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Long-term Changes in Handgrip Strength in Men and Women—Accounting the Effect of Right Censoring Due to Death

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Background. Age-related decline in muscle strength is among of the most important factors in the aging process leading to disability. This study examines age-related changes in handgrip strength through a 22-year follow-up in men and women. Because handgrip strength is associated with mortality, this study also accounts for the selection effect of right censoring by comparing the estimates of handgrip strength decline based either on only the handgrip strength data or on the data of both the handgrip strength and survival times.

Methods. Data are from 1,890 men and women aged 30 years or more at baseline participating in the population-based Mini-Finland Health Examination Survey (1978–1980) with repeated handgrip strength measurement in 2000–2001.

Results. In men aged 31–41 years, the annual decrease in handgrip strength was approximately 3.5 Newtons (N). After that, the decrease accelerated and stabilized around the age of 75 years, being approximately 7.3 N per year. In women, respectively, prior to 45 years, the annual decrease was approximately 2 N and after age 80 years approximately 4 N per year. The estimates for the handgrip strength decline were more pronounced when the right censoring due to death was accounted for, especially for persons aged 65 years and older.

Conclusions. Our work confirms that the right censoring, which depends on the outcome of interest, should be accounted for in analyses.

Key Words: Aging—Muscle strength—Mortality—Right censoring.

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AN escalating number of older people and associated increase in incidence of physical disability and need of help have increased scientific interest in the biology of aging. It is widely recognized that age-related decrease in muscle mass and especially muscle strength are among of the most important factors in the aging process leading to mobility problems, increased risk of falls, and disability in older persons (1–4). Cross-sectional studies have shown that muscle strength peaks between the second and third decade, remains relatively unchanged until the fourth or the fifth decade of life and there after declines (3,5–10).

Although cross-sectional studies have provided relatively comparable results about muscle strength distribution at various ages, they tend to underestimate the true changes seen in longitudinal studies. This is partly due to cohort effect and natural selection, which favors stronger individuals in older cohorts. To properly examine age-related trajectories in muscle strength, longitudinal studies are needed. However, today only few studies have reported changes in muscle strength over 10 years of follow-up. Rantanen and colleagues (11) and Metter and colleagues (10,12) reported significant changes in muscle strength over adult life span based on Honolulu Heart Study and Baltimore Longitudinal Study on Aging, respectively. In addition, few smaller scale studies have examined changes in muscle strength with a relatively long follow-up (13–15), but participants were initially old (>65 years).

Because low muscle strength is strongly associated with mortality (16–19), stronger individuals survive and remain in the prospective studies. Thus, even the results based on longitudinal data may underestimate the true age-related muscle strength decline. To our knowledge, no previous studies have taken into account the effect of right censoring due to deaths when examining the age-related trajectories in muscle strength, although the problems related to the right censoring have been widely recognized, see for example (20,21). By using a Mini-Finland Survey with 22 years of follow-up, this study aimed to examine changes in handgrip strength with age in men and women and to account for the selection effect of right censoring by comparing the estimates of handgrip strength decline based either on only the handgrip strength data or on the data both the handgrip strength and survival times.

Materials and Methods

Study Population

The study is based on the population-based Mini-Finland Health Examination Survey, which was conducted in 1978–1980 with sample size 8,000 (22). Of the 7,217 participants, those who lived in one of the nine selected municipalities across the country were included in this study (n = 2,049). Baseline handgrip strength values were available from 1,890 participants aged 30 years or more, and they comprised the study population. Those participants still alive were invited to take part in the follow-up study carried out in conjunction with the Health 2000 Survey in 2000–2001 (23). Repeated handgrip strength measurement was obtained from 882 participants, whereas 369 deceased before follow-up measurement and 742 remained alive but did not have follow-up grip measured (of these 501, no longer lived in the selected cities and 241 were unwilling or unable to participate the follow-up measurements).

Mortality follow-up was continued until December 31, 2008, and 530 of the participants deceased after the follow-up measurement took place. The follow-up information on all-cause mortality was obtained from the Statistics Finland.

