A microsimulation framework for modelling AD

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Key limitations in previous models

- Cohort simulation
  – Tracking of individual characteristics not possible
- Artificial stratification into states
  – Disease progression is continuous
- Based on cognitive function only
  – ADLs are more important cost drivers

Individual patient simulation

- Microsimulation rather than simulating cohorts of patients
- Tracking individual characteristics
  - Representing a diverse patient group at baseline
  - Incorporating memory of previous events
- Results still presented as means from a large sample
  - No robust estimates of individual progression

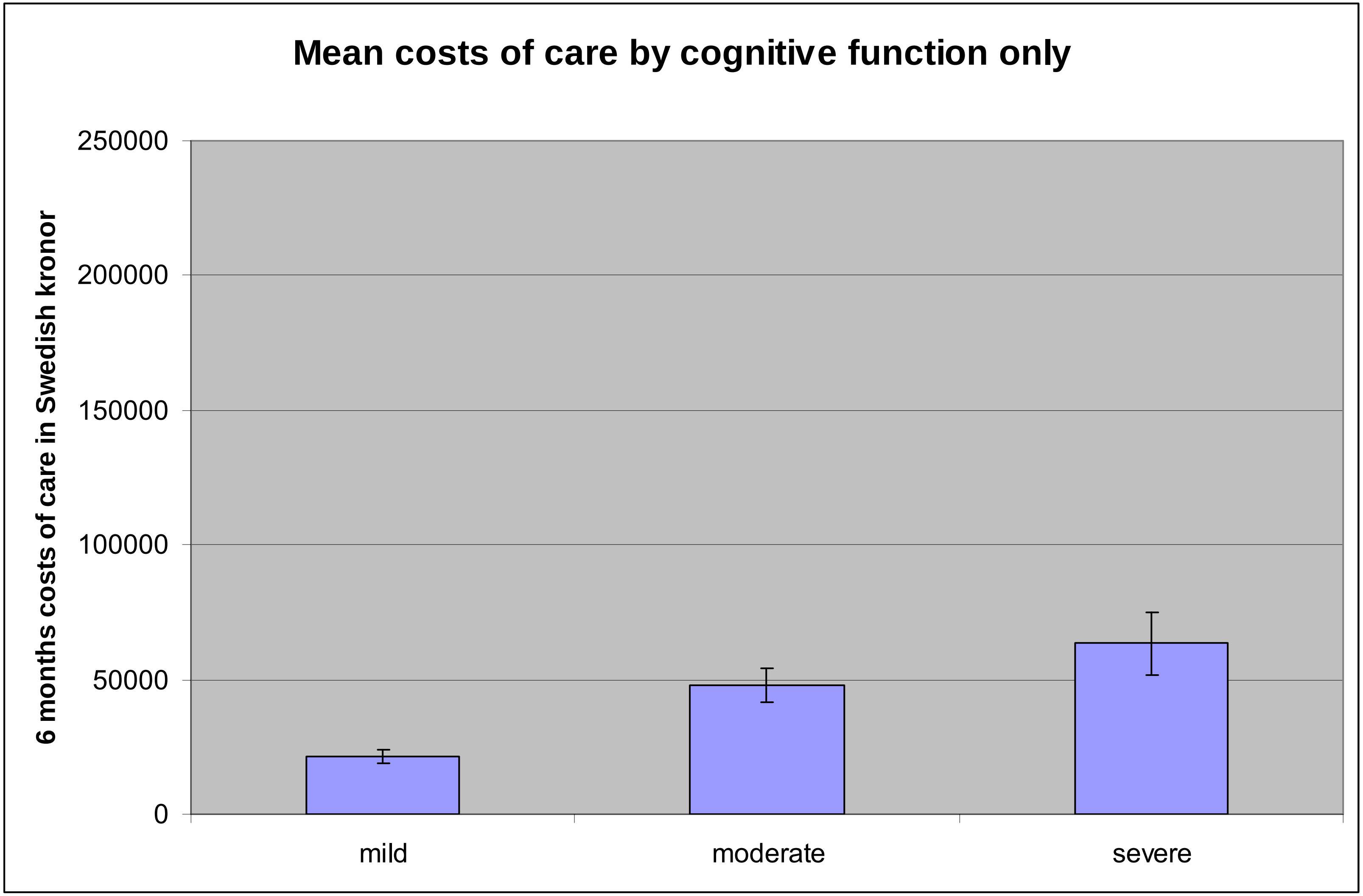
Avoiding state stratification

- What is the appropriate level of detail?
  - Only as sensitive as the disease indicators
    - ADAS-cog (0-70)
    - MMSE (0-30)
  - Should translate into relevant differences in outcomes
    - Uncertainty in data estimates
- Conclusion: choice should be guided by the data available

