

Changes in Biological Markers of Health: Older Americans in the 1990s

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Background. Many studies that show improved health in older adults have relied on subjective measures of health. This article assesses changes in the physiological status of older Americans during the 1990s using biological measures of high-risk for morbidity and mortality.

Methods. Changes in the prevalence of clinically-defined, high risk for 10 biological markers were assessed in respondents age 65 years and older from National Health and Nutrition Examination Surveys (NHANES) III (1988–1994) and IV (1999–2000).

Results. Some changes in prevalence of high-risk values of biological markers indicate improved health among older adults in the 1990s: a 6% reduction in the prevalence of high-risk total cholesterol ($p < .001$) and a 7% reduction in the prevalence of high-risk homocysteine ($p < .001$). Other changes indicate worsening health: a 9% increase in the prevalence of high-risk systolic blood pressure ($p < .01$), a 10% increase in obesity ($p < .001$), and an 8% increase in the prevalence of high-risk C-reactive protein ($p < .001$). These changes remained significant after adjusting for age, sex, and education. Results of logistic regressions indicate that changes in the frequency of medication usage, medication efficacy, prevalence of chronic disease, and diet explained some of these changes.

Conclusions. Changes in the prevalence of high-risk values of biological markers in the 1990s are mixed. Greater use and effectiveness of lipid-lowering medication has contributed to the reduction in percentage of the population with high-risk lipid levels, and folate supplementation accounted for a decline in the percentage with high-risk homocysteine. However, increases in the percentage with high-risk systolic blood pressure occurred despite an increase in the use of antihypertensive medications, in part because of the limited ability of antihypertensive medications to bring blood pressure below high-risk levels.

HEALTH in the older population, as measured by many dimensions, appears to have improved during the last two decades (1–4). Mortality has continued to decline, and disability and loss of functioning are less common than in the past. Not all indicators point toward improving health, however. The prevalence of most diseases has increased in the older population (1,5,6).

Most studies examining trends in the health of older adults have focused on self-reports of health that can be affected by circumstances other than the intrinsic health of the individual (7,8). For instance, self-reports of conditions and diseases are subject to variations in knowledge, access to health care, and disease diagnosis. Disability measures can be confounded by role expectations and living environments (9,10).

In contrast, the physiological status that underlies disability, loss of functioning, disease, and mortality can be more directly measured through biological indicators of risk. Trends in these biological markers should be a good indicator of trends in the innate health status of the older population as all of these markers have been linked to higher mortality, poorer physical and cognitive functioning, and more heart disease (11–16).

Past research on trends in biological risk markers has focused on cardiovascular risk factors, namely blood pressure, serum cholesterol levels, and relative weight

(17–19). From the 1960s through the early 1990s, decreases in hypertension were fueled by increased diagnosis and treatment of blood pressure problems (17,20). However, there is some evidence that improvement in blood pressure may have stopped and that blood pressure may have actually increased through the 1990s (21). Cholesterol appears to have decreased steadily from the 1960s through 2000 (22). One of the most adverse health trends in recent decades has been the increase in weight and obesity (23). Several other markers, such as triglycerides, glycated hemoglobin, C-reactive protein (CRP), and homocysteine level, are increasingly considered clinically relevant and change over time in these markers also requires attention. The intent of this article is to examine changes in the prevalence of high-risk values for indicators of physiological functioning in older Americans through the 1990s and to explore reasons for these observed changes.

METHODS

Data

The National Health and Nutrition Examination Surveys (NHANES) are cross-sectional studies of the noninstitutionalized U.S. population including interview, clinical

Table 1. Percentage of Population Aged 65+ Years at High Risk for Biological Markers in NHANES III and IV

Indicator	High-Risk Cut Point (Reference)	N (NHANES III/IV)	% High Risk				Odds Ratio	(95% CI)
			NHANES III	NHANES IV	Change	p for Change		
Diastolic blood pressure [†]	>90 mmHg (27)	3893/1052	4.7	5.4	0.8	.81	1.17	(0.86–1.61)
Systolic blood pressure [†]	>140 mmHg (27)	3906/1076	43.5	52.3	8.9	.01	1.43	(1.24–1.64)
HDL cholesterol [‡]	<40 mg/dl (28)	4152/1088	23.0	21.3	–1.7	.40	0.90	(0.76–1.06)
Fasting LDL cholesterol [‡]	>160 mg/dl (28)	1631/441	27.0	18.1	–8.9	.02	0.60	(0.45–0.79)
Total cholesterol [‡]	>240 mg/dl (28)	4174/1090	31.2	25.1	–6.1	<.001	0.74	(0.63–0.86)
Glycated hemoglobin [§]	>6.4% (29)	4187/1112	12.1	13.2	1.1	.42	1.11	(0.90–1.36)
Body mass index	>30 kg/m (30)	4457/1156	21.4	30.8	9.5	<.001	1.64	(1.41–1.91)
Fasting triglycerides [¶]	>200 mg/dl (28)	1656/451	18.4	21.8	3.4	.06	1.24	(1.41–1.90)
C-reactive protein [#]	>4.0 mg/l	4075/1090	21.3	29.6	8.3	<.001	1.65	(1.42–1.93)
Serum homocysteine ^{**}	>15 µmol/l (31,32)	1715/1115	17.6	10.3	–7.3	<.001	0.54	(0.42–0.68)

