Reversal of Fortune: Income Disparities in Cholesterol before and after the Era of Statins

[EXTENDED ABSTRACT]

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ABSTRACT

Cholesterol levels, a central risk factor for cardiovascular disease, have been significantly altered in recent years by pharmaceutical innovation. Introduced in the late 1980's, statins (HMG-CoA reductase inhibitors) offered, for the first time, highly effective drug control. In this paper, we examine income disparities in cholesterol in before and after the introduction of statins. As an expensive and potent new technology, statins may be disproportionately adopted those who are better resourced, creating or exacerbating social disparities. Using NHANES data from 1976 to 2004, we find that income gradients for both total cholesterol and fasting LDL were initially positive, but then reversed and became negative in the era of statin use. While the advantaged were once more likely to have high levels of cholesterol, they are now less likely to have such unhealthy outcomes. These secular changes serve as forceful example of social conditions as a fundamental cause of disease.

INTRODUCTION

Though cardiovascular disease (CVD) remains a leading cause of death in post-industrial nations such as the U.S., the past few decades have yielded tremendous progress in the reduction of cardiovascular mortality. In fact, the increase in overall life expectancy observed for the last half of the 20th century is attributed, in large part, to a concomitant, steady decline in cardiovascular mortality, as this decline has far outpaced progress in other realms of disease (e.g., cancer mortality) (National Center for Health Statistics 2007). Hence, these improvements in CVD are widely applauded in the medical community and beyond, and they are frequently used as an exemplar for successful returns on investments in the domains of medical research and technology (Murphy and Topel 2003). For example, in the National Institutes of Health (NIH) Budget Requests presented to Congress, advances in the treatment and prevention of heart disease have figured quite prominently in recent years as examples of the successful impact of federally funded research (National Institutes of Health 2007). With respect to the source of this progress, Cutler and Kadiyala (2003) estimate that about one-third of the reduction in cardiovascular mortality stems from high-tech invasive treatment (e.g., angioplasty); one-third stems from changes in lifestyle (e.g., reduced smoking and dietary changes); and a final third results from pharmaceutical innovation (e.g., drugs to lower blood pressure and cholesterol).

In this paper, we examine secular trends in cholesterol levels, a central risk factor for cardiovascular disease, and a risk factor that has been significantly altered in recent years by pharmaceutical innovation, specifically, the introduction of statins (or HMG-CoA reductase inhibitors). While dietary modification has undoubtedly played a substantive role in the reduction of cholesterol levels in the era following landmark studies such as the *Framingham Heart Study*, the advent of statins offered, for the first time, highly effective pharmaceutical control. In this paper, we focus in particular on income disparities in cholesterol levels, and we consider how such disparities may have changed over time with the introduction of statins in the late 1980s. While statins have largely been welcomed as a potent agent in the (primary and secondary) prevention of heart disease and a key contributor to our overall progress against cardiovascular mortality, less attention is devoted to the fact that statins, as an expensive new technology that requires continuous monitoring, may be disproportionately adopted those who are better resourced.

As noted by researchers studying the diffusion of technology, new technologies can exacerbate existing differentials in health by socioeconomic status (SES), despite offering great potential for improving overall population health (Goldman and Smith 2005; Rogers 1995). In addition to being costly, new technologies can also be complex, requiring additional resources such as patient time and the ability to adhere to treatment and follow-up regimens (Goldman and Lakdawalla 2005). In a related vein, medical sociologists have long argued that certain social conditions may function over time as "fundamental causes of disease" (House, Kessler and Herzog 1990; Link and Phelan 1995). SES, for example, operates as a persistent and fundamental cause of disease because it involves access to a variety of resources that allow individuals to avoid diseases and their undesirable consequences (Link and Phelan 1995). Hence, the correlation between SES and health overall is not eliminated by simply addressing the specific mechanisms that link SES to any one particular disease, at any one particular point in time. Over the long term, as certain risk factors or diseases are eradicated or brought under

control, new risk factors and diseases arise, and those with more resources are better able to take advantage of new developments with respect to prevention (e.g., knowledge and avoidance of risk factors), diagnosis, and treatment.