Details of the design and implementation of the Mini-Finland Health Examination Survey (22,24) as well as the Health 2000 Survey (23) have been reported elsewhere. At the reexamination survey, all participants signed a written informed consent, and the study was approved by the Ethical Committee for epidemiology and public health in the hospital district of Helsinki and Uusimaa in Finland. The baseline survey preceded current legislation on medical research, and participants were fully informed about the study.

Measurement of Handgrip Strength

At baseline, maximal handgrip strength was measured using a handheld dynamometer based on strain gage sensors (Bruel-Kjaer Type 1526; Denmark; [25]). The measurement was taken from both hands with the participant seated. Width of the handle was adjusted for the participant's hand size. There was a high correlation between the test–retest results (r = 0.91–0.93, n = 449; [25]). The best result of the dominant hand (same as in the follow-up measurement) was chosen for the analysis. Information about the measurement side was missing in 20 persons. In these cases, the best result of the stronger hand was used in the analysis.

At follow-up, maximal handgrip strength was measured using a handheld dynamometer based on strain gage sensors (Good Strength, IGS01; Metitur Oy, Jyväskylä, Finland). The measurement was taken with the dominant hand with the participant seated. If the two results differed more than 10%, a third attempt was conducted. The best result was chosen for the analysis. The reliability of the particular handgrip strength test, measured using the intraclass correlation coefficient (ICC) was shown to be excellent (intraclass correlation coefficient = 0.95, n = 265; [26]).

Table 1. Agreement Between Devices Used at Baseline and Follow-up Handgrip Strength Measures Among 46 Volunteers; Results Are Shown in Newtons

	Mean	*SD*
Baseline	359.5	108.1
Follow-up	359.0	108.4
Difference	0.5*	0.3
Intraclass correlation	0.96	

* Nonsignificant difference between values.

To examine the agreement of these two handgrip strength measurements, 46 volunteers performed both tests following previously described measurement protocols. Handgrip strength was measured first with baseline dynamometer and every other with follow-up dynamometer so that there was 5–10 minutes break between measures. Table 1 shows the results from the comparison. The agreement between best values of each handgrip strength measures was nearly perfect (intraclass correlation coefficient = 0.96) with no statistical significant difference in mean strength levels. Based on these results, it was feasible to calculate the absolute handgrip strength change between the baseline and follow-up measurements.

Baseline Characteristics

At baseline, information about the education, leisure time physical activity, work-related physical activity, smoking, alcohol consumption, and physical function was collected with interview. In addition, body weight and height were measured in light indoor clothing without shoes, and body mass index was defined as body weight divided by the square of height (kilograms per square meter). Furthermore, standardized clinical examinations were carried out by specially trained physicians who diagnosed chronic diseases on the basis of clinical findings, symptoms, disease histories, and related documentation using uniform criteria (22,27). Following chronic conditions were included in this study: coronary heart disease, other cardiovascular disease, hypertension, diabetes, asthma, osteoarthritis, chronic back syndrome (24), and chronic neck syndrome (27).

Statistical Analysis

Study population characteristics at baseline are reported as mean (*SD*) values for continuous variables and proportions for categorical variables. The selective right censoring was accounted for by applying a selection model by Diggle and Kenward (28). An individual was assumed to drop out from the follow-up at the time of death and the probability of death to depend on the grip strength, age, and gender. We applied the data augmentation method (29), Bayesian inference (30), and the OpenBUGS software (31) version 3.1.1. The details of the model are presented in the Appendix 1. The results were compared with an analogous model assuming no association between the grip strength and risk of death.

