Health 2011 Survey: An overview of the design, missing data and statistical analyses examples

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Outline

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- 80 health center districts (HCD) including
    - 15 largest towns with probability 1 and
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- Oversampling of people aged 80 and older using double inclusion probabilities.
- Total sample size was 9,922.

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Mini-Finland Resurvey data

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  - Sample was based on a complex sampling design similar to the Health 2000 sample, and it represented the population
  - Sample size 8,000 and participation rate 90 %

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- In Health 2000 Survey, 1,278 participants of Mini-Finland Survey, who lived in **9 towns** in 2000, were invited

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- In Health 2000 Survey, 1,278 participants of Mini-Finland Survey, who lived in **9 towns** in 2000, were invited
- Does not represents population due to **left truncation**
    - We do not know who were the members of the baseline sample, who would have
        - moved to (or stayed in) one of the 9 towns between 1978-80 and 2000, and
        - not died
    - This would require further investigations but could be done

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Missing data in Health 2000 Survey

- Participation rates in age group 30 years and above:
  - Home interview 89 %
  - Health examination 85 %
  - Any part of the survey 93 %

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- Participation rates in the Mini-Finland Resurvey:
  - Health examination 80 %
  - Any part of the survey 89 %

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Handling of missing data in the Health 2000 Survey

- **Post-stratification weights** were calibrated by Statistics Finland
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    All respondents any section of the survey or separate non-response interviews or inquiries $n = 9,125$

    Respondents' union any section of the survey $n = 8,617$

    Nutrition several sections and especially in the nutrition inquiry $n = 6,794$

    Intersection interviews or corresponding inquiries and in most clinical sections and inquiries $n = 6,774$

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- **Multiple imputation** has also been applied in several analyses

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Options for analyses

- Most analyses were **design-based analyses** based on
  - generalized estimating equations and
  - post-stratification weights
- Some **model-based** analyses using hierarchical models have also been conducted

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Sampling desing of The Health 2011 Survey

- **Health 2000 Survey** data (aged 29 or older)
  - The Health 2000 sampling design (strata and PSUs)
  - Repeated measurements on the members of the Health 2000 sample
  - 7,964 were invited in the age group 30 years or older
  - 59 % participated in the health examination
  - 73 % participated in any part of the survey

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- **Mini-Finland Resurvey** data (aged 61 years or older)
  - 922 were invited and 81 % participated

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- **Mini-Finland Resurvey** data (aged 61 years or older)
  - 922 were invited and 81 % participated
- **New sample** of 1,994 young adults (aged 18 to 28)
  - Same geographical areas as in 2000
    Amalgamations of municipalities/HCDs were handled using GIS coordinates[1] in some cases
  - 415 were invited in the health examination and 52 % participated
  - 1,579 were sent a questionnaire and 40 % participated

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Representativeness of the original Health 2000 sample

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[2] www.thl.fi/maamu

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- The same selection mechanisms, which apply to the population in 2000, also apply to the sample:
  - Mortality, emigration and migration in Finland, but
  - not immigration after 2000 (there is a separate survey[2] on the immigrants)

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- We consider that the original sample still provides representative results in cross-sectional analyses in 2011

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Substudies

Additional protocols were applied on randomly selected subgroups.

Table : Sample sizes in different age and substudy groups.

Age group	Sample	Courage	Exercise	Courage and Exercise
18-28	1994	415	415	415
29-49	3306	884	2088	0
50-74	3840	1885	1908	0
75-79	384	181	193	5
80+	605	568	294	294
All	10129	3933	4898	714

Clustering

Clustering effects can emerge from various sources, e.g.

- Original Health 2000 sampling design:
  - Stratification: largest towns (15) and university hospital district (5)
  - Primary sampling units (PSUs): health center districts (HCDs)
- Municipality vs. HCD
- Distances (spatial analyses using GIS coordinates)

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this can depend on the variable of interest.

For example, blood pressure appeared to have strong clustering effects in Health 2000, but BMI did not.

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Clustering in statistical analyses

Design-based methods Traditional methods to handle clustering, usually methods based on linearization and estimating equations (GEE)

Model-based methods Clustering has been handled by e.g. mixed effects (hierarchical) models

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Some differences exist:

- Model-based methods can be useful when having several levels of hierarchy $\Rightarrow$ variance on different levels can be compared.
- Model-based methods can be more efficient but also more sensitive to model assumptions.

