The times we are born into and our lifestyle choices determine our health trajectories in older age - Results from the KORA*-Age study

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Highlights

- Birth cohort membership may affect health deficit accumulation in older age.
- We compared Frailty Index (FI) values in five 5-year birth cohorts at ages ≥65.
- Both birth cohort and individual factors influenced FI levels.
- FI levels increased in cohorts born >1933 as compared to earlier cohorts.
- BMI, physical activity and smoking also suggested high prevention potential.

Abstract

Health projections often extrapolate from observations in current ageing cohorts, but health in older age may depend not only on individual characteristics but also on a person's historical context. Our objective was to investigate how health deficit accumulation trajectories after age 65 differed in five adjacent birth cohorts and according to individual life course characteristics.

Data originate from the 2008/09 KORA (Cooperative Health Research in the Region of Augsburg)-Age cohort study from Southern Germany and their 2012 and 2016 follow-ups. Deficit accumulation was assessed using a Frailty Index. The effects of birth cohort membership and individual life course characteristics on deficit accumulation trajectories were analyzed using generalized linear mixed models. Out of 2,701 participants (49% male) from five birth cohorts (1919-23, 1924-28, 1929-33, 1934-38, 1939-43), we included 2,512 individuals with 5,560 observations. Frailty Index levels were higher for women, smokers, alcohol abstainers, obese participants and persons with a sedentary lifestyle or living below the poverty threshold. We found higher age-specific Frailty Index levels for the two most recent birth cohorts (e.g. 61%, CI: [13%; 130%] for the 1934-38 as compared to the 1919-23 cohort), but the rate of deficit accumulation with age (7% per life year, (CI: [5%, 9%]) was cohort-independent. Results indicate that the historical context (birth cohort membership) may influence the number of accumulated health deficits after age 65 in addition to poverty and other individual life course characteristics, but BMI, physical activity and smoking remain the modifiable risk factors offering the highest prevention potential.

Key Words: *Older adults, Health trajectories, Frailty index, Birth cohorts, Life course epidemiology, Risk factors*

Introduction

Analyses on current health trajectories are often supposed to inform projections on future population health and associated health care costs, as well as potential health effects of non-health policies (Hoogendijk et al., 2018; Lu et al., 2017; Rogers et al., 2017). This is relevant because of the implicit assumption that ageing can be considered a biologically determined process which repeats itself independently of a person's historical context (Holliday, 2006). However, as soon as ageing is regarded as a "fundamentally […] event-dependent, and not a time-dependent process" (Arking and Arking, 2006), it seems plausible that a 65-year-old in 2059 may not follow the same health deficit accumulation trajectory as a 65-year old in 2019, because societal, medical and environmental circumstances may have changed, potentially leading to entirely different life experiences. Thus, disentangling cohort from age effects is crucial for adequate health care planning.

To complicate matters even more, cohort differences may not only stem from contextual changes, but apparent cohort effects may be induced by generation-specific patterns of accumulation of individual risk, such as smoking, physical activity, overweight or alcohol consumption frequency and should also be statistically attributed as such to identify prevention potential in future generations. As a consequence of these challenges in correctly attributing observed health trends to age, cohort membership or individual accumulation of risk, the concept of life course epidemiology has increasingly found attention (Kuh et al., 2014). When investigating biological ageing, life course epidemiological approaches try to capture both an individual's specific biographical characteristics and the historical context. To date, though, most studies which investigate the interplay of cohort effects and individual life course characteristics on health deficit accumulation in older age focus on socio-economic characteristics such as income, education and wealth (Marshall et al., 2015; Stolz et al., 2017; Yang and Lee, 2009). A British study, for example, suggested higher levels of deficit accumulation for more recent cohorts (born after 1932), with cohort differences being highest for the poorest and non-existent in the richest population tertile (Marshall et al., 2015). Also a study using data from several European countries suggested higher deficit accumulation levels and growth rates for cohorts born after 1930 as compared to earlier-born cohorts, additionally suggesting education as one of the main factors explaining deficit accumulation differences between individuals, especially in later-born cohorts (Stolz et al., 2017). A US study

reported similar results for cohort differences, and additional cohort-specific effects of sex, education and poverty on deficit accumulation (Yang and Lee, 2009). A study from England (Rogers et al., 2017) suggested that cohort differences were largest for participants with sedentary lifestyles as opposed to those who were moderately to vigorously active, and additionally found higher age-specific deficit levels for later-born cohorts. Apart from this, to date, evidence on the role of health risk behaviours with regard to potential cohort differences in deficit accumulation remains sparse. Furthermore, it remains unclear to what extent the process of health deficit accumulation in older age depends on a person's historical context. The objective of this study was thus to investigate how deficit accumulation trajectories after age 65 differed in five adjacent birth cohorts after controlling for individual life course characteristics including socio-economic and socio-demographic characteristics as well as health risk behaviours.