Note: [†]Average of three sets of blood pressure measurements.

[‡]Hitachi 737 Analyzer (Boehringer-Mannheim Diagnostics).

[§]Boronate affinity chromatography.

^{||}Examination weight, standard anthropometry.

[¶]H₂O₂ biproduct spectroscopy.

[#]Enzyme-linked immunosorbent assay (ELISA): low-sensitivity in NHANES III, high-sensitivity in NHANES IV.

^{**}Waters Expertise Chromatography Software (Waters Corp., Milford, MA).

NHANES = National Health and Nutrition Examination Survey; CI = confidence interval; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

examination, and laboratory tests (24). In this analysis, data from NHANES III (1988–1994) and NHANES IV (1999–2000) were used to examine change in biological risk in the population aged 65 years and older. Although data collection for these studies took place over a number of years, each person was interviewed only once. NHANES III centered on 1991, and NHANES IV centered on 1999; differences between the two surveys represent change for an average of 8 years. There were 4495 respondents 65 and older in NHANES III and 1196 in NHANES IV who completed both the interview and the examination and laboratory components. All analyses were conducted using STATA (25) to account for the design effect, and the sample completing the laboratory components was weighted to reflect the noninstitutionalized population of the United States.

Measures

We examined change across the two studies in the percentage of the population with measured values above (or below) clinically defined “high risk” levels for 10 biological markers: diastolic blood pressure, systolic blood pressure, high-density lipoprotein (HDL) cholesterol, fasting low-density lipoprotein (LDL) cholesterol, total cholesterol, glycated hemoglobin, body mass index (BMI), fasting triglycerides, CRP, and homocysteine. Clinical cut points used to define high-risk levels are shown in Table 1. For all variables, at least 87% of those eligible to provide data did so at both dates. Measures of LDL cholesterol and triglycerides were available for the participants in the morning sample fasting at least 6 hours (about 40% of the total laboratory sample), and measures of homocysteine were only available for the second half of NHANES III (1991–1994). For these reasons, these three indicators have data for a smaller number of respondents.

Because assays used to measure CRP differed somewhat at the two dates, an adjustment of NHANES IV assay values was performed using information derived from comparisons made by the laboratory doing both sets of assays. The

correlation between the two assays at levels greater than 3.0 mg/l was 0.993, with a slope indicating that NHANES IV values need to be reduced by 9.9% for comparability. Because the lower level of sensitivity changed, we used 4.0 mg/l as the cut point for risk across the surveys (26). Persons with levels of CRP >10 mg/l were assumed to have acute infections and were eliminated from CRP analyses.

Measured values of biological markers were used to identify individuals with high-risk levels of each indicator, regardless of medication use status. Thus, persons on medication whose measured levels were outside the risk range were not considered to be at risk. Subsequent analyses examined the changing prevalence of medication usage relative to measured risk. Self-report data were used to examine age, gender, education, disease diagnosis, and medication prescription.

Analysis

First, we examined change across the surveys in the percentage with high-risk values. For each biomarker, we then used logistic regression to examine the relative odds of being at high risk in the NHANES IV sample versus the NHANES III sample. Regression models examined the relative odds of being high-risk after controlling for changes in age and sex of the population (Model 1) and educational level (Model 2). Because weight increased markedly between the two surveys, Model 3 also controlled for BMI. A final set of analyses explored changes in factors likely to affect change in individual biomarkers, including diagnosis and medication use, prevalence of chronic disease, and the level of serum folate.