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- Model-based methods can be more efficient but also more sensitive to model assumptions.
- Design-based methods can effectively handle only one level of clustering. In **Health 2011 repeated measurements** analyses it is advisable to **choose the individual level** as the primary sampling unit (PSU).

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Similarities and differences of hierarchical models and GEE

- Linear mixed effects models produce similar point estimates as GEE.

[3] E.g. http://courses.washington.edu/b571/lectures/set5.pdf (Johnson and Kotz, 1970).

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- In non-linear models the point estimates generally differ [3]!
    - Generalized linear mixed effects (GLME) models (e.g. logistic regression analyses with random effects) estimate **conditional effects**.
    - GEE estimates **marginal effects**, which are attenuated towards zero (towards OR=1).

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  Marginal effect of a covariate is the **average** effect of a covariate in the population.

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  Marginal effect of a covariate is the **average** effect of a covariate in the population.

  Conditional effect is the effect of a covariate for a particular **individual** (or a cluster of observations cf. the hierarchical model).

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Conditional **OR = 2.7**

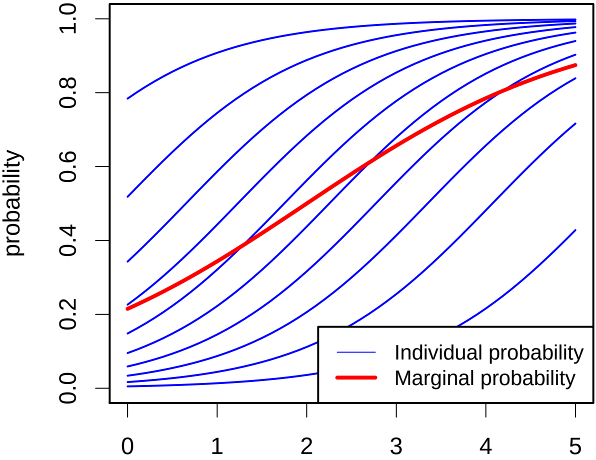
Marginal **OR = 1.9**

Example by Jon Wakefield (2009)[a]

- Note that e.g. near probability 1 the individual curves of those individuals, who are in higher risk, bend. (*"ceiling effect"*)
- On the other hand the curves of the individuals with low risk are much lower.

⇒ The average of the curves (marginal effect) also bends.

⇒ Covariate X has a **smaller marginal effect** on the outcome



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Participation rates

Table : Participation rates in different age and substudy groups. HES refers to health examination.

	Age groups					
	18-28	29-49	50-74	75-79	80+	All
Total sample	1994	3306	3840	384	605	10129
Participation (%)	**42**	68	**79**	74	59	67
HES sample	415	3306	3840	384	605	8550
HES participation (%)	**29**	50	**66**	61	50	57
Courage sample	415	884	1885	181	568	3933
Courage participation (%)	52	67	78	76	58	70
Physical exercise sample	415	2088	1908	193	294	4898
Physical exercise participation (%)	52	68	80	73	59	71

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Nonresponse in 2000 vs. 2011

Table : Distribution of the participation of the invitees in the Health 2011 Resurvey. The Health 2000 Survey (2000) vs. in the Health 2011 Resurvey (2011).

	Participated in 2011 (%)		
Participated in 2000 (%)	Yes	No	Sum
Yes	69	20	88
No	4	8	12
Sum	73	27	100

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Factors which are often associated with nonresponse

- Low social activity, low education

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Missing completely at random (MCAR) Nonresponse can be ignored in all analyses, only statistical power is lower.
Usually unrealistic.

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Missing at random (MAR) Probability of nonresponse depends only on observed data. Effects of nonresponse can be corrected.

Missing not at random (MNAR) Probability of nonresponse depends also on **un**observed data. **Untestable assumptions** are needed.

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How to handle effects of missing data?

Weighting Probability of participation varies individually.
Each participant is given a weight indicating the **number of similar sample members**, which the participant represents:

- Ideally, participation rate 100% $\Rightarrow$ weight equals 1.

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  $\Rightarrow$ **unstable results**.

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Other methods E.g. data augmentation using Bayesian inference can allow flexible incorporation of prior/expert information on missing data mechanisms.

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Weights

Separate weights for each wave:

- **The Health 2000 Survey** Use the original Health 2000 poststratification weights.

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  Participants in 2000 Inverse probability weights (IPW) method based on logistic regression model. Predictors based on observed information in 2000, e.g.
    - risk factors of diseases and disabilities
    - various lifestyle factors (social activity etc.)

