A Poisson-Like Model of Sub-Clinical Signs from the Neurological Examination of Healthy Aging Subjects

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Clinical Application

- Healthy aging individuals age 53-84.
- Given a “standard neurologic exam”
- Complicated clinical data (“sign” present or not) in a neurologic exam which examined a large number characteristics.
- From these characteristics 6 aspects were created (combinations of the characteristics that were assumed to be independent).
- The goal was to characterize normal neurologic aging. [to compare groups or test effects of drugs]

The Model

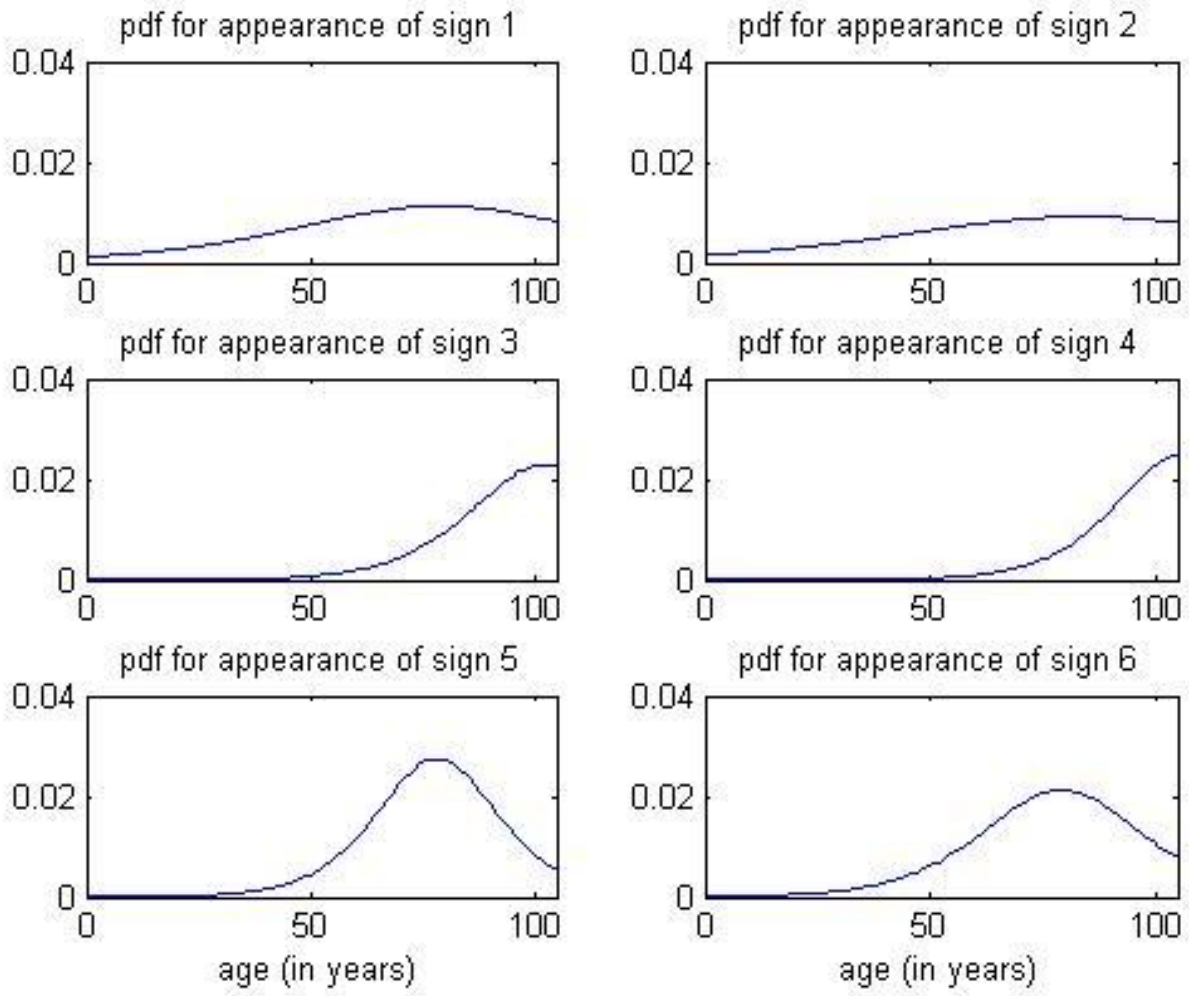
- Assume that each of the 6 signs were arriving <u>independently</u> and at <u>different rates</u>
- The rates were determined through logistic regression.
- To describe normal aging, we would like to compute the number of signs $N(t)$ present at time t. This requires the determination of the distributions $P(N(t)=n_i, n_i=0, 1, \ldots, 6)$ at different times t.

