Impact of preventive policy regarding dementia's risk factors, on several health indicator projections.

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Context

Context

- in France in 2010: more than 990 000 case of dementia,
- increase of number of older people.

  ⟶ consequences in 2030 ?

Motivating question

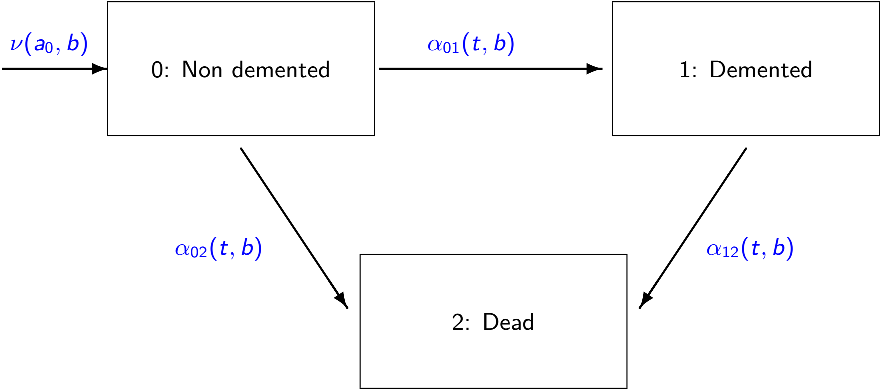
How evaluate the impact of preventive policy on population at risk to develop dementia?

Objectives

Consider the impact of an intervention targeting a risk factor of dementia:

- on health indicator projections (prevalence, life expectancy...),
- under several intervention scenarios,
- to compare and assess the intervention interest.

Multi-state model: illness-death



with t the calendar time, b the birth, $t - b$ the age at t time,
$\nu(a_0|b)$ number of people of age a_0 born at b.
NB: $\alpha_2(t, b)$ defines the death risk in overall population.

Assumptions

Incidence

- $\forall t - b \leq 65, \alpha_{01}(t, b) = 0$, (then $a_0 = 65$),
- homogeneity over calendar time: $\alpha_{01}(t, b) = \alpha_{01}(t - b)$,

Death risk for demented

For $t - b > 65$, $\alpha_{12}(t, b)$ is:

- independent of time spent in dementia,
- variable over calendar time: $\alpha_{12}(t, b) = g(t - b)\alpha_{02}(t - b|t)$,
  $\rightarrow$ with $g(t - b)$ the relative risk of death of demented versus non-demented.

Data

Cohort study (PAQUID) to estimate:

- α_{01} by age and gender,
- $g(t-b)$ by age and gender

Demographics data (from INSEE) to estimate:

- α_2 by age, gender and year,
- $\nu(65|b)$ by gender and year.

$\hookrightarrow$ Then we estimate α_{02} et α_{12}

- by resolution of a differential equation (Runge Kutta 4)

Intervention

We introduce z=(0,1), a variable exposure to a risk factor,

Proportional intensities model:

$$\alpha_{ij}(t-b|t,z) = \alpha_{ij}^{0}(t-b|t)(\theta_{ij})^{z}$$

→ with α_{ij}^{0} baseline transition intensities between state i and state j and θ_{ij} relative risk associated to z.

Observations:

- α_{ij}^{0} are estimate by resolution of an equation system.
  → least square method, and cubic spline approximation.
- Assumed to be known
  - $p_0(65)$, the risk factor prevalence at 65 years old, for non-demented subjects (state '0').
  - θ_{ij} in the context without intervention.

↪ then the risk factor can have an effect on death and/or on the risk to develop dementia.

Intervention

Targeting dementia risk factors from a given year τ

- on subjects aged a_τ since a given year (with $a_\tau \geq 65$ years old),

May change:

- the risk factor prevalence at age a_τ (when the intervention occurs),
- and/or each θ_{ij} independently.

Consequences:

- must take into account state demented/non-demented at τ,
- a change in exposure status is possible after 65 years.

Remarks: the risk factor can't be acquired after 65 years old.

