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

Mathilde Wanneveich
Hélène Jacqmin-Gadda, Catherine Helmer and Pierre Joly

University of Bordeaux, Isped - Inserm U 897

GDR Toulouse, October 3rd 2014.
Context

Context

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

\[ \nu(a_0, b) \]

0: Non demented

\[ \alpha_{01}(t, b) \]

1: Demented

\[ \alpha_{02}(t, b) \]

2: Dead

\[ \alpha_{12}(t, b) \]

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:
- $\alpha_{01}$ by age and gender,
- $g(t - b)$ by age and gender

Demographics data (from INSEE) to estimate:
- $\alpha_2$ by age, gender and year,
- $\nu(65|b)$ by gender and year.

Then we estimate $\alpha_{02}$ et $\alpha_{12}$
- 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:

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

→ with $\alpha^0_{ij}$ baseline transition intensities between state $i$ and state $j$
and $\theta_{ij}$ relative risk associated to $z$.

Observations:

▶ $\alpha^0_{ij}$ 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').
  ▶ $\theta_{ij}$ 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 $\tau$
  - on subjects aged $a_\tau$ since a given year (with $a_\tau \geq 65$ years old),

May change:
  - the risk factor prevalence at age $a_\tau$ (when the intervention occurs),
  - and/or each $\theta_{ij}$ independently.

Consequences:
  - must take into account state demented/non-demented at $\tau$,
  - 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:

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

→ 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 \( t \):

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

**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
  - $1.a$: $p_0(65) = 0.2$, $\theta_{ij}$ unchanged.
  - $1.b$: $\theta_{01} = 1.27$, $\theta_{02} = \theta_{12} = 1.74$, $p_0(65)$ unchanged.

Scenario 2:

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

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Prevalence</th>
<th>Change#</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Women</td>
<td>Men</td>
</tr>
<tr>
<td>Projections without intervention</td>
<td>1,146,000</td>
<td>604,000</td>
</tr>
<tr>
<td>Projections with intervention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.a</td>
<td>1,410,000</td>
<td>733,000</td>
</tr>
<tr>
<td>1.b</td>
<td>1,149,000</td>
<td>605,000</td>
</tr>
<tr>
<td>2</td>
<td>1,297,000</td>
<td>664,000</td>
</tr>
</tbody>
</table>

# 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.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>$p$</td>
</tr>
<tr>
<td>Projections in 2030 without intervention</td>
<td>15.06</td>
<td>17.79</td>
</tr>
<tr>
<td>Projections in 2030 with intervention in 2015</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.a</td>
<td>0.4</td>
<td><strong>0.2</strong></td>
</tr>
<tr>
<td>1.b</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>2</td>
<td>0.4</td>
<td><strong>0.2</strong></td>
</tr>
<tr>
<td>Projections in 2030 without intervention</td>
<td>16.73</td>
<td>21.68</td>
</tr>
<tr>
<td>Projections in 2030 with intervention in 2015</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.a</td>
<td>0.4</td>
<td><strong>0.2</strong></td>
</tr>
<tr>
<td>1.b</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>2</td>
<td>0.4</td>
<td><strong>0.2</strong></td>
</tr>
</tbody>
</table>

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


