Adverse generational changes in obesity development converge at midlife without increased cardiometabolic risk

Ibi, D.; Rietman, M.L.; Picavet, H.S.J.; Klinken, J.B.; Dijk, K.W.; Dolle, M.E.T.; Verschuren, W.M.M.

Received: 25 April 2021 | Revised: 30 June 2021 | Accepted: 1 July 2021

DOI: 10.1002/oby.23260

Obesity A Research Journal | THE OBESITY SOCIETY | WILEY

ORIGINAL ARTICLE

Epidemiology/Genetics

Adverse generational changes in obesity development converge at midlife without increased cardiometabolic risk

Dorina Ibi[1,2] | M. Liset Rietman[2] | H. S. J. Picavet[2] | Jan Bert van Klinken[1] | Ko Willems van Dijk[1] | Martijn E. T. Dollé[1,2] | W.M. Monique Verschuren[2,3]

[1]Leiden University Medical Center, Leiden, the Netherlands

[2]National Institute for Public Health and the Environment, Bilthoven, the Netherlands

[3]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands

Correspondence
Dorina Ibi, Department of Human Genetics, Leiden University Medical Center, Einthovenweg 20, 2333 ZC, Leiden, the Netherlands; Postzone S4-P, Postbus 9600, 2300 RC Leiden, the Netherlands.
Email d.ibi@lumc.nl

Funding information
This study was supported by the Ministry of Health, Welfare and Sport of the Netherlands and the National Institute for Public Health and the Environment.

Abstract

Objective: Obesity is becoming a global public health problem, but it is unclear how it impacts different generations over the life course. Here, a descriptive analysis of the age-related changes in anthropometric measures and related cardiometabolic risk factors across different generations was performed.

Methods: The development of anthropometric measures and related cardiometabolic risk factors was studied during 26 years of follow-up in the Doetinchem Cohort Study ($N = 6{,}314$ at baseline). All analyses were stratified by sex and generation, i.e., 10-year age groups (20-29, 30-39, 40-49, and 50-59 years) at baseline. Generalized estimating equations were used to test for generational differences.

Results: Weight, BMI, waist circumference, and prevalence of overweight and obesity were higher, in general, in the younger generations during the first 10 to 15 years of follow-up. From age 50 to 59 years onward, these measures converged in all generations of men and women. Among cardiometabolic risk factors, only type 2 diabetes showed an unfavorable shift between the two oldest generations of men.

Conclusions: It was observed that, compared with the older generations, the younger generations had obesity at an earlier age but did not reach higher levels at midlife and beyond. This increased exposure to obesity was not (yet) associated with increased prevalence of cardiometabolic risk factors.

INTRODUCTION

The prevalence of obesity has increased dramatically over the past decades, and it is estimated that, by 2030, more than 1 billion people will have obesity (1). This poses a global public health problem, as obesity is strongly associated with cardiometabolic risk factors and diseases such as hypertension, hypercholesterolemia, insulin resistance, type 2 diabetes (T2D), and cardiovascular disease (CVD) (2-5), all of which are associated with morbidity and reduced life expectancy (6).

Obesity prevalence increases with age, with more progressive changes taking place from age 20 to 60 years (7,8). This upward trend follows a sex-specific course, with men reaching a BMI plateau at a younger age than women (9). In addition to age and sex, obesity differs by birth cohorts, which are defined as groups of people born in the same period of time (10). Individuals belonging to a particular birth cohort are likely to share a cumulative set of experiences that may be different from those born earlier or later (11). For instance, the oldest generations in their younger years were exposed

to a less obesogenic food environment and a less sedentary lifestyle than more recent generations (12). The extent of exposure to such obesity-promoting environments and, consequently, to obesity affects development of obesity-related conditions; a longer exposure to obesity is associated with higher risk of T2D (13,14) and CVD (15). Altogether, both timing and duration of obesity are important in the development of cardiometabolic disease. Therefore, a more comprehensive evaluation of the development of obesity prevalence and its long-term effects on associated cardiometabolic risk factors is important.

We have previously studied the development of overweight and obesity during 16 years of follow-up in a Dutch population of men and women aged 20 to 59 years at baseline, in which we showed an unfavorable increase of overweight and obesity in the most recently born generations compared with the older ones (8). However, at the end of the 16-year follow-up, the most recently born generations had barely reached midlife, which is typically a period that predates the manifestation of cardiometabolic disease and is a strategic window for early detection and prevention of CVD. Therefore, our previous study could not adequately assess trends of obesity and related cardiometabolic factors beyond midlife in the most recently born generations (16). Another limitation of our previous study was that it used only BMI as a measurement of overweight and obesity. However, BMI measurements alone are insufficient to assess visceral obesity, thereby failing to fully capture cardiometabolic risk. Recent studies emphasize the importance of using waist circumference in addition to BMI as an important measure of visceral obesity to better assess and predict obesity and cardiometabolic risk (17). Therefore, in the current analyses, we further assessed the development of obesity and related cardiometabolic risk factors in the same population by including data from more recent measurements, extending the follow-up period by 10 years to a total of 26 years, and assessing waist circumference. Our aim was to perform descriptive analyses of the changes in anthropometric measures and related cardiometabolic risk factors over the life course by sex and generation.

Study Importance

What is already known?

- The most recently born generations are exposed to a more obesogenic environment compared with older generations, resulting in an earlier and longer exposure to obesity.

What does this study add?

- Our study shows that, despite having a higher and earlier exposure to obesity, the younger generations do not reach higher levels of BMI and obesity prevalence at midlife and beyond, which was an unanticipated observation given the expected further rise of BMI throughout middle age.
- Moreover, thus far we found no evidence that cardiometabolic risk factors are elevated in the younger generations when compared at midlife with the older generations.

How might these results change the direction of research?

- Further research beyond the age of 50 years is needed to assess the progression of cardiometabolic and other obesity-related diseases in younger generations.
- Future research should focus on developing alternative markers for BMI that could better capture cardiometabolic health.
- The BMI plateau for all younger generations at a similar level suggests that, apparently, at this plateau, a population-specific energy balance is reached. Research into the determinants of this energy balance is needed.

METHODS

Population

The Doetinchem Cohort Study (DCS) is a prospective, population-based cohort study including, at baseline, 7,769 men and women aged 20 to 59 years living in Doetinchem, the Netherlands, who were predominantly of Dutch Caucasian descent, between 1987 and 1991 (round 1). Participants from the first round were invited for follow-up examinations every 5 years. The response rates varied between 75% and 80% in all rounds. The study design of DCS has previously been described in more detail (18,19). For the present analyses, we included participants who took part in at least two rounds ($N = 6,391$) and excluded pregnant women only for that specific round (round 1-6: 77, 43, 18, 3, 1, and 1, respectively). This resulted in a total of 6,314, a total of 6,069, a total of 4,897, a total of 4,516, a total of 4,015, and a total of 3,437 participants in rounds 1, 2, 3, 4, 5, and 6, respectively. This selection process is described in a participant flowchart (Figure 1). All participants gave written informed consent, and the study was approved according to the guidelines of the Helsinki Declaration by the external Medical Ethics Committee of the University Medical Center Utrecht.

Measures

Demographic characteristics, medical history of chronic diseases, medication use, and lifestyle factors were collected using standardized questionnaires. Trained staff performed standardized measurements of anthropometric traits (height, weight, and waist circumference), blood pressure, and blood sampling during a visit to the municipal health service. A detailed description of these measures has been reported elsewhere (8). Having overweight was defined as BMI between 25 and 30 kg/m^2, and having obesity was defined