Methods

Study design, participants and data collection procedures

Data originate from participants of the population-based KORA (Cooperative Health Research in the Region of Augsburg)-Age study from Bavaria, Southern Germany. KORA-Age includes all participants from four former population representative surveys conducted between 1984 and 2001, the MONICA (Monitoring of Trends and Determinants in Cardiovascular Diseases)/KORA surveys. All former MONICA/KORA participants aged ≥65 years on December 31st 2008 were eligible for participation in the KORA-Age cohort.

For the 2008/09 KORA-Age baseline assessment 4,123 individuals aged ≥65 years (i.e. born ≤1943) completed structured telephone interviews and mailed questionnaires (response rate: 68.8%). An age- and sex-stratified random sub-sample (n=1,079) additionally completed medical examinations.

For the first follow-up wave in 2012 only participants from the 2008/09 medical examination sub-sample were re-invited. Out of these sub-sample participants 975 were still eligible (i.e. still alive, and not living abroad or refusing to be contacted) and 822 individuals participated in the first follow-up (response: 84.3%). For the current analysis we included all participants aged 65-89 years at baseline with at least one follow-up observation. These criteria applied to 821 out of the 822 follow-up 1 participants.

For the second follow-up wave in 2016, not only the 2008/09 medical examination sub-sample participants, but all individuals formerly eligible for KORA-Age baseline were re-invited. Thus, in 2016, 3,982 of all individuals formerly eligible for KORA-Age baseline were still eligible, of which 2,625 completed structured telephone interviews and paper-based questionnaires (response rate: 65.9%).

In total, 567 participants participated in all three waves. Longitudinal data from two waves (either baseline and follow-up 1 or baseline and follow-up 2) were available for 2,136 participants (Appendix A). Thus, for the main analysis we included a total of 2,703 participants. Details about study design, sampling, data collection and response rates for KORA-Age can be found elsewhere (Holle et al., 2005; Peters et al., 2011).

Approval for KORA-Age was obtained from the Ethics Committee of the Bavarian Medical Association. Written informed consent was obtained from all participants.

Frailty index

To examine cohort-specific deficit accumulation trajectories, we calculated a Frailty Index (Searle et al., 2008) for each participant and each follow-up wave (2008/09, 2012 and 2016). The KORA-Age Frailty Index was published for the first time in 2016 (Stephan et al., 2016), and has been slightly modified since (Stephan et al., 2017; Stephan et al., 2019) to be uniformly applicable to all three KORA-Age waves.

The most recent index version (Stephan et al., 2019) was used for all three waves in the present analysis and calculated following the standard procedure published by (Searle et al., 2008). It comprises 33 health deficits, covering 10 comorbidities, 13 measures of functioning and 10 (pre-)clinical signs and symptoms. A list of included deficit items can be found in Appendix B.1. Details on the item selection methodology can be found elsewhere (Searle et al., 2008).

All deficits were coded from 0 (deficit absent) to 1 (deficit present). A participant's Frailty Index results as the number of the person-specific deficits divided by the total number of listed deficits. Frailty Index scores range from 0 (no deficits present) to 1 (all deficits present). If a participant scored missing on one or more of the deficits, the Frailty Index denominator was reduced accordingly (Searle et al., 2008). If ≥20% of the items were missing for a participant, the Frailty Index was set to missing (Yang and Lee, 2009).

Exposure: birth cohorts

To obtain birth cohort trajectories with overlapping age intervals over the 7-year follow-up period, birth cohorts were defined in brackets of five years (1919-23, 1924-28, 1929-33, 1934-38 and 1939-43).