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  Nonparticipants in 2000 A small number of individuals without observed baseline information

  $\Rightarrow$ Poststratification weights based on age groups.

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Resulting weights were further calibrated so that they match the population sizes in different areas.

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Different definitions of weights

- Different definitions of participation (DoP) in 2011, e.g.
  1. any part of the survey
  2. the health examination (HES)
  3. the Courage subsample
  4. the physical exercise subsample (4 different criteria)
  5. (even more, e.g. food frequency questionnaire?)

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  - The DoP should match one-to-one to the participation to the analysis variables.
    E.g. in analyses involving HES variables, the HES weights are the best choice.

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Different definitions of weights

- Different definitions of participation (DoP) in 2011, e.g.
  1. any part of the survey
  2. the health examination (HES)
  3. the Courage subsample
  4. the physical exercise subsample (4 different criteria)
  5. (even more, e.g. food frequency questionnaire?)
- **How to choose** the correct weight for my analysis?
  - The DoP should match one-to-one to the participation to the analysis variables.
    E.g. in analyses involving HES variables, the HES weights are the best choice.
  - Can be problematic, if the variables were collected at different sections of the survey (item nonresponse).

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Weights

Pros:

- weights are **easy to use** in analyses
- weights can work well in case of **unit-nonresponse** (no additional item-nonresponse)

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Pros:

- weights are **easy to use** in analyses
- weights can work well in case of **unit-nonresponse** (no additional item-nonresponse)

Cons:

- There are generally **considerable amounts of item-nonresponse** thus participation indicator of the weight variable often differ from observed analysis variable
  $\Rightarrow$ weights do not work optimally
- item-nonresponse in any analysis variable drops the individual out of the analysis
  $\Rightarrow$ **loss of information**

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Example on using different weights on 3 register variables

Table : Comparison of prevalences (%) in age group 30 years and older.

Variable	Clustering	Missing data	Prevalence	SE
Disability pension	SRS	None	8.8	0.4
	Complex	Baseline weights	8.9	0.4
	Complex	Resurvey weights	9.4	0.4
	Complex	True prevalence	9.5	0.4
Hospitalization	SRS	None	16.6	0.5
	Complex	Baseline weights	16.7	0.5
	Complex	Resurvey weights	17.3	0.6
	Complex	True prevalence	17.8	0.5
Reimbursement	SRS	None	40.2	0.7
	Complex	Baseline weights	40.6	0.8
	Complex	Resurvey weights	42.0	0.8
	Complex	True prevalence	42.1	0.6

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Multiple imputation (MI)

- MI in short:
  1. Create **several copies** of the original data set
  2. Impute missing values using **predictive distributions** based on the associations and variable values of the observed data
     - Various methods exist, some are available in general-purpose statistical software
  3. **Analyze separately** the copies using standard statistical methods
  4. **Join** the results

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[4] ftp.cdc.gov/pub/Health_Statistics/NCHS/nhanes/nhanes3/7a/doc/mimodels.pdf

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  4. **Join** the results
- For example, MI has been used in NHANES [4]
  - MI based on multivariate **linear** mixed effects models
  - 67 health examination and lifestyle variables were imputed
  - MI separately in 9 age groups
  - clustering in the data was accounted for
  - R package *pan* by Schafer

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Multiple imputation (MI)

- Pros:
  - Item-nonresponse can be better accounted for by replacing missing values with randomly drawn values from a predictive distribution
  - MI is generally more efficient than weighting
  - Imputation model does not have to be the same as the analysis model

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- Cons:
  - Difficult to produce one MI data set for the whole Health 2011 survey
  - More laborious as the imputation model should be tuned separately for most analyses:
    - variable selection, level of measurement, interactions, nonlinearities, heteroscedasticity etc.

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The imputation models and methods must be documented in great detail in the publications!

This allows other researchers to apply the same imputation model (possibly with some additional variables etc..)

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Example: Weighting vs. MI

Table : Kendall correlations of body mass index (BMI), systolic blood pressure (SBP) and walking speed (WSp).

	BMI 2000	BMI 2011	SBP 2000	SBP 2011	WSp 2000	WSp 2011	N
BMI 2000	1.00	0.65	0.24	0.21	-0.12	-0.18	7,585
BMI 2011	0.65	1.00	0.17	0.18	-0.11	-0.15	4,253
SBP 2000	0.24	0.17	1.00	0.40	-0.10	-0.20	5,561
SBP 2011	0.21	0.18	0.40	1.00	-0.02	-0.13	4,239
WSp 2000	-0.12	-0.11	-0.10	-0.02	1.00	0.43	1,833
WSp 2011	-0.18	-0.15	-0.20	-0.13	0.43	1.00	4,191

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Example: Estimating BMI means using weighting vs. MI

Table : Comparison of different methods to handle missing data in the estimation of the body mass index (BMI) mean.

