Multivariate Mixture Models to Describe Longitudinal Patterns of Frailty in American Seniors

Jason Connor
Thesis Proposal

January 24, 2006

Abstract

Large, longitudinal, multivariate population surveys are increasingly common. Many analytic methods inspect changing rates of individual outcomes but ignore heterogeneous subpopulations that may exist. In this document I propose two analytical methods which extend group-based trajectory models to multivariate outcomes. I use group-based longitudinal finite mixture models (i.e., developmental trajectory models) to identify and describe latent subpopulations for the multivariate outcomes of interest. I use the National Long Term Care Survey, which measures various disabilities in American elderly from 1982 to 2004, as an example. Both models of longitudinal pathways of disability clearly illustrate the various frailty patterns in latent subpopulations of American seniors. These models recognize that within group some disabilities may coincide while others may follow at a later time. Finally, I demonstrate latent frailty patterns with illustrative plots that show multivariate temporal patterns within latent class.

Introduction

The number and proportion of older Americans is rapidly increasing [6, 45]. This demographic shift increases demands on the public health system while decreasing the American income and social security tax base [11, 43]. Factors causing this dramatic demographic shift include declining birthrates, increases in average lifespan, and elevated fertility from 1945-1965 (the baby boom) [13, 44].

The proportion of Americans over 65 is expected to rise from 12.4% to 19.6% from 2000 to 2030 (and by 35,000,000 people). The proportion of Americans over age 80 is expected to more than double. This demographic shift will have severe consequences on health care expenditures. Persons 65 and older have health care costs, on average, 3-5 times higher than individuals under 65. Already the United States has the highest annual per-capita spending for seniors ($12,100 in 1997).

Long term care, as typically necessitated by chronic disability, is a substantial portion of this cost. Chronic disability, most often seen in older citizens, places great burdens on families and the American health care system. Nursing home and home health care costs doubled from 1990 to 2001 [15]. Individuals and families pay a larger share, 25%, of this form of health care than for doctor's visits, hospital stays, and treatments [3].

First we must define disability. The Americans with Disability Act (ADA) [1] states a person is disabled if he or she (1) has a physical or mental impairment that substantially limits one or more major life activities, (2) has a record of such an impairment, or (3 is regarded as having such an impairment. This definition, particularly part (3), is not precise and the Supreme Court of the United States has had to repeatedly clarify and interpret the legal definition of disability.

In the context of aging, disability typically refers to the set of functional problems in performing fundamental activities related to community living, specifically, activities of daily living (ADLs), such as bathing, dressing, and eating, and instrumental activities of daily living (IADLs) such as preparing meals, caring for the home, maintaining finances, and mobility in walking and climbing stairs.

To partially alleviate the need for long term care, either disabilities need to be delayed or technologies that permit independent living with disabilities need to be developed or more widely available. One recent study estimates that 35% of seniors live without would-be-useful assistive devices or tools [17].

But to understand and characterize disability patterns in 40 million Americans, we must identify heterogeneous subpopulations that comprise the Amer-

ican elderly population. This work aims to identify latent patterns of frailty in elderly Americans, identify how they changed over the past twenty years, and determine what factors may predict these frailty pathways.

Because frailty has specific meanings in the geriatrics literature and statistical literature, I will mean the vague geriatric definition of frailty unless noted. While there is not an official definition, Rockwood writes [37]

> "Some consensus on a definition [of frailty] is likely to emerge, but the basis for a successful definition needs to be explored. Here, a classic approach to validation is proposed: a successful definition of frailty should be multifactorial but must also manage the many factors in a way that takes their interactions into account. It is likely to be correlated with disability, co-morbidity and self-rated health, and should identify a group that is vulnerable to adverse outcomes."

Therefore we interpret the latent groups we identify as longitudinal patterns of frailty and assume they are the underlying mechanism for the observed disability.

Past investigations of disability have typically compared years' age-adjusted disability rates cross-sectionally [14, 18, 19] rather than inspecting disability in individuals longitudinally [42]. This analysis uses the National Long Term Care Survey (henceforth NLTCS) to investigate longitudinal patterns of disability in seniors. The NLTCS is a large, national dataset initiated by the Census Bureau in 1982 and resampled every 5 years from 1984 to 2004. Using these multivariate longitudinal data we can identify latent patterns of frailty and study how these patterns are evolving.

Cross-sectional investigations of disability may indicate gross changes in particular function areas but can not provide information about the relationship between various disabilities, nor how, within individuals, disabilities compound with age. For example Reynolds et al. suggest that obesity at 70 does not decrease expected remaining life, but increases disability throughout the remainder of life [36]. This analysis, however, simply compared static population proportions for activities of daily living. Only longitudinal studies of a large cohort of seniors can provide information on the length of disability, how physical and mental abilities jointly or sequentially deteriorate, and how individual disabilities compound with additional disabilities with age.

By longitudinally studying patterns of disability, we can estimate latent multivariate trajectories of disability and identify common patterns of frailty in the United States elderly population.

The NLTCS Data

The National Long Term Care Survey was initiated in 1982 by the National Institute on Aging. 35,000 seniors were selected from Medicare enrollment files and have been longitudinally tracked in successive waves in 1984, 1989, 1994, 1999, and 2004. Approximately 5,000 additional seniors passing 65 are added to the survey each wave. The survey is administered by the U.S. Census Bureau. They employ trained interviewers and response rates are at least 95% for all waves. Duke University's Center for Demographic Studies has been the home of the survey for the last several waves.

The physiologic limitations that lead to disability include cognitive impairments, mobility limitations, loss of fine motor control, and vision or hearing problems. Each of these physiologic restrictions or combination of impairments causes a distinct set of activities seniors are no longer able to perform independently. Using the NLTCS I study 6 activities of daily living and 10 instrumental activities of daily living to quantify disability and identify disability patterns.

I identify disabilities by studying seniors' abilities to independently perform activities of daily living (ADLs) and instrumental activities of daily living (IADLs). ADLs are activities related to personal care. IADLs are activities related to independent living. Table 1 lists the 6 ADLs and 10 IADLs.

Activities of Daily Living	
Eating	Getting In/Out of Bed
Inside Mobility	Dressing
Bathing	Toileting
Instrumental Activities of Daily Living	
Heavy Housework	Light Housework
Laundry	Cooking
Grocery Shopping	Outside Mobility
Travel	Managing Money
Taking Medicines	Phoning

Table 1: Activities of daily living (ADLs) and Instrumental Activities of daily living (IADLs). ADLs relate to personal care while IADLs relate to independent living.

Interviewers asked subjects or their proxy responders about their ability to independently perform each of the ADLs over the last seven days. Anyone needing assistance (either from another person or a device) is classified as

having the disability. Subjects fail IADL queries if they reported needing general assistance (no time period specified) performing any of these tasks.

All subjects responded to ADL questions; only subjects living in the community answered the IADL questions. Therefore we lack IADL responses for all institutionalized subjects (e.g., seniors in nursing homes or assisted living facilities). While ADLs measure gross disability, IADLs provide a finer measure of quality of life. Therefore the IADLs may offer the most insight into finer changes in function and may be indicative of the initial descent down the frailty path.

The 2004 data are being finalized by the Center for Demographic Studies at Duke University. Therefore I use the 1982, 1984, 1989, 1994, and 1999 waves of the NLTCS in this analysis. 41,947 unique subjects provide data in the first five waves of the study. A plurality provide just one year of data but 10,000+ provide three or more years worth of data. For this proposal I simplify the data to the 3447 subjects with four or more waves of data and at least one ADL at some time. Furthermore the NLTCS is based on a complex sampling design. The analysis thus far ignores sampling weights.