Life course predictors

Based on findings from the literature, we controlled for socio-demographic (age, sex, marital status (Hoogendijk et al., 2018; Yu et al., 2017)), socio-economic (education (Chamberlain et al., 2016; Hoogendijk et al., 2018; Stolz et al., 2017), income (Stolz et al., 2017)) and lifestyle factors (physical activity (Brinkman et al., 2018; Rogers et al., 2017), smoking status (Brinkman et al., 2018; Yu et al., 2017), alcohol intake

(Chamberlain et al., 2016; Yu et al., 2017), body mass index (BMI)) as potential life course characteristics. For details on covariate measurement and categorization see Appendix B.2. Covariates were regarded as time-constant and included as measured at baseline to allow a longitudinal perspective without introducing unnecessary complexity.

Descriptive statistics

Absolute and relative frequencies of baseline categorical characteristics were presented for each cohort.

Descriptive plots

We graphically examined mean observed Frailty Index trajectories stratified by sex and birth cohort to find first indications for time trends: For each five-year birth cohort resulted a two-year age overlap in observed trajectories both with the previous and with the following cohort, respectively. Converging trajectories in adjacent cohorts indicate no cohort differences whereas non-converging trajectories indicate changes in Frailty Index levels across birth cohorts (Marshall et al., 2015).

Regression model

Determinants of deficit accumulation trajectories were analyzed using negative binomial generalized linear mixed models (GLMMs) with random intercepts, a log-link, the number of accumulated deficits as outcome and the number of possible deficits as offset term. The offset term (i.e. the logarithmized denominator of the individual participant's Frailty Index) counterbalances the impact of missing values for single index items on the deficit count. A generalized linear mixed model was chosen because the Frailty Index distribution has been shown to be skewed to the right and overdispersed (Mitnitski et al., 2001; Stephan et al., 2016). Age was used as time variable and centered at the median age at baseline (71 years).

We fitted a restricted model including only the exposures of primary interest (birth cohort, sex and age) and an extended model to see if including additional life course characteristics (marital status, income, education, BMI, smoking status, alcohol consumption, and physical activity) as covariates would change the birth cohort effect

estimates compared to the restricted model. In both models we included an interaction effect of birth cohort with age to see if ageing effects depended on birth cohort. We experimented with age and cohort squared terms, which both did not turn out significant and were not kept in the models.
Furthermore, we checked the need for a random age slope, which was not included in the final models as this resulted in model overparametrization (perfect correlation of random effects). Also, random slope variance was low and inclusion did only marginally change fixed effect estimates.
Exponentiated regression coefficients ceteris paribus represent Frailty Index ratios for the respective covariate category as compared to the respective reference group.
For all longitudinal analyses we used the R package lme4. Mean predicted sex- and cohort-specific trajectories and 95% prediction intervals (taking into account the variance of fixed and random effects, but not residual individual variance) were plotted using predictInterval from R package merTools.

Sensitivity analyses

To explore whether trajectories for birth cohorts varied in slope for socio-economic and socio-demographic characteristics or health risk behaviours, we calculated one additional model per covariate which included interactions of the respective covariate with cohort and age in addition to the extended model specifications described above. Covariate-specific predicted trajectories were then plotted for each cohort.

To facilitate comparisons with some previous analyses (Marshall et al., 2015; Rogers et al., 2017; Stolz et al., 2017) on cohort differences in deficit accumulation which applied linear mixed models (LMMs) using the Frailty Index as outcome variable, we recalculated our main analysis as a LMM, even though it should be kept in mind that this assumes a normal distribution of Frailty Index values and discounts the fact that Frailty Index values cannot be negative.

Results

Study participants

Out of the 2,703 participants who had participated in at least two KORA-Age waves and were aged between 65 and 89 years at baseline, Frailty Index values were set to missing due to ≥20% missing deficit items in two cases. Frailty Index values were thus available for 2,701 participants at baseline (51.4% female, range 65-89 years). Out of these, 806 (49.5% female, range 68-92 years) participants had Frailty Index values in 2012 (Frailty Index values were set to missing for 15 participants). In 2016, 2,438 baseline participants (51.4% female, range 72-96 years) had valid Frailty Index values (Frailty Index values were set to missing for 11 participants). Out of the 2,701 baseline participants with valid Frailty Index values, 562 (21%) participated in both follow-ups, 244 (9.1%) participated in follow-up 1 only, and 1,876 (69.9%) participated in follow-up 2 only (Appendix A).