Logistic Regression

- In logistic regression, the log odds ratio of the probability that a sign of that type is present at age *t* is fit to the data. The result was that for each of the six categories, the probability $F_i(t)$ that a sign of type i has appeared by age *t,* was determined.

$$F_i(t) = \frac{\exp(a_i + b_i t)}{1 + \exp(a_i + b_i t)}$$

The six pdf's


pdf for appearance of sign 1
pdf for appearance of sign 2
pdf for appearance of sign 3
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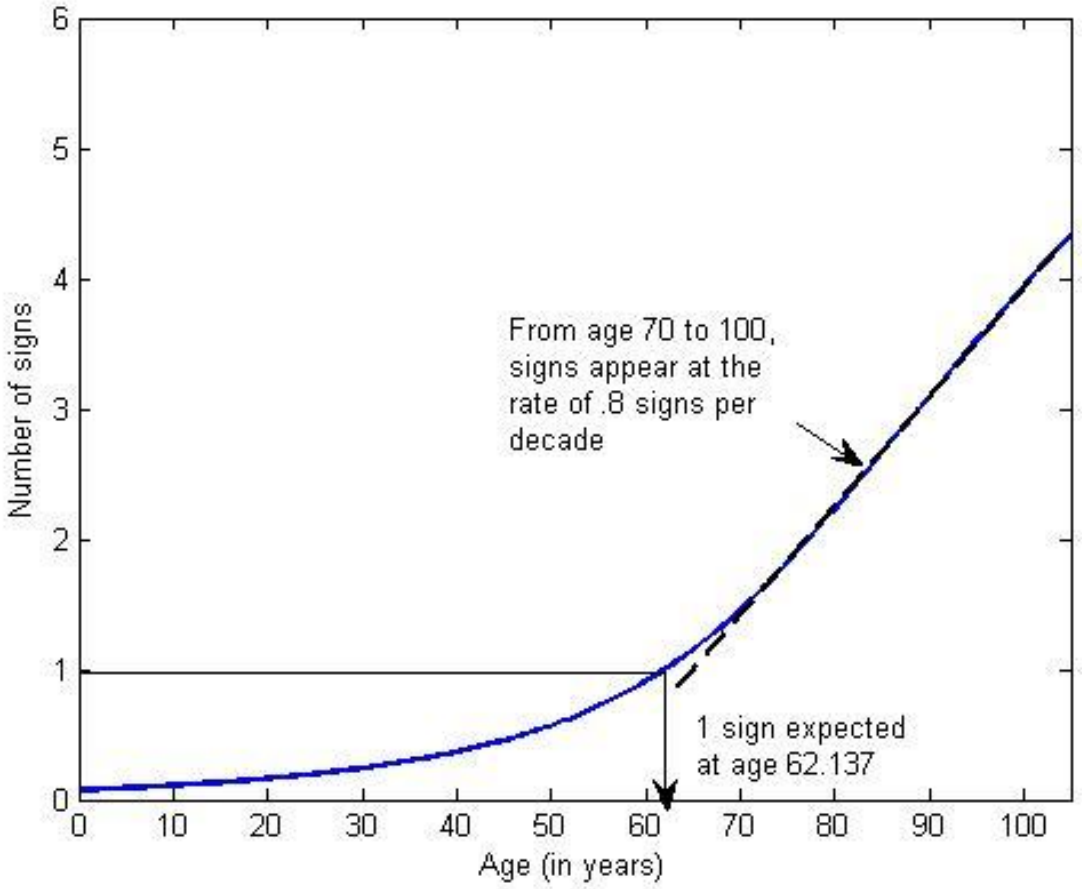
pdf for appearance of sign 6
0.04
0.02
0
0
50
100
age (in years)