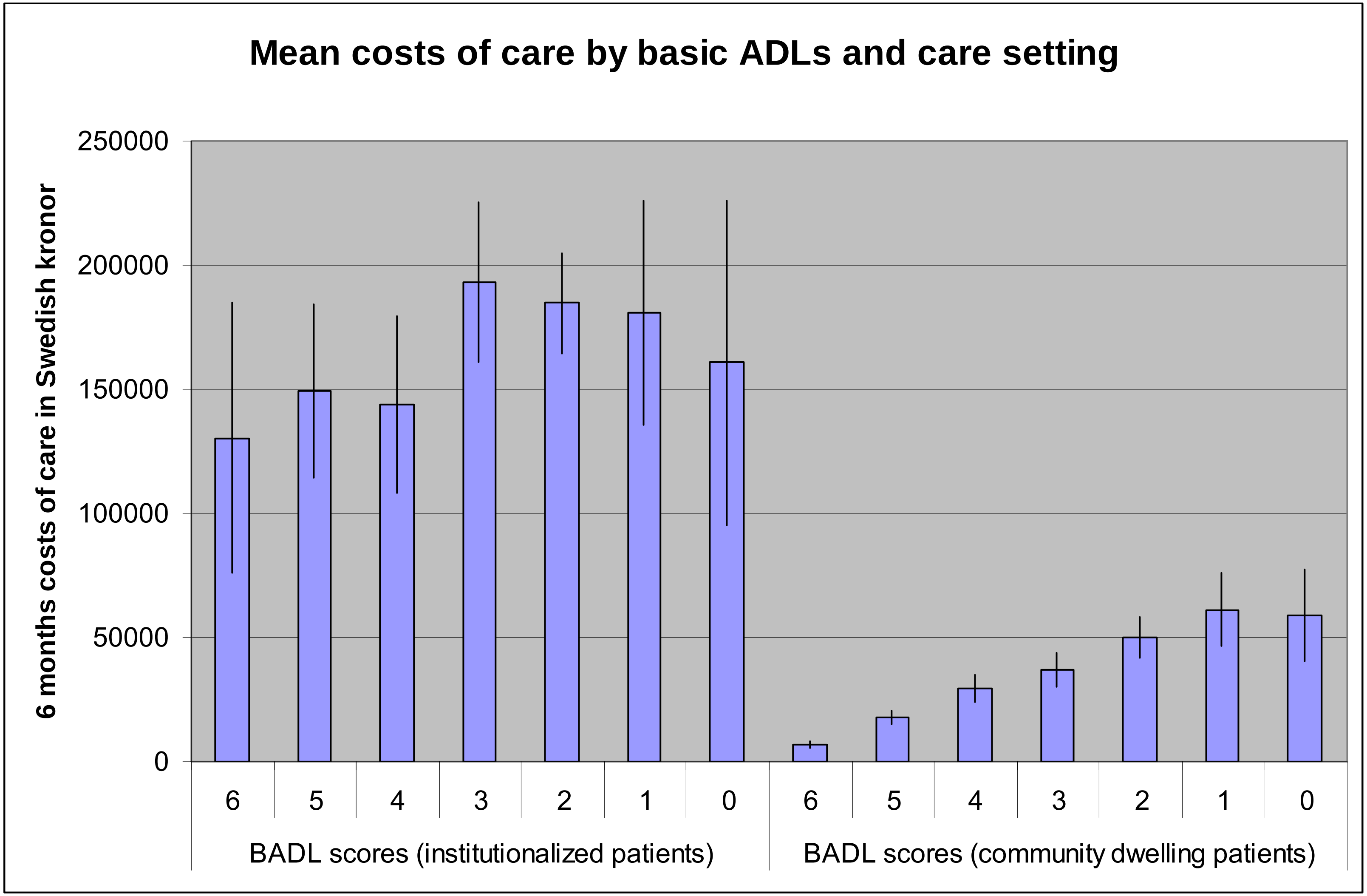
Including multiple indicators

- Avoiding unconvincing direct linkage between outcomes and cognitive function
- What disease indicators should be included?
  - Should include all indicators adding to the precision of outcomes
- Potential determinants of costs of care
  - ADL-ability
  - Care setting
  - Behavioural disturbances
- Conclusion: choice should be guided by the data available

Costs of care in a Swedish sample



Costs of care in a Swedish sample…



Proposed microsimulation framework

Summary of objectives for model

- Microsimulation
  - Diverse patient cohort at baseline
  - Track individual characteristics over time
- Sensitive disease indicators
  - No artificial states
  - Sensitive enough to explain relevant differences in outcome
- Multiple disease indicators
  - Cognitive function not sufficient
  - ADL-ability, dependency, care setting and behavioural disturbances important determinants of outcome