Main Functions

Probability for a subject born in b and alive at 65 years old **to be non demented and alive** at $t-b$, depending on the risk factor exposure:

$$P_{00}(65, t-b|t, z) = e^{-A_{01}(65, t-b|z) - A_{02}(65, t-b|t, z)}$$

$\rightarrow$ with $A_{ij}(65, t-b|t, z) = \int_{65}^{t-b} \alpha_{ij}^{0}(u|t)(\theta_{ij})^{z} du$, the cumulative transition intensities between state i and j, depending on the risk factor exposure.

Probability for a subject born in b and non demented at 65 years old **to be demented and alive** at $t-b$, depending on the risk factor exposure:

$$P_{01}(65, t-b|t, z) = \int_{65}^{t-b} e^{-A_{01}(65, u|z) - A_{02}(65, u|t, z)} (\theta_{01})^{z} \alpha_{01}^{0}(u) e^{-A_{12}(u, t-b|t, z)} du$$

Probability for a subject born in b, demented at a_1 (with $a_1 > 65$) **to be alive** at $t-b$, depending on the risk factor exposure:

$$P_{11}(a_1, t-b|t, z) = e^{-A_{12}(a_1, t-b|t, z)}$$

Life expectancy at age x, for a given year t

Life expectancy without dementia, depending on the risk factor exposure:

$$LE_{00}(x|t,z) = \int_{x}^{\infty} P_{00}(x,u|t,z)du$$

Life expectancy for demented at age x, depending on the risk factor exposure:

$$LE_{11}(x|t,z) = \int_{x}^{\infty} P_{11}(x,u|t,z)du$$

Life expectancy for non demented at age x, depending on the risk factor exposure:

$$LE_{0.}(x|t,z) = \int_{x}^{\infty} (P_{00}(x,u|t,z) + P_{01}(x,u|t,z))du$$

Life expectancy at age x, for a given year t

Remarks:

To obtain life expectancy independently of z, we weight by the proportion of exposed/unexposed subjects at age x and time t (distinguishing demented or non-demented status).

Overall life expectancy:

$$LE_{..}(x|t) = \pi_0(x|t)LE_{0.}(x|t) + (1 - \pi_0(x|t))LE_{11}(x|t)$$

$\rightarrow$ with $\pi_0(x|t)$ the proportion of non-demented subjects at age x and time t among subjects alive

Other health indicators

Prevalence of dementia on ages 65 to 100, for a given years t:

$$Prev(t) = \sum_{z=0}^{1} \sum_{i=0}^{35} \nu(65, t-100+i|z) P_{01}(65, 100-i|t-100+i, z)$$

Number of years spent in dementia at age x and time t:

$$T_{11}(x|t) = LE_{0.}(x|t) - LE_{00}(x|t)$$

Overall risk to develop dementia at age x and time t, depending on the risk factor exposure:

$$F_{01}(x|t, z) = \int_{x}^{\infty} P_{00}(x, u|t, z)(\theta_{01})^{z} \alpha_{01}^{0}(u) du$$

Example of scenario

Objective

Studying the impact of high blood pressure (HBP) effect modifications.

Context

- Prevalence of HBP at 65 year: $p_0(65) = 0.4$,
- The intervention takes place in $\tau = 2015$, on people older than 65 years.

Scenario 1:

- effect of HBP stronger on death than on dementia: $\theta_{01} = 1.5$ and $\theta_{02} = \theta_{12} = 2$
- intervention impact

$\rightarrow$ 1.a: $p_0(65) = 0.2$, θ_{ij} unchanged.

$\rightarrow$ 1.b: $\theta_{01} = 1.27$, $\theta_{02} = \theta_{12} = 1.74$, $p_0(65)$ unchanged.

Scenario 2:

- effect of HBP stronger on dementia than on death: $\theta_{01} = 2$ and $\theta_{02} = \theta_{12} = 1.5$
- intervention impact $\rightarrow p_0(65) = 0.2$, θ_{ij} unchanged.

Results: Prevalence in 2030

Table: Estimated prevalence of dementia in France for subjects between 65 and 99 years in 2030 under 3 scenarios of preventive intervention, compared to projections without intervention.

