Remembering IMaCh
The complex case
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Ideas for the future of IMaCh
Optimal delay between two waves REVES Canberra 1994
Conclusions

Could IMaCh treat irreversible deterioration of health?

Nicolas Brouard [1] and Karine Pérès [2]

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[1] brouard@ined.fr French National Institute for Population Studies (INED) Paris

[2] Karine.Peres@isped.u-bordeaux2.fr Epidemiology and neuropsychology of brain aging, ISPED/INSERM Bordeaux

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Outline

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- The complex case
- The advantage of the reversibility

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IMaCh

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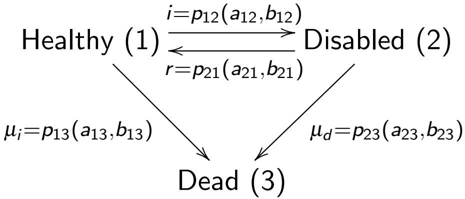
IMaCh is a statistical computer program which aims is to solve a realistic process where incidence of disability estimated from two interviews of a longitudinal studies on health is usually compensated by a recovery which can also be observed and estimated.

But for some disability states, it is sometimes hard to observe recovery cases. Sometimes also, we would like to use IMaCh for estimating an incidence to a state which by definition is not reversible, like having "had a stroke" or "demented". IMaCh hasn't been designed for the double decrement model. But IMaCh fails when reversibility is weak and should be adapted to work.

We will explore the different possibilities and constraints offered by current version of IMaCh in order to treat the case of Dementia in a famous French longitudinal study named Paquid with 5 medical exams from 1989 to 2000.

Statistical model behind IMaCh

$$\text{logit}(p_{ij}) = a_{ij} + b_{ij} * \text{age} + c_{ij} * \text{covariate}_1 + \cdots \qquad (1)$$



Likelihood with reversibility and without

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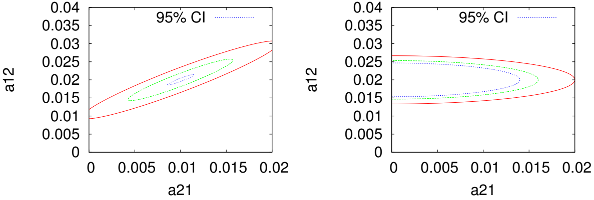
- Even if there is a strong relation between both incidences, we often find a meaningful likelihood and a 95% CI (blue)



- When recovery is rare (few cases, low level): likelihood distortion amongst recovery p_{21} . Maximum Likelihood doesn't converge.

Incidences are correlated and not as accurately estimated as prevalences

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- If $\hat{a_{12}}$ is high, $\hat{b_{12}}$ is also high.

Incidences are correlated and not as accurately estimated as prevalences

- If $\hat{a_{12}}$ is high, $\hat{b_{12}}$ is also high.
- In a model without differential mortality and similar to

$$\text{Healthy (1)} \underset{r}{\overset{i}{\rightleftarrows}} \text{Disabled (2)}$$

incidences can't be estimated separately, but period prevalence as a combination of both incidences are not affected.

Incidences are correlated and not as accurately estimated as prevalences

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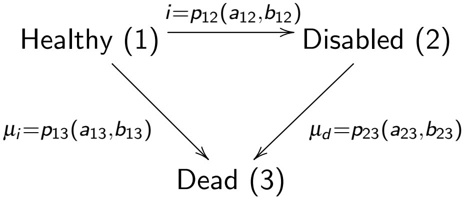
- If $\hat{a_{12}}$ is high, $\hat{b_{12}}$ is also high.
- In a model without differential mortality and similar to

$$\text{Healthy (1)} \underset{r}{\overset{i}{\rightleftarrows}} \text{Disabled (2)}$$

  incidences can't be estimated separately, but period prevalence as a combination of both incidences are not affected.
- Can IMaCh estimate such an irreversible model?



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Simplest case: the life table

- IMaCh is able to solve partially a simple model: the life table

Healthy or disabled (1 or 2) $\xrightarrow{\mu}$ Dead (3)

Using IMaCh for estimating the total mortality

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The parameter file (mle=-3)

```
title=paquid-don datafile=paquid-dem-esp.txt lastobs=1237 firstpass=1 lastpass=6
ftol=1.000000e-008 stepm=12 ncovcol=2 nlstate=2 ndeath=1 maxwav=6 mle=-3 weight=0
model=.
```

The data file

```
#  NUMERO   SEXE cep weightdatenais datedc  date0  etat0 date1  etat1 date3  etat3 date5  etat5
etat8 date10 etat10
# Case A (mle=-3) mortality of the sample
   65      1    0    1   02/1910 11/1997 01/1988   1  10/1989   1  05/1991   2  03/1993   2
11/1995   2  99/9999   3
   72      1    0    1   01/1906 12/1995 01/1988   1  03/1989   1  04/1991   1  04/1993   1
99/9999   3  99/9999   3
```