As such, the development of new medical research and technologies can both exacerbate existing SES differentials in health and cause new differentials to arise. In the case of cholesterol levels, however, socioeconomic disparities may have actually *reversed* or changed directions over time. While those who were economically advantaged once had had richer and heavier diets because they could afford them and, hence, higher cholesterol levels, the introduction of statins, accompanied by continued dietary adjustments, may have precipitated a discrete reversal of this disparity. In this paper, we examine income disparities in cholesterol levels over the last three decades in the U.S. We hypothesize that income gradients were positive (e.g., cholesterol levels increasing with income) in the period preceding the introduction and diffusion of statins, and negative in the period after.

METHODS

We use three successive "waves" of the National Health and Nutrition Examination Survey (NHANES): II (1976-1980), III (1988-1994), and Continuous (1999-2004). The NHANES are designed to provide nationally-representative, cross-sectional estimates at successive points in time and obtain health information through in-person interviews and examinations, which include both physical and laboratory examinations. Our outcomes of interest are total cholesterol levels and fasting low density lipoprotein (fasting LDL) levels, the fraction of total cholesterol that is most directly targeted by statin therapy. In analyses of total cholesterol values, we restrict our samples to adults aged 20 and over and those who were examined and not pregnant. In analyses of fasting low density lipoprotein values (fasting LDL), we additionally restrict our sample to those who (1) had their blood drawn in a morning session and (2) had fasted for an appropriate amount of time prior to having their blood drawn.

We use the poverty income ratio (PIR) to measure income status. PIR is the ratio of a family's income to its appropriate poverty threshold. In contrast to household income, PIR is continuous rather than interval data; adjusts for household characteristics; and accounts for inflation both between waves and across years within the same wave. PIR is top-coded at different values in the three survey waves, so we top-code the PIR variable at 5.0 for all waves to create consistency across waves. We focus on income rather than education as an indicator of SES because educational categories have shifted in meaning and value during the period under study. Furthermore, "high school graduate" is the highest category provided in the most recent data. Given the current education distribution in the country, this is not an adequately detailed categorization to address our study questions. Covariates include age, sex, race, body mass index (BMI: weight [kg]/height [m^2]), and survey year. For NHANES II, we define non-Hispanic white or black as persons who are coded as white or black for race but do not have any of several Hispanic ancestry codes. For later waves, a combined race/ethnicity recode is available. Survey year is based on the midpoint for each wave of the NHANES, with the first wave (1976-1980) coded as 0, and subsequent waves coded as 1.30 (for 1988-1994) and 2.35 (for 1999-2004). Hence, a change of one unit in the survey year variable represents 10 years.

Age includes a squared term, as preliminary analyses revealed a curvilinear relationship with lipid (cholesterol and LDL) outcomes.

We use multivariate linear regression to assess the influence of income on lipid levels over time. Cholesterol (or fasting LDL) is modeled as the dependent variable and income and survey year, along with other covariates, are included as predictor variables. To formally test our hypothesis that income disparities have changed over time, we also include an interaction term between income and survey year. As noted above, we hypothesize the coefficient for income will change from positive to negative over the course of this thirty year period. Lastly, as statins are predominately indicated and prescribed in the setting of high lipid values, we also consider high cholesterol (cholesterol >240) and high fasting LDL (LDL >160) as dichotomous outcomes and model them using logistic regression. All analyses are stratified by sex and incorporate the appropriate NHANES sampling weights.

RESULTS

Sample characteristics for each of the three survey waves are given in TABLE 1. For both women and men, average total cholesterol levels as well as average fasting LDL levels show considerable declines in the period from NHANES II (1976-1980) to the most recent data (1999-2004). Among women, cholesterol dropped from 221 to 204, and LDL dropped from 139 to 120. Among men, cholesterol dropped from 213 to 201, and fasting LDL dropped from 137 to 122. Average weight status, as measured by BMI, has also increased over this period for both sexes, while average PIR has remained relatively stable.

