SPECIAL ARTICLE

DOES FREE CARE IMPROVE ADULTS' HEALTH?

Results from a Randomized Controlled Trial

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Abstract Does free medical care lead to better health than insurance plans that require the patient to shoulder part of the cost? In an effort to answer this question, we studied 3958 people between the ages of 14 and 61 who were free of disability that precluded work and had been randomly assigned to a set of insurance plans for three or five years. One plan provided free care; the others required enrollees to pay a share of their medical bills. As previously reported, patients in the latter group made approximately one-third fewer visits to a physician and were hospitalized about one-third less often. For persons with poor vision and for low-income persons with high blood pressure, free care brought an improvement (vision better

by 0.2 Snellen lines, diastolic blood pressure lower by 3 mm Hg); better control of blood pressure reduced the calculated risk of early death among those at high risk. For the average participant, as well as for subgroups differing in income and initial health status, no significant effects were detected on eight other measures of health status and health habits. Confidence intervals for these eight measures were sufficiently narrow to rule out all but a minimal influence, favorable or adverse, of free care for the average participant. For some measures of health in subgroups of the population, however, the broader confidence intervals make this conclusion less certain. (N Engl J Med 1983; 309:1426-34.)

SPENDING at least some money on medical care is indisputably worthwhile. But does spending yet more buy still better health? In individual cases, the answer may be an obvious yes or no, but in the population as a whole the point of diminishing (or absent) returns has been difficult to identify.¹⁻⁷

Critics of the existing system have contended that developed countries spend too much on medicine; they argue that this practice increases iatrogenous illness. 8,9 The extreme versions of this argument, constituting a kind of "therapeutic nihilism," have been cogently criticized, 10,11 and in this country public policy has proceeded for more than five decades on the assumption that if some medical care is good, more would be better. The main instrument of this policy has been increased insurance coverage, both public and private.

While this policy has been in effect, the national outlay on medical care has steadily increased and has now reached a level that causes concern in many quarters. One of the few potential methods for reducing expenditure appears to be to increase the proportion of costs borne by the people who are consuming medical care.

What fraction of their costs, if any, patients should be required to pay is thus a central and serious question of policy. Proponents of cost-sharing argue that it curtails frank abuse and restrains the purchase of care that yields little or no benefit. Opponents counter that if people must pay out of pocket for medical care, their access to appropriate levels of care will decrease and they will suffer accordingly. Data in support of either position have been all but nonexistent.

This dearth of information prompted the federal government to support a controlled trial. Known as the Rand Health Insurance Experiment, the project randomly assigned a sample of families to a variety of different insurance plans; one group received all their medical care free of charge; others paid some percentage of their health bills up to a stipulated maximum. We have already reported that when cost sharing was higher, use of medical care (visits to physicians, adult hospitalizations) and accordingly total expenditures were lower. ¹² To take one example, people enrolled in cost-sharing plans made only about two thirds as many outpatient visits as those receiving free care. ¹³

These earlier analyses left an important question unanswered: Were the people who received free medical care, and who thus used more of it, healthier as a result? Here we report what happened to several health-status measures among a group of adults under age 65 who received free care, as compared with a similar group that was required to share in the cost of care.

METHODS

Sample and Sites

The experiment, which ran from November 1974 through January 1982, enrolled 3958 people between the ages of 14 and 61 who belonged to 2005 families; 70 per cent of the sample participated for three years, and the remainder for five years. Families lived in one of six sites (Seattle, Washington; Dayton, Ohio; Fitchburg or Franklin County, Massachusetts; and Charleston or Georgetown County,

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representative of the general population of the area where they lived. 12,14,15

Excluded from the experiment were families with an annual income above \$54,000 (1982 value), who constituted about 3 per cent of those initially contacted; persons who were too badly disabled to work and therefore eligible for Medicare; and family members over the age of 61 at entry to the study. Included in the overall experiment but not in this analysis (nor in the above numbers) were children under the age of 14 and a group of families in a prepaid group practice; they are the subjects of separate analyses.