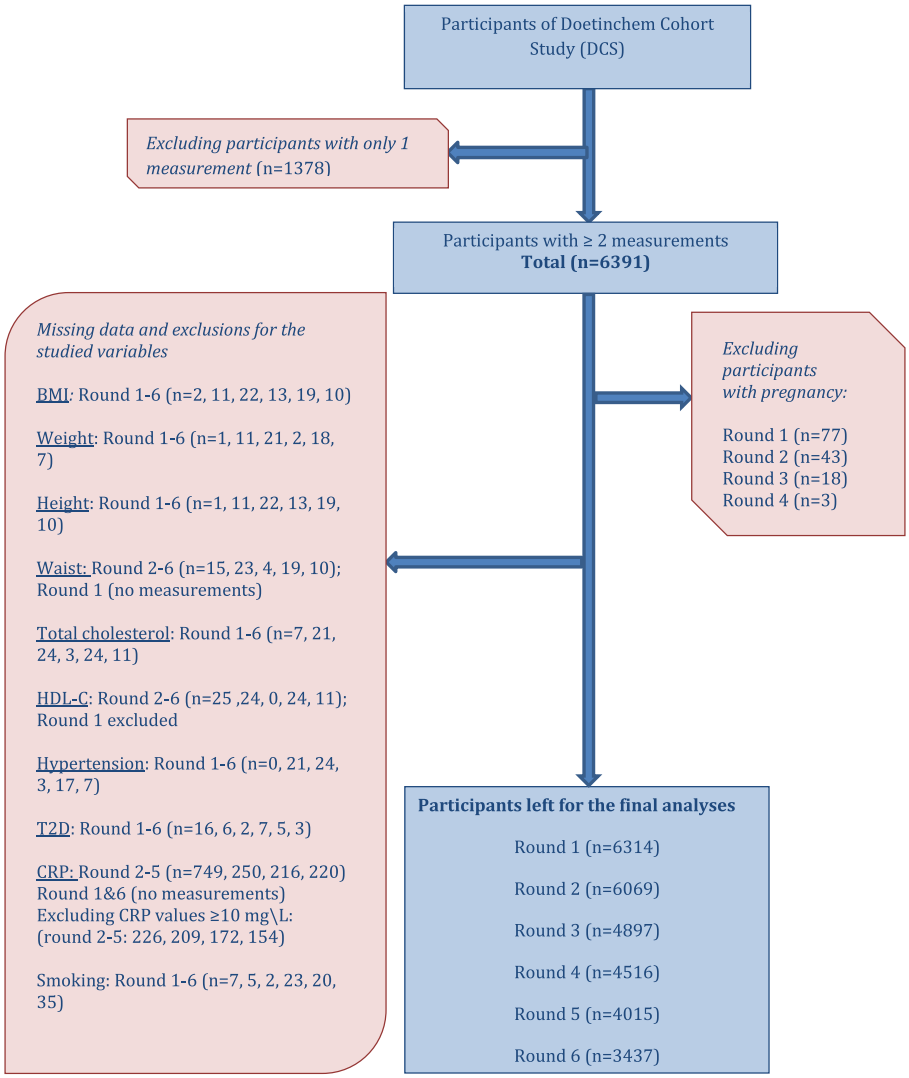

FIGURE 1 Flowchart of study participant selection. CRP, C-reactive protein; HDL-C, high-density lipoprotein cholesterol; T2D, type 2 diabetes [Color figure can be viewed at wileyonlinelibrary.com]

as BMI equal to or greater than 30. The mean value of two blood pressure measurements was used in the analyses. Hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and/or use of antihypertensive medication (according to World Health Organization definition) (20). Total cholesterol and high-density lipoprotein cholesterol (HDL-C) were measured until 1998 in non fasting EDTA plasma and, from 1998 onward, in serum at the Lipid Reference Laboratory using standardized enzymatic methods. Hypercholesterolemia was defined as total cholesterol of 6.5 mmol/L and/or use of cholesterol-lowering medication, and low HDL-C was defined based on the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII) definition of cardiometabolic syndrome as HDL-C < 1.03 mmol/L and < 1.29 mmol/L in men and women, respectively (21). For C-reactive protein (CRP), standardized enzymatic methods were used to retrospectively determine CRP in four rounds (rounds 2, 3, 4, and 5) using blood plasma that had been stored in freezers. This examination of all available samples from consecutive rounds (rounds 2, 3, 4, and 5) in one assay run was performed to reduce the chance of measurement error and batch effects.

T2D cases were defined on the basis of self-report or level of random glucose (>11.1 mmol/L). Most self-reported diabetes cases were verified with information from the general practitioner or pharmacist (86%). The highest level of completed education during follow-up was classified into the following three categories: 1) low (intermediate secondary education or less); 2) intermediate (intermediate vocational or higher secondary education); and 3) high (higher vocational education or university). Smoking was assessed by means of a questionnaire and categorized into current, ex-, and never smokers.

Statistical analyses

The development in the prevalence of anthropometric measures and cardiometabolic risk factors over time in four 10-year generations was described. The generations were defined on the baseline age of the

participants: 20 to 29, 30 to 39, 40 to 49, and 50 to 59 years, further referred to as those who were in their 20s, 30s, 40s, and 50s, respectively. The prevalence or mean (median for non-normally distributed variables of anthropometric measures and cardiometabolic risk factors) was plotted against the mean age of these generations at the time of measurement for men and women separately. A generation shift occurs when the difference in the prevalence or mean of a particular measure of obesity or cardiometabolic risk factor between generations at a similar age is significantly different, as determined by logistic regression for dichotomous outcomes and linear regression for continuous outcomes. In order to take the correlations among repeated observations on the same participants into account, we used generalized estimating equations (GEE) with an autoregressive structure similar to Hulsegge et al. (8). In order to distinguish between differences in earlier and later lifetime points, we performed the analyses separately for earlier development (rounds 1, 2, 3, and 4), later development (rounds 3, 4, 5, and 6), and then for the time development over the total period, comprising all six rounds. At rounds 3, 4, 5, and 6, the mean age of a generation was approximately the same as the mean age of a generation born 10 years earlier at rounds 1, 2, 3, and 4, respectively. Therefore, for the earlier development, measures of obesity and cardiometabolic risk factors at rounds 3 and 4 of a generation were compared with those of a generation born 10 years earlier at rounds 1 and 2, respectively. In the later development, rounds 5 and 6 of a generation were compared with the generation born 10 years earlier at rounds 3 and 4, respectively. Finally, for the time development over the total period, the data at rounds 3, 4, 5, and 6 of a generation were compared with those of a generation born 10 years earlier at rounds 1, 2, 3, and 4, respectively. As waist circumference was not measured in round 1, GEE was performed comparing rounds 4, 5, and 6 (total period), rounds 4 and 5 (earlier development), and rounds 5 and 6 (later development) of a generation with rounds 2, 3, and 4 (total period), rounds 2 and 3 (early development), and rounds 3 and 4 (later development), respectively, of a 10-year older generation. As the HDL-C values in the first round deviated markedly from the values in the other rounds, these data were omitted in the current analyses, and, therefore, GEE for HDL-C was performed comparing the same rounds as for waist circumference. CRP was not measured in rounds 1 and 6, and, therefore, only rounds 4 and 5 of a generation were compared with rounds 2 and 3 of a 10-year older generation.

The analyses were adjusted for age, and a p value < 0.05 was considered statistically significant. Descriptive analyses were performed in SPSS Statistics version 23 (IBM Corp., Armonk, New York), and GEE analyses were performed in SAS version 9.2 (SAS Institute Inc., Cary, North Carolina).

RESULTS

Population characteristics

The general characteristics of the study population at baseline are presented in Table 1. In the total population, the mean age was 40.0 years, and 48% were men. Participants in the older generations had a lower educational level and a lower percentage of current smokers, but a higher percentage were former smokers compared with the younger generations. The oldest generation of women had the highest percentage of never smokers and the lowest percentage of current smokers. Participants in the older generations had more unfavorable baseline levels of systolic blood pressure, diastolic blood pressure, and total cholesterol and used antihypertensive and cholesterol-lowering medication more often. Women in the younger generations entered the menarche earlier. The oldest generation of women (50-59 years at baseline) had the highest mean number of children ($n = 2.9$) compared with the other three generations ($n = 2.1$).

Anthropometric measures

Figure 2 shows the development of anthropometric measures and BMI as well as the prevalence of overweight and obesity. Weight increased whereas height decreased with age in both men and women in all generations and they were both significantly higher in the younger generations ($p < 0.001$) when compared at a similar age with participants born 10 years earlier (Figure 2A-2D and Tables 2 and 3). BMI, waist circumference, and prevalence of overweight and obesity increased with age in all generations and they were, in general, significantly higher in the younger generations compared with the older generations (Figure 2E-2L and Tables 2 and 3). Among men, such unfavorable generation shifts in the aforementioned traits were present between all consecutive generations when they were compared over the life course and especially with respect to earlier development, but not to later development. For example, at an average age of 35 years, the obesity prevalence was 8.6% (round 3) in men who were in their 20s at baseline and 4.0% (round 1) in men who were born 10 years earlier (those in their 30s at baseline; Table 2). However, as also seen in Figure 2, BMI, waist circumference, and obesity prevalence in the younger generations did not reach significantly higher levels in later life than in the older generations ($p > 0.05$). For example, at the average age of 50 years, the obesity prevalence was 14.6% (round 6) in men who were in their 20s at baseline and 13.9% (round 4) in men who were born 10 years earlier (those in their 30s at baseline). Among women, initially unfavorable but ultimately converging generation shifts were evident for the three youngest generations. However, the oldest generation of women showed elevated levels for BMI, weight, waist circumference, and prevalence of overweight and obesity already within the first three rounds compared with the younger three generations. The youngest generation of women (those in their 20s at baseline) had the most unfavorable shift in obesity development, whereas the prevalence of obesity almost doubled when they reached a similar age compared with those who were in their 30s at baseline ($p < 0.001$).