TABLE 2 displays the results of linear regression models for total cholesterol and fasting LDL. Given the inclusion of an interaction term between survey year and PIR, we have coded the survey year variable so that the coefficient for the main effect of PIR represents the estimated effect of PIR on the outcome variable for the baseline survey wave (NHANES II: 1976-1980). Among women and men, the association between PIR and lipid levels is positive for both total cholesterol and fasting LDL in the baseline survey wave. As income increases, lipid levels are estimated to increase. This relationship statistically significant only among men and is also stronger for men. For both sexes and both outcomes, however, the interaction term between PIR and survey year is negative and significant, showing significant change over time. Specifically, the initially positive gradient declines and becomes negative with time. Despite a positive association in the first wave, the estimated association between PIR and lipid levels in the final wave (1999-2004) is negative for both sexes and both outcomes. For total cholesterol, the estimated coefficient for PIR in the final wave is -0.812 (p=0.027) among women and -0.731 (p=0.073) among men (values are calculated, not shown in table). For fasting LDL, the estimated coefficient for PIR in the final wave is -1.504 (p=0.002) among women and -0.849 (p=0.073) among men. Figures 1 and 2 graph the estimated income gradients for cholesterol and LDL in the first and last waves of the NHANES. Values are estimated for whites who are 40 years of age with a BMI of 25. As previously discussed, all gradients change from positive to negative for both sexes and each outcomes. Additionally, the figures highlight the fact that over this period of time, those at the upper end of the income scale (PIR=5) have experienced a much larger decline in average lipid levels than those at the lower end.

Lastly, TABLE 3 displays the results of logistic regression models for high total cholesterol (>240) and high fasting LDL (>160). Results are similar to those found for the continuous versions of these variables. The estimated coefficient for the interaction term between income and survey year is again significantly negative for both sexes and both outcomes, and income gradients again shift from positive to negative over the thirty year period under consideration. For women in the last wave (1999-2004), each unit (value of 1) increase in PIR is associated with a 10% decline in the odds of having high cholesterol (OR: 0.90, p<0.00) and a 14% decline in the odds of having high LDL (OR: 0.16, p=0.001) (values are calculated, not shown in table). Hence, compared to a woman with at a PIR of 1, a woman with a PIR of 5 has 0.67 times lower odds of having high cholesterol, and 0.54 times lower odds of having a high LDL. For men, the estimated odds ratios for PIR in the last wave are 0.92 (p=0.003) for high cholesterol and 0.91 for high LDL.

PRELIMINARY CONCLUSIONS

In sum, we find that income disparities in lipid levels (as measured by total cholesterol and fasting LDL) have undergone dramatic changes during a period in which statins, or HMG-CoA reductase inhibitors, were introduced. Income gradients were positive in an era prior to the introduction of statins (which occurred in the late 1980s), but became negative in the period subsequent to the advent and dissemination of statins. While the more advantaged were once more likely to have high levels of cholesterol and LDL, they are now definitively less likely to have such unhealthy outcomes. While statins, as a relatively recent pharmaceutical development, hold great promise for improving cardiovascular health and mortality, they have, at least in the initial period, reversed social disparities, turning a positive gradient into a negative one. Statins are both expensive and highly effective drugs, easily outperforming prior generation drugs aimed at controlling lipid levels. The use of statins also requires consistent monitoring via blood work not only to monitor cholesterol levels, but also to monitor liver function tests. Given that these drugs are expensive, highly effective, and require continuous follow-up, it is perhaps not surprising that social disparities in cholesterol have shifted so dramatically in this period. In addition to such pharmaceutical changes, it may also be the case that the wealthy have been more likely to engage in effective dietary changes in this period. Indeed, our findings are likely driven by a combination of pharmaceutical intervention and dietary modifications. From a clinical standpoint, however, the use of statins is generally more effective than dietary modifications for those with very high lipid levels (REFS). Finally, regardless of the degree to which our findings are driven by drugs vs. lifestyle changes, the secular changes we find for cholesterol levels serve as forceful example of socioeconomic status as a fundamental cause of disease.