$$E[N(t)] = \sum_{i=1}^{6} F_i(t)$$



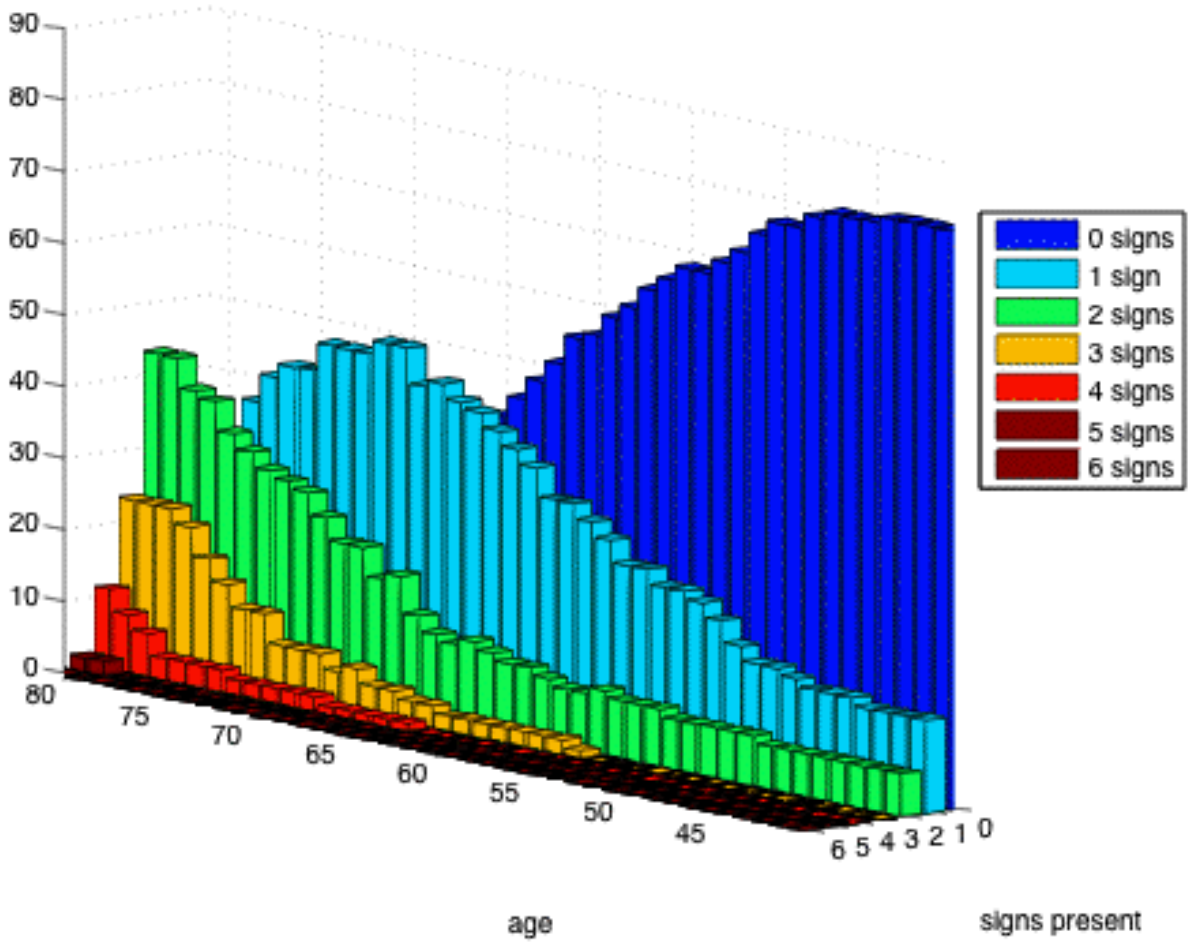
Expected number of signs at time t is the sum of the distribution functions .

Longitudinal Simulation of 100 Individuals

- For each compute the age at which each of the 6 signs will appear. This gives us a 100x6 matrix.

$$[t_1 \quad t_2 \quad t_3 \quad t_4 \quad t_5 \quad t_6]$$

- Zero a 100x6 array. At each time t, assign a 1 if $t > t_i$. For each row, sum across to count the number of signs present. In this way, at each time a distribution of counts is created.


90
80
70
60
50
40
30
20
10
0
80
75
70
65
60
55
50
45
6 5 4 3 2 1 0
0 signs
1 sign
2 signs
3 signs
4 signs
5 signs
6 signs
age
signs present

Reference and Acknowledgements

S.J. Merrill[1], B. Myklebust[2], J. Myklebust[3], N. Reynolds[4], and E. Duthie[5,6], A Poisson-like model of sub-clinical signs from the examination of healthy aging subjects, *Aging Clinical and Experimental Research*, **20** (2008), 368-375.

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TABLE 2: HEALTHY AGING SUBJECTS TESTED BY NEUROLOGIC EXAMINATION

CATEGORIES OF THE NEUROLOGIC EXAM	SUBJECT GROUPS				
	53 - 57 years (54.4 ± 1.9) n=5 3 males	**58 - 62 years** (59.9 ± 1.1) n=12 2 males	**63 - 67 years** (65.5 ± 1.1) n=19 9 males	**68 - 72 years** (69.4 ± 1.4) n=20 14 males	**73 - 84 years** (76.7 ± 4.2) n=10 5 males
SENSORY DEFICIT	**0**	**5** 5/12 = 0.42	**6** 6/12 = 0.50	**8** 8/20 = 0.40	**5** 5/10 = 0.50
DTR DEFICIT	**1** 1/5 = 0.20	**2** 2/12 = 0.17	**8** 8/19 = 0.42	**9** 9/20 = 0.45	**3** 3/10 = 0.30
INCREASED TONE	**0**	**0**	**1** 1/19 = 0.05	**1** 1/20 = 0.05	**1** 1/10 = 0.10
DECREASED STRENGTH	**0**	**0**	**1** 1/19 = 0.05	**0**	**1** 1/10 = 0.10
CEREBELLAR SIGNS	**1** 1/5 = 0.20	**2** 2/12 = 0.17	**4** 4/19 = 0.20	**5** 5/20 = 0.25	**6** 6/10 = 0.60
FRONTAL RELEASE SIGNS	**0**	**0**	**5** 5/19 = 0.26	**11** 11/20 = 0.55	**2** 2/10 = 0.20