Cardiometabolic risk factors

Levels of cardiometabolic risk factors increased with age during the 26-year follow-up in all generations of men and women, except

TABLE 1 General baseline characteristics for four generations in the Doetinchem Cohort Study (*N* = 6,314)

		20-29 years		30-39 years		40-49 years		50-59 years	
	Total (*N* = 6,314)	Men (*n* = 469)	Women (*n* = 589)	Men (*n* = 941)	Women (*n* = 1,040)	Men (*n* = 928)	Women (*n* = 955)	Men (*n* = 659)	Women (*n* = 733)
Baseline age (y)	40.0 ± 10.2	25.4 ± 2.9	25.3 ± 2.8	35.1 ± 2.9	35.0 ± 2.7	44.3 ± 2.6	44.2 ± 2.8	54.5 ± 2.8	54.6 ± 2.9
Men (%)	48	-	-	-	-	-	-	-	-
Education (%)									
Low	63	52	49	49	65	59	76	61	83
Intermediate	21	37	41	27	19	21	12	17	9
High	16	11	10	23	16	21	13	22	8
Smoking (%)									
Current smokers	35	39	40	37	38	34	33	31	25
Former smokers	29	13	17	30	31	39	25	46	19
Non smokers	37	48	44	33	31	28	42	23	57
BMI (kg/m^2)	24.6 ± 3.5	23.4 ± 2.8	22.6 ± 3.4	24.5 ± 2.9	23.5 ± 3.5	25.6 ± 3.0	24.6 ± 3.6	26.0 ± 3.0	26.3 ± 4.0
SBP (mmHg)	122 ± 15	125 ± 12	114 ± 11	124 ± 12	113 ± 12	125 ± 14	118 ± 15	130 ± 16	126 ± 16
DBP (mmHg)	78 ± 10	74 ± 9	72 ± 9	78 ± 10	73 ± 9	81 ± 10	77 ± 10	82 ± 11	80 ± 11
Antihypertensive medication (%)	19	3	3	8	7	12	16	33	43
Total cholesterol (mmol/L)	5.47 ± 1.08	4.79 ± 0.90	4.95 ± 0.86	5.41 ± 1.06	5.04 ± 0.91	5.84 ± 1.09	5.43 ± 0.94	5.98 ± 0.96	6.18 ± 1.04
HDL-C (mmol/L)[a]	1.25 ± 0.31	1.13 ± 0.24	1.36 ± 0.29	1.12 ± 0.26	1.35 ± 0.30	1.12 ± 0.27	1.39 ± 0.32	1.09 ± 0.26	1.35 ± 0.32
Cholesterol-lowering medication (%)	2	0	0	0	0	2	0	2	4
Female-specific									
Age at menarche	13.4 ± 1.5	-	13.1 ± 1.5	-	13.2 ± 1.4	-	13.5 ± 1.5	-	13.7 ± 1.7
Number of children[b]	2.4 ± 1.0	-	2.1 ± 0.9	-	2.2 ± 0.9	-	2.2 ± 0.8	-	2.9 ± 1.4

Values are mean ± SD or %. All data are from baseline (round 1), unless otherwise specified.

Abbreviations: DBP, diastolic blood pressure; HDL-C, high-density lipoprotein; SBP, systolic blood pressure.

[a]These are data from round 2 because of a marked deviation of HDL-C values in round 1.

[b]Number of children is given as the maximum value of the available rounds.

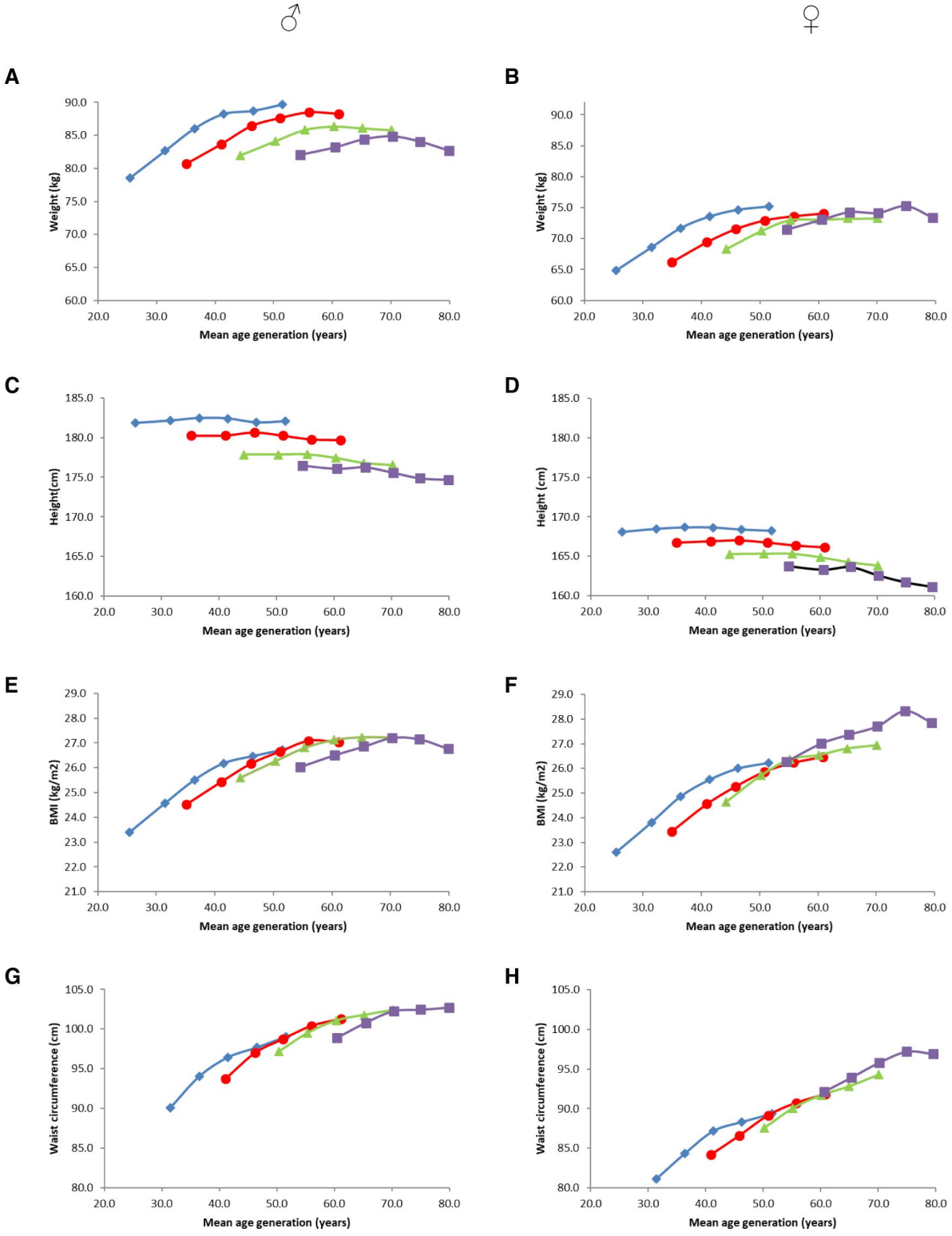

FIGURE 2 Age-specific mean (SD) or prevalence of anthropometric measures over 26 years of follow-up (six rounds) in those who were in their 20s (20-29 years; -◆- [blue]), 30s (30-39 years; -●- [red]), 40s (40-49 years; -▲- [green]), and 50s (50-59 years; -■- [purple]) at baseline, stratified by sex: (A,B) weight; (C,D) height; (E,F) BMI; (G,H) waist circumference; (I,J) overweight ($25 \leq \text{BMI} < 30\,\text{kg/m}^2$); and (K,L) obesity (BMI ≥ 30)

for low HDL-C (Figure 3). Hypertension and hypercholesterolemia were more prevalent in men before age 50 years than in women. After age 50 years, hypercholesterolemia was more prevalent in women. However, hypertension and hypercholesterolemia did not differ across the generations, except for the youngest generation of women, who started with a significantly higher prevalence of