FORTHCOMING:

- Analyses adjusting for medication use and other conrols
- Analyses on the differential uptake of cholesterol medications by income status over time
- Analyses on how the distribution of cholesterol has changed with time. Given that statins are prescribed at certain thresholds, the right-hand tail of the distribution (or the portion above these thresholds) should be changing disproportionately.
- Additional discussion

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TABLE 1. Sample Characteristics

Mean (SD)/ Frequency (%)				
NHANES II (1976-1980)				
Variable	**Women (N=5,916)**		**Men (N=5,394)**	
Total Cholesterol	221.40	(51.85)	213.20	(45.89)
Fasting LDL	138.92	(44.19)	137.37	(41.06)
Poverty Income Ratio (PIR)	2.48	(1.47)	2.75	(1.52)
Age	47.93	(17.13)	47.49	(17.20)
Race/Ethnicity (%)				
Non-Hispanic White	82.94		83.72	
Non-Hispanic Black	11.29		10.38	
Mexican-American	-		-	
Other Race	5.76		5.90	
BMI	25.62	(5.72)	25.51	(4.03)
NHANES III (1988-1994)				
Variable	**Women (N=7,415)**		**Men (N=6,863)**	
Total Cholesterol	207.69	(46.27)	203.82	(43.08)
Fasting LDL	125.87	(38.55)	129.81	(37.65)
Poverty Income Ratio (PIR)	2.31	(1.73)	2.53	(1.80)
Age	48.45	(19.25)	48.77	(19.40)
Race/Ethnicity (%)				
Non-Hispanic White	44.10		43.09	
Non-Hispanic Black	27.42		25.57	
Mexican-American	24.21		27.73	
Other Race	4.28		3.61	
BMI	27.52	(6.53)	26.69	(4.86)
NHANES 1999-2004				
Variable	**Women (N=5,469)**		**Men (N=5,678)**	
Total Cholesterol	204.30	(41.66)	200.62	(43.70)
Fasting LDL	119.94	(35.24)	122.29	(36.43)
Poverty Income Ratio (PIR)	2.55	(1.61)	2.72	(1.60)
Age	50.82	(18.56)	50.09	(18.51)
Race/Ethnicity (%)				
Non-Hispanic White	51.25		52.11	
Non-Hispanic Black	19.40		18.35	
Mexican-American	22.12		22.65	
Other Race	7.22		6.89	
BMI	28.74	(6.86)	27.90	(5.37)

TABLE 2. OLS Regression Models for Cholesterol and LDL

Total Cholesterol

	Women		Men	
Variable	**β**	**SE**	**β**	**SE**
Poverty Income Ratio (PIR)	0.722	(0.455)	1.661**	(0.485)
Year (10 year increments)	-5.812**	(0.822)	-2.809**	(0.918)
PIR x Year	-0.653*	(0.262)	-1.021**	(0.286)
Age	2.918**	(0.124)	3.953**	(0.136)
Age^2	-0.019**	(0.001)	-.0354**	(0.001)
Race				
Non-Hispanic Black	-4.208**	(1.001)	-2.435*	(1.105)
Mexican-America	-3.525*	(1.1)	2.566*	(1.192)
Other Race	-3.636*	(1.499)	4.277*	(2.032)
Non-Hispanic White	-	-	-	-
BMI	0.616**	(0.060)	.810**	(.090)
Constant	110.638**	(3.049)	89.672**	(3.543)
N	18,800		17,935	

Fasting LDL

	Women		Men	
Variable	**β**	**(SE)**	**β**	**(SE)**
Poverty Income Ratio (PIR)	0.984	(0. 639)	1.712*	(0.688)
Year (10 year increments)	-5.387**	(1.099)	-3.304**	(1.203)
PIR x Year	-1.059**	(0.365)	-1.089**	(0.379)
Age	2.146**	(0.169)	3.033**	(0.175)
Age^2	-0.015**	(0.002)	-0.028**	(0.002)
Race				
Non-Hispanic Black	-3.544**	(1.301)	-4.155**	(1.416)
Mexican-America	-4.008**	(1.450)	0.570	(1.522)
Other Race	-2.749	(2.097)	0.262	(2.079)
Non-Hispanic White	-	-	-	-
BMI	0.707**	(0.081)	0.435**	(0.107)
Constant	52.377**	(4.230)	49.051**	(4.859)
N	7,292		7,492	