Figure 1 shows the probability of not being able to do the six activities of daily living by age, plus the probability of institutionalization. Bathing is the most common ADL with which elderly need assistance. Eating is the activity elderly are most able to do on their own. All disability rates increase essentially monotonically with age.

Modeling Strategies

Various diseases and chronic conditions and their combinations are associated with particular sets of disabilities. To appropriately model disability, these latent subpopulations must be identified and described. Thus far the Grade of Membership (GoM) model [5, 20, 21, 22, 39] has been the instrument of choice for identifying and describing these latent populations. These explorations, however, have ignored the longitudinal nature of the survey. Stallard has more recently proposed a longitudinal GoM model based upon transition probabilities between pure types [42] . Other initial explorations also use Markov transition matrices to detail changes in disability [46].

In the Stallard model, individual subjects are assigned grades of membership into one or more "pure types", thereby being viewed as a weighted mixture of multiple homogeneous groups. In more standard mixture models [24], a subject may be assumed to come from just one group, but the group of origin is unknown and therefore assigned a vector of probabilities.

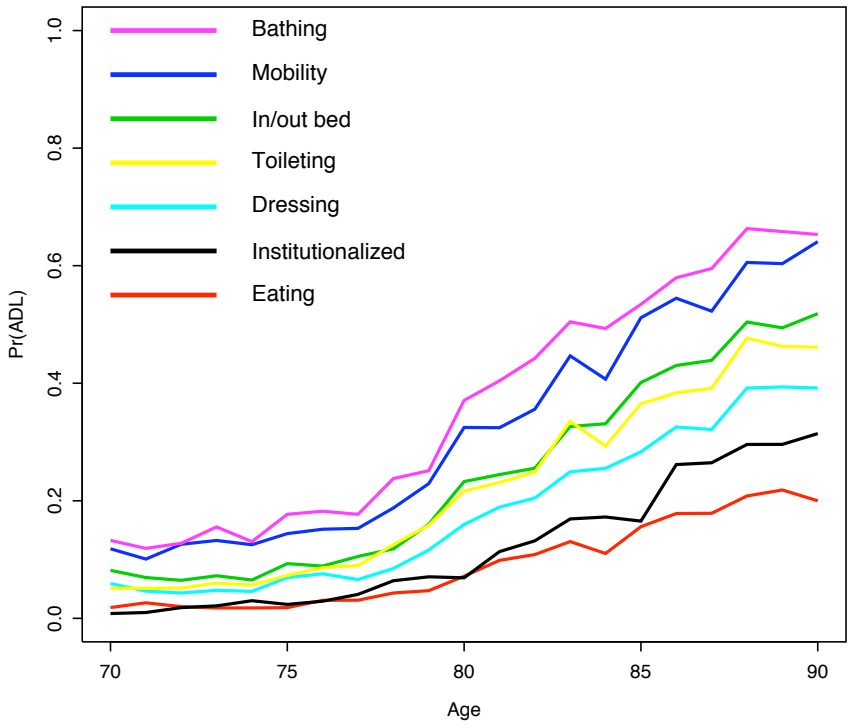

Figure 1: Yearly proportion of patients who can not complete ADL unassisted.

The GoM model emphasizes that an individual's outcomes result from a combination of properties from various pure types (an analogy would be being 50% French and 50% Italian versus having 50% chance of being *entirely* French and a 50% chance of being *entirely* Italian.) However, "pure types" are a hypothetical class to which potentially no subjects may belong. The standard (i.e., non-longitudinal) GoM model is easily interpretable but becomes more difficult when considering transition probabilities between already hypothetical groups. Therefore illustrating patterns of disability in typical seniors (vs. idealized groups) is less straightforward than the comprehensible method I propose.

I propose a mixture model to model multivariate longitudinal pathways of frailty that clearly illustrates the various disability patterns in latent subpopulations of American seniors. This model recognizes that within group some

disabilities may coincide while others may follow at a later time. For instance bathing and dressing each require some strength but more flexibility and may most often coincide. Meanwhile each of these events may precede the inability to eat independently.

To model these latent subpopulations I start with the univariate group-based trajectory approach of Nagin and collaborators [12, 27, 28, 29, 30, 31, 32, 33]. The goal of their methodology is to identify clusters of subjects with similar univariate trajectories. Given an individual i's longitudinal vector of outcomes, $Y_i = \{y_{i,1}, ..., y_{i,T}\}$, and assuming he belongs to group j of J unique latent groups, then $P^j(y_{i,t}) = f(\beta_{0,j} + \beta_{1,j}t)$ is the probability of observing outcome $y_{i,t}$ assuming subject i is in latent group j. Here f may be any generalized linear model link function. Thus there are J unique longitudinal trajectories. The distribution of subjects to the J latent trajectories may be denoted as $\pi = \{\pi_1, ...\pi_J\}$.
Therefore the likelihood for a single subject's data is

$$\ell(Y_i|\beta_{0,1}, \beta_{1,1}, ..., \beta_{0,J}, \beta_{1,J}, \pi_1, ..., \pi_J) = \sum_{j=1}^{J} \left(\pi_j \prod_{t=1}^{T_i} (P^j)^{Y_{i,k.t}} (1 - P^j)^{1-Y_{i,k,t}} \right), \tag{1}$$

and the likelihood for the sample is

$$\ell(Y|\beta_{0,1}, \beta_{1,1}, ..., \beta_{0,J}, \beta_{1,J}, \pi_1, ..., \pi_J) = \prod_{i=1}^{N} \left(\sum_{j=1}^{J} \left(\pi_j \prod_{t=1}^{T_i} (P^j)^{Y_{i,k.t}} (1 - P^j)^{1-Y_{i,k,t}} \right) \right). \tag{2}$$

I expand this modeling strategy to multiple outcome variables using two different group-based trajectory modeling strategies which I label the marginal mixture model and the joint mixture model.

Marginal Mixture Model

In the marginal model, I assume there are J latent trajectories per ADL, then use finite mixture models with a logit link [26] to estimate these latent trajectories separately for each ADL. Let $Y_{i,k,t} = 0$ or 1 for whether subject i was or was not able to independently perform ADL k at time t. Then separately for $k = 1...K$ I can estimate parameters in Equation (2) above. I expand the polynomial to

$$\text{logit}(P^j(Y_{i,k,t})) = \beta_{0,j,k} + \beta_{1,j,k} Age_{i,t} + \beta_{2,j,k} Age_{i,t}^2 \text{ for } j \in 1...J \tag{3}$$

where $Age_{i,t}$ is the age of subject i in year t. The independence assumption is most likely false since a serial correlation of ADL and IADLs exists. This assumption, however, significantly reduces computational complexity. However with sufficiently many mixture groups, the group-based modeling method serves to restore much of this serial correlation [26].

The likelihood for a single ADL is

$$\ell(Y|\Theta_k) = \prod_{i=1}^{N} \left(\sum_{j=1}^{J} \left(\pi_j \prod_{t=1}^{T_i} (P^j)^{Y_{i,k.t}} (1 - P^j)^{1-Y_{i,k,t}} \right) \right) \text{ for } k = 1...7. \quad (4)$$

I calculated maximum likelihood estimates for the parameters for each of the 6 ADLs plus institutionalization. For each individual, I can estimate the probability of membership in each group, $j = 1...J$, for each ADL, $k = 1...7$. Initially I've used $J = 3$ latent classes per ADL. Figure 2 shows the estimated latent trajectories, shown in red, green, and blue for the healthiest to most frail, for each ADL. The table below shows the proportion of the sample following each longitudinal trajectory.