Table 2. Baseline Characteristics for Men and Women; The Mini-Finland Health Survey 1978–1980

	Men (n = 832)		Women (n = 1058)	
	n	Mean (*SD*)	*n*	Mean (*SD*)
Age (y)	832	47.1 (12.3)	1,058	49.4 (13.7)
BMI	832	25.7 (3.4)	1,057	25.2 (4.4)
	n	%	*n*	%
Education				
Higher (>12 y)	277	33.5	250	23.7
Intermediate (9–12 y)	129	15.6	212	20.1
Basic (<9 y)	421	50.9	594	56.3
Physical activity				
Regular exercise activity	215	25.8	199	18.8
Occasional exercise/ lifestyle activity	381	45.8	496	46.9
Sedentary	236	28.4	362	34.3
Work-related physical activity				
Light	392	58.0	514	67.3
Moderate	129	19.1	215	28.1
Strenuous	155	22.9	35	4.6
BMI (kg/m^2)				
<18.5	5	0.6	22	2.1
18.5–24.9	362	43.5	574	54.3
25–29.9	381	45.8	308	29.1
≥30	84	10.1	154	14.6
Alcohol use				
Not at all	186	22.4	491	46.4
Moderate	562	67.6	526	49.7
Heavy	83	10.0	41	3.9
Smoking				
Never	227	27.4	717	67.8
Former	281	33.9	151	14.3
Current	320	38.7	189	17.9
Coronary heart disease*	79	9.5	72	6.8
Other cardiovascular disease†	81	9.7	90	8.5
Hypertension	66	9.2	92	9.7
Diabetes	29	3.5	43	4.1
Asthma	16	1.9	30	2.8
Osteoarthritis‡	45	5.4	182	17.2
Chronic back syndrome	134	16.1	189	17.9
Chronic neck syndrome	64	7.7	129	12.2
Difficulties running 500 m	245	29.5	438	41.4
Difficulties walking 500 m	97	11.7	166	15.7

Notes: BMI = body mass index.

*Angina pectoris or myocardial infarction.

†Heart failure, peripheral artery disease, stroke, arrhythmia, valvular heart disease, or congenital heart disease.

‡Hip, knee, or hand osteoarthritis.

We reported both the annual changes in grip strength (drift) and the cumulative changes in grip strength over a time interval of 10 years (trajectory) defined as the sum of the corresponding 10 annual drifts. Since only few persons were 30 years old at the time of the baseline examination, the presentation of numerical results was based on the ages of 31, 41, 51, 61, 71, and 81 years.

Results

Baseline characteristics of study population are shown in Table 2. The mean age for men was 47.1 years and for women 49.4 years. The prevalence of chronic conditions was relatively low, and nearly half of the study population did not have any disease at baseline. Functional limitations were also rare: 11.7% of men and 15.7% of women reported difficulties in 500 m walking.

In men aged 31–41 years, the annual decrease (drift) in handgrip strength was approximately 3.5 N (Figure 1a). After that the decrease accelerated and stabilized around the age of 75 years being approximately 7.3 N per year. In women aged 31–45 years, the annual decrease was approximately 2 N and after age of 80 years approximately 4 N per year (Figure 1b). The credible intervals (CI) were wide due to the relatively small sample size in addition to the long time interval between the measurements, which hindered accurate estimation of the handgrip strength drift in a single age year.

At baseline, handgrip strength was equally high among men aged 31 and 41 years, whereas women aged 31 years had highest handgrip strength compared with other ages (Appendix Table 1, Figure 2a and 2b). Participants aged 51, 61, 71, and 81 years at baseline had always lower baseline handgrip strength than those aged 10 years younger. Handgrip strength declined in an accelerated manner in each age decade with more pronounced decrease in men than in women. The start and end points of the subsequent trajectories do not seem to match in both young and old age groups. Especially, in the younger ages, this could indicate that there were some differences between birth cohorts.

There were negative associations between the handgrip strength and the risk of death. The odds ratio for mortality with 100 N increase of the handgrip strength was 0.87 (95% CI 0.70–1.07) for men younger than 65 years, 0.78 (95% CI 0.67–0.91) for men at least 65 years old, and 0.65 (95% CI 0.43–0.93) for women younger than 65 years, and 0.82 (95% CI 0.65–1.00) for women at least 65 years old.