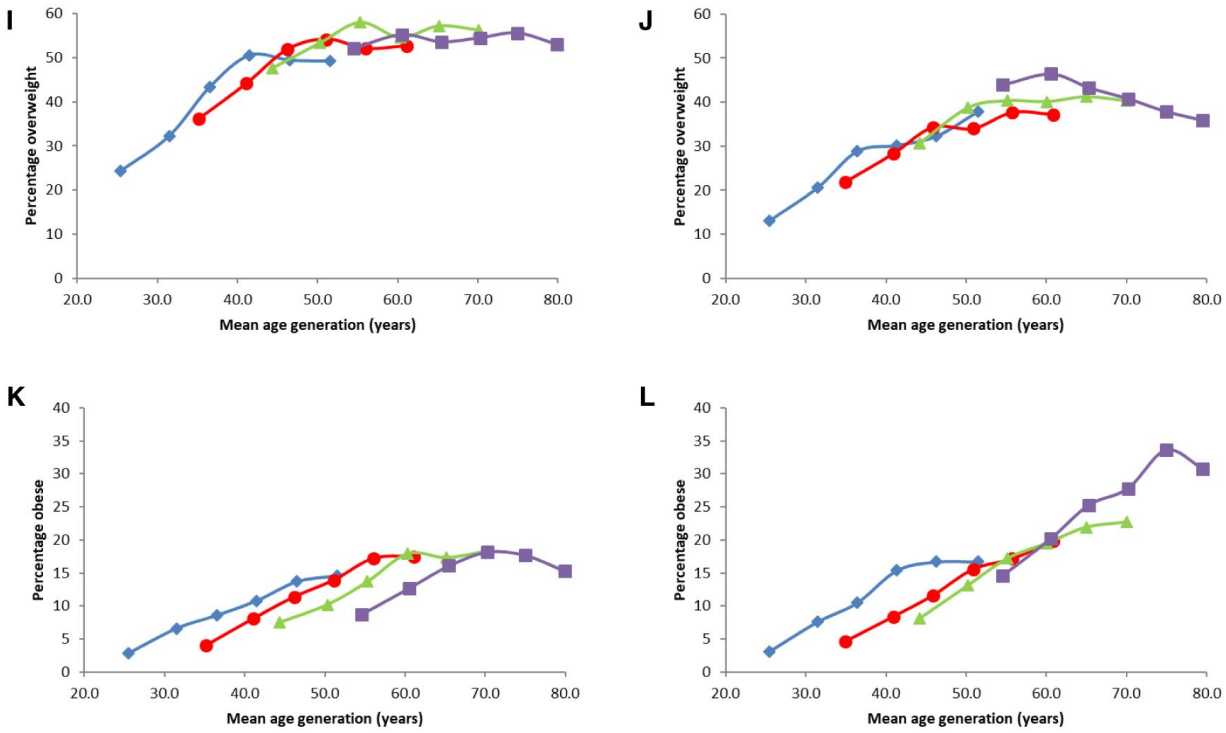

FIGURE 2 (Continued)

hypertension compared with those born 10 years earlier ($p = 0.013$; Figure 3 and Table 3). In addition, an unfavorable generation shift ($p = 0.042$) was observed in the later development for hypercholesterolemia in men who were in their 30s at baseline compared with those in their 40s at baseline (Figure 3 and Table 2). Interestingly, the percentage of low HDL-C was significantly lower in the younger generations, resulting in favorable generation shifts, particularly in women. Overall, T2D development did not differ across the generations. An unfavorable generation shift for T2D was only observed when comparing the development in men who were in their 50s at baseline with those born 10 years earlier ($p = 0.007$). However, CRP showed a favorable generation shift between men in their 30s at baseline and those in their 40s ($p = 0.018$) and between the two oldest generations of men and women ($p = 0.009$ and $p = 0.003$, respectively). Owing to the fact that CRP is strongly associated with smoking, we assessed smoking prevalence during the follow-up of our cohort (Figure 4). Prevalence of current smoking decreased with age in both sexes and all generations. Furthermore, for both men and women, a favorable generation shift was observed in the younger generations compared with the older ones ($p < 0.05$; Figure 4).

DISCUSSION

Our results show that the prevalence of overweight and obesity increased with age and reached a sex-specific plateau at late midlife. This was apparent for all generations of men and women, except for the oldest generation of women, whose BMI still increased beyond late midlife. At the same age, the younger generations had higher weight, BMI, waist circumference, and prevalence of overweight and obesity compared with the older generations but did not reach much higher levels in later life. In general, these developments did not translate into unfavorable generation shifts in cardiometabolic risk factors.

Evidence that younger birth generations are heavier than the ones born earlier was observed in high-income countries such as the United States (22,23), UK (24), Australia (11,25), Norway (26), Finland (9), and Austria (27), as well as in middle-income countries such as China (28). The Atherosclerosis Risk in Communities Study examined associations of age with mean BMI across three bi-ethnic birth cohorts (1920-1930, 1930-1935, and 1935-1945) ranging from 45 to 64 years of age, and reported that, except for White women, participants in the more recent cohorts gained more weight as they aged (22). In our study, we observed unfavorable generation shifts in the anthropometric measures and obesity prevalence between every generation of men, whereas, in women, they were evident especially between the two youngest generations. Our results are in line with a recent Australian study (25) reporting a higher prevalence of obesity in women born in 1989 through 1995 compared with women born in 1973 through 1978 when they were the same age. Other studies with similar age groups as in our cohort support the consistent unfavorable shifts we found among men, whereas their results for women partially contradict ours. For example, a Norwegian cohort study (26) with a comparable range of birth years to our DCS showed that BMI increased in every birth cohort of men and women during a 15 to 20-year period of follow-up. However, the study found that this increase was larger in the younger birth cohorts of men than the older ones but did not differ among female birth cohorts. The lack of BMI differences in the female birth cohorts reported in these two studies contradicts the unfavorable BMI shift found between

TABLE 2 Comparison of anthropometric measures and cardiometabolic risk factors over six rounds between consecutive generations in men

	Round 1	Round 2	Round 3	Round 4	Round 5	Round 6	*p* value[a]	*p* value[b]	*p* value[c]
Weight (kg)			a		b				
20-29	78.5 ± 11.0	82.6 ± 12.0	86.0 ± 12.5	88.2 ± 13.7	88.7 ± 13.7	89.7 ± 14.1	<0.001	0.013	<0.001
30-39	80.7 ± 10.6	83.7 ± 11.2	86.4 ± 11.5	87.6 ± 12.0	88.5 ± 12.4	88.3 ± 12.3	<0.001	<0.001	<0.001
			c						
40-49	82.0 ± 10.6	84.1 ± 11.3	85.8 ± 11.7	86.3 ± 11.8	86.1 ± 11.3	85.8 ± 11.8	<0.001	0.03	<0.001
50-59	82.1 ± 10.1	83.2 ± 10.5	84.4 ± 10.9	84.8 ± 11.0	84.1 ± 11.0	82.7 ± 11.4	-	-	-
Height (cm)									
20-29	181.8 ± 6.7	182.1 ± 6.6	182.4 ± 6.9	182.4 ± 6.4	181.9 ± 6.2	182.0 ± 6.2	<0.001	<0.001	<0.001
30-39	180.2 ± 6.5	180.3 ± 6.5	180.7 ± 6.6	180.2 ± 6.4	179.8 ± 6.3	179.7 ± 6.3	<0.001	<0.001	<0.001
40-49	177.8 ± 6.3	177.8 ± 6.3	177.8 ± 6.3	177.4 ±6.0	176.8 ± 6.0	176.5 ± 6.2	<0.001	0.055	<0.001
50-59	176.5 ± 6.5	176.1 ± 6.5	176.3 ± 6.5	175.6 ± 6.2	174.9 ± 6.3	174.7 ± 6.5	-	-	-
BMI (kg/m^2)									
20-29	23.4 ± 2.8	24.6 ± 3.1	25.5 ± 3.2	26.2 ± 3.6	26.5 ± 3.7	26.7 ± 3.8	<0.001	0.39	0.013
30-39	24.5 ± 2.9	25.4 ± 3.1	26.2 ± 3.2	26.6 ± 3.3	27.1 ± 3.6	27.0 ± 3.5	0.033	0.71	0.13
40-49	25.6 ± 3.0	26.3 ± 3.2	26.8 ± 3.4	27.1 ± 3.5	27.2 ± 3.5	27.2 ± 3.6	<0.001	0.23	0.001
50-59	26.0 ± 2.9	26.5 ± 3.1	26.9 ± 3.3	27.2 ± 3.4	27.2 ± 3.3	26.8 ± 3.4	-	-	-
Waist circumference (cm)[d]									
20-29	-	90.1 ± 9.2	94.1 ± 9.3	96.5 ± 10.2	97.7 ± 10.7	99.1 ± 11.4	0.0048	0.48	0.015
30-39	-	93.8 ± 8.9	97.0 ± 9.1	98.9 ± 9.4	100.4± 10.0	101.3 ± 10.0	0.039	0.54	0.11
40-49	-	97.2 ± 9.3	99.5 ± 9.9	101.1 ± 101	101.8 ± 10.0	102.4 ± 10.7	<0.001	0.26	0.005
50-59	-	98.9 ± 9.0	100.8 ± 9.6	102.3 ± 9.8	102.5 ± 9.7	102.7 ± 10.3	-	-	-
Overweight (%)									
20-29	24.4	32.3	43.4	50.6	49.5	49.3	0.0033	0.29	0.008
30-39	36.2	44.2	51.9	54.2	52.1	52.7	0.65	0.096	0.29
40-49	47.7	53.4	58	54.6	57.2	56.3	0.25	0.29	0.23
50-59	52.1	55.2	53.6	54.5	55.6	53	-	-	-
Obesity (%)									
20-29	2.8	6.6	8.6	10.8	13.7	14.6	0.043	0.53	0.01
30-39	4	8.1	11.4	13.9	17.2	17.5	0.021	0.55	0.006
40-49	7.5	10.2	13.7	17.9	17.3	18.3	0.0013	0.8	<0.001
50-59	8.7	12.7	16.1	18.2	17.7	15.3	-	-	-
Hypertension (%)									
20-29	14.3	15	19.9	21.2	28.6	32	0.76	0.11	0.28
30-39	17.9	23.1	33.3	35.2	44.7	51.1	0.083	0.86	0.3
40-49	23.8	34.9	42.8	51.5	61.6	63.9	0.093	0.71	0.16
50-59	35.4	51	59.2	66.2	70.5	70.4	-	-	-
Hypercholesterolemia (%)									
20-29	3.8	6.8	14.6	14	22.1	25.2	0.32	0.58	0.23
30-39	15	16.2	24.1	25.9	33.2	35.4	0.11	0.042	0.35
40-49	23.7	20.6	29.6	28.9	33.8	38.4	0.1	0.079	0.33
50-59	29.4	22.8	31.3	32	42.5	48.1	-	-	-
Low HDL-C (%)[d]									
20-29	-	25.7	30.9	27.6	29.9	21.8	0.52	0.35	0.23