Each individual may be clustered in his group of highest posterior probability or may be weighted by his vector of posterior probabilities of group membership. Using hard clustering for simplicity in this illustration the distribution of ADL deficiency per trajectory is

ADL #	ADL	Red %	Green %	Blue %
1	Eating	3	82	15
2	In/Out Bed	46	48	6
3	Inside Mobility	40	50	10
4	Getting Dressed	85	5	10
5	Bathing	23	63	14
6	Toileting	62	33	5
	Institutionalized	72	25	3

Now we may consider the joint probability of group membership between 2 or more ADLs. For instance, classifying subjects into their most likely group, we could create a 3×3 table that shows the distribution of trajectory group classification of the getting in and out of bed ADL by the inside mobility ADL. For example:

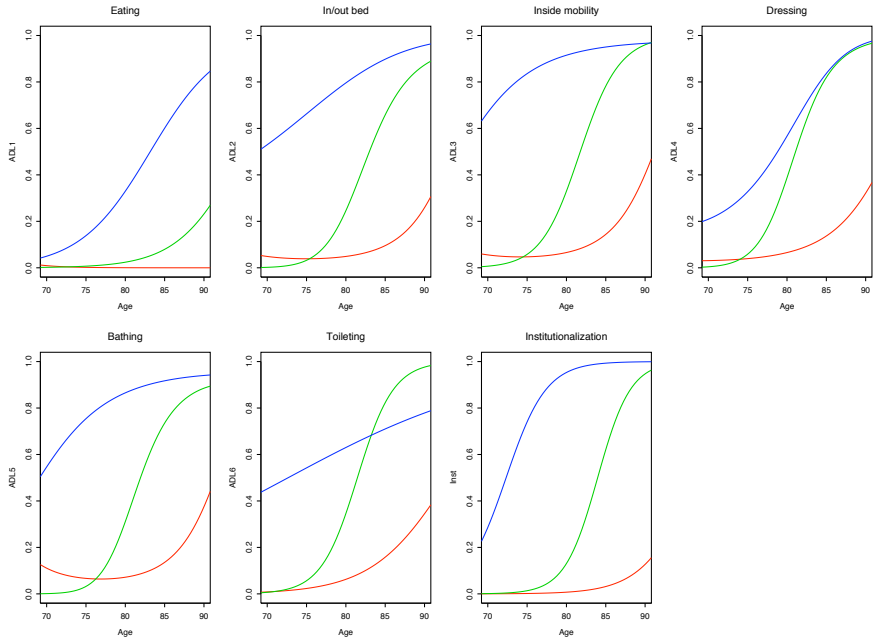

Figure 2: Mixture models fit separately for each ADL. Each plot illustrates the three latent trajectories estimated for that ADL.

	Inside Mobility			
In/Out Bed	Red	Green	Blue	Total
Red	1127	415	44	1586
Green	253	1282	108	1643
Blue	6	33	179	218
Total	1386	1730	331	3447

The latent trajectory groups for getting in and out of bed and inside mobility look similar (Figure 2). Likewise we would expect similar physiological capabilities to contribute to these two ADLs. Therefore it is expected that subjects would fall into similar trajectory patterns for the two ADLs. In fact 75% of subjects fall on the diagonal. But it's informative that 7 times as many subjects are in the highest disability group for inside mobility and lowest trajectory group for getting in and out of bed than vice versa. While both ADLs require mobility, we would expect seniors to need assistance with general inside mobility sooner than assistance getting in and out of bed.

We can expand this 3×3 table to a $3 \times 3 \times 3 \times 3 \times 3 \times 3 \times 3 = 3^7$ table

that includes each of the three estimated latent trajectories for each ADL plus institutionalization.

But as shown, ADLs are highly correlated so we expect very many non-existent combinations of ADL trajectory groups (i.e., empty cells in our 3^7 table). In fact, although we have 3447 subjects, 1864 of the 2187 cells (85%) have 0 counts. 144 cells have just 1 count, 56 cells have just 2 counts. So 94% of all cells have 2 or fewer counts.

Just 101 (of the possible 2187) patterns appear four or more times, or 1 in 1,000 seniors. Only 19 patterns appear 34 times or more – and 34 subjects to a pattern is just 1% of the data.

So 2420 of the 3447 subjects have patterns in just 20 of the cells. Therefore 70% of the data exists in $< 1\%$ of the cells. Figure 3 shows the 20 most common patterns.

Thus the initial result of this analysis is a major data reduction with very descriptive and easily understandable results.

For example, Figure 4 shows the 6 most highly populated cells in our contingency table (but not in order of frequency). This clearly shows distinct pathways of frailty. For instance Plot (a), the most common set of trajectories, shows generally healthy subjects who exhibit slightly increased frailty in all ADLs after age 80. Plot (b), the second most frequent set of trajectories, shows similar trajectories but an increased rate of trouble bathing at early ages. Plot (c) shows the the next level of frailty, the addition of needing help with inside mobility at an earlier age. From plots (d) through (f) the frailty pathway continues with ADLs being added to the list of disabilities.

Also noteworthy is that although the mixture model for each ADL was separately estimated, frailty trajectories are extremely similar across ADLs. This is further evidence of possible data reduction and leads to our second modeling strategy, the joint mixture model.

Joint Mixture Model

There are so few populated cells in the 3^7 matrix that it encourages us to simply fit a mixture model (with a large, e.g., 15-30, number of components) that jointly identifies common trajectories rather than models the 7 ADLs individually and then studies the joint distribution of group membership.

Now for instance I assume a larger, e.g., $J = 20$, number of groups, and I estimate latent disability groups using all 6 ADLs and institutionalization simultaneously.

I use the similar parametric form as above except I drop the quadratic term. However, instead of estimating $\Theta_k = \{\beta_{0,1,k}, \beta_{1,1,k}, ..., \beta_{0,J,k}, \beta_{1,J,k}, \pi_1, ..., \pi_J\}$

