol{\alpha_{01}}$ (per 100 000) by period for several five-year age groups. Points represent observed data and solid lines represent the estimated incidences with the age-cohort model.

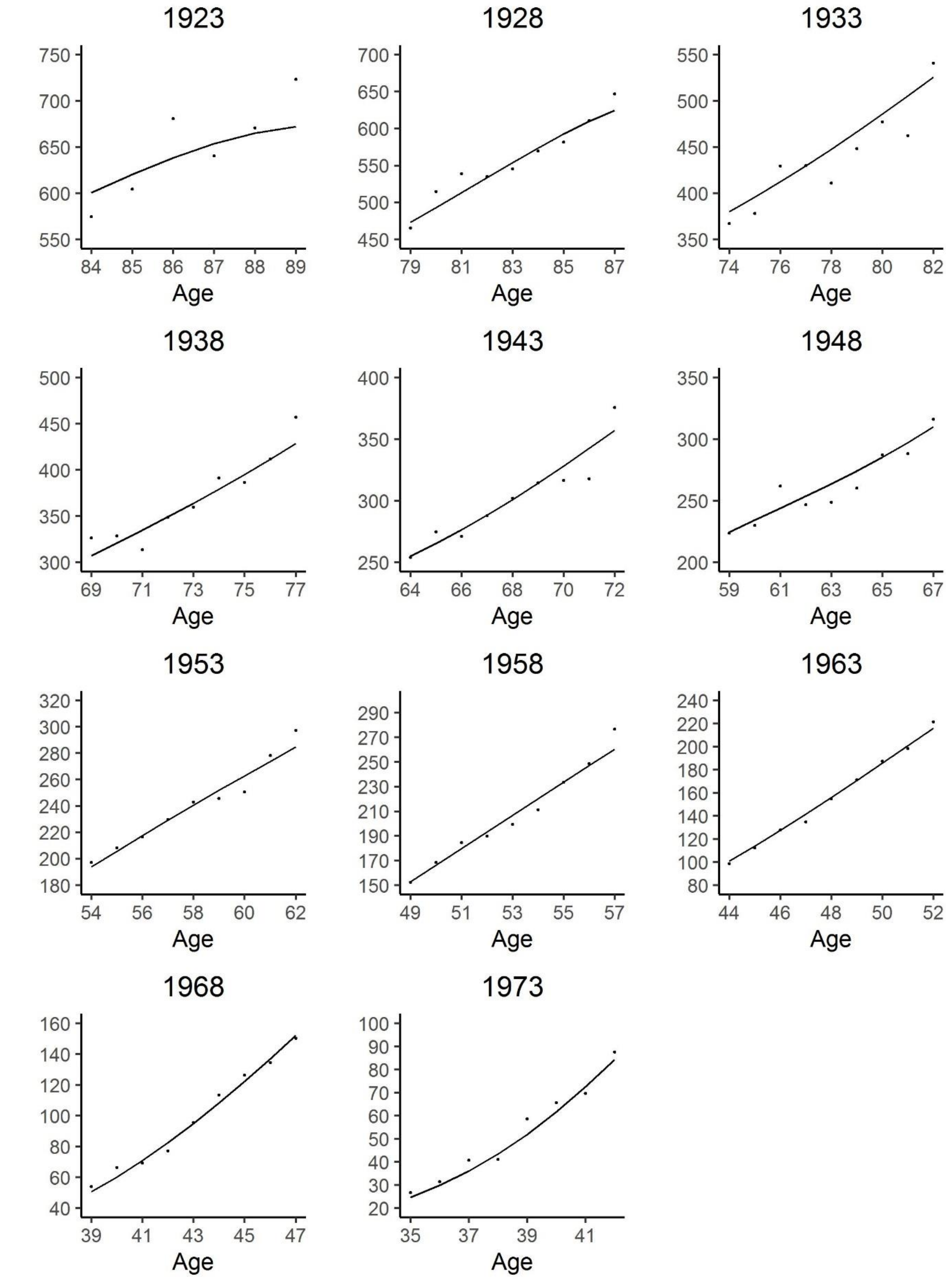


Figure S5. Incidence rate of hospitalizations of men for myocardial infarction $\boldsymbol{\alpha_{01}}$ (per 100 000) by age for several cohorts (five-year intervals) between 1923 and 1973. Points represent observed data and solid lines represent the estimated incidences with the age-cohort model.