*p<0.05
**p<0.01

TABLE 3. Logistic Regression Models for High Cholesterol and High LDL

High Total Cholesterol (>240)

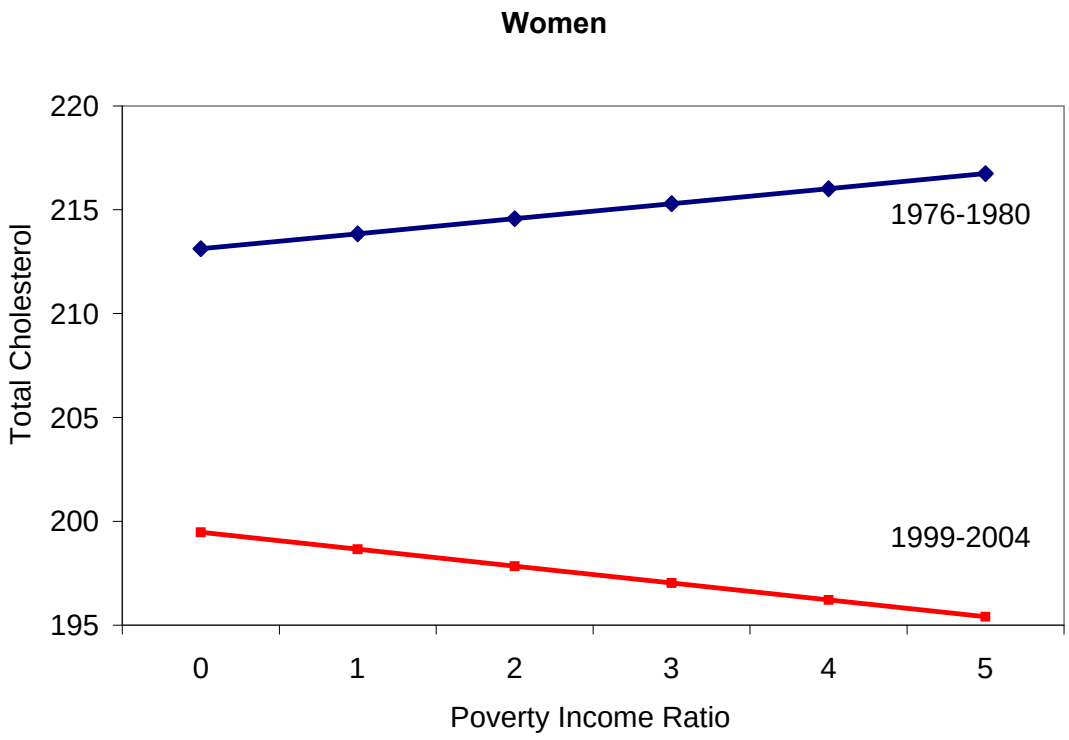
	Women			Men		
Variable	**β**	**(SE)**	**OR**	**β**	**(SE)**	**OR**
Poverty Income Ratio (PIR)	0.042	(0.026)	1.04	0.076**	(0.028)	1.08
Year (10 year increments)	-0.244**	(0.053)	0.78	-0.085	(0.058)	0.92
PIR x Year	-0.061**	(0.017)	0.94	-0.068**	(0.018)	0.93
Age	0.178**	(0.011)	1.19	0.186**	(0.011)	1.20
Age^2	-0.001**	(<0.001)	1.00	-0.002**	(<0.001)	1.00
Race						
Non-Hispanic Black	-0.263**	(0.065)	0.77	-0.165*	(0.072)	0.85
Mexican-America	-0.412**	(0.086)	0.66	-0.037	(0.084)	0.96
Other Race	-0.184	(0.108)	0.83	0.213	(0.111)	1.24
Non-Hispanic White	-	-	-	-	-	-
BMI	0.026**	(0.004)	1.03	0.030**	(0.005)	1.03
Constant	-7.006**	(0.284)		-6.714**	(0.271)	
N	18,800			17,935		