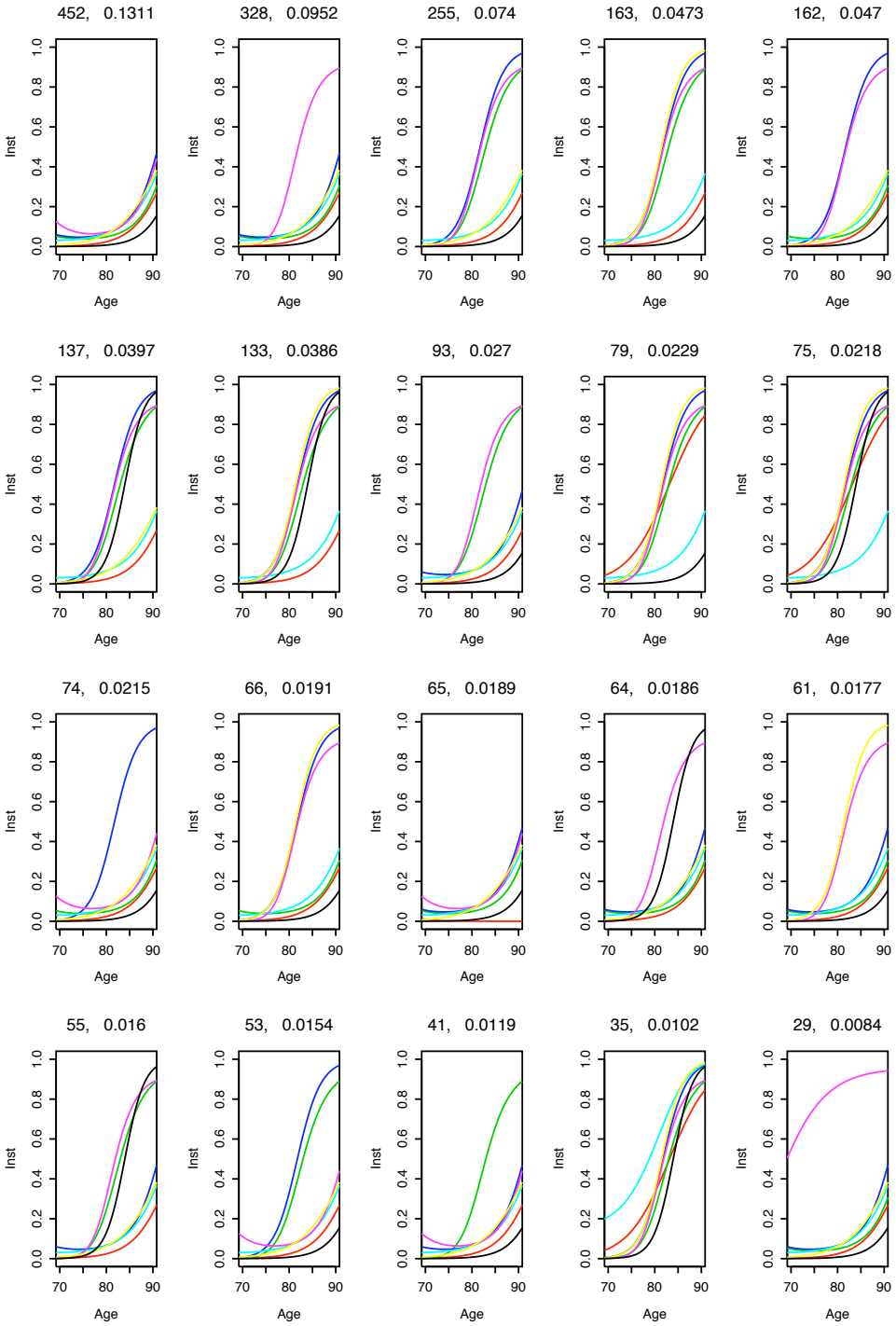

Figure 3: 20 most common sets of trajectories. Each graph represents one cell in the 3^7 table. Colors are defined in Fig 1. The title of each plot shows the number and proportion of subjects classified to each cell. There are 3447 total subjects.

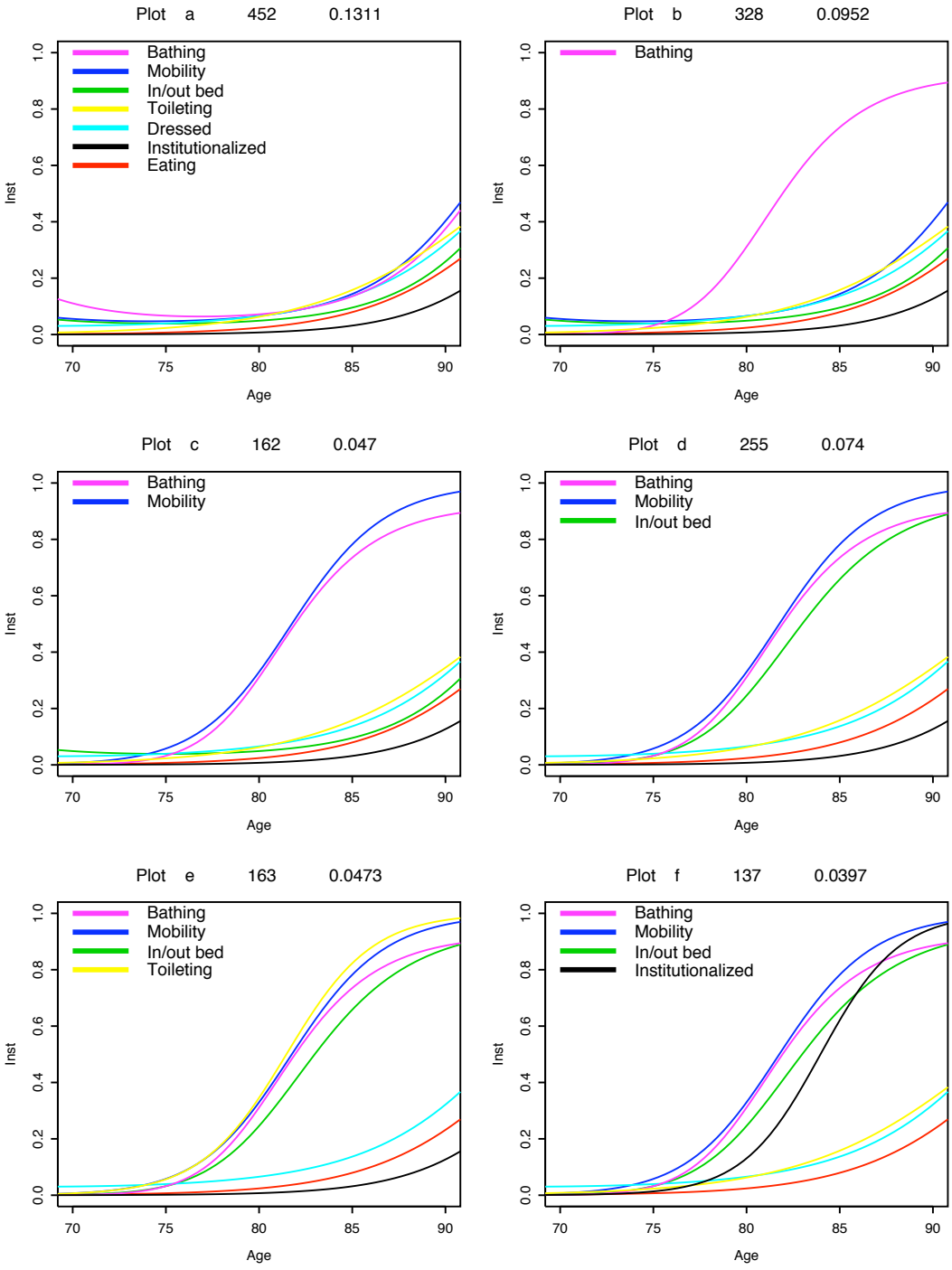

Figure 4: Six most common sets of trajectories. Each graph represents one cell in the 3^7 table and therefore one latent group. The title of each plot shows the number and proportion of subjects classified to each cell. There are 3447 total subjects.

separately for each of the K ADLs, I can estimate
$\Theta = \{\beta_{0,1,1}, \beta_{1,1,1}, ..., \beta_{0,J,1}, \beta_{1,J,1}, ...\beta_{0,1,K}, \beta_{1,1,K}, ..., \beta_{0,J,K}, \beta_{1,J,K}, \pi_1, ..., \pi_J\}$ jointly.

The likelihood for subject i is

$$\ell(Y_i|\Theta) = \sum_{j=1}^{J} \left(\pi_j \left(\prod_{k=1}^{7} \prod_{t=1}^{T_i} (P^j)^{Y_{i,k.t}} (1 - P^j)^{1-Y_{i,k,t}} \right) \right), \tag{5}$$

and the likelihood for the sample is

$$\ell(Y|\Theta) = \prod_{i=1}^{N} \left(\sum_{j=1}^{J} \left(\pi_j \left(\prod_{k=1}^{7} \prod_{t=1}^{T_i} (P^j)^{Y_{i,k.t}} (1 - P^j)^{1-Y_{i,k,t}} \right) \right) \right) \tag{6}$$

The marginal model had $3^7 = 2187$ possible latent trajectories, although 19 described 70% of our data. The joint model estimated with 20 groups will not create latent group for subjects with unique disability patterns as will the marginal model. However it will estimate up to 20 unique trajectories for an individual ADL whereas the marginal model used just 1 of 3 trajectories per each ADL. Figure 5 shows the 20 groups estimated with this model. The number of subjects and proportion all subjects in each latent group is shown at the top of each plot.