RESULTS

Table 1 presents the percentage of the U.S. population aged 65 years and older with high-risk levels of each biological measure in the two studies. By NHANES IV, a majority of older Americans had high-risk levels of systolic blood pressure, almost one third had weight levels

Table 2. Likelihood of Being in a High-Risk Group in NHANES IV Relative to NHANES III

Indicator	Model 1*		Model 2 [†]		Model 3 [‡]	
	Odds Ratio	(95% CI)	Odds Ratio	(95% CI)	Odds Ratio	(95% CI)
Diastolic blood pressure	0.94	(0.68–1.28)	0.94	(0.68–1.30)	0.88	(0.64–1.23)
Systolic blood pressure	1.26	(1.09–1.46)	1.27	(1.10–1.48)	1.28	(1.10–1.48)
HDL cholesterol	0.93	(0.79–1.11)	0.96	(0.81–1.14)	0.89	(0.75–1.06)
Fasting LDL cholesterol	0.72	(0.54–0.95)	0.73	(0.55–0.97)	0.72	(0.54–0.95)
Total cholesterol	0.65	(0.55–0.78)	0.65	(0.55–0.78)	0.65	(0.55–0.78)
Glycated hemoglobin	1.05	(0.86–1.28)	1.10	(0.90–1.34)	0.98	(0.80–1.21)
Body mass index	1.43	(1.22–1.68)	1.47	(1.25–1.73)		
Fasting triglycerides	1.29	(0.98–1.70)	1.33	(1.00–1.76)	1.27	(0.96–1.69)
C-reactive protein	1.68	(1.44–1.97)	1.70	(1.45–1.99)	1.59	(1.35–1.87)
Serum homocysteine	0.60	(0.48–0.76)	0.63	(0.50–0.80)	0.62	(0.49–0.79)

Note: *Model 1 controlled for years of age and gender.

[†]Model 2 controlled for age, gender, and education (>12 y, 12 y, <12 y).

[‡]Model 3 controlled for age, gender, education, and body mass index.

CI = confidence interval; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

considered obese, and one quarter had high-risk levels of total cholesterol. The percentage of older Americans with high-risk systolic blood pressure increased by 9% from NHANES III to IV, but there was no significant change in the prevalence of high-risk diastolic blood pressure (Table 1). The prevalence of high-risk levels of total and LDL cholesterol declined significantly (6.1% and 8.9%, respectively); however, there was no significant change in the percentage with high-risk levels of HDL cholesterol or glycated hemoglobin. The prevalence of obesity among the elderly population increased from 21.4% to 30.8%. The prevalence of high-risk levels of triglycerides appears to have increased marginally, from 18.4% to 21.8%, and the prevalence of CRP greater than 4.0 mg/l increased significantly (from 21.3% to 29.6%). However, the prevalence of high-risk levels of homocysteine declined by 7%, from 17.6% to 10.3%.

Explanations for Changes in Percentage of Population With High-Risk Values of Biological Markers

Table 2 presents results from regression models testing the robustness of the observed differences in prevalence of high risk to controls for change in population composition. Model 1 indicates the odds ratios for being in the high-risk group in NHANES IV versus NHANES III adjusted for age and sex. Generally, the results are the same as those in Table 1, indicating that changes in age and in sex composition, or both, do not explain observed changes over time. The odds for high-risk levels of systolic blood pressure were 26% higher, the odds for high-risk BMI were 43% higher, and the odds for high-risk CRP were 68% higher for the NHANES IV sample than for the NHANES III sample. However, the odds of having high-risk levels of LDL and total cholesterol were 28% and 35% lower, respectively, and the odds of having a high-risk level of homocysteine were 40% lower. The odds of having high-risk diastolic blood pressure, HDL cholesterol, glycated hemoglobin, and fasting triglycerides did not change significantly.

Because educational attainment has been linked to better health and the educational level of the older population increased markedly in the last decade (the percentage of

Americans aged 65 and older who have more than a high school education increased from 26% in NHANES III to 34% in NHANES IV), Model 2 adjusted for years of education. This did not significantly change any of the results. Because body weight is related to many other biological indicators of risk, Model 3 controlled for BMI. Controlling for BMI did not change the significance or direction of the results, although results indicate that the increase in prevalence of high-risk CRP would have been somewhat smaller without the concurrent increase in obesity.

Explanations for Changes in Specific Markers

To further investigate the causes for these changes, we assessed changes in related factors. For blood pressure and cholesterol, we examined changes in diagnosis, medication prescription, and use and effectiveness of medication. To do this, we divided the sample by diagnosis, use of medication, and measured risk group. For CRP, we examined changes in the prevalence of concurrent disease. For homocysteine, we examined changes in level of serum folate.