The results: Life table

```
iter=5 MLE=-4695.805345 Eq=0.024669*exp(0.125162*(age-75))
0.024669 [0.019143 ; 0.030195]
0.125162 [0.105487 ; 0.144837]

Age   lx     qx     dx    Lx     Tx      e(x)
75  100000  0.024669 2467 98767 1208488 12.084877
76  97533  0.027958 2727 96170 1109721 11.377896
77  94806  0.031686 3004 93304 1013552 10.690772
78  91802  0.035911 3297 90154 920247 10.024245
79  88505  0.040699 3602 86704 830094 9.379010
80  84903  0.046126 3916 82945 743389 8.755709
```

Trying the full reversible model

Dementia incidence is known to be related to Primary School Education level which is linked to Socio-Economic status

The parameter file (mle=1)

```
title=paquid-don datafile=paquid-dem-esp.txt lastobs=1237 firstpass=1 lastpass=6
ftol=1.000000e-008 stepm=12 ncovcol=2 nlstate=2 ndeath=1 maxwav=6 mle=1 weight=0
model=.
```

The results: divergence after iteration 5 in the recovery a21 and b21

```
#iter -2*LL    a12       b12       a13      b13          a21       b21        a23       b23
1 12629.526190  1   0.000 2 0.000 3  0.000 4 0.0000 5   0.000 6    0.000 7   0.00 8 0.00
2  7884.473816  1  -0.802 2 0.000 3 -3.318 4 0.0004 5   1.784 6   -0.000 7   0.53 8 0.00
3  7057.571262  1  -2.315 2 0.001 3 -3.275 4 0.0077 5   1.769 6   -0.001 7  -0.00 8 0.01
4  6328.764347  1  -3.431 2 0.002 3 -3.522 4 0.0134 5  -3.161 6   -0.009 7  -2.91 8 0.01
5  6295.182854  1  -3.486 2 0.004 3 -3.676 4 0.0131 5  -4.716 6   -1.009 7  -2.90 8 0.02
OK until here and the deterioration
6  6272.401008  1   -5.467 2 0.027 3  -4.995 4 0.0264 5  85.636 6   -58.029 7  -4.60 8 0.04
7  6229.277492  1   -9.585 2 0.076 3  -7.467 4 0.0549 5 282.087 6 -174.930 7  -8.36 8 0.08
8  6158.0285    1  -17.211 2 0.167 3 -11.77 4 0.1082 5 651.942 6 -392.075 7 -15.46 8 0.16
9  6150.0348    1  -16.710 2 0.161 3 -11.41 4 0.1056 5 631.882 6 -374.857 7 -15.05 8 0.15
10    6149.845  1  -16.868 2 0.162 3 -11.49 4 0.1066 5 640.435 6 -375.896 7 -15.21 8 0.16
11    6149.578  1  -17.001 2 0.164 3 -11.60 4 0.1077 5 678.981 6 -345.895 7 -15.21 8 0.16
12    6148.447  1  -17.205 2 0.166 3 -11.83 4 0.1105 5 827.417 6 -212.166 7 -14.76 8 0.15
13    6147.755  1  -17.156 2 0.165 3 -11.86 4 0.1108 5 892.329 6 -144.480 7 -14.41 8 0.15
14    6145.453  1  -17.063 2 0.164 3 -11.91 4 0.1115 5 1018.22 6 -13.2846 7 -13.74 8 0.14
15     nan      1  -18.145 2 0.177 3 -12.61 4 0.1200 5 1170.58 6 57.12102 7 -14.29 8 0.14
```

Estimating Life expectancy of Demented

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The parameter file (mle=-3)

```
title=paquid-don datafile=paquid-dem-esp.txt lastobs=1237 firstpass=1 lastpass=6
ftol=1.000000e-008 stepm=12 ncovcol=2 nlstate=2 ndeath=1 maxwav=6 mle=-3 weight=0
model=.
```

The data file (changing status 1 into unknown!)

```
#  NUMERO   SEXE cep weightdatenais datedc   date0   etat0 date1   etat1 date3   etat3 date5   etat5
etat8 date10 etat10
# Case A (mle=1) doesn't converge
    65       1     0     1    02/1910 11/1997 01/1988    1   10/1989    1   05/1991    2   03/1993    2
11/1995    2  99/9999    3
    72       1     0     1    01/1906 12/1995 01/1988    1   03/1989    1   04/1991    1   04/1993    1
99/9999    3  99/9999    3
# Case B (mle=-3) Changing state 1 (Healthy) into -1 (Unknown)
    65       1     0     1    02/1910 11/1997 01/1988   -1   10/1989   -1   05/1991    2   03/1993    2
11/1995    2  99/9999    3
    72       1     0     1    01/1906 12/1995 01/1988   -1   03/1989   -1   04/1991   -1   04/1993   -1
99/9999    3  99/9999    3
```