Descriptive statistics

Earlier-born cohorts were older at KORA-Age baseline and had higher mean Frailty Index values. The share of women and people with low education was higher in the 1919-23 as compared to all other cohorts. The share of widowed individuals and individuals with no or low physical activity increased with cohort age, while the share of obese participants and frequent alcohol consumers was higher in later-born cohorts. Also the share of people living below poverty threshold varied over birth cohorts, but without a clear time trend (Table 1).

Table 1: Distribution of the 2008/09 baseline sample characteristics over birth cohorts (n=2,703 individuals, thereof 2,701 with valid baseline Frailty Index values and at least one follow-up measurement)

	Cohort				
Baseline covariates	**1919-23**	**1924-28**	**1929-33**	**1934-38**	**1939-43**
N	81	246	474	803	1099
Frailty index, mean (sd)	0.27 (0.13)	0.2 (0.1)	0.17 (0.1)	0.14 (0.09)	0.12 (0.08)
Missing (n, (%))	0 (0%)	2 (0.8%)	0 (0%)	0 (0%)	0 (0%)
Wave participation					
Baseline & 1st follow-up	44 (54.3%)	72 (29.3%)	56 (11.8%)	49 (6.1%)	33 (3%)
Baseline & 2nd follow-up	11 (13.6%)	74 (30.1%)	294 (62%)	601 (74.8%)	902 (82.1%)
Baseline & 1st follow-up & 2nd follow-up	26 (32.1%)	100 (40.7%)	124 (26.2%)	153 (19.1%)	164 (14.9%)
Age, mean (sd)	86.38 (1.25)	81.56 (1.34)	76.83 (1.34)	71.83 (1.39)	67.08 (1.41)
Sex, n (%)					
Male	32 (39.5%)	119 (48.4%)	247 (52.1%)	367 (45.7%)	548 (49.9%)
Female	49 (60.5%)	127 (51.6%)	227 (47.9%)	436 (54.3%)	551 (50.1%)
Baseline education, n (%)					
Low	25 (30.9%)	54 (22%)	99 (20.9%)	122 (15.2%)	114 (10.4%)
Lower intermediate	41 (50.6%)	119 (48.4%)	236 (49.8%)	453 (56.4%)	639 (58.1%)
Higher intermediate	9 (11.1%)	42 (17.1%)	85 (17.9%)	129 (16.1%)	206 (18.7%)
High	6 (7.4%)	31 (12.6%)	54 (11.4%)	99 (12.3%)	140 (12.7%)
Baseline income, n (%)					
Below the poverty threshold[a]	10 (12.3%)	53 (21.5%)	108 (22.8%)	143 (17.8%)	160 (14.6%)
Above poverty threshold, below highest income decile	58 (71.6%)	143 (58.1%)	299 (63.1%)	520 (64.8%)	750 (68.2%)
Highest income decile	7 (8.6%)	27 (11%)	42 (8.9%)	95 (11.8%)	145 (13.2%)
Missing	6 (7.4%)	23 (9.3%)	25 (5.3%)	45 (5.6%)	44 (4%)
Baseline marital status, n (%)					
Married	22 (27.2%)	131 (53.3%)	319 (67.3%)	581 (72.4%)	846 (77%)
Single	2 (2.5%)	9 (3.7%)	15 (3.2%)	27 (3.4%)	44 (4%)
Divorced	3 (3.7%)	4 (1.6%)	21 (4.4%)	39 (4.9%)	72 (6.6%)
Widowed	50 (61.7%)	94 (38.2%)	113 (23.8%)	152 (18.9%)	129 (11.7%)
Missing	4 (4.9%)	8 (3.3%)	6 (1.3%)	4 (0.5%)	8 (0.7%)
Baseline BMI, n (%)					
Underweight or normal weight	39 (48.1%)	85 (34.6%)	121 (25.5%)	221 (27.5%)	308 (28%)
Overweight	31 (38.3%)	116 (47.2%)	230 (48.5%)	377 (46.9%)	530 (48.2%)
Obesity grade I	10 (12.3%)	37 (15 %)	101 (21.3%)	163 (20.3%)	210 (19.1%)
Obesity grade II or III	1 (1.2%)	7 (2.8%)	22 (4.6%)	36 (4.5%)	45 (4.1%)