Scenario									Prevalence			Change#
No.	p	p^*	θ_{01}	θ_{01}^*	θ_{02}	θ_{02}^*	θ_{12}	θ_{12}^*	Women	Men	Total	%
Projections without intervention												
									1,146,000	604,000	1,750,000	-
Projections with intervention												
1.a	0.4	**0.2**	1.5	1.5	2	2	2	2	1,410,000	733,000	2,143,000	+22.4
1.b	0.4	0.4	1.5	**1.27**	2	**1.74**	2	**1.74**	1,149,000	605,000	1,754,000	+0.2
2	0.4	**0.2**	2	2	1.5	1.5	1.5	1.5	1,297,000	664,000	1,961,000	+12.1

change as compared with the predicted prevalence without intervention.

Results: Life expectancy without dementia

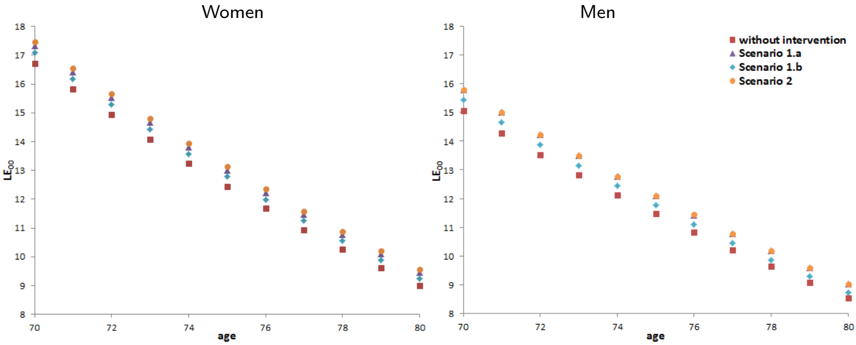


Figure: LE_{00} in 2030 between 70 and 80 years old by gender, with or without intervention in 2015.

Overview of results

Table: Projections in 2030 for men and women aged 70 years old.

Scenario									Men					
No.	p	p^*	θ_{01}	θ^*_{01}	θ_{02}	θ^*_{02}	θ_{12}	θ^*_{12}	LE_{00}	$LE_{0.}$	LE_{11}	$LE_{..}$	T_{11}	F_{01}
Projections in 2030 without intervention									15.06	17.79	9.73	17.68	2.73	0.484
Projections in 2030 with intervention in 2015														
1.a	0.4	**0.2**	1.5	1.5	2	2	2	2	15.80	18.73	11.02	18.64	2.93	0.493
1.b	0.4	0.4	1.5	**1.27**	2	**1.74**	2	**1.74**	15.44	18.19	10.52	18.09	2.75	0.480
2	0.4	**0.2**	2	2	1.5	1.5	1.5	1.5	15.80	18.49	10.46	18.40	2.69	0.467

Scenario									Women					
No.	p	p^*	θ_{01}	θ^*_{01}	θ_{02}	θ^*_{02}	θ_{12}	θ^*_{12}	LE_{00}	$LE_{0.}$	LE_{11}	$LE_{..}$	T_{11}	F_{01}
Projections in 2030 without intervention									16.73	21.68	12.26	21.54	4.95	0.708
Projections in 2030 with intervention in 2015														
1.a	0.4	**0.2**	1.5	1.5	2	2	2	2	17.96	22.60	13.80	22.48	5.26	0.716
1.b	0.4	0.4	1.5	**1.27**	2	**1.74**	2	**1.74**	17.10	22.10	13.20	21.98	5	0.704
2	0.4	**0.2**	2	2	1.5	1.5	1.5	1.5	17.48	22.39	13.08	22.28	4.91	0.693

In bold the value modified after the intervention

Discussion / Prospects

The actual model: markov non homogeneous

- doesn't take into account time spent in dementia.

Alternative: semi-markov model

- doesn't take into account age.

Solution: a semi-markov model

- taking into account both age of subject and time spent in dementia.

Others prospects:

- more various intervention (before 65 years; risk factor acquire after 65 years...)
- impact on others health indicators.

Thank you for your attention.

References

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