The most common group is similar to the marginal model's most common. But the two methods have few similarities. In both eating and institutionalization tend to be the events that are least likely to occur, even at older ages. Likewise the order of frailty typically follows the path of failure bathing, inside mobility, in/out bed toileting, dressing, then eating. Many of the patterns have dissimilar ADL trajectories within class unlike the joint model which typically has just a few paths that numerous ADLs follow within trajectory group. This illustrates this model's added flexibility since an individual ADL may take up to 20 different paths in the 20 groups unlike in the marginal model in which only 3 distinct paths apply across the 20 groups.

Model Comparison

The marginal model with 3 groups per ADL has $3 \times 3 \times 7 + 2 \times 7 = 77$ parameters. The joint model with 20 groups has $2 \times 7 \times 20 + 19 = 299$ parameters, and estimation, as expected, is less stable.

The marginal model may better describe unique or outlying patterns of disability because it produces $3^7 = 2187$ latent groups, more latent classes with fewer parameters. The joint model certainly fails at this task. In fact,

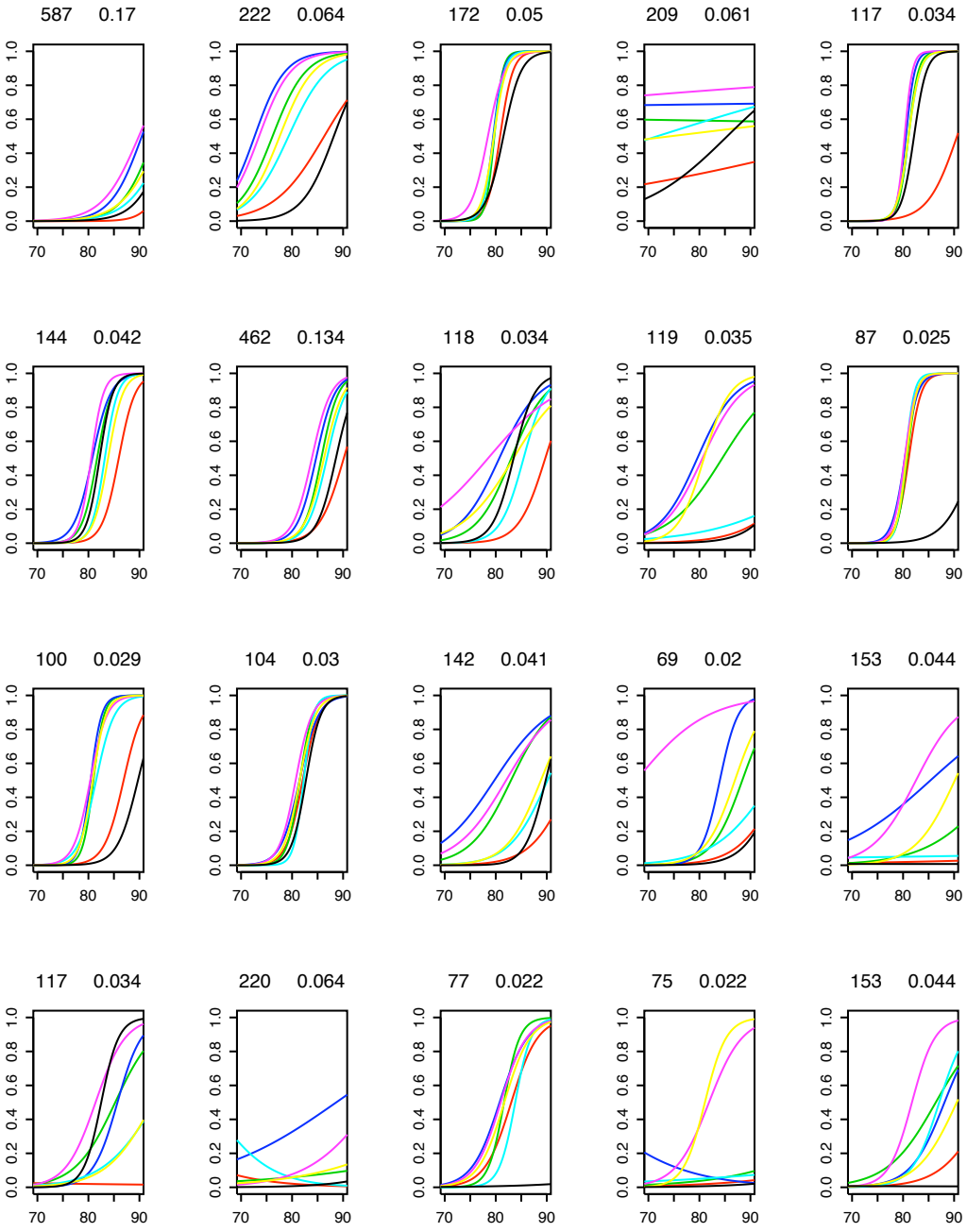

Figure 5: 20 latent trajectories from the joint mixture model. Colors are defined in Fig 1. The title of each plot shows the number and proportion of subjects classified to each cell. There are 3447 total subjects.

unique disability patterns may exert influence over the modeling of just 20 common paths meant to describe a population of 40 million seniors. The joint model, however, is more flexible in that each ADL's path may differ across the 20 groups. For the marginal model, only 3 unique trajectories for each ADL are used to produce the various latent trajectory groups.

Using mean squared error as a simple metric for model fit, the MSE for the marginal model is 0.077. The MSE for the joint model is 0.071.

For comparisons sake I calculated the MSE under two simple models. Using $\hat{p}_k = (0.092, 0.232, 0.306, 0.177, 0.342, 0.211, 0.120)$ for the 6ADLs and institutionalization (the simple proportion of subjects requiring assistance regardless of time or age) the MSE is 0.160.

Fitting a logistic regression by age separately for each ADL, the MSE = 0.131. So the marginal model reduces the MSE by 41% compared to logistic regression. The joint model reduces the MSE just 14%.

This simple comparison based on mean square error does not test either model's ability to correctly and logically estimate pairs or higher combinations of ADLs. I will expand the model comparison component to test each model's ability to estimate pairwise combinations of ADLs and IADLs.

For instance Pr(Need assistance eating|Do not need assistance bathing) = 0.003 while Pr(Need assistance bathing|Do not need assistance eating) = 0.27. Using the estimated probability from the marginal mixture model with cutoffs at 0.5, Pr(Need assistance eating|Do not need assistance bathing) = 0.001 while Pr(Need assistance bathing|Do not need assistance eating) = 0.33.

In the table below, NN, NY, YN, YY refer to needing assistance with neither eating nor bathing, need assistance with only bathing, needing assistance with only eating, and needing assistance with both eating and bathing, respectively. 80% of the counts fall on the diagonal indicating that the marginal model precisely estimated the pairwise combination of the eating and bathing ADLs 80% of the time.

Estimated from Marginal Model					
True	NN	NY	YN	YY	Total
NN	8690	1051	6	26	9773
NY	881	2795	0	85	3761
YN	21	7	1	3	32
YY	194	741	2	401	1338
Total	9786	4594	9	515	

The joint model estimated 67% of pairwise results for eating correctly and never predicted the a subject would need assistance eating but not require

assistance bathing. This also illustrates the joint model's inability to classify rare combinations of ADLs.

Estimated from Joint Model					
True	NN	NY	YN	YY	Total
NN	9490	270	0	13	9773
NY	3190	503	0	68	3761
YN	27	4	0	1	32
YY	932	324	0	82	1338
Total	13639	1101	0	164	

Further model comparisons and diagnostics will tests both models' ability to not only marginally predict ADLs, but also test their ability to correctly predict pairwise and higher order combinations of ADLs.

Proposed Work

The models estimated in this proposal use a subset of the data, only ADLs, and are fit by maximum likelihood. I propose to expand from my subset of 3447 subjects to the 40,000 subjects in the NLTCS including the 2004 wave, to use all 6+10 ADLs and IADLs, and to estimate a full Bayesian model.