(Continues)

TABLE 2 (Continued)

	Round 1	Round 2	Round 3	Round 4	Round 5	Round 6	*p* value[a]	*p* value[b]	*p* value[c]
30-39	-	30.2	30.2	27.3	27.7	25.3	0.14	0.54	0.37
40-49	-	30.4	31.5	25.5	25.1	23.8	0.01	0.089	0.07
50-59	-	30.6	31.5	24.4	24.5	23.6	-		-
T2D (%)									
20-29	0.6	0.9	1.1	0.9	2.2	3.1	0.07	0.34	0.13
30-39	0.1	0.4	0.7	2.3	4.3	5.6	0.55	0.96	0.63
40-49	0.9	2.2	3.2	5.5	8.9	10	0.0073	0.22	0.11
50-59	1.2	3.2	6.4	9.2	14.4	13.9	-	-	-
C-reactive protein (mg/L)[e]									
20-29	-	0.60 (0.86)	0.72 (1.03)	0.88 (1.24)	0.90 (1.44)	-	-	-	0.72
30-39	-	0.81 (1.17)	0.94 (1.29)	1.02 (1.33)	1.07 (1.61)	-	-	-	0.018
40-49	-	1.10 (1.59)	1.10 (1.70)	1.22 (1.72)	1.20 (1.69)	-	-	-	0.009
50-59	-	1.36 (2.16)	1.43 (2.07)	1.41 (2.03)	1.44 (2.13)	-	-	-	-

Values are mean ± SD, median (interquartile range), or percentage. Logistic and linear regression using generalized estimating equations, adjusted for age, were used to test whether a generation was, at a similar age, statistically significantly different compared with the consecutive generations born 10 years earlier. The colored rectangles and the arrows in the first rows exemplify the comparisons performed for the corresponding *p* values.

Abbreviations: HDL-C, high-density lipoprotein cholesterol; T2D, type 2 diabetes.

[a]For the earlier development, the difference in all indicated outcomes, except waist circumference, low HDL-C, and C-reactive protein, at rounds 3 and 4 of a generation was compared with the generation born 10 years earlier at rounds 1 and 2, respectively (blue).

[b]For the later development, rounds 5 and 6 of a generation were compared with the generation born 10 years earlier at rounds 3 and 4, respectively (red).

[c]Finally, for the time development over the total period, the data at rounds 3, 4, 5, and 6 of a generation were compared with those of a generation born 10 years earlier at rounds 1, 2, 3, and 4, respectively (green).

[d]Rounds 4, 5, and 6 (whole development), rounds 4 and 5 (earlier development), and rounds 5 and 6 (later development) were compared with rounds 2, 3, and 4 (whole development), rounds 2 and 3 (earlier development), and rounds 3 and 4 (later development), respectively, of a 10-year older generation using linear regression (waist circumference) and logistic regression (low HDL-C).

[e]Rounds 4 and 5 were compared to rounds 2 and 3 of a 10-year older generation using linear regression. Consecutive generations had approximately a similar age at those moments.

our two youngest generations of women. However, our study also showed that there was no difference in the BMI development up to 50 years among the other generations of women, which is in concordance with results from the two aforementioned studies.

The higher BMI and obesity prevalence observed in the oldest generation of women after the age of 50 years in our study could be due to several lifestyle and environmental factors. The number of children in the oldest generation was higher compared with the rest, which could be one factor explaining the differences in the obesity development of the oldest women. Previous research has demonstrated a positive association between parity (the number of times a woman has given birth) and obesity in women, particularly after menopause (29). A study in middle-aged retired US women reported that women had a 7% increase in obesity for each additional child born, even after controlling for potential confounders (30). From a biological point of view, this positive association of parity and obesity can be explained by the numerous metabolic changes that occur during the pregnancy and can persist even after, including insulin resistance and fat accumulation (31,32).

Previously, we reported on 16 years of follow-up in the Doetinchem study (8) and already showed that the younger generations have overweight and obesity at a younger age. However, based on our follow-up of 26 years in total, we now observe that, despite having obesity at an earlier age, the younger generations do not reach much higher levels of BMI and obesity at midlife and beyond. This was an unanticipated observation given the expected further rise of BMI throughout middle age. For example, when participants of the youngest generation were at an average age of 45 years, the obesity prevalence in men was 13.7%, and, after 5 years, it reached 14.6%. This increase between the last two rounds was smaller than the increase in earlier rounds, which suggests that the rate of increase in obesity prevalence in the youngest generation of men starts to slow down after the age of 45 years and points to a probable plateau in obesity after the age of 50 years. In women, the obesity prevalence remained the same in the last two rounds, already showing evidence of a leveling off in obesity prevalence after the age of 50 years in the younger generations. Therefore, data from the last 10 years of follow-up in the current study point to an obesity plateau in both men and women, which was somewhat unexpected. However, it is important to emphasize that although the younger generations do not reach higher levels of obesity in later life, their lifetime exposure to obesity will be longer. This is of particular

TABLE 3 Comparison of anthropometric measures and cardiometabolic risk factors over six rounds between consecutive generations in women