Clustering	Missing data	Mean	SE
SRS	None	27.06	0.08
Complex	Baseline weights	27.16	0.08
Complex	Resurvey weights[5]	27.03	0.08
Complex	Resurvey HES weights[6]	26.47	0.13
Complex	Baseline weights; Multiple imputation	26.84	0.08

[5] Participation in any part of survey

[6] Participation in health examination

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Example: Estimating systolic blood pressure means using weighting vs. MI

Table : Comparison of different methods to handle missing data in the estimation of the systolic blood pressure (SBP) mean.

Clustering	Missing data	Mean	SE
SRS	None	131.21	0.28
Complex	Baseline weights	131.77	0.32
Complex	Resurvey weights[7]	131.04	0.32
Complex	Resurvey HES weights[8]	128.36	0.43
Complex	Baseline weights; Multiple imputation	129.04	0.33

[7] Participation in any part of survey
[8] Participation in health examination

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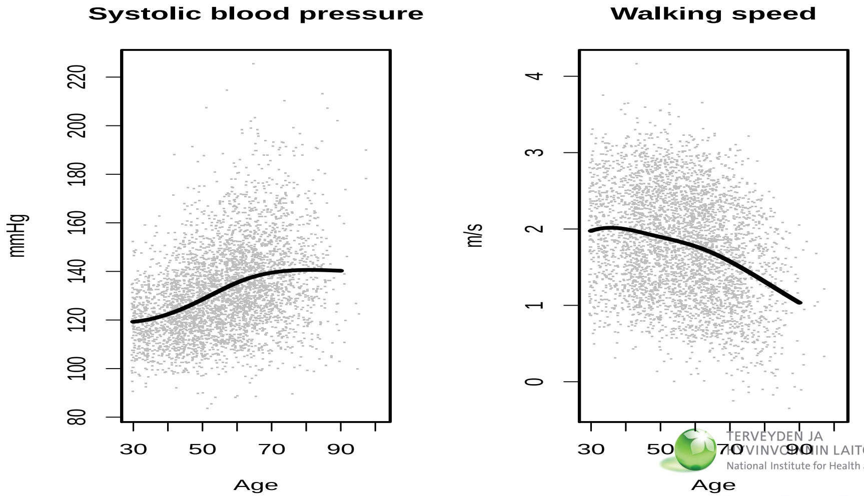
Assumptions in MI

Associations of continuous variables are not always linear and errors terms not homoscedastic and symmetric.



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Cross-sectional analyses

- "What was the population distribution and/or the associations between variables?"
- What needs to be accounted for in the analyses?
  - Analyses for Mini-Finland Survey or the Health 2000 Survey:
    - Clustering in the data (strata and PSUs, especially the 80 health center districts)
    - Missing data handled using the weights
  - Analyses for Health 2011:
    - More options in handling clustering effects (health center districts in 2000 vs. 2011) due to
      environmental effects (which can influence the outcome after migration) or
      selection effects due to migration
    - **More** missing data

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Longitudinal analyses: Changes in population distributions from (1980 to) 2000 to 2011

- "What was the difference of means between 2000 and 2011 in age group X?"
- Repeated measurements design – standard methodology
  - Mini-Finland and Health 2000 were independent samples
    - At most **one** measurement per individual in Mini-Finland data

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- Example: A simple regression model could be defined as
  `MODEL Y = AGEGROUP + TIME`
  - Outcome: `Y`
  - Categorical covariates: `AGEGROUP` is age of study subject at **measurement time**, and measurement is `TIME` (note that subjects are 11 years older at the end of follow-up!)
  - The term `TIME` represent the overall change.