The results: Coefficients are not significant (absence of a slope with age: -0.007355)

```
iter=5 MLE=-420.038801 Eq=0.205107*exp(-0.007355*(age-77))
0.205107 [0.060569 ; 0.349645]
-0.007355 [-0.075483 ; 0.060772]

Age   lx      qx      dx     Lx     Tx      e(x)
77 100000 0.205107 20511 89745 452471 4.524709
```

Estimating Life expectancy without Dementia

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The parameter file (mle=-3)

```
title=paquid-don datafile=paquid-dem-esp.txt lastobs=1237 firstpass=1 lastpass=6
ftol=1.000000e-008 stepm=12 ncovcol=2 nlstate=2 ndeath=1 maxwav=6 mle=-3 weight=0
model=.
```

The data file: changing status 2 into dead (no reversibility of dementia)

```
#  NUMERO    SEXE cep  weightdatenais datedc   date0   etat0 date1   etat1 date3   etat3 date5   etat5
etat8 date10 etat10
# Case  A  (mle=1)  doesn't  converge
   65       1     0     1    02/1910  11/1997  01/1988    1   10/1989    1   05/1991    2   03/1993    2
11/1995    2   99/9999    3
   72       1     0     1    01/1906  12/1995  01/1988    1   03/1989    1   04/1991    1   04/1993    1
99/9999    3   99/9999    3
# Case  C  (mle=-3)  Changing  2  (Disable)  into  3  (Dead)
   65       1     0     1    02/1910  11/1997  01/1988    1   10/1989    1   05/1991    3   03/1993    3
11/1995    3   99/9999    3
   72       1     0     1    01/1906  12/1995  01/1988    1   03/198
```

The results: 11.76 at age 75 to be compared with 12.08

```
 iter=6  MLE=-4546.831739  Eq=0.021545*exp(0.147751*(age-75))
0.021545 [0.016626 ; 0.026464]
0.147751 [0.127648 ; 0.167854]

Age   lx      qx      dx     Lx      Tx      e(x)
75 100000 0.021545 2154 98923 1176026 11.760255
76 97846 0.024975 2444 96624 1077103 11.008198
77 95402 0.028952 2762 94021 980479 10.277367
78 92640 0.033562 3109 91085 886458 9.568882
79 89531 0.038906 3483 87789 795373 8.883821
80 86047 0.045101 3881 84107 707584 8.223205
```

Life expectancy by level of education

- Low education (CEP): 11.72 years
- High (CEP): 12.35 years
- IMaCh is measuring life expectancy nicely using the survival times detailed by month.

Ideas for IMaCh

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- Detecting when the likelihood is flat among a particular direction (ideas?).

Ideas for IMaCh

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- Detecting when the likelihood is flat among a particular direction (ideas?).
- Suppressing the recovery parameters a_{21} and b_{21}, reducing from 8 to 6 parameters from the estimation.
- Skipping the computation of the period prevalence.

Ideas for IMaCh

- Detecting when the likelihood is flat among a particular direction (ideas?).
- Suppressing the recovery parameters a_{21} and b_{21}, reducing from 8 to 6 parameters from the estimation.
- Skipping the computation of the period prevalence.
- Fixing arbitrary values of a_{21} and b_{21} in order to keep the program unchanged.
- Keeping the computation of the period prevalence.

Core of IMaCh and design variables I

- Core of IMaCh, currently too complex in managing design variables.

```
cov[1]=1.;
cov[2]=age+((h-1)*hstepm + (d-1))*stepm/YEARM;
for (k=1; k<=cptcovn;k++) // V1+V2+...
  cov[2+k]=nbcode[Tvar[k]][codtab[ij][Tvar[k]]];
for (k=1; k<=cptcovage;k++)  // V1*age
  cov[2+Tage[k]]=cov[2+Tage[k]]*cov[2];
for (k=1; k<=cptcovprod;k++)  // V1*V2 + V3*V4
  cov[2+Tprod[k]]=nbcode[Tvard[k][1]][codtab[ij][Tvard[k][1]]]*
    nbcode[Tvard[k][2]][codtab[ij][Tvard[k][2]]];
```

- IMaCh has to be simplified before being designed for new purposes.
- Agnès Lièvre implemented the 'easy' use of a unique design variable V1 coded for example:
  - 1 (low education)
  - 2 (middle)
  - 3 (high).