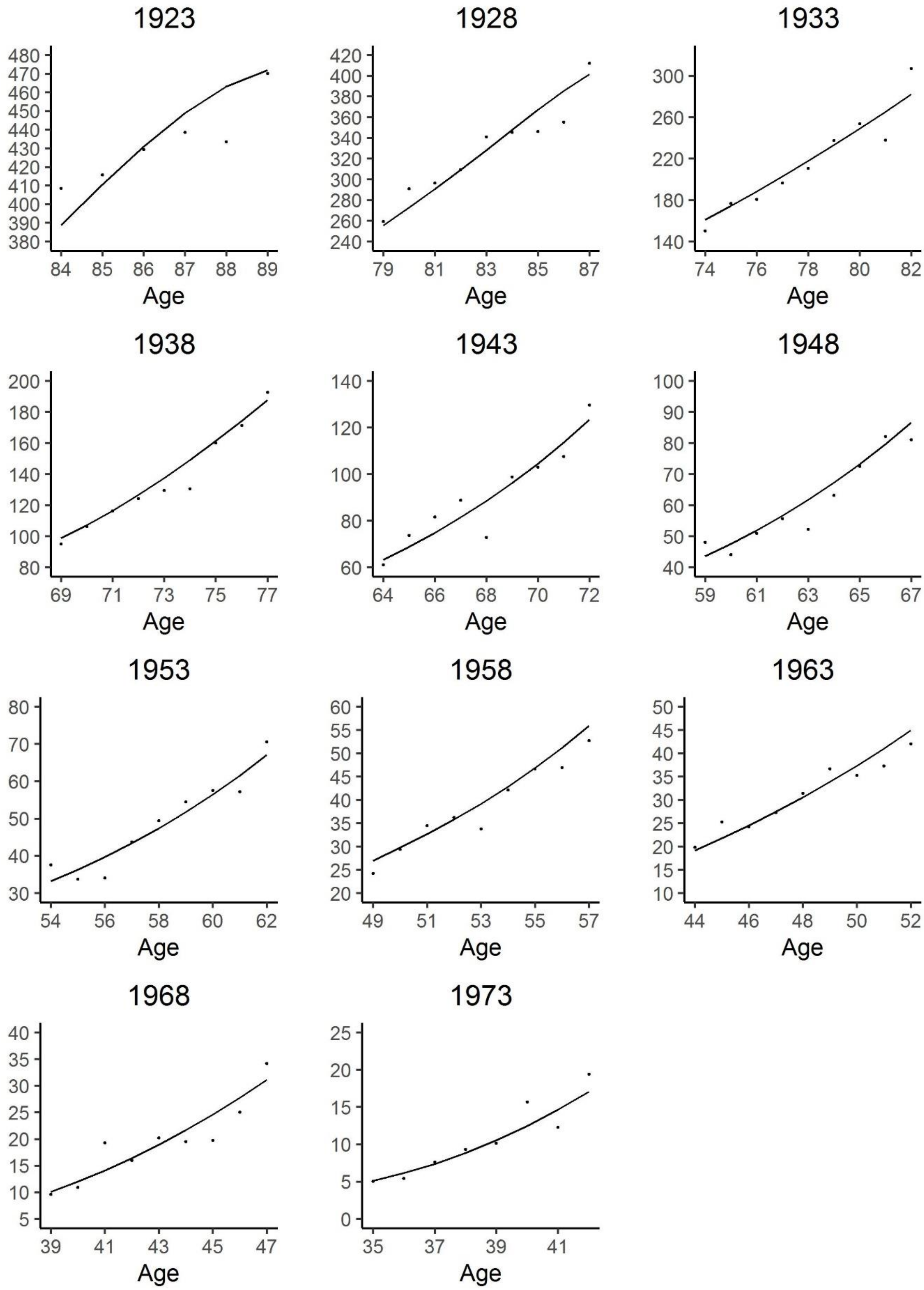


Figure S6. Incidence rate of hospitalizations of women for myocardial infarction $\boldsymbol{\alpha_{01}}$ (per 100 000) by age for several cohorts (five-year intervals) between 1923 and 1973. Points represent observed data and solid lines represent the estimated incidences with the age-cohort model.