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Longitudinal analyses: Individual changes

- "What has been the average change of variable X during the follow-up?"
- Repeated measurements design – standard methodology, e.g. hierarchical models

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  - The term `TIME` represent the average individual change between 2000 and 2011
- **But** informative right-censoring can complicate the interpretation of the results
  - Mortality at older age can influence the results if the outcome is associated with risk of death
  - Individuals with weak condition are more likely to die, but those of them, who do not die, can have more positive progression of the outcome
    $\Rightarrow$ Trend estimates can be too positive

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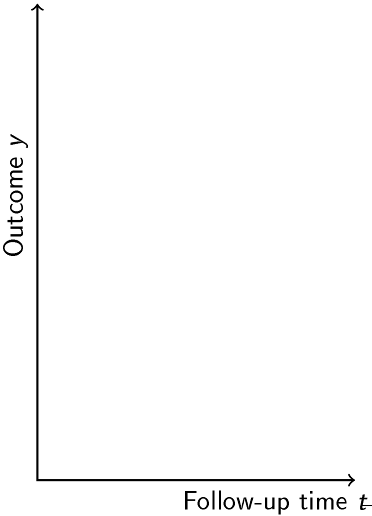
Example on informative right-censoring



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- We want to estimate the average speed of change

[a] Stenholm, Härkänen et al. (2012)

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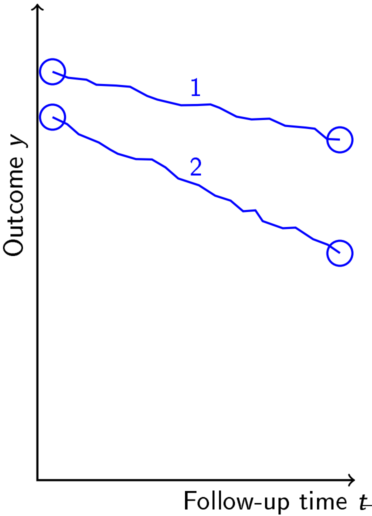

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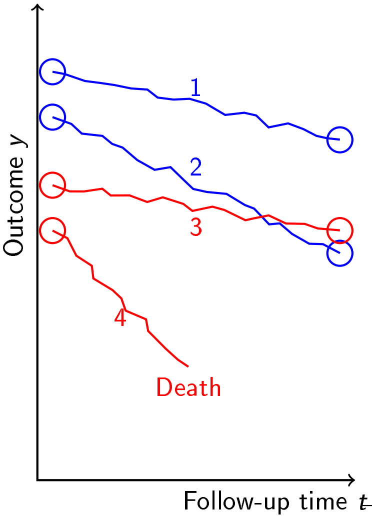

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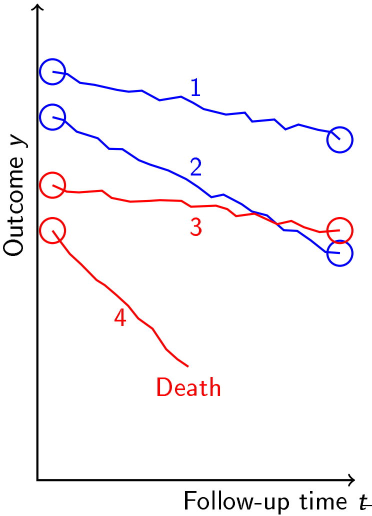

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  ⇒ No problems in estimating the speed of change
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- There is a **selection process**
  ⇒ Problems in estimating the speed of change – speed of change is underestimated!

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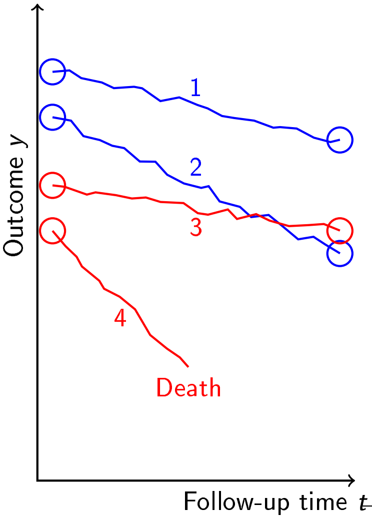

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- There is a **selection process**
  $\Rightarrow$ Problems in estimating the speed of change – speed of change is underestimated!
- Possible solution is to use a **selection model**[a]

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Summary

- Nonresponse has increased considerably from 2000 to 2011, and its effects should be corrected for
  - The Health 2011 organization will provide IPW weights to handle missing data
  - Researchers are encouraged to use better methods such as multiple imputation (MI) or data augmentation

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  - The Health 2011 organization will provide IPW weights to handle missing data
  - Researchers are encouraged to use better methods such as multiple imputation (MI) or data augmentation
- Clustering needs to be accounted for, and in longitudinal studies the individual variation is likely to be most important
- Register-based follow-up
  - Important in handling missing data (of the Health 2011 Survey)
  - Important also in cohort analyses as outcome variables
  - Methodology for joint analysis of time-to-event data and repeated measurements is likely to be needed

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