This full model of all subjects sampled in the National Long Term Care Survey will provide inferences applicable to the entire population of U.S. seniors over the last 20 years. The results will clearly illustrate multivariate, longitudinal patterns of frailty and provide for descriptive differences of frailty patterns by a wide variety of patient characteristics and behaviors.

Inclusion of soon-to-be released 2004 wave will provide another wave of data for those previously sampled and a new cohort of seniors who turned 65 since 1999.

The Bayesian model will provide correct estimates of standard errors by correctly accounting for all levels of uncertainty. The likelihood functions described above can be easily adapted to a fully Bayesian model. Currently R and SAS are used for analysis. I have begun to use C++ to estimate the Bayesian model with 40,000+ subjects.

Additionally, I will conduct a more thorough comparisons of the marginal mixture model to the joint mixture model including comparisons that test each model's ability to correctly predict combinations of ADL and IADLs. For instance some combinations of capabilities are extremely rare (e.g. it's very rare to need help eating but to be able to bathe independently) and a reliable model must predict such codependencies.

Beyond the above additions and improvements which will lead to novel inferences and illustrations of disability in American seniors I may also explore the following three additions to the models:

Data imputation for IADLs for institutionalized subjects

The models above do not use IADL data which measure finer degrees of functionality, e.g., ability to travel, do housework, or manage money. The ability to perform IADLs without assistance is far more indicative of independent living. Therefore classification of function can be improved by using IADLs. IADLs, however, are not known for institutionalized seniors. IADLs are not known for 6-8% of any wave and are unknown at at least one wave for 13% of subjects who are sampled in three or more waves.

Incorporating IADLs into the models described above may offer finer gradations and therefore keener insights into the frailty pathway. Having finer measures of disability is particularly important in the models, such as the promised full model, which include fewer waves of data for some subjects. To fully incorporate IADLs into these models, I will impute the missing-by-design IADLs for institutionalized subjects. Understandably, many institutionalized patients need assistance with all or more IADLs.

Imputation of missing IADLs is necessary to have complete disability patterns for all individuals and therefore the imputation is necessary to profile and classify all subjects. The key to this imputation method is not only to impute the missing values, but with a particular subject's survey, impute the missing IADLs so that there remains logical conditional probabilities between IADLs. For instance

$$\Pr(\text{Can't do laundry}|\text{Can't do heavy housework}) = 0.50,$$

however,

$$\Pr(\text{Can't do heavy housework}|\text{Can't do laundry}) = 0.97.$$

A simple univariate imputation may result in many rare combinations of IADLs. Therefore I propose two methods of multiple imputation that will have the correct conditional dependencies. Using multiple imputation [16, 40, 41] for the multivariate IADL data, I can simulate IADLs for the missing data, and our final models will correctly account for the uncertainty associated with the missing values.

One potential method for imputation is using empirical distributions of ADLs. For six ADLs, there are $2^6 = 64$ possible ADL patterns. 58 of these 64 are observed in the community sample, the sample for which IADLs are

also known. 43 unique ADL patterns are observed in the institutionalized sample, subjects for whom I need to impute IADLs. Only 2 institutionalized subjects have unique ADL patterns – patterns not observed in the community sample. Therefore, for an institutionalized subject with unknown IADLs, I can randomly select a subject with the exact same ADL pattern and use that subject's IADLs for the institutionalized subject.

Repeating this method at each step of the multiple imputation process will effectively integrate over likely but unknown IADL patterns while maintaining the correlation structure inherent to disability patterns. The one drawback is that there may be high bias for institutionalized subjects whose ADL patterns have just one or two matches in the community sample.

A second multiple imputation method uses log-linear models estimated from the community sample. I estimated a log-linear model using all 6+10 ADLs and IADLs using second order terms. This model provides an adequate fit according to the likelihood ratio statistic, and since all second order terms were used in the model, pairwise conditional probabilities pass visible inspection, i.e. pairwise 2×2 tables of imputed IADLs have similar off-diagonal proportions to 2×2 tables of known IADLs. Now for any known pattern of 6 ADLs, I may use the fitted model to estimate the probability distribution across the $2^{10} = 1024$ patterns of IADLs. Using multiple imputation I may sample from these likely combinations of IADLs which retain the correct conditional dependencies given the observed set of ADLs.

Predictive distributions for unknown IADLs using the empirical distributions or the Bayesian log-linear model will be incorporated into the fully Bayesian model for estimating trajectories.

The primary assumption for using data imputation assumes the data is missing at random, i.e. given the observed data, the probability of missing data is independent of the true but unknown values of that missing data. So in this circumstance, the missing at random assumption implies that institutionalization is independent of IADLs status given the known ADL vector. Because the need for institutionalized is more dependent upon person care, which is measured by ADLs, I believe this assumption is clinically reasonable, though it will be tested.

An alternative to imputing missing IADLs for institutionalized subjects is to estimate latent classes solely based upon the observed data for each subject.

Inference based upon demographics and behaviors

Often times policy makers or collaborators will have very broad questions, e.g., "How do patterns of disability differ in senior citizens with and without

MediGap insurance?" The current geriatrics research on disability typically compares subjects' disability rates demographically [2, 6, 25] or by other personal characteristics such as weight [36] or lifestyle [10]. Because these comparisons tend to be cross-sectional, standard linear modeling methods are used to adjust for factors such as gender and age.

Currently, the group-based trajectory modeling approach enables researchers to compare distributions of disability patterns across demographic groups. For example, Figure 6 shows the six most common multivariate disability patterns using the marginally specified method. The gender breakdown of the sample used in this example is 75% female / 25% male. Figure 6 shows that this distribution is similar within each disability pattern. The racial breakdown in the survey is 91% white / 9% non-white. Figure 6 shows that amidst the most common trajectory groups, non-white seniors are far less likely to be institutionalized (Plot f) and slightly more likely to require assistance toileting at earlier ages (Plot e). The six most common patterns tended to have similar distributions of race, gender, and urban vs. rural.

This inference is very informative, however, some consumers of this data may want a formal test of differences in disability patterns by groups while considering the frailty patterns in their multivariate, longitudinal form. Two current models I plan to explore are (1) making probabilities of group membership functions of demographic and behavioral variables and (2) relaxing the dependence on age and replacing it with a latent frailty term.

1. Currently the probability of group membership is a function only of an individual's observed longitudinal ADL pattern. We may expand the model so that an individual's probability of group membership is also a function of demographic characteristics, physiological attributes, or behaviors.

2. Currently all trajectories are dependent upon age. But age is merely a proxy for frailty. There is frequently a seminal event that sparks an elderly person's descent down the disability pathway. A contrary model in the geriatric literature espouses a cumulative model of chronic disability that indicates subsequent disabilities may rely less on age and more on recently experienced disabilities. Actual age may have very little to do with the disability pathway we're trying to model. I may relax the model's dependency on age and introduce a latent frailty term (frailty in the statistical sense) that describes excess risk, i.e., *frailty*, for distinct categories or individuals. In such a model two individuals may have similar disability trajectories that manifest at different ages