Missing	0 (0%)	1 (0.4%)	0 (0%)	6 (0.7%)	6 (0.5%)
Baseline smoking status, n (%)					
Never-smoker	50 (61.7%)	131 (53.3%)	283 (59.7%)	457 (56.9%)	518 (47.1%)
Ex-smoker	30 (37%)	105 (42.7%)	175 (36.9%)	306 (38.1%)	481 (43.8%)
Smoker	1 (1.2%)	10 (4.1%)	16 (3.4%)	40 (5%)	100 (9.1%)
Baseline alcohol consumption, n (%)					
(almost) daily	19 (23.5%)	80 (32.5%)	150 (31.6%)	247 (30.8%)	325 (29.6%)
Multiple times a week	10 (12.3%)	26 (10.6%)	58 (12.2%)	130 (16.2%)	217 (19.7%)
Once a week	7 (8.6%)	31 (12.6%)	54 (11.4%)	121 (15.1%)	164 (14.9%)
Less than once a week	19 (23.5%)	65 (26.4%)	132 (27.8%)	205 (25.5%)	274 (24.9%)
(almost) never	26 (32.1%)	44 (17.9%)	80 (16.9%)	100 (12.5%)	119 (10.8%)
Baseline physical activity, n (%)					
High	12 (14.8%)	50 (20.3%)	120 (25.3%)	289 (36%)	387 (35.2%)
Moderate	13 (16%)	49 (19.9%)	136 (28.7%)	239 (29.8%)	374 (34%)
Low	9 (11.1%)	38 (15.4%)	71 (15%)	124 (15.4%)	163 (14.8%)
No	47 (58%)	108 (43.9%)	147 (31%)	151 (18.8%)	175 (15.9%)
Missing	0 (0%)	1 (0.4)	0 (0%)	0 (0%)	0 (0%)

sd = standard deviation
[a]Poverty threshold: 859 Euro per person per month for Bavaria in 2009

Descriptive plots

For men, trajectories converged for the three most recent (1929-33, 1934-38, and 1939-1943) birth cohorts, with a gap to their two predecessor cohorts (1924-28 and 1919-23). For women, trajectories converged for all cohorts. For those age years in which observed trajectories of two adjacent cohorts overlapped, mean Frailty Index levels were generaly lower for earlier-born cohorts as compared to later-born cohorts. Sex-specific trajectories converged for later-born but diverged for earlier-born birth cohorts, with higher FI levels for women (Figure 1).