The right censoring due to death had virtually no effect on the estimates of handgrip strength on the drift or trajectory of handgrip strength before the age of 65 years (Figure 1). After that the effect of right censoring on the handgrip strength increased as the overall risk of death increased. For example, for men aged 71 (and 81) years, the 10-year decline appeared to be 5.2 N (6.6 N) larger and in women about 3.8 N (5.2 N), when the right censoring was accounted for in estimating the drift parameters (Figure 2, Appendix Table 1).

Discussion

This work appears to be first in the field of muscle strength studies, in which the effect of right censoring due to death has been accounted for when estimating age-related changes in muscle strength. It was found that the right censoring had the largest effect on the handgrip strength drift and trajectory results on people aged 65 years and older. The main reason is that most deaths occurred after that age. Without taking into account the deaths, the pronounced handgrip strength decline in the older population would be underestimated. If the sample size had been larger and the

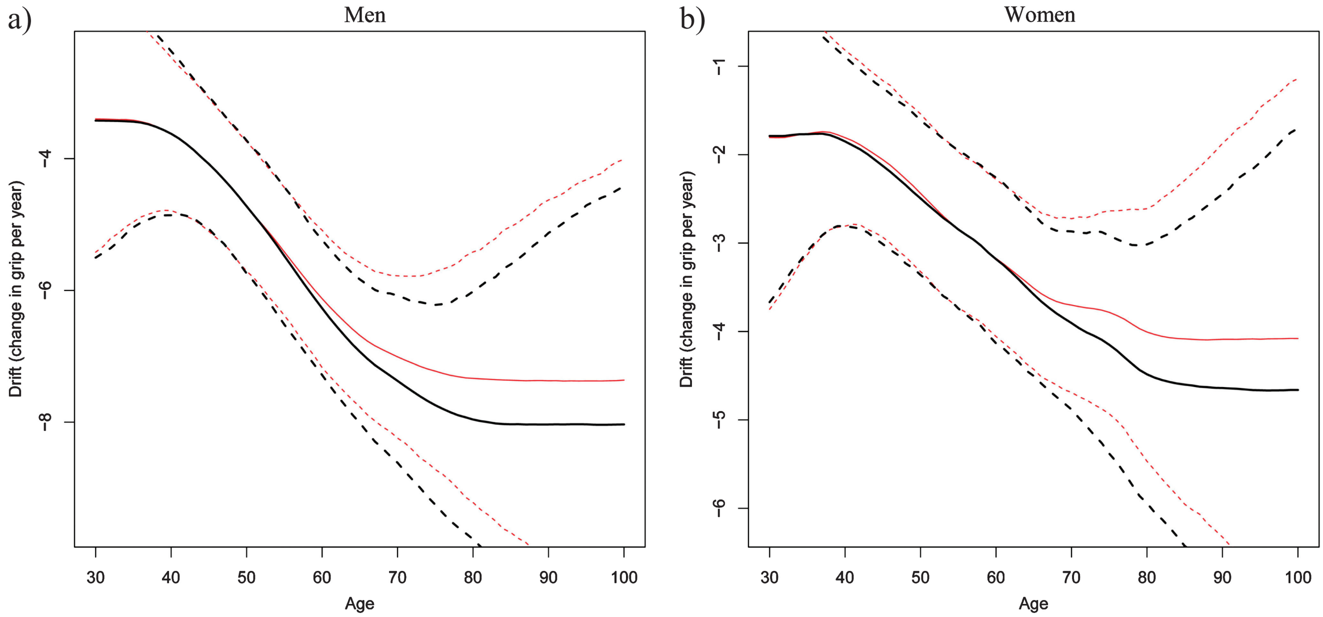

Figure 1. Posterior expectations of the age-related annual change (drift) in handgrip strength according to crude values (red line) and values in which the effect of right censoring due to deaths was accounted for (black line) and their corresponding 95% credible intervals (dashed lines). The Mini-Finland Health Survey 1978–1980, The Health 2000 Survey 2000–2001, and Mortality Data 1978–2008. (**a**) Men and (**b**) women.

measurement points had been closer to each others, the effect of right censoring could have been even more significant.