Core of IMaCh and design variables II

- IMaCh no more treats such variables because of lot of confusions in the analyses of results.
- Current IMaCh needs 2 covariates for this unique 'education' dimension V1 and V2:
  - low education is for example the reference (coded 0 0);
  - middle (coded 1) vs low (0) is V1;
  - high (coded 1) vs low (0) is V2.
- More complex but correct results and easier program to maintain.

Optimal delay between two waves I

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If we only know that an individual died before time h without any more precision on the exact age at death, its contribution to the likelihood is simply $(1-p(h))$ where $p(h)$ is the probability to survive until time h. On the opposite if an individual survived after time h, its contribution is still $p(h)$. The total likelihood for n individuals is then:

$$L = (1-p)^d p^{n-d}, \quad \text{and its logarithm} \tag{2}$$

$$\log(L) = d\log(1-p) + (n-d)\log(p) \tag{3}$$

where d is the number of individuals dead before time h.

Optimal delay between two waves II

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Let us notate $\tilde{p} = (1 - \frac{d}{n})$ the observed proportion of survivors (at time h), then first and second derivatives of the loglikelihood are:

$$\frac{\partial \log(L)}{\partial p} = n \frac{\tilde{p} - p}{p(1-p)}, \qquad (4)$$

$$\frac{\partial^2 \log(L)}{\partial p^2} = n \frac{p^2 - 2p\tilde{p} + \tilde{p}}{p^2(1-p)^2}. \qquad (5)$$

Clearly the maximum likelihood estimator (MLE) $\hat{p}$ of p is $\tilde{p}$. And the Fisher's information at $\hat{p}$ is the classical formula of the variance of a binomial law:

$$\left[\frac{\partial^2 \log(L)}{\partial p^2}\right]^{-1} = \frac{\tilde{p}(1-\tilde{p})}{n} \qquad (6)$$

Optimal delay between two waves III

Let us now suppose again that the force of mortality is constant between age a and $a+h$:

$$p(a) = \exp(-\mu(a)h), \quad (7)$$

$$\mu(a) = K\exp(a). \quad (8)$$

Also, $\log(h)$ is a better scale of time:

$$h = \exp(k). \quad (9)$$

Some easy computations described below will exhibit the MLE of a and its variance:

$$\frac{\partial \log(L)}{\partial a} = \frac{\partial \log(L)}{\partial p}\frac{\partial p}{\partial a},$$

$$\frac{\partial^2 \log(L)}{\partial a^2} = \frac{\partial^2 \log(L)}{\partial p^2}\left[\frac{\partial p}{\partial a}\right]^2 + \frac{\partial \log(L)}{\partial p}\frac{\partial^2 p}{\partial a^2}.$$

Optimal delay between two waves IV

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The MLE of a is $\hat{a} = p^{-1}(\hat{p}) = \log(-\log(\hat{p})) - k$ after a particular time h of observation.
Fisher's information computed at point $\hat{a}$ is then:

$$\left[\frac{\partial^2 \log(L)}{\partial a^2}\right]^{-1} = \left[\frac{\partial^2 \log(L)}{\partial p^2}\left[\frac{\partial p}{\partial a}\right]^2\right]^{-1} = \frac{1-\tilde{p}}{n\tilde{p}\log^2(\tilde{p})}. \quad (10)$$

The last function has a minimum for $p = 0.20319 = 1 - 0.7968$, which means that whatever the incidence level the optimum delay for the second pass is when about 80% of the initial cohort have already died.

Delay between waves should vary and are usually too short I

- According to the former result concerning a simple life table, we can extrapolate to other incidences like disability or recovery.
- With an incidence of μ per year, the optimal delay is $\frac{-\log(0.2)}{\mu}$ years.
- Taking the age of 90, with a risk dying or entering disability of 0.2 per year, the optimal delay is $\frac{-\log(0.2)}{0.2} = 8$ years.
- At 80, with a risk dying or entering disability of 0.1 per year, the optimal delay is $\frac{-\log(0.2)}{0.1} = 16$ years.
- At 70, with an incidence to recovery of 0.1 per year, the optimal delay is also $\frac{-\log(0.2)}{0.1} = 16$ years.
- These are rather long delays compared to 2 to 5 years used in standard LSOAs.

Delay between waves should vary and are usually too short II

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- Contradiction when having the same delay for measuring incidence of disability (longer delays are needed for young < 70) and recovery (low levels and longer delay at old ages).
- The loss of follow-up being the main reason of shortening the delay but short delays are far from optimum, partly explaining the non convergence (lack of cases).

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Conclusions I

- Low level of recovery incidences are not estimated by current IMaCh and are blocking estimates of other incidences.
- Some workarounds presented let you investigate the irreversibility.

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Conclusions II

- IMaCh has to be simplified before being designed for new purposes.
- Thanks for your attention