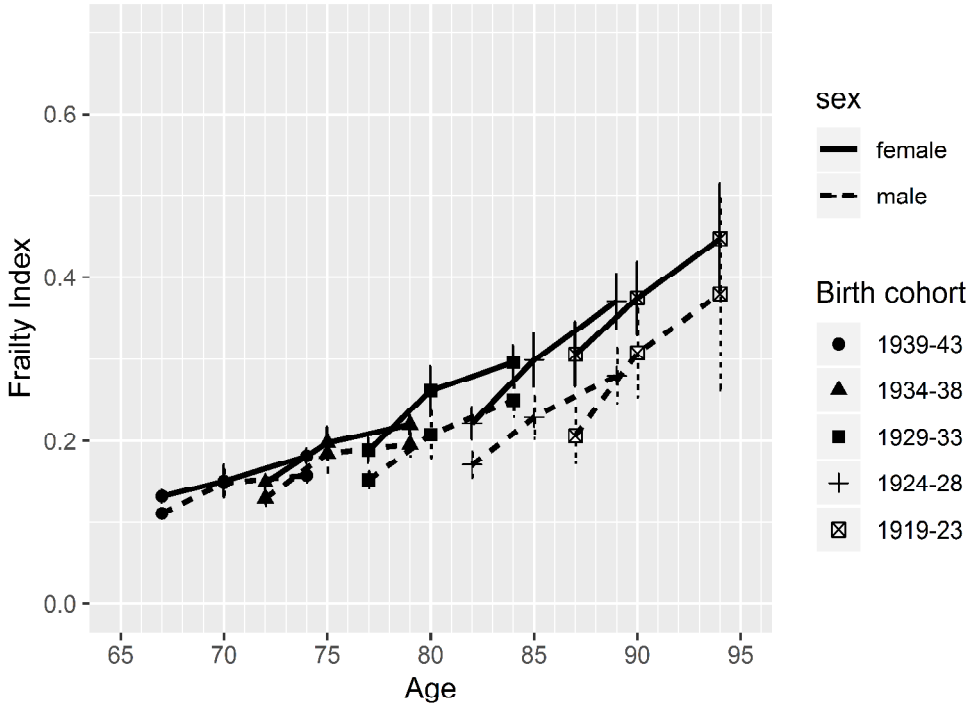

Fig 1. Observed overall Frailty Index trajectories by birth cohort and sex. Frailty Index means are positioned at the mean age of the respective cohort (e.g. for the cohort born 1939-43, which contains adults aged 65-69 years in 2008/09, mean cohort Frailty Index values are positioned in the plot at 67 years). Error bars represent the 95% confidence intervals for mean Frailty Index values by cohort, sex and measurement period.

Regression model

Out of the 2,701 baseline participants with valid Frailty Index values, 2,512 individuals with complete covariate information contributed 5,560 observations to the analysis.

In the restricted model including only the exposures of interest, women had 18% higher Frailty Index values than men (CI: [13%, 23%]). The two youngest cohorts (born 1934-38 and 1939-43) both had significantly higher Frailty Index values than earlier-born cohorts (e.g. 57% (CI: [9%, 125%]) higher for the 1934-38 as compared to the 1919-23 cohort). Frailty Index ratios increased significantly by 8% with each additional life year (CI: [6%, 10%]). Increases with age did not differ significantly between the cohorts.

Inclusion of further covariates did not substantially alter these results: While the sex effect was reduced to 12% (CI: [7%; 18%]), the effects for later-born cohorts increased (e.g. for the 1934-38 cohort as compared to the 1919-23 cohort to 61% (CI: [13%, 130%]). Additional increases in Frailty Index ratios were found for higher BMI, being divorced as opposed to married, current or former smokers, alcohol abstainers, living below the poverty threshold and lower physical activity (Table 2).

Predictions of cohort trajectories from both the restricted and main model are visualized in Appendix C.

Table 2: Results from the restricted and extended generalized linear mixed models (5,560 observations from 2,512 individuals) using baseline covariate values.

		Frailty index ratio	
		Restricted model	Extended model
Intercept		0.00 (0.00, 0.00)	0.06 (0.04, 0.08)
Age	Factor for each additional life year	1.08 (1.06, 1.10)	1.07 (1.05, 1.09)
Sex	Men	Reference	
	Women	1.18 (1.13, 1.23)	1.12 (1.07, 1.18)
Birth cohort	1919-23	Reference	
	1924-28	1.09 (0.74, 1.62)	1.09 (0.74, 1.61)
	1929-33	1.31 (0.91, 1.90)	1.29 (0.90, 1.86)
	1934-38	1.57 (1.09, 2.25)	1.61 (1.13, 2.30)
	1939-43	1.73 (1.21, 2.48)	1.77 (1.24, 2.53)
	Interaction birth cohort 1924-28 and age	1.00 (0.98, 1.02)	1.00 (0.98, 1.02)
	Interaction birth cohort 1929-33 and age	1.00 (0.98, 1.02)	1.00 (0.98, 1.02)
	Interaction birth cohort 1934-38 and age	0.99 (0.97, 1.00)	0.99 (0.97, 1.01)
	Interaction birth cohort 1939-43 and age	0.97 (0.96, 0.99)	0.98 (0.96, 1.00)
Baseline marital status	Married		Reference
	Single		1.08 (0.98, 1.20)
	Divorced		1.11 (1.02, 1.21)
	Widowed		1.04 (0.99, 1.09)
Baseline BMI	Underweight or normal weight		Reference
	Overweight		1.09 (1.05, 1.15)
	Obesity grade I		1.26 (1.19, 1.33)
	Obesity grade II or III		1.53 (1.40, 1.69)
Baseline smoking status	Never-smoker		Reference
	Ex-smoker		1.08 (1.03, 1.13)
	Smoker		1.15 (1.06, 1.25)
Baseline alcohol consumption	(almost) daily		Reference
	Multiple times / week		1.01 (0.95, 1.07)
	Once / week		0.99 (0.93, 1.06)
	Less than once / week		1.04 (0.99, 1.10)
	(almost) never		1.12 (1.05, 1.20)
Education	Low		Reference
	Lower intermediate		1.01 (0.95, 1.06)
	Higher intermediate		1.00 (0.93, 1.07)
	Aigh		0.93 (0.85, 1.01)
Baseline income	above poverty threshold, below highest income decile		Reference
	Below poverty threshold[a]		1.06 (1.01, 1.12)
	Highest income decile		0.94 (0.88, 1.01)
Baseline physical activity	High		Reference
	Moderate		1.10 (1.05, 1.16)
	Low		1.13 (1.06, 1.19)
	No		1.30 (1.24, 1.38)
Goodness of fit	AIC	26442.7	26016.1
	BIC	26528.8	26234.7
Random intercept variance		0.1812	0.1440