The results of this study suggest that handgrip strength starts to decline already at age of 30 years with more accelerated decline after 40 years of age. This is somewhat earlier compared with findings in other studies (3,5,10,12). Based on this study, the rate of handgrip strength decline stabilizes around the age of 75 years in men and 80 years in women but is still greater than in preceding years. Previous studies have also reported accelerated decline in muscle strength with aging (5,10–12,32), but not many studies have been able to follow-up persons until the age of 80 or 90 years. Based on Baltimore Longitudinal Study on Aging study, Metter and colleagues (10) also reported increases in muscle strength decline even among the oldest old.

Despite extensive investigations, the mechanisms leading to muscle strength decline with aging are not completely understood. In addition to age-related changes in muscle mass, several other factors including decreasing physical activity with age, nutritional deficiencies, impairments in

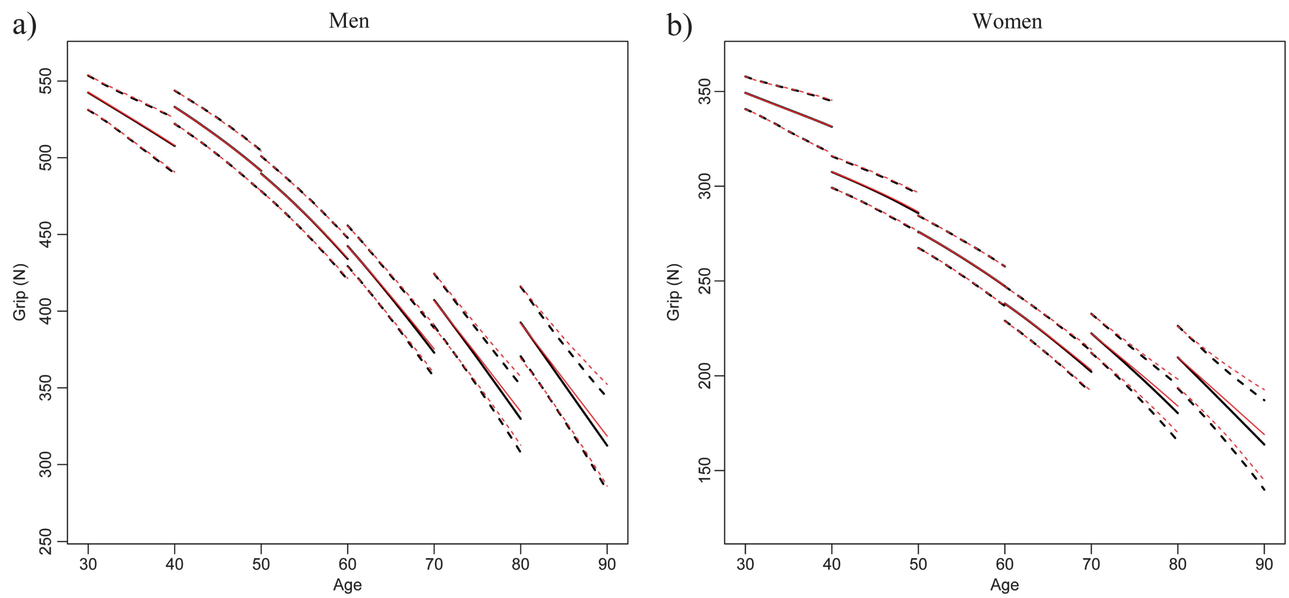

Figure 2. Posterior expectations of the longitudinal trajectories in handgrip strength according to baseline age decade. Red lines indicate crude values and black lines values in which the effect of right censoring due to deaths was accounted for and their 95% credible intervals (dashed lines). The Mini-Finland Health Survey 1978–1980, The Health 2000 Survey 2000–2001, and Mortality Data 1978–2008. (**a**) Men and (**b**) women.

neural activation and contractile quality, as well as changes in circulatory mediators such as hormones, growth factors, and inflammatory factors may play role in age-associated decline in muscle strength (33,34). It is also unclear whether these factors have different effect at a specific boundary age. For example, changes in sex hormones (especially in women) may predispose to muscle strength decline in middle age, but in older ages, poor nutrition or muscle disuse, that is, drastically decreased physical activity may have a highlighted effect on strength decline.