High Fasting LDL (>160)

	Women			Men		
Variable	**β**	**(SE)**	**OR**	**β**	**(SE)**	**OR**
Poverty Income Ratio (PIR)	0.032	(0.042)	1.03	0.104*	(0.044)	1.11
Year (10 year increments)	-0.265**	(0.087)	0.77	-0.137	(0.092)	0.87
PIR x Year	-0.079**	(0.028)	0.92	-0.086**	(0.028)	0.92
Age	0.138**	(0.016)	1.15	0.172**	(0.016)	1.19
Age^2	-0.001**	(<0.001)	1.00	-0.002**	(<0.001)	1.00
Race						
Non-Hispanic Black	-0.072	(0.105)	0.93	-0.139	(0.107)	0.87
Mexican-America	-0.476**	(0.153)	0.62	-0.004	(0.133)	1.00
Other Race	-0.086	(0.169)	0.92	-0.014	(0.176)	0.99
Non-Hispanic White	-	-	-	-	-	-
BMI	0.026**	(0.006)	1.03	0.012	(0.008)	1.01
Constant	-5.927**	(0.430)		-5.827**	(0.407)	
N	7,972			7,492		

*p<0.05
**p<0.01

FIGURE 1. Income Gradients for Total Cholesterol: 1976-1980 and 1999-2004



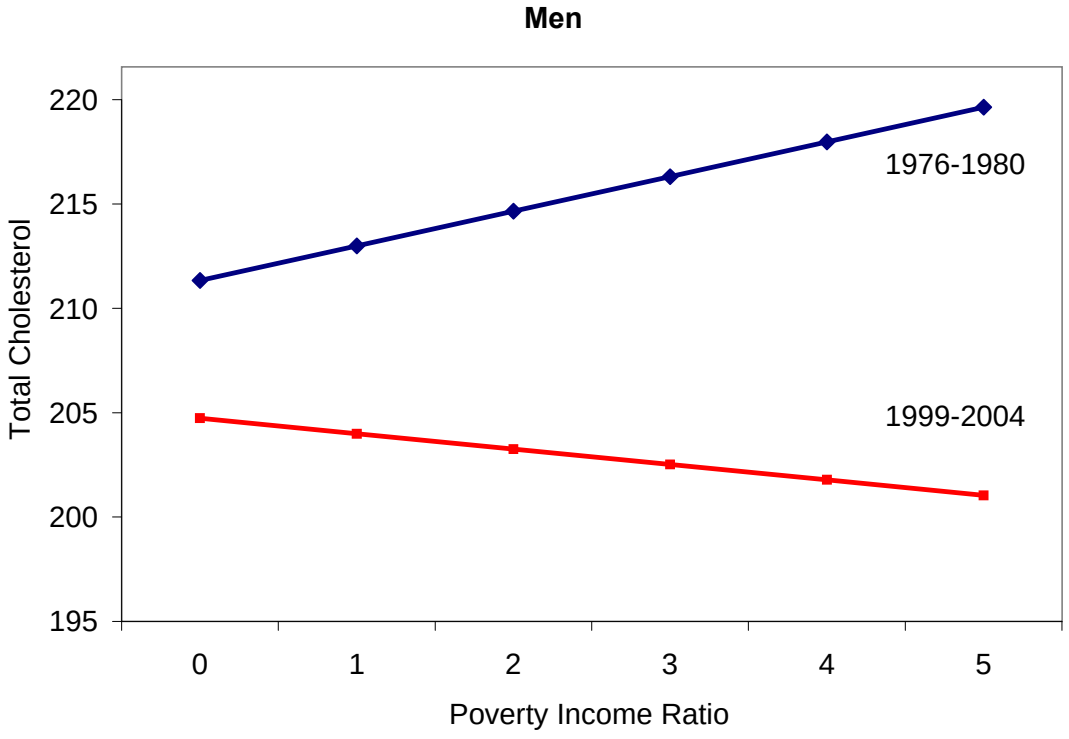


FIGURE 2. Income Gradients for Fasting LDL: 1976-1980 and 1999-2004