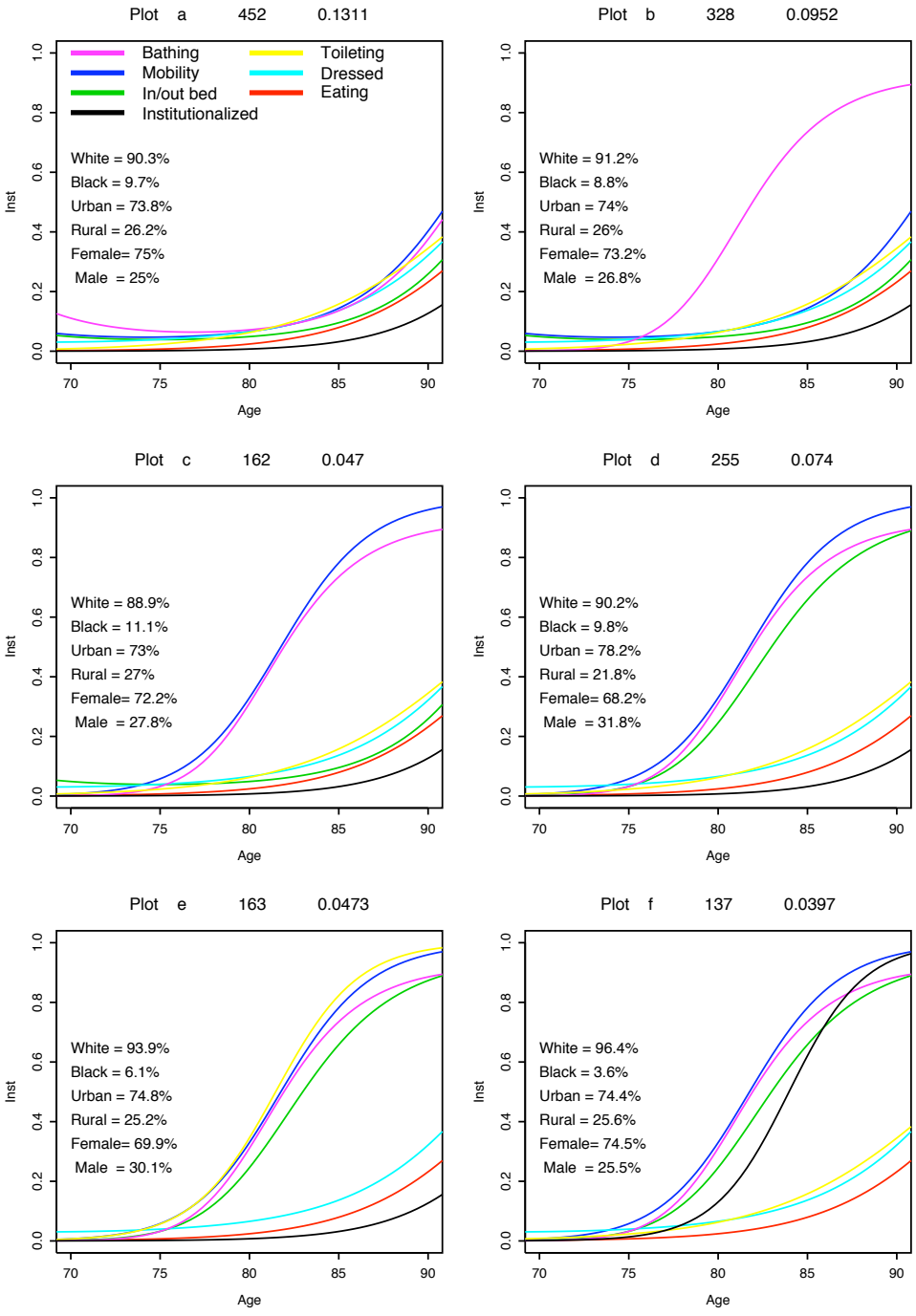

Figure 6: Six most common disability patterns with distributions of gender, race, and urban vs. rural. Marginal distributions are 25% male, 75% female; 91% white, 9% black (includes 0.8% other races); 74% urban, 26% rural.

but would considered in the same group since they would be identified as having similar frailties.

a) One complicated alternative is apply a random effect to age to Equation (3) and replace $Age_{i,t}$ with $Age_{i_t} + \delta_i$ where $\delta_i \sim N(0, \Delta)$. This model allows an individual's set of trajectories to shift left or right as shown in panels such as Figure 6. This model, however, adds 40,000+ parameters that need to be estimated.

b) Another, simpler-to-estimate, alternative is make the δ_i a function of subject characteristics, behaviors, or demographics. For instance

$$\delta_i = \delta_a Race_i + \delta_b Insurance_i + \delta_c Gender_i + ...$$

For example if $Race_i$ is coded 0 for white and 1 for non-white, and if $\delta_a > 0$ it means that the average non-white senior ages δ_a years faster than an average white senior, assuming all other characteristics in this model are the same. In both models we may consider $Age_{i,t} + \delta_i$ as "functional age."

The National Long Term Care Survey contains thousands of demographic, behavior, and physiologic variables including blood samples, buccal washes, and particular genes believed to be related to delayed aging and longevity (e.g., APOE and SOD2) so that many additional comparisons are possible.

These inferences, particularly the addition of the frailty term in either of the stated forms, will substantially complicate the model and may not be computational feasible. If, however, the model is estimable, it may provide insightful inferences.

Understand consequences of short follow-up times and censoring due to death

In order to identify changing patterns of frailty over time (i.e., are today's 75-year-olds more capable than the past's 75-year-olds?), our analysis must include longitudinal patterns for younger seniors. Since sampling begins only at age 65, the newer cohorts provides less data for analysis, and therefore less data for classification. Likewise seniors who die young provide less data.

Because the properties that distinguish trajectory groups frequently occur at older ages, correctly identifying groups with only data at younger ages (e.g., 65-75) is more difficult. Subjects who die younger may die without ever being disabled. While early deaths are becoming less common, we must understand

the effect of such subjects on our models which currently do not account for death.

A key question in the geriatrics / disability literature is the theory of Expansion of Morbidity [4, 7, 8, 23, 38] versus the Compression of Morbidity [9, 34, 35]. Because early sudden deaths (due to heart disease, workplace accidents, etc.) are decreasing, expansion theorists argue that chronic disability may increase as more Americans are living to older ages and may therefore experience longer periods of chronic illness and disability in their lifetimes. Gruenberg predicted improvements in health care would save people from dying without curing them. He labeled this "the failure of success" [9].

Compression theorists hypothesize that healthier lifestyles and medical improvements will delay the onset of disability hence compressing chronic disabilities at older ages near the end of life. This state of health is ideal: American seniors live longer and higher quality lives. Thus far, NLTCS data has supported the compression of morbidity hypothesis [18].

To definitively answer this question, however, we must use longitudinal data to estimate the length of time individuals are disabled near the end of life. This component may also use the frailty term we may introduce as described above. In addition to being at risk for more disabilities, frail seniors will also be at higher risk for early death.

To quickly see how well group membership can be estimated with less data, I estimated the probability of group membership (assuming the groups estimated by using 5 waves of data are correct) using just 3-waves of data. 90% of subjects are classified to the same group both times for the dressing ADL (the highest agreement) and 66% of subjects are classified to the same group for the getting in and out of bed ADL (the lowest agreement).

This limitation of group assignment based on just three waves may provide further reason to jointly model latent trajectory groups – though subjects can not be distinguished based upon individual ADLs, perhaps they are distinguishable when simultaneously considering all ADLs. Furthermore the slope of the medium frailty groups is typically steeper than the low frailty group. A concern with the marginal model based upon age is that health declines are more rapid than my estimated trajectories with just three groups show because fitting over age masks these affects leading to flatter slopes. This concern may also be addressed using the frailty component in the previous section.

Summary

The population of American seniors is a heterogeneous group in terms of health and functional abilities. The two multivariate group-based trajectory models I describe identify seniors with similar patterns of disability of time and clearly illustrates trajectories of frailty within group.

Bibliography

[1] Americans With Disabilities Act. (1990). Public Law 101-336 (42 U.S.C. Sec. 12101 et seq). Became public law January 26, 1992.

[2] Arbeev KG, Butov AA, Manton KG, Sannikov IA, and Yashin AI. (2004), "Disability Trends in Gender and Race Groups of Early Retirements Ages in the USA," *Soz Praventivmed*, 49, 142-151.

[3] Congressional Budget Office. (1999), "Projections for Long-term Care Services for the Elderly," Available at: http://www.cbo.gov/showdoc.cfm ?index=1123&sequence=0. Accessed December 10, 2005.