	Round 1	Round 2	Round 3	Round 4	Round 5	Round 6	*p* value[a]	*p* value[b]	*p* value[c]
Weight (kg)			a		b				
20-29	64.9 ± 10.3	68.6 ± 11.8	71.7 ± 12.1	73.6 ± 13.6	74.7 ± 13.7	75.2 ± 13.6	<0.001	<0.001	<0.001
30-39	66.2 ± 10.2	69.4 ± 11.4	71.5 ± 12. 1	72.9 ± 12.7	73.6 ± 13.1	74.0 ± 13.3	<0.001	0.42	0.003
			c						
40-49	68.3 ± 10.4	71.2 ± 11.7	73.0 ± 12.4	73.1 ± 12.5	73.2 ± 12.0	73.3 ± 12.8	0.096	0.25	0.46
50-59	71.5 ± 11.4	73.1 ± 11.4	74.3 ± 12.4	74.1 ± 13.4	75.2 ± 15.0	73.4 ± 14.0	-	-	-
Height (cm)									
20-29	168.5 ± 6.6	168.6 ± 6.6	168.6 ± 6.4	168.4 ± 6.5	168.2 ± 6.4	<0.001	<0.001	<0.001	<0.001
30-39	166.7 ± 6.0	166.9 ± 6.0	167.0 ± 6.0	166.7 ± 6.1	166.3 ± 6.1	166.1 ± 6.0	<0.001	<0.001	<0.001
40-49	165.3 ± 5.9	165.3 ± 6.0	165.3 ± 5.8	164.9 ± 5.8	164.3 ± 5.7	163.8 ± 5.9	<0.001	0.0046	<0.001
50-59	163.8 ± 6.1	163.3 ± 6.1	163.6 ± 6.0	162.6 ± 6.1	161.7 ± 6.2	161.1 ± 6.0	-	-	-
BMI (kg/m^2)									
20-29	22.6 ± 3.4	23.8 ± 3.9	24.9 ± 4.1	25.5 ± 4.7	26.0 ± 4.8	26.2 ± 4.8	<0.001	0.026	<0.001
30-39	23.5 ± 3.5	24.6 ± 4.0	25.3 ± 4.1	25.9 ± 4.4	26.2 ± 4.6	26.5 ± 4.7	0.2	0.35	0.65
40-49	24.6 ± 3.6	25.7 ± 4.1	26.4 ± 4.4	26.5 ± 4.5	26.8 ± 4.5	26.9 ± 4.6	0.68	0.017	0.2
50-59	26.3 ± 4.0	27.0 ± 4.3	27.4 ± 4.4	27.7 ± 4.9	28.3 ± 5.4	27.9 ± 5.0	-	-	-
Waist circumference (cm)[d]									
20-29	-	81.2 ± 10.3	84.4 ± 10.5	87.2 ± 11.6	88.3 ± 2.2	89.3 ± 11.9	<0.001	0.18	0.008
30-39	-	84.2 ± 10.5	86.6 ± 10.8	89.1 ± 11.0	90.7 ± 11.4	91.8 ± 12.3	0.057	0.84	0.24
40-49	-	87.6 ± 10.5	90.1 ± 11.0	91.7 ± 11.1	92.8 ± 11.2	94.3 ± 12.0	0.25	0.065	0.15
50-59	-	92.1 ± 11.4	93.9 ± 11.6	95.8 ± 12.0	97.2 ± 12.8	96.9 ± 12.4	-	-	-
Overweight (%)									
20-29	13.1	20.6	28.9	30.2	32.3	37.9	0.054	0.83	0.012
30-39	21.8	28.3	34.3	34	37.7	37.2	0.38	0.31	0.82
40-49	30.7	38.7	40.3	40.1	41.2	40.3	0.016	0.49	0.069
50-59	43.9	46.4	43.3	40.8	37.9	35.9	-	-	-
Obesity (%)									
20-29	3.1	7.6	10.5	15.4	16.7	16.7	<0.001	0.071	<0.001
30-39	4.6	8.4	11.6	15.6	17.2	19.9	0.1	0.55	0.007
40-49	8.1	13.1	17.2	19.5	21.9	22.7	0.31	0.089	0.18
50-59	14.6	20.2	25.3	27.8	33.6	30.8	-	-	-
Hypertension (%)									
20-29	4.6	7.6	11.8	16.1	22.7	27.6	0.013	0.79	0.36
30-39	6.3	12.8	23.2	27.2	36	38.5	0.45	0.011	0.38
40-49	16.1	27.9	38.1	44.8	54.3	57.1	0.07	0.42	0.48
50-59	31.8	44.4	54.6	60.6	71.4	72.4	-	-	-
Hypercholesterolemia (%)									
20-29	4.6	3.2	6.7	8	11	16.7	0.98	0.017	0.025
30-39	7	7.5	13.2	20.9	34.6	42.9	0.45	0.22	0.75
40-49	13.4	17.4	34.2	36.8	51.9	52.3	0.85	0.078	0.54
50-59	34.7	37.4	47	47	54.5	51	-	-	-
Low HDL-C (%)[d]									
20-29	-	28.7	31.8	23.2	25.4	26	0.092	0.63	0.95
30-39	-	26.7	28.7	20.6	21.2	19.5	0.0048	0.014	0.008
40-49	-	24.9	26.9	23.7	25	23.7	<0.001	0.003	<0.001

(Continues)

TABLE 3 (Continued)

	Round 1	Round 2	Round 3	Round 4	Round 5	Round 6	*p* value[a]	*p* value[b]	*p* value[c]
50-59	-	32.8	33.5	28.3	29.4	25.4	-	-	-
T2D (%)									
20-29	0.2	0	0	0.4	0.7	1.9	0.15	0.85	0.8
30-39	0.3	1.2	0.8	2	4	4.9	0.81	0.45	0.81
40-49	0.7	1.6	2	4.2	6.4	9.7	0.3	0.9	0.65
50-59	1.6	3.5	5.5	10.7	15.3	16.3	-	-	-
C-reactive protein (mg/L)[e]									
168.1 ± 6.6	-	1.35 (2.35)	1.33 (2.56)	1.20 (2.38)	1.16 (2.11)	-	-	-	0.061
30-39	-	0.97 (1.83)	1.20 (2.10)	1.15 (1.75)	1.07 (1.57)	-	-	-	0.16
40-49	-	1.07 (1.69)	1.21 (1.94)	1.23 (1.84)	1.25 (1.76)	-	-	-	0.003
50-59	-	1.44 (2.06)	1.65 (2.27)	1.60 (2.32)	1.40 (1.93)	-	-	-	-

Values are mean ± SD, median (interquartile range), or %. Logistic and linear regression using generalized estimating equations, adjusted for age, were used to test whether a generation was, at a similar age, statistically significantly different compared with the consecutive generations born 10 years earlier. The colored rectangles and the arrows in the first rows exemplify the comparisons performed for the corresponding *p* values.

Abbreviations: HDL-C, high-density lipoprotein cholesterol; T2D, type 2 diabetes.

[a]For the earlier development, the difference in all indicated outcomes, except waist circumference, low HDL-C, and C-reactive protein, at rounds 3 and 4 of a generation was compared with the generation born 10 years earlier at rounds 1 and 2, respectively (blue).

[b]For the later development, rounds 5 and 6 of a generation were compared with the generation born 10 years earlier at rounds 3 and 4, respectively (red).

[c]Finally, for the time development over the total period, the data at rounds 3, 4, 5, and 6 of a generation were compared with those of a generation born 10 years earlier at rounds 1, 2, 3, and 4, respectively (green).

[d]Rounds 4, 5, and 6 (whole development), rounds 4 and 5 (earlier development), and rounds 5 and 6 (later development) were compared with rounds 2, 3, and 4 (whole development), rounds 2 and 3 (earlier development), and rounds 3 and 4 (later development), respectively, of a 10-year older generation using linear regression (waist circumference) and logistic regression (low HDL-C).

[e]Rounds 4 and 5 were compared to rounds 2 and 3 of a 10-year older generation using linear regression. Consecutive generations had approximately a similar age at those moments.

concern, as an earlier exposure and longer duration of obesity have been shown to increase risk of several metabolic conditions, including T2D and CVD (13-15).

It is important to mention that although BMI is the standard measure of overweight and obesity, it does not assess body composition or fat distribution. It has previously been shown that visceral fat, which is stored in the abdominal cavity, secretes more pro-inflammatory cytokines than other types of fat, which are thought to play an important role in the pathogenesis of insulin resistance and T2D (33). Waist circumference is a simple way of assessing visceral fat, and a higher waist circumference has also been associated with increased T2D risk (34). In our study, the waist circumference followed a similar pattern to BMI, increasing more in the early development between each generation of men and the two youngest generations of women and starting to level off in the latest years of follow-up. These results point to increased weight-related chronic systemic inflammation in the younger generations, which could, in turn, increase the risk for T2D in these groups. However, in our study, CRP levels, a marker for inflammation, were not higher in the younger generations compared with the older ones, but, on the contrary, in some generations of men and women CRP showed a favorable generation shift. In men, the lack of increased inflammation in the younger generations, given their unfavorable shifts in waist circumference, could be explained by the counterbalancing effects of decreased smoking prevalence in the recent generations of the Doetinchem study, shown by Raho et al. (35). Our latest follow-up rounds further support this observation, pointing to favorable smoking generation shifts in men. Therefore, the reduced prevalence of smoking in the younger generations of men may have reversed the adverse effects of increased waist circumference and obesity on inflammation, which could, in turn, partially account for the general lack of unfavorable generation shifts in T2D prevalence. However, the unfavorable generation shift in T2D prevalence observed only between the two oldest generations of men suggests that, in addition to reduced smoking prevalence, a possible delay between obesity and onset of T2D may explain the discrepant pattern of increased visceral fat and obesity without an increase in T2D prevalence. Among women, the large unfavorable generation shift in waist circumference and obesity that was found only between the two youngest generations is probably not (yet) reflected in T2D shifts because the prevalence of diabetes is too low at that age. It is hard to predict the impact that increased obesity in the youngest generation of women will have on T2D prevalence in the future if we take into consideration the large favorable shift in current smoking in the youngest generation of women, further supported by Raho et al. (35).