Table S5. Estimated mean age of incident cases of myocardial infarction (with 95% uncertainty intervals) in France, according to gender, for the three INSEE scenarios studied

Year	Men			Women		
	Low scenario	Central scenario	High scenario	Low scenario	Central scenario	High scenario
2015	64.56 [64.47 – 64.65]	64.61 [64.52 – 64.70]	64.67 [64.59 – 64.76]	74.08 [73.95 – 74.21]	74.13 [74.00 – 74.26]	74.17 [74.04 – 74.30]
2018	64.80 [64.66 – 64.93]	64.87 [64.73 – 65.01]	64.96 [64.83 – 65.09]	73.47 [73.27 – 73.68]	73.55 [73.35 – 73.76]	73.62 [73.40 – 73.82]
2021	65.18 [64.99 – 65.37]	65.27 [65.08 – 65.46]	65.39 [65.20 – 65.58]	72.92 [72.63 – 73.21]	73.04 [72.74 – 73.33]	73.13 [72.83 – 73.43]
2024	65.69 [65.42 – 65.93]	65.79 [65.53 – 66.04]	65.94 [65.70 – 66.20]	72.57 [72.18 – 72.94]	72.71 [72.32 – 73.08]	72.83 [72.44 – 73.22]
2027	66.28 [65.94 – 66.60]	66.41 [66.07 – 66.73]	66.60 [66.28 – 66.92]	72.45 [71.98 – 72.93]	72.62 [72.14 – 73.10]	72.77 [72.26 – 73.25]
2030	66.97 [66.55 – 67.37]	67.11 [66.68 – 67.51]	67.35 [66.94 – 67.74]	72.67 [72.09 – 73.24]	72.85 [72.26 – 73.42]	72.90 [72.44 – 73.59]
2033	67.71 [67.19 – 68.20]	67.86 [67.33 – 68.34]	68.15 [67.64 – 68.63]	73.21 [72.54 – 73.86]	73.38 [72.72 – 74.03]	73.60 [72.91 – 74.24]
2035	68.21 [67.62 – 68.76]	68.36 [67.78 – 68.91]	68.69 [68.11 – 69.23]	73.69 [72.96 – 74.40]	73.85 [73.13 – 74.57]	74.11 [73.35 – 74.80]

Table S6. Estimated prevalence (in percentages) for myocardial infarction (with 95 % uncertainty intervals) in France for 2015, 2025 and 2035 based on the three INSEE scenarios studied

Year	Scenario	Men		Women	
		Prevalence (%)	95% UI	Prevalence (%)	95% UI
2015					
	Low	2.50	[2.46 – 2.54]	0.82	[0.80 – 0.83]
	Central	2.52	[2.48 – 2.56]	0.85	[0.83 – 0.87]
	High	2.55	[2.51 – 2.59]	0.83	[0.82 – 0.85]
2025					
	Low	3.16	[3.12 – 3.21]	0.98	[0.97 – 1.00]
	Central	3.19	[3.15 – 3.23]	1.04	[1.02 – 1.05]
	High	3.25	[3.21 – 3.29]	1.02	[1.00 – 1.04]
2035					
	Low	3.98	[3.89 – 4.09]	1.37	[1.32 – 1.43]
	Central	4.02	[3.92 – 4.12]	1.44	[1.38 – 1.50]
	High	4.11	[4.02 – 4.21]	1.44	[1.38 – 1.50]
Evolution (2015-2035)					
	Low	+1.48		+0.55	
	Central	+1.50		+0.59	
	High	+1.56		+0.61	

Table S7. Estimated number of prevalent cases (N) of myocardial infarction (with 95% uncertainty interval) in France for 2015 and 2035 based on the three INSEE scenarios tested