Marginal[b] pseudo R^2	Delta	0.016751556	0.02132485
	Lognormal	0.045092378	0.05800057
	Trigamma	0.003033277	0.00381025
Conditional[c] pseudo R^2	Delta	0.048018399	0.045477239
	Lognormal	0.129257473	0.123691666
	Trigamma	0.008694901	0.008125716

[a]Poverty threshold: 859 Euro per person per month for Bavaria in 2009
[b]variance explained by the fixed effects (calculated with r.squared.GLMM from library MuMIn)
[c]variance explained by the entire model including fixed and random effects (calculated with r.squared.GLMM from library MuMIn)

Sensitivity analyses

Visual inspection of prediction plots for models including covariate*cohort*age interactions suggested potential between-cohort differences in both levels and slopes for BMI especially for younger cohorts with obesity grade II or III and for income below the poverty threshold (Appendix D).

Results from the LMM parametrization confirmed the direction of effects from our main model (Appendix E).

Discussion

In our analyses of five different cohorts born between 1919 and 1943, we found higher age-specific health deficit levels in earlier-born as compared to later-born cohorts. Regression analysis confirmed the break in deficit accumulation trajectories seen in descriptive plots between cohorts born after 1933 and earlier cohorts. Interestingly, also other international European studies report increases in older-age Frailty Index levels for cohorts born after the early 1930s (Marshall et al., 2015; Stolz et al., 2017). In contrast, in a US study, the same trend was not found until a decade later (Yang and Lee, 2009). Contextual factors which may have influenced cohort health in the late 20th century could be the unprecedented treatment improvements for conditions such as cardiovascular diseases, cancer, and diabetes, which may have lead, accompanied by stable or increasing incidence of these conditions, to higher survival rates in spite of health deficits in later-born cohorts (Crimmins and Beltrán-Sánchez, 2011). Another potential pathway to higher deficit levels in the 1934-1943 birth cohorts may be related to their specific childhood experiences in sensitive developmental age due to World War II such as hunger, trauma, prosecution, or separation from family members (Kesternich et al., 2014).

Not only contextual factors such as war experiences vary between birth cohorts, but also lifestyles change between generations. For example, BMI increases between 20 and 50 years of age have been considerably larger and physical activity levels in this age interval have been reported to be constantly lower for later-born as compared to earlier-born cohorts. In later-born cohorts, the number of female smokers approached the number of male smokers and female alcohol consumption increased (Raum et al., 2007). One of the strengths of this analysis is that it not only differentiates between age and cohort effects, but additionally constitutes one of the first attempts to narrow down the plethora of potential pathways for cohort effects by investigating the contribution of individual life course characteristics which might vary across different cohorts. In our study, cohort differences further increased when we additionally controlled for individual life course factors. One explanation might be that some more advantageous individual socio-economic and health behavior related characteristics (such as higher socio-economic position and higher physical activity) in the later-born cohorts obscured not only the detrimental effects of other contextual

factors related to cohort membership, but also effects stemming from their less advantageous individual characteristics (higher obesity rates).

Although individually, obesity, physical inactivity, smoking and poverty each contributed less to deficit accumulation than membership in certain birth cohorts, one should keep in mind that all these individual risk factors may affect a person simultaneously. As a consequence, appropriate prevention strategies targeting physical activity levels, BMI reduction, smoking cessation and poverty may help reduce deficit levels independent of and with a higher effect than (not modifiable) cohort membership.

We also observed that controlling for life course factors reduced sex effects, confirming that differences in life course factors contribute to health differences between the sexes (Oksuzyan et al., 2008).

As opposed to other findings reported in the literature (Stolz et al., 2017; Yang and Lee, 2009), the speed of deficit accumulation with age did not differ between birth cohorts in our analysis. The respective effect estimates were close to zero and had very narrow confidence limits convincing us that this finding was not an artefact of our relatively small sample size. Nevertheless, we cannot fully exclude that the analysis may have been insufficiently powered to identify significant differences in growth rates across birth cohorts.