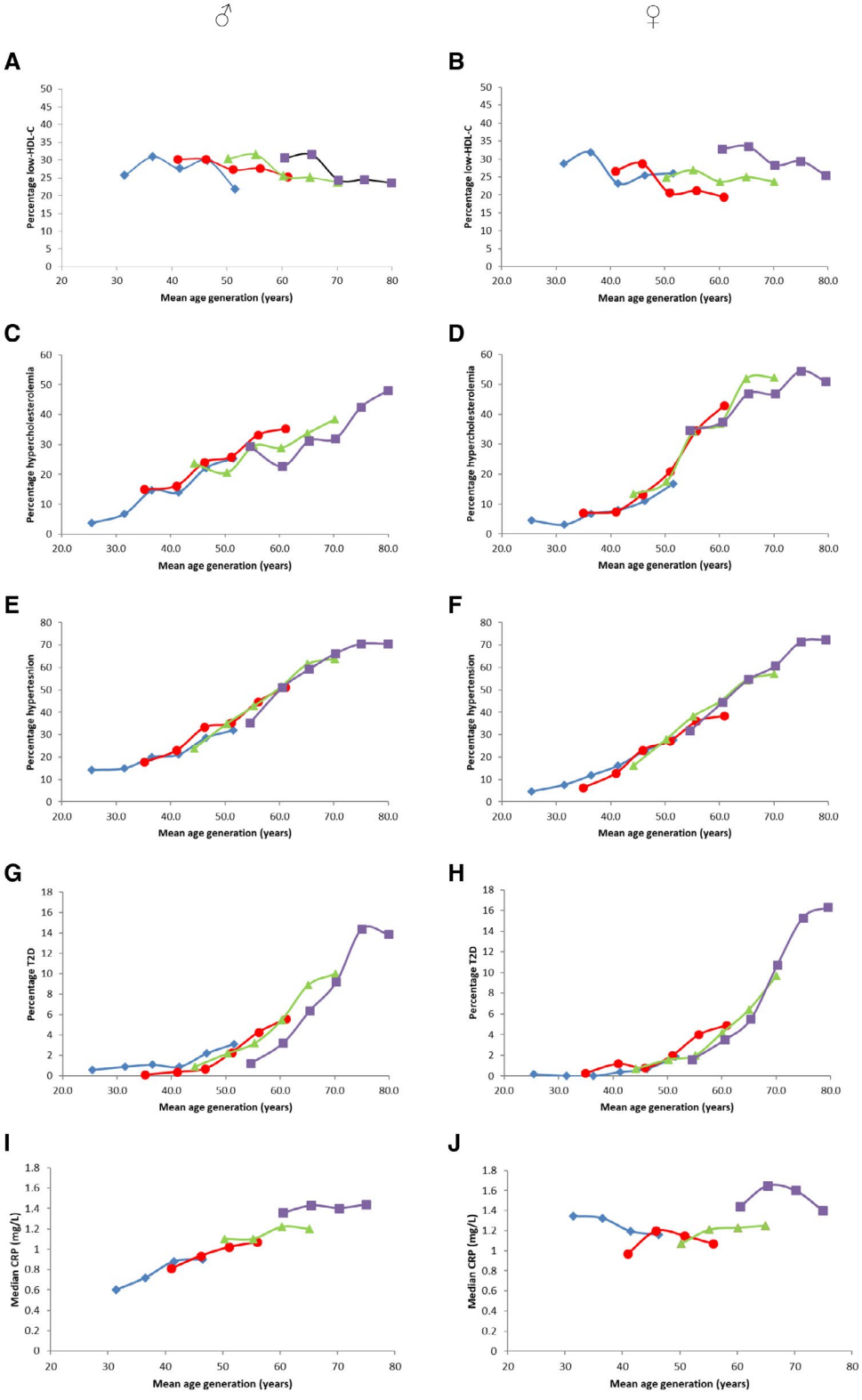

FIGURE 3 Age-specific prevalence of cardiometabolic risk factors over 26 years of follow-up (six rounds) in those who were in their 20s (20-29 years; -◆- [blue]), 30s (30-39 years; -●- [red]), 40s (40-49 years; -▲- [green]), and 50s (50-59 years; -■- [purple]) at baseline, stratified by sex: (A,B) low HDL-C; (C,D) hypercholesterolemia (total cholesterol = 6.5 mmol/L and/or on cholesterol-lowering medication); (E,F) hypertension; (G,H) T2D; and (I,J) CRP, expressed as median (interquartile range). CRP, C-reactive protein; HDL-C, high-density lipoprotein cholesterol; T2D, type 2 diabetes

Obesity A Research Journal THE OBESITY SOCIETY –WILEY

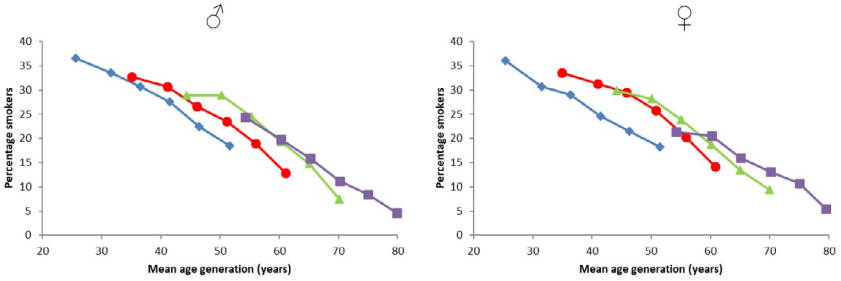

FIGURE 4 Age-specific prevalence of current smoking over 26 years of follow-up (six rounds) in those who were in their 20s (20-29 years; -◆- [blue]), 30s (30-39 years; -●- [red]), 40s (40-49 years; -▲- [green]), and 50s (50-59 years; -■- [purple]) at baseline, stratified by sex

In our study, despite the increasing obesity prevalence in the younger generations, prevalence of hypertension and hypercholesterolemia showed, in general, no evident generation shifts in the younger individuals with more overweight and obesity. One explanation for these results could be the increased use in the last decades of antihypertensive and lipid-lowering medication, particularly among individuals with obesity (36,37). In fact, in our data, we observed that the younger generations used more antihypertensive and lipid-lowering medication compared with the older ones (data not shown).

Our study has some limitations that should be taken into account when interpreting the results. First, participants who take part in long-lasting prospective studies are usually slightly healthier and more educated than the general population. This means that the actual prevalence of obesity and cardiometabolic risk factors in the general Dutch population is probably slightly higher than what is presented in this study. However, the trends of anthropometrics and cardiometabolic risk factors in complete case analyses (including participants with measurements at all rounds) were similar to the trends in the main analyses (including participants with at least two measurements), indicating that they were not caused by a selective drop out during the follow-up (data not shown). Second, another limitation is that we did not examine specific trends in dietary intake and diet quality or changes in physical activity. However, one of the strengths of the present study is the long follow-up period of 26 years, comprising six rounds of measurements. Another advantage is that we extensively studied multiple anthropometric traits, including BMI, waist circumference, weight, and prevalence of overweight and obesity.

In summary, we found that younger generations have a higher and earlier exposure to obesity but do not reach higher levels of BMI and obesity prevalence at midlife and beyond compared with the older generations. Although, in general, these unfavorable generation shifts in anthropometric traits and prevalence of obesity were not associated with increased prevalence of cardiometabolic risk factors, the increased prevalence and duration of obesity in the younger generations should not be neglected and they might still lead to negative health effects further down the line. Owing to the fact that the most recently born generations had reached merely age 50 years at the end of our follow-up, further research beyond this age is needed to assess the progression of cardiometabolic and other obesity-related diseases in the current generations because of their long exposure to obesity. Furthermore, the observation that BMI plateaued for all younger generations at a similar level suggests that apparently, at this plateau, a population-specific energy balance is reached. Research into the determinants of this state of energy balance could provide insight into population-wide measures to decrease adiposity. This would require quantitative research to explore the effects of genetic influences and environmental factors and their interactions over the life course. Another consideration for future research would be focusing on developing alternative markers that could better assess and capture adiposity and cardiometabolic health and disease, such as metabolomics-based biomarkers. Finally, individuals with obesity in the current generations still have higher levels of cardiometabolic risk factors and risk of CVD than those with normal weight (38,39), calling for the need to maintain a healthy weight and prevent a further increase in obesity in the current generations.O

ACKNOWLEDGMENTS

The authors would like to thank the field workers of the Municipal Health Services in Doetinchem for their contribution to the data collection, P. Vissink for logistic management, and A. Blokstra for data management (all from the National Institute for Public Health and the Environment).

CONFLICT OF INTEREST

The authors declared conflict of interest.

DATA AVAILABILITY STATEMENT

Processed data for every figure are made available/will be made available, study protocol has been published, and analysis plan can be shared. Access to the data will be granted by the Scientific Advisory Board of the National Institute for Public Health and the Environment, which can be contacted through VPZ (secretariaat@rivm.nl). We are willing to share, but, preferably, access is through remote access.