Year	Scenario	Men		Women	
		N	95% UI	N	95% UI
2015					
	Low	446 000	[439 000 – 453 000]	164 000	[161 000 – 168 000]
	Central	450 000	[442 000 – 457 000]	166 000	[163 000 – 170 000]
	High	455 000	[448 000 – 462 000]	168 000	[164 000 – 172 000]
2035					
	Low	789 000	[770 000 – 809 000]	302 000	[290 000 – 316 000]
	Central	815 000	[795 000 – 835 000]	312 000	[300 000 – 327 000]
	High	863 000	[844 000 – 885 000]	331 000	[319 000 – 346 000]
Evolution (2015-2035)					
	Low	+ 343 000 (+76.9 %)		+ 138 000 (+84.1 %)	
	Central	+ 365 000 (+81.1 %)		+ 146 000 (+88.0 %)	
	High	+ 408 000 (+89.7 %)		+ 163 000 (+97.0 %)	

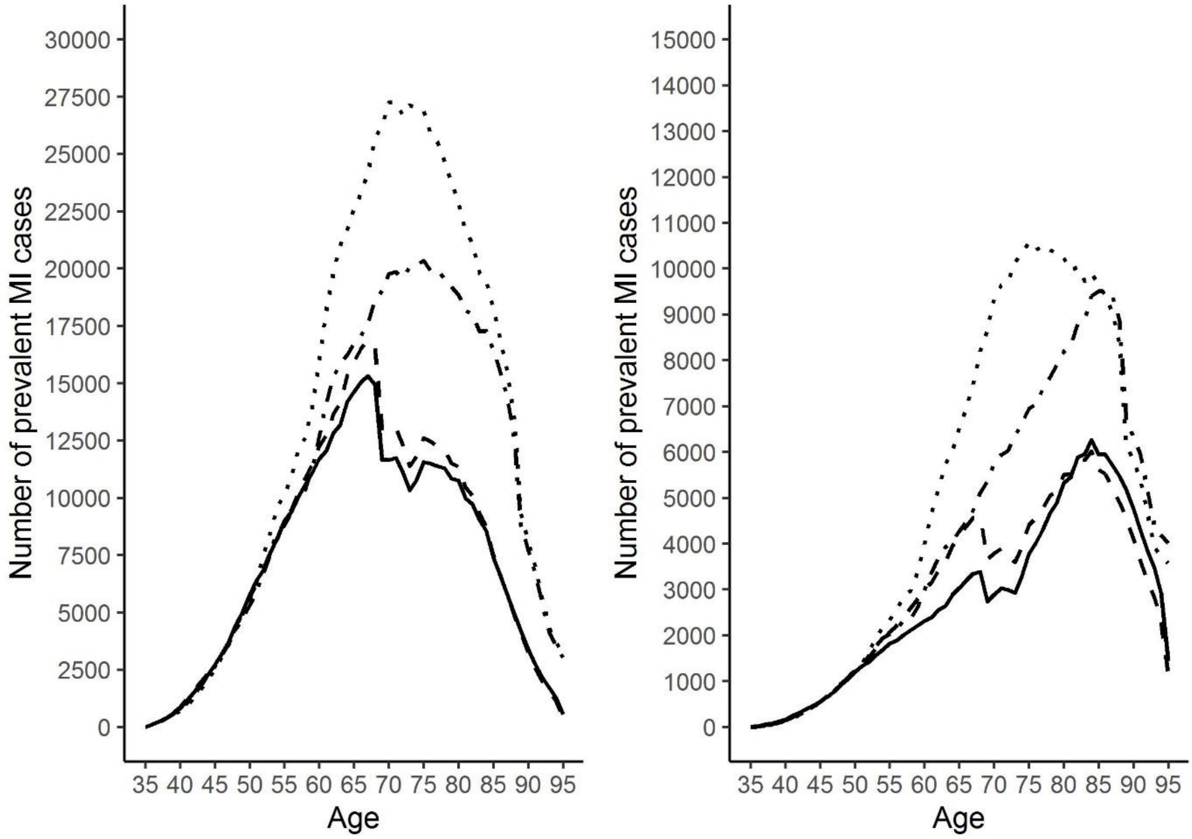


Figure S7. Number of prevalent myocardial infarction cases in 2015 and 2035 by age in men (left) and women (right) according to the central INSEE scenario. Solid and dotted lines represent prevalent cases estimated with the age-cohort model. Dashed and dot-dashed lines represent the number of prevalent cases estimated with an incidence depending only on age.