Some aspects concerning our statistical approach are discussed in the Appendix 1.

In conclusion, this 22-year follow-up study provides new information about muscle strength change and trajectories throughout adult life span. In addition, our results suggest that the right censoring can influence the results of a repeated measurements study, especially if the study population is old.

Funding

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Conflict of Interest

The authors declare no conflict of interest.

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Appendix 1: Statistical Appendix

Let y_{i0} and y_{ia_i} denote the observed values of grip strength of participant i at baseline (time zero) and during the follow-up at time $a_i > 0$. Let d_i denote the time of death, and $T_i^{\max} > 0$ the maximum follow-up time. y_{ia_i} was missing, if participant i (a) died before the follow-up measurement ($d_i < a_i$), (b) emigrated out of the study area, or (c) refused to participate. Reasons (b) and (c) were considered to be ignorable, but reason (a) was likely to depend on the partially missing grip strength values and therefore be nonignorable, thus it required special treatment, which is described below.

Diggle and Kenward (28) proposed a model in which a multivariate normal model was applied for the longitudinal outcome process and a logistic regression model for the dropout process.

In our case, the follow-up time was discretized so that Y_{it} represented the annual grip strength in year $t = 0, 1, 2, \ldots$

Model

The grip strength Y_{it} was modeled as a sum of baseline mean $\mu_{X_{i0}}$, individual variation at baseline represented by U_i, the expected annual changes in grip strength $\delta_{X_{is}}$, which was called the drift, and individual residual variation ε_{is}:

$$Y_{it} := \mu_{X_{i0}} + U_i + \sum_{s=1}^{t} (\delta_{X_{is}} + \varepsilon_{is}), \quad 0 \le t \le \min(d_i, T_i^{\max}).$$

The baseline mean and drift depended on time-dependent covariates X_{is}, which contained gender and age at time $s \ge 0$.

Survival indicator R_{it} had value zero if individual i was alive in year t ($d_i > t$) and one if individual i died in year t ($d_i = t$). The risk of death depended on the grip strength, which was assumed to have a possibly different association in four categories defined by an indicator whether individual was under 65 years old or older together with gender, in addition to gender and age at time t, and these factors were denoted by time-dependent covariate vector z_{it}, and we applied a logistic regression model:

$$\Pr\{R_{it} = 1\} = 1/[1 + \exp(-\beta Z_{it})] \text{ for } t = 0, 1, \ldots, \min(d_i, T_i^{\max}).$$

Missing data were induced not only by deaths, migration, and nonresponse but also by discretization of time using 1 year as the length of a time interval. The maximum follow-up time was from 1978 to 2008, and at most two measurements of the grip strengths were conducted during that time. The missing data were handled by Bayesian inference and data augmentation, in which the missing annual grip strengths were imputed during the Markov chain Monte Carlo simulation.