ORCID

Dorina Ibi https://orcid.org/0000-0003-0908-4039

REFERENCES

1. Kelly T, Yang W, Chen CS, Reynolds K, He J. Global burden of obesity in 2005 and projections to 2030. *Int J Obes* (Lond). 2008;32:1431-1437.
2. Boden G. Obesity, insulin resistance and free fatty acids. *Curr Opin Endocrinol Diabetes Obes*. 2011;18:139-143.
3. Agha M, Agha R. The rising prevalence of obesity: part A: impact on public health. *Int J Surg Oncol (N Y)*. 2017;2:e17. doi:10.1097/IJ9.0000000000000017
4. Klop B, Elte JWF, Cabezas MC. Dyslipidemia in obesity: mechanisms and potential targets. *Nutrients*. 2013;5:1218-1240.
5. Khaodhiar L, McCowen KC, Blackburn GL. Obesity and its comorbid conditions. *Clin Cornerstone*. 1999;2:17-31.
6. Olshansky SJ, Passaro DJ, Hershow RC, et al. A potential decline in life expectancy in the United States in the 21st century. *N Engl J Med*. 2005;352:1138-1145.
7. Villareal DT, Apovian CM, Kushner RF, Klein S. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, the Obesity Society. *Am J Clin Nutr*. 2005;82:923-934.
8. Hulsegge G, Picavet HSJ, Blokstra A, et al. Today's adult generations are less healthy than their predecessors: generation shifts in metabolic risk factors: the Doetinchem Cohort Study. *Eur J Prev Cardiol*. 2014;21:1134-1144.
9. Lahti-Koski M, Jousilahti P, Pietinen P. Secular trends in body mass index by birth cohort in eastern Finland from 1972 to 1997. *Int J Obes* Relat Metab Disord. 2001;25:727-734.
10. Keyes KM, Utz RL, Robinson W, et al. What is a cohort effect? Comparison of three statistical methods for modeling cohort effects in obesity prevalence in the United States, 1971-2006. *Soc Sci Med*. 2010;70:1100-1108.
11. Allman-Farinelli MA, Chey T, Bauman AE, Gill T, James WP. Age, period and birth cohort effects on prevalence of overweight and obesity in Australian adults from 1990 to 2000. *Eur J Clin Nutr*. 2008;62:898-907.
12. Swinburn BA, Sacks G, Hall KD, et al. The global obesity pandemic: shaped by global drivers and local environments. *Lancet*. 2011;378:804-814.
13. Luo J, Hodge A, Hendryx M, Byles JE. Age of obesity onset, cumulative obesity exposure over early adulthood and risk of type 2 diabetes. *Diabetologia*. 2020;63:519-527.
14. Abdullah A, Stoelwinder J, Shortreed S, et al. The duration of obesity and the risk of type 2 diabetes. *Public Health Nutr*. 2011;14:119-126.
15. Abdullah A, Amin FA, Stoelwinder J, et al. Estimating the risk of cardiovascular disease using an obese-years metric. *BMJ Open*. 2014;4:5629. doi:10.1136/bmjopen-2014-005629
16. Barinas-Mitchell E, Duan C, Brooks M, et al. Cardiovascular disease risk factor burden during the menopause transition and late midlife subclinical vascular disease: does race/ethnicity matter? *J Am Heart Assoc*. 2020;9:e013876. doi:10.1161/JAHA.119.013876
17. Ross R, Neeland IJ, Yamashita S, et al. Waist circumference as a vital sign in clinical practice: a Consensus Statement from the IAS and ICCR Working Group on Visceral Obesity. *Nat Rev Endocrinol*. 2020;16:177-189.
18. Verschuren WMM, Blokstra A, Picavet HSJ, Smit HA. Cohort profile: the Doetinchem Cohort Study. *Int J Epidemiol*. 2008;37:1236-1241.
19. Picavet HSJ, Blokstra A, Spijkerman AMW, Verschuren WMM. Cohort profile update: the Doetinchem Cohort Study 1987-2017: lifestyle, health and chronic diseases in a life course and ageing perspective. *Int J Epidemiol*. 2017;46:1751.
20. Chalmers J, MacMahon S, Mancia G, et al. 1999 World Health Organization-International Society of Hypertension Guidelines for the management of hypertension. Guidelines sub-committee of the World Health Organization. *Clin Exp Hypertens*. 1999;21:1009-1060.
21. Huang PL. A comprehensive definition for metabolic syndrome. *Dis Model Mech*. 2009;2:231-237.
22. Juhaeri, Stevens J, Jones DW, Arnett D. Associations of aging and birth cohort with body mass index in a biethnic cohort. *Obes Res*. 2003;11:426-433.
23. Leveille SG, Wee CC, Iezzoni LI. Trends in obesity and arthritis among baby boomers and their predecessors, 1971-2002. *Am J Public Health*. 2005;95:1607-1613.
24. Johnson W, Li L, Kuh D, Hardy R. How has the age-related process of overweight or obesity development changed over time? Co-ordinated analyses of individual participant data from five United Kingdom birth cohorts. *PLoS Med*. 2015;12:e1001828. doi:10.1371/journal.pmed.1001828
25. Dobson A, Hockey R, Chan HW, Mishra G. Flexible age-period-cohort modelling illustrated using obesity prevalence data. *BMC Med Res Methodol*. 2020;20:16. doi:10.1186/s12874-020-0904-8
26. Jacobsen BK, Njølstad I, Thune I, Wilsgaard T, Løchen ML, Schirmer H. Increase in weight in all birth cohorts in a general population: the Tromsø Study, 1974-1994. *Arch Intern Med*. 2001;161:466-472.
27. Peter RS, Fromm E, Klenk J, Concin H, Nagel G. Change in height, weight, and body mass index: longitudinal data from Austria. *Am J Hum Biol*. 2014;26:690-696.
28. Chen Y, Peng Q, Yang Y, Zheng S, Wang Y, Lu W. The prevalence and increasing trends of overweight, general obesity, and abdominal obesity among Chinese adults: a repeated cross-sectional study. *BMC Public Health*. 2019;19:1293. doi:10.1186/s12889-019-7633-0
29. Weng HH, Bastian LA, Taylor DH Jr, Moser BK, Ostbye T. Number of children associated with obesity in middle-aged women and men: results from the Health and Retirement Study. *J Womens Health (Larchmt)*. 2004;13:85-91.
30. We JS, Han K, Kwon HS, Kil K. Effect of maternal age at childbirth on obesity in postmenopausal women: a nationwide population-based study in Korea. *Medicine (Baltimore)*. 2016;95:e3584. doi:10.1097/MD.0000000000003584
31. Pacyga DC, Henning M, Chiang C, Smith RL, Flaws JA, Strakovsky RS. Associations of pregnancy history with BMI and weight gain in 45-54-year-old women. *Curr Dev Nutr*. 2020;4:45-54.
32. Lain KY, Catalano PM. Metabolic changes in pregnancy. *Clin Obstet Gynecol*. 2007;50:938-948.
33. Feller S, Boeing H, Pischon T. Body mass index, waist circumference, and the risk of type 2 diabetes mellitus. *Dtsch Arztebl Int*. 2010;107:470-476.
34. Zhang C, Rexrode KM, van Dam RM, Li TY, Hu FB. Abdominal obesity and the risk of all-cause, cardiovascular, and cancer mortality: sixteen years of follow-up in US women. *Circulation*. 2008;117:1658-1667.
35. Raho E, van Oostrom SH, Visser M, et al. Generation shifts in smoking over 20 years in two Dutch population-based cohorts aged 20–100 years. *BMC Public Health*. 2015;15:142. doi:10.1186/s12889-015-1481-3
36. Eriksson M, Holmgren L, Janlert U, et al. Large improvements in major cardiovascular risk factors in the population of northern Sweden: the MONICA study 1986-2009. *J Intern Med*. 2011;269:219-231.
37. Gregg EW, Cheng YJ, Cadwell BL, et al. Secular trends in cardiovascular disease risk factors according to body mass index in US adults. *J Am Med Assoc*. 2005;293:1868-1874.
38. Landi F, Calvani R, Picca A, et al. Body mass index is strongly associated with hypertension: results from the longevity check-up 7+ study. *Nutrients*. 2018;10:1976. doi:10.3390/nu10121976
39. Khan SS, Ning H, Wilkins JT, et al. Association of body mass index with lifetime risk of cardiovascular disease and compression of morbidity. *JAMA Cardiol*. 2018;3:280-287.

How to cite this article: Ibi D, Rietman ML, Picavet HSJ, et al. Adverse generational changes in obesity development converge at midlife without increased cardiometabolic risk. *Obesity (Silver Spring)*. 2021;29:1925–1938. https://doi.org/10.1002/oby.23260