Systolic blood pressure.—Self-report of physician diagnosis of high blood pressure increased during the 1990s, with 41% of older adults reporting that they had been diagnosed with high blood pressure in NHANES III (46% in NHANES IV). However, the use of medication to control hypertension in the older population also increased during the 1990s, from 35% in NHANES III to 43% in NHANES IV. If we used an alternative approach to defining high-risk blood pressure that included those taking medication as well as those with measured high-risk systolic blood pressure, the increase in the presence of high-risk blood pressure between NHANES III and NHANES IV would have been even greater, from 59% to 70%.

Among those persons who reported having been diagnosed with high blood pressure, almost all (90%) had been told to take medication in each survey. Taking blood pressure medication does not necessarily reduce an individual's blood pressure below the risk level; among those taking medication, 56% in NHANES III and 60% in NHANES IV (19.4% and 25.1% of the total samples) had

high measured systolic blood pressure. Another reason for the rise in measured systolic blood pressure is the increase in undiagnosed high blood pressure, in which participants measured at-risk did not report prior diagnosis (17% in NHANES III to 22% in NHANES IV). Thus, despite the increase in treatment, an increase in undiagnosed high blood pressure and diagnosed, but inadequately controlled, hypertension are factors in the growing prevalence of high-risk systolic blood pressure.

Cholesterol.—Although we observed a decline in measured high-risk LDL and total cholesterol, the percentage reporting that they had been diagnosed with high cholesterol increased (31% in NHANES III vs 45% in NHANES IV). There was also an increase in the use of medication to control cholesterol, from 20% to 35%. Medication prescription among those diagnosed with high cholesterol increased markedly during the 1990s (from 33% in NHANES III to 62% in NHANES IV). In addition, the effectiveness of medications available to treat high cholesterol increased (33). In NHANES III, 40% of those taking medication still had high-risk levels of cholesterol; this figure fell to only 21% in NHANES IV. Thus, increases in cholesterol testing and diagnosis, as well as increased use and efficacy of medications, may have contributed to the observed decrease in high-risk total cholesterol.

C-reactive protein.—The increase in CRP observed here was paralleled by an increase in BMI (Table 2, Models 2 and 3). Controlling for BMI suggests that, without the increase in weight, the odds of high-risk CRP in NHANES IV versus NHANES III would have been 59% higher, instead of 70%. Higher CRP levels in NHANES IV may also be associated with the increased prevalence of chronic diseases in the later survey period. Controlling for the change in prevalence of seven chronic conditions related to inflammation (hypertension, diabetes, chronic heart failure, heart attack, asthma, chronic bronchitis, and arthritis) reduced the odds ratio (OR) for the indicator of change in high-risk CRP by 0.12 (results not shown), suggesting that some of the observed increase in CRP was related to the concurrent increasing prevalence of chronic conditions.

Homocysteine.—We considered whether the decreasing prevalence of high-risk homocysteine might be the result of changes in folate supplementation. Higher levels of serum folate led to lower levels of homocysteine (34), and folate consumption in the population increased after 1998 because of regulated folate supplementation of cereals and flours to prevent neural tube defects in fetuses (35). Although this policy was oriented toward improving pregnancy outcomes, it also resulted in improved dietary intake of folate among elderly persons. The mean level of serum folate in the older population increased from 9.8 ng/ml in NHANES III to 20.9 ng/ml in NHANES IV. These increasing levels of serum folate appear to completely explain the decrease in high-risk homocysteine levels between the two surveys, as addition of serum folate to Model 3 in Table 2 resulted in an insignificant OR for the indicator of change in homocysteine (OR = 1.14, results not shown).

DISCUSSION

Comparisons of the prevalence of high-risk levels of a range of clinically relevant biological markers in older adults at the beginning versus the end of the 1990s revealed a mixed pattern of changes in health. There was an increase in the prevalence of high-risk systolic blood pressure reflecting increases in both diagnosed and undiagnosed cases and in the fact that blood pressure may not be reduced below risk levels even among those using medication. There were also significant increases in the percentage of the older population with high-risk levels of CRP during the 1990s. Concurrent changes in factors related to CRP, including weight and the prevalence of diseases, may explain part of the increase.

In contrast to these patterns of increasing risk, prevalence of high-risk cholesterol showed considerable improvement during the 1990s. This appears to partially result from the dramatic increase in the use of more effective lipid-lowering medications. Another notable health improvement during the 1990s was the reduction in high-risk homocysteine—a change that appears to have been accomplished through public health efforts that led to elevations in serum folate levels in the older U.S. population.

Conclusion

We found mixed patterns of change in the prevalence of high-risk levels of various clinically relevant biomarkers in older Americans through the 1990s: increasing prevalence of high-risk levels for some measures, but decreasing levels for others. Overall, the data suggest that the prevalence of high-risk levels would have risen more without the increased use of medications.

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