Although the KORA-Age study population derived from four former population representative surveys, men are slightly overrepresented in our sample (49%) as compared to the general Bavarian population (43%), largely due to the relatively balanced sex distribution in the older KORA-Age groups. Also, health care resource utilization has been reported to be lower in the KORA-Age study population, suggesting healthier participants (Hunger et al., 2013) and KORA-Age has shown a middle class response bias not uncommon for population-based cohorts (Holle et al., 2006). This might, in part, explain why in contrast to literature (Chamberlain et al., 2016; Hoogendijk et al., 2018; Stolz et al., 2017) we did not find any effect of education on deficit levels. Alcohol abstinence seemed to additionally increase the risk for higher deficit counts, potentially due to reverse causation: Individuals with deteriorating health may restrict their alcohol consumption or even refrain from it completely (“sick quitter” effect) (Shaper et al., 1988). An additional limitation

concerns the low number of longitudinal measurements per individual, due to which our analysis may not yet have had full power to properly disentangle age and cohort effects. This limitation might recede in the future as the KORA-Age study matures with additional waves. Further limitations include the comparatively low number of observations in the 1919-23 birth cohort and, as in other analyses (Marshall et al., 2015), the relatively short age overlap between adjacent birth cohorts. As our focus was on the interplay of age and cohort effects and as the maximum difference between measurement periods was only seven years in our analysis, we constrained the period effect to zero, assuming that being measured in 2016 as opposed to 2008/09 would not make a difference for health status. In doing so we avoided the so-called “age-period-cohort analysis conundrum” (Yang and Land, 2016), which refers to the fact that from information on two out of the three characteristics age, measurement period and birth cohort membership, the third quantity can always be calculated unambiguously, posing identification challenges to statistical analysis. Nevertheless, we cannot fully exclude that period effects, induced for example by the aftermath of the 2007-2009 financial crisis, may have exerted an influence on the KORA-Age participants’ health. Still, we assumed that these contextual effects would not have had a birth-cohort-specific impact on the KORA-Age participants. Also, as observed ages only partly overlapped for cohorts, residual confounding of age and cohort variables may remain.

As cohorts entered the KORA-Age study at different ages (earlier-born cohorts were older at entry in KORA-Age than later-born cohorts), one might want to argue that survivorship bias may have additionally affected our results: Later-born cohorts may seem less healthy simply because they still contain the less healthy part of the population who dies or retracts from the study early as opposed to the earlier-born cohorts who were measured in older age, potentially after the less healthy cohort part had already died or retracted their survey participation. Although there is reason to assume that sample attrition only marginally affects the assessment of frailty trajectories in older age (Stolz et al., 2018), to counteract the abovementioned arguments it is helpful to remember that birth cohorts were defined in such a way that their observed trajectories overlapped both with the next older and the next younger birth cohort, resulting in a total overlap with other birth cohorts in four out of seven observed life years for each cohort: In these intervals, individuals were measured at the same age and can thus not have been affected by differential attrition due to age,

leaving observed differences between trajectories only attributable to cohort membership (Yang and Lee, 2009). Nevertheless, it remains unclear to what extent our results can be extrapolated to cohorts born after World War II and the subsequent development of a democratic system in Germany.

Finally, the Frailty Index represents a very broad measure for health status (covering both disabilities and chronic diseases), and exploring which health deficits predominantly drive cohort differences would go beyond the scope of this analysis. As morbidity expansions tend to be found for analyses of chronic disease outcomes, whereas compression of morbidity tends to be reported with regard to disability (Chatterji et al., 2015) we can only hypothesize that the cohort effects we found would be stronger with pure chronic disease outcomes and potentially less clear for purely disability-related outcomes.

In conclusion, our results confirmed that age and individual life course characteristics determine health trajectories after age 65, with some additional influences attributable to cohort membership. This potential additional source of variation in health trajectories should be kept in mind when trying to make predictions for the future. BMI, physical activity and smoking were the modifiable risk factors with the highest prevention potential, offering the chance to keep future health care costs at a sustainable level through timely investments in appropriate behavioural prevention strategies.

Compliance with Ethical Standards

Declaration of competing interest: The authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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