Baseline patient characteristics

- A patient with baseline characteristics is defined
  - Age
  - Sex
  - Duration of illness
  - Baseline ADAS-cog
- Random draw from sample distributions
  - Distributions representing the eligible population
  - Narrowed down for sub group analysis

Cognitive progression

- Baseline characteristics are used to predict disease progression in the next time period
- Cognitive function is predicted using a regression function
  - $\text{ADAS-cog}_t = \beta_1 X_{1t} + \beta_2 X_{2t} + \beta_3 X_{3t-1} + \ldots + \varepsilon_t$
  - Regression function estimated from longitudinal data on patients in clinical practice
  - Wide potential of predictors
    - Previous ADAS-cog level
    - Previous ADAS-cog progression
    - Age
    - Education level
    - etc.

ADL-ability and other disease indicators

- Similarly, cognitive function and other patient characteristics in each time period are used to predict ADL-ability and other disease indicators
  - $ADL_t = \beta_1 X_{1t} + \beta_2 X_{2t} + \beta_3 X_{3t-1} + \ldots + \varepsilon_t$
  - $NPI_t = \beta_1 X_{1t} + \beta_2 X_{2t} + \beta_3 X_{3t-1} + \ldots + \varepsilon_t$
- Performed over time, a complete disease trajectory of the patient is simulated
- Mortality is modelled either dependent or independent of disease indicators

Care setting and outcomes

- The probability of institutionalization is estimated in each time period
  - $P(\text{Instit})_t = \beta_1 X_{1t} + \beta_2 X_{2t} + \beta_3 X_{3t-1} + \ldots + \varepsilon_t$
  - Determining the care setting of the patient over time
- The disease indicators, care setting and other patient characteristics are translated into the outcomes of interest
  - Quality of life
  - Caregiver burden
  - Resource Utilization
  - Costs of care
- Resulting in an estimate of all outcomes over the simulation period

Multiple individual patient simulations

- Multiple simulations are performed each time defining a new patient
  – Each simulation includes randomization of patient characteristics at baseline
- All prediction functions include a random component
  – Corresponding to the uncertainty in prediction function estimates
- Estimates of mean outcomes and confidence intervals for all simulations are calculated

Economic evaluation of treatment

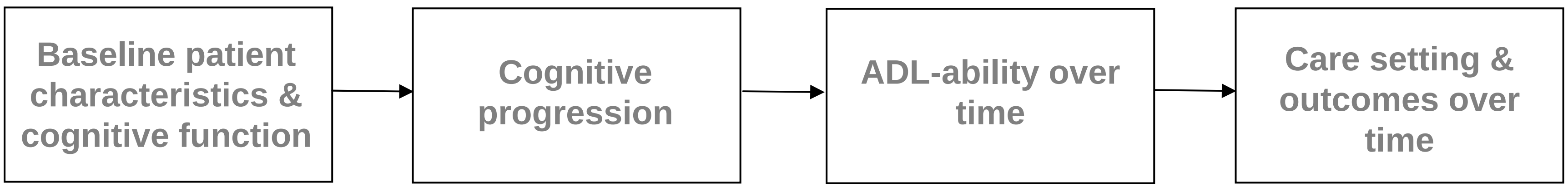
- Multiple microsimulations are performed in pairs comparing a control patient and an initially identical patient on treatment
  - Also, random component of prediction functions equal within pairs
- Treatment is added in one or several prediction functions resulting in different outcomes within the pairs
- Incremental cost effectiveness is estimated based on differences between multiple simulation pairs

Data need for prediction functions

- Longitudinal data on disease indicators
  - For estimating prediction function of disease progression
- Cross-sectional data on outcomes
  - Linking to relevant disease indicators
- RCT data on treatment effect
  - Generalizable to clinical practice
  - Long term effect

Model summary

- Multiple nested prediction functions are used to depict disease progression over time and relevant outcomes
  - Derived from observational data



- Multiple simulations are performed each time defining a new patient
- Pairs of treated patients and controls are simulated estimating the consequences of treatment over time
  - Treatment effect from RCT

Benefits of microsimulation

- Simulates individual patients rather than groups (cohorts) of patients
  - Individual characteristics and memory
- Avoids artificial classification of patients into states
- Possible to incorporate multiple disease indicators
  - Cognitive deterioration
  - ADL-ability
  - Behavioural disturbances
- Somewhat more complex programming and requires more computing power than cohort simulations