Prior Distributions

Relatively uninformative prior distributions were chosen so that the identifiability of the model was maintained. The following model parameters were defined separately for both genders $k \in \{\text{male, female}\}$. The prior distribution of the baseline mean of the grip strength for the youngest participants was $\mu_{k,30} \sim \mathrm{N}(500, 100)$. For the older ages t > 30, the priors were defined using an autoregressive structure $\mu_{kt} \sim \mathrm{N}(\mu_{k,t-1}, 10)$. The prior distributions of the individual variation at baseline were $U_i \sim \mathrm{N}(0, \sigma_0^2)$ and $\sigma_0^2 \sim \mathrm{InverseGamma}(2,1)$, and the residual variation was $\varepsilon_{it} \sim \mathrm{N}(0, \sigma^2)$ and $\sigma^2 \sim \mathrm{InverseGamma}(25,1)$. The drift parameters were also given an autoregressive structure $\delta_{k,30} \sim \mathrm{N}(0,100)$. For the older ages $t > 30$, large prior variances did not provide stable results, thus we applied $\delta_{kt} \sim \mathrm{N}(\delta_{k,t-1}, 0.1)$. The regression coefficients of the logistic regression model were $\beta_{\mathrm{Grip},k,j} \sim \mathrm{N}(0, 0.01)$ for the association of grip strength and risk of death in age categories $j \in \{\text{30 to 64 years, 65 years or older}\}$ and $\beta_{\mathrm{Age},k,30} \sim \mathrm{N}(0,100)$ and $\beta_{\mathrm{Age},k,t} \sim \mathrm{N}(\beta_{\mathrm{Age},k,t-1}, 1)$ ($t > 30$) for the risk of death at age t.

Outcome Statistics

The point estimates were posterior expectations, and the 95% CI were based on the 2.5% and 97.5% quantile points of the posterior distributions.

Figure 1a and b presents the posterior expectations and CI of the drift parameters δ_{kt}. To demonstrate the cumulative changes of grip strength over s years of follow-up assuming no deaths, we defined expected grip strength as a sum of the baseline value at age t and the s drift parameters after age t:

$$\Delta_{k,t,s} := \mu_{kt} + \sum_{l=1}^{s} \delta_{k,t+l}.$$

Appendix Table 1 and Figure 2a and b present the posterior expectations and CI of $\Delta_{k,t,10}$ for $\in \{31, 41, \ldots, 81\}$.

Discussion

In the selection model, the mechanism inducing missingness was assumed to be missing not at random, in which the probability of an observation being missing depends on the partly unobserved outcome in addition to some baseline factors, which were in this case age and gender. The risk of death (as well as the changes in the grip strength) might have depended on confounding factors, which can be unobservable such as those discussed above, and on model assumptions (21). However, if the right censoring is ignored in the analyses, the results would be subject to bias as discussed above.

Note that this model has similarities with a hidden Markov model (35). In our case, the observed variable is the binary survival indicator R_{it} and the latent variable is grip strength Y_{it}, which is partly observed, whereas in the standard HMM, the latent variable is categorical and the observed variable is continuous.

Appendix Table 1. Means (posterior expectations) and Their 95% CI of Handgrip Strength at Baseline and After 10 Years of Follow-up Assuming No Deaths Without or With Adjustment for the Right Censoring Due to Death; The Mini-Finland Health Survey 1978–1980, The Health 2000 Survey 2000–2001, and Mortality Data 1978–2008

		Baseline	10 y Follow-up Without Adjustment for the Right Censoring	10 y Follow-up With Adjustment for the Right Censoring
Gender	Age*	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)
Men	31	543 (532–554)	508 (491–526)	508 (490–526)
Men	41	533 (522–544)	491 (478–504)	491 (478–505)
Men	51	490 (478–501)	435 (421–448)	434 (420–448)
Men	61	442 (429–456)	375 (359–391)	373 (357–389)
Men	71	407 (389–425)	335 (313–357)	330 (308–352)
Men	81	392 (369–416)	318 (286–352)	312 (283–344)
Women	31	349 (341–358)	332 (317–345)	331 (318–345)
Women	41	308 (299–316)	287 (276–297)	286 (276–296)
Women	51	276 (267–285)	247 (237–258)	247 (237–258)
Women	61	238 (229–247)	203 (192–214)	202 (191–213)
Women	71	222 (212–233)	184 (170–198)	180 (166–195)
Women	81	210 (194–226)	169 (145–193)	164 (140–187)

Notes: CI, credible interval.

* Since there were only few persons aged 30 years in the sample, the presentation of numerical results was based on the ages of 31, 41, 51, 61, 71, and 81 years.