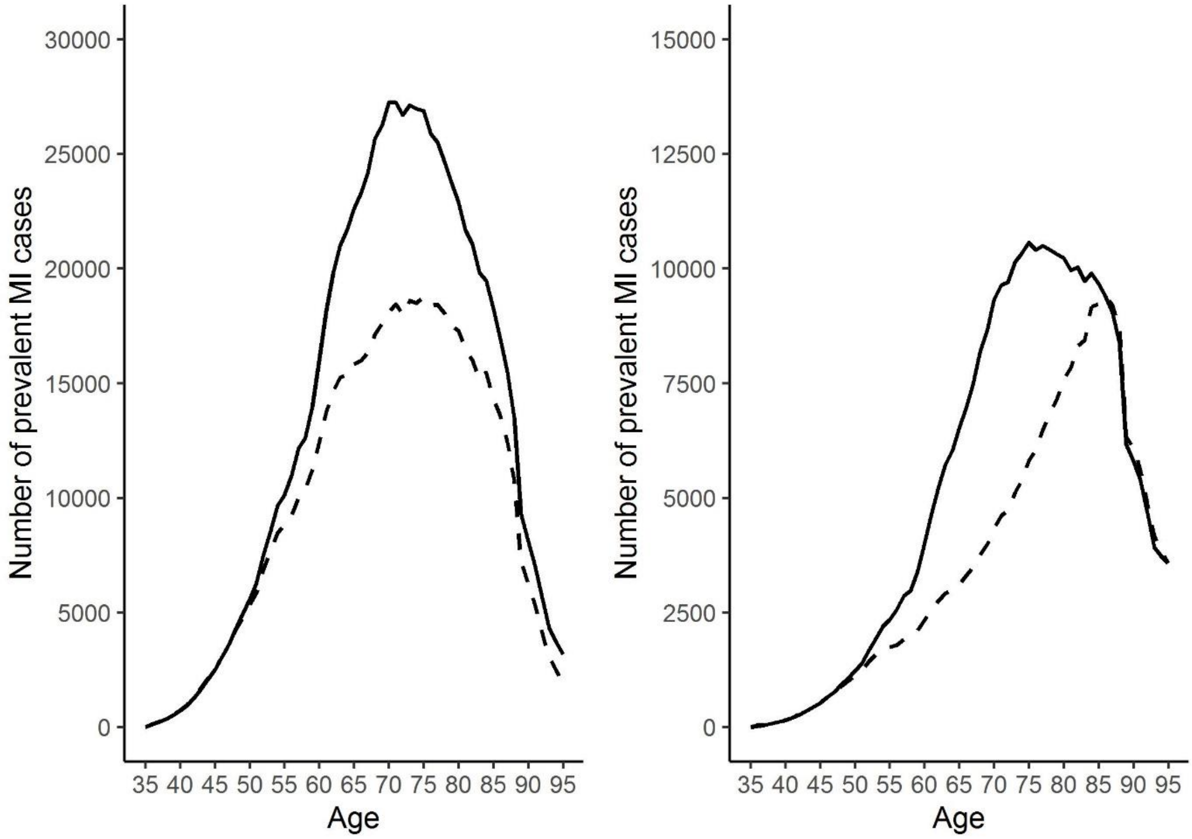


Figure S8. Number of prevalent myocardial infarction cases in 2035 by age in men (left) and women (right) according to the central INSEE scenario. Solid lines represent the number of prevalent cases estimated with our projection methodology. Dashed lines represent the number of prevalent cases computed by applying the prevalence we estimated in 2015 to the population in 2035.

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