[4] Cressie H. (1998), "Compression of morbidity: evidence in relation to the age of onset of neurological disorders," *Compression of Morbidity Workshop Papers*, [Australian] Department of Health and Aged Care, Occassional Papers Series No. 4. 69-78.

[5] Erosheva EA. (2002), "Grade of Membership and Latent Structure Models with Application to Disability Survey Data," Ph.D. Thesis, Carnegie Mellon University.

[6] Freedman VA, Martin LG, Schoeni RF. (2002), "Recent Trends in Disability and Functioning Among Older Adults in the United States," *Journal of the American Medical Association*, 288, 3137-3146.

[7] Fries JF. (1980), "Aging, Natural Death, and the Compression of Morbidity," *New England Journal of Medicine*, 303, 130-5.

[8] Fries JF. (1989), "The Compression of Morbidity: Near or Far?" *Milbank Quarterly*, 67, 20832.

[9] Gruenberg EM. (1977), "The Failures of Success," *Millbank Quarterly*, 83, 779-880.

[10] Hubert H, Bloch D, Oehlert J, Fries J. (2002), "Lifestyle habits and compression of morbidity," *Journal of Gerontology Series A*, 57, M347-M351.

[11] Jacobzone S and Oxley H. (2002), "Ageing and Health Care Costs," *Internationale Politik und Gesellschaft Online*. Available at http://fesportal.fes.de/pls/portal30/docs/folder/ipg/ipg1_2002/artjacobzone.htm. Accessed December 10, 2005.

[12] Jones BL, Nagin DS, and Roeder K. (2001), "A SAS Procedure Based on Mixture Models for Estimating Developmental Trajectories," *Soc. Methods and Research*, 29, 374-393.

[13] Kinsella K and Velkoff V. (2001), "An Aging World: 2001," U.S. Census Bureau, Washington, DC: U.S. Government Printing Office, 2001, series P95/01-1.

[14] Kunkel S and Applebaum R. (1992), "Estimating the Prevalence of Long-term Disability for an Aging Society," *Journal of Gerontology*, 47, S253-260.

[15] Levit K, Smith C, Cowan C, Lazenby H, Sensenig A, Catlin A. (2003), "Trends in U.S. Health Care Spending," *Health Affairs*, 22, 154-64.

[16] Little RJA and Rubin DB. (1987), *Statistical Analysis with Missing Data.* J. Wiley & Sons, New York.

[17] Manton K. (1989), "Epidemiological, Demographic, and Social Correlates of Disability Among the Elderly," *Milbank Quarterly*, 67, Supplement 2, Part 1, 13-58.

[18] Manton K, Corder L, Stallard E. (1997), "Chronic Disability Trends in Elderly United States Populations: 1982-1994," *PNAS*, 94, 2593-2598.

[19] Manton K, and Gu X. (2001), "Changes in the Prevalance of Chronic Disability in the United States Black and Non-black Population Above Age 65 from 1982 to 1999," *PNAS*, 98, 6354-6359.

[20] Manton KG, Stallard E, and Woodbury MA. (1991), "A Multivariate Event History Model Based Upon Fuzzy States: Estimation from Longitudinal Surveys with Informative Nonresponse," *Journal of Official Statistics* 7, 261-293.

[21] Manton KG and Woodbury MA. (1991), "Grade of Membership Generalizations and Aging Research," *Experimental Aging Research*, 17, 217-226.

[22] Manton KG, Woodbury MA, and Tolley HD. (1994), *Statistical Applications Using Fuzzy Sets,* J. Wiley & Sons, New York.

[23] Mathers C. (1998), "International trends in health expectancies: do they provide evidence for expansion or compression of morbidity?", *Compression of Morbidity Workshop Papers*, [Australian] Department of Health and Aged Care, Occassional Papers Series No. 4. 33-56.

[24] McLachlan G and Peel D. (2000), *Finite Mixture Models*, J. Wiley & Sons, New York.

[25] Meyer MH. (1994), "Gender, Race, and the Distribution of Social Assistance: Medicaid Use Among the Frail Elderly," *Gender & Society*, 8, 8-28.

[26] Nagin DS. (2005), *Group-Based Modeling of Development*. Harvard University Press. Cambridge.

[27] Nagin DS, Farrington DP, and Moffitt TE. (1995), "Life-Course Trajectories of Different Types of Offenders," *Criminology*, 33, 111-139.

[28] Nagin DS and Land KC. (1993), "Age, Criminal Careers, and Population Heterogeniety: Specification and Estimation of a Nonparametric, Mixed Poisson Model," *Criminology*, 31, 327-362.

[29] Nagin DS, Pagani L, Tremblay RE, and Vitaro F. (2003), "Life Course Turning Points: The Effect of Grade Retention on Physical Aggression," *Developmental Psychopathology*, 15, 343-361.

[30] Nagin DS, Pogarsky G, Farrington DP. (1997), "Adolescent Mothers and the Criminal Behavior of Their Children," *Law & Society Review*, 31, 137-162.

[31] Nagin DS and Tremblay RE. (1999), "Trajectories of Boys' Physical Agression, Opposition, and Hyperactivity on the Path to Physically Violent and Nonviolent Juvenile Delinquency," *Child Development*, 70, 1181-1196.

[32] Nagin DS and Tremblay RE. (2001), "Analyzing Developmental Trajectories of Distinct but Related Behaviors: A Group-Based Method," *Psychological Methods*, 6, 18-34.

[33] Nagin DS and Tremblay RE. (2001), "Parental and Early Childhood Predictors of Persistent Physical Aggression in Boys from Kindergarten to High School," *Archives of General Psychiatry*, 58, 389-394.

[34] Olshansky SJ, Carnes BA, and Cassell C. (1990), "In Search of Methuselah: Estimating the Upper Limits to Human Longevity," *Science*, 250, 634-640.

[35] Olshansky SJ, Rudberg MA, Carnes BA, Cassel VK, and Brody JA. (1991). "Trading Off Longer Life for Worsening Health: The Expansion of Morbidity Hypothesis." *Journal of Aging Health*, 3, 194-216.

[36] Reynolds SL, Saito Y, and Crimmins EM. (2005), "The Impact of Obesity on Active Life Expectancy in Older American Men and Women," *The Gerontologist*, 45, 438-444.

[37] Rockwood K. (2005), "What would make a definition of frailty successful?" *Age and Aging*, 34, 432-434.

[38] Romeu Gordo L. (2005), "Compression of Morbidity and the Labor Supply of Older People," Submitted.

[39] Romoren TI and Blekeseane M. (2003), "Trajectories of Disability Among the Oldest Old," *Journal of Aging and Public Health*, 15, 548-566.

[40] Rubin DB. (1987), *Multiple Imputation for Nonresponse in Surveys*. J. Wiley & Sons, New York.

[41] Rubin DB. (1996), "Multiple Imputation After 18+ Years," *Journal of the American Statistical Association*, 91, 473-489.

[42] Stallard E. (in preparation), "Trajectories of Disability and Mortality Among the U.S. Elderly Population: Evidence from the 1984-1999 NLTCS."

[43] Trupin L, Rice DP, and Max W. (1995), "Medical Expenditures for People With Disabilities in the United States, 1987," Washington: DC: US Dept of Education, National Institute on Disability and Rehabilation Research.

[44] United Nations. (2002), "Report of the Second World Assembly on Aging," Madrid, Spain: United Nations, April 8-12, 2002.

[45] U.S. Census Bureau. International database.Table 094. Midyear population, by age and sex. Available at http://www.census.gov/population/www/projections/natdet-D1A.html.

[46] White T. (Working paper), [NLTCS] Exploratory Data Analysis – Condensed Report.