Insurance Plans and Benefits

Families were assigned to one of 14 experimental insurance plans by a random-sampling technique that made the distribution of family characteristics in each as similar as possible. ¹⁶ No premium was charged for any plan. Any family assigned to a plan that offered less coverage than its current insurance was reimbursed an amount equal to its maximal possible loss. This money was paid in installments every four weeks, and the family was not required to spend it on health care. Such payments had a negligible effect on use. ¹⁵

All plans covered ambulatory and hospital care, preventive services, most dental services, psychiatric and psychological services (limited to 52 visits a year), and prescription drugs. 12

For this analysis, each of the 14 insurance plans was assigned to one of four categories (one providing free care, the other three requiring cost sharing) as follows: the free plan, under which the

family received all services without charge; the individual-deductible plan, under which the family paid 95 per cent of the cost of each outpatient service up to an annual out-of-pocket expenditure of \$150 for each person (\$450 for a family), and all outpatient care beyond that amount, as well as all inpatient care, was free; the nine intermediate coinsurance plans, under which the family paid 25 or 50 per cent of all its health bills each year, inpatient and outpatient, until it had spent 5, 10, or 15 per cent of its income or \$1,000, whichever was less (in three of these nine plans the family paid 50 per cent for dental and mental-health services and 25 per cent for all other services; in some sites and years the maximum expenditure was limited to \$750); and finally the three income-related catastrophic plans, under which the family paid for 95 per cent of all its health bills up to 5, 10, or 15 per cent of its income or \$1,000, whichever was less.

In many analyses we have grouped the cost-sharing plans and compared them with the free-care plan.

Health-Status Variables

Starting with the World Health Organizations's definition of health, ¹⁷ we developed or adapted measures to evaluate the effect of cost-sharing on health status. This comprehensive set comprised four distinct categories — general health, health habits, physiologic health, and the risk of dying from any cause related to risk factors (i.e., high blood pressure, high serum cholesterol level, or cigarette smoking). Because actual deaths in our experimental population

Table 1. Operational Definitions and Mean Scores for Self-Assessed General Health Measures at Enrollment.

HEALTH VARIABLE AND OPERATIONAL DEFINITION	TYPICAL ÎTEM	Mean Sc Enroli		Interpretation of Effect Size	
		"GOOD" HEALTH *	"ILL" HEALTH [†]		
Physical functioning: A standardized (0-100) scale (23 items) that indicates the degree to which the person has limitations in personal self-care, mobility, or physical activities. ^{19,20} A high score means greater capacity for physical activity.	"Do you have any trouble either walking one block or climbing one flight of stairs because of your health?"	100	44.8	A 10-point difference = the effect of having chronic, mild osteoarthritis. ‡§	
Role functioning: A dichotomous measure (2 items) that indicates whether the person can perform work, school, or housework activities free of limitations due to poor health. 19,20 A high score means a higher probability of role functioning. Mean probabilities are expressed as percentages.	"Does your health keep you from working at a job, doing work around the house, or going to school?"	100	0	A 1-point difference = a probability 1 percentage point higher of being limited in the performance of one's principal role.	
Mental health: A standardized (0–100) scale (38 items) that measures anxiety, depression, emotional ties, behavioral/ emotional control, and psychological well-being during the previous month. ²¹⁻²³ A high score reflects higher or more positive levels of mental health.	"How much of the time, dur- ing the past month, have you felt downhearted and blue?"	86.4	53.0	A 3-point difference = the impact of being fired or laid off from a job.	
Social contacts: A standardized (0–100) scale (3 items) that measures contacts with friends and relatives during the past month or year. ²⁴ A high score reflects higher levels of social activity.	"About how often have you visited with friends at their homes during the past month? (Do not count relatives.)"	94.3	29.1	A 10-point difference = an increase of 2 percentage points in the probability of being psychiatrically impaired.	
Health perceptions: A standardized (0-100) scale (22 items) that measures the person's perceptions of past, present, and future health, susceptibility to illness, and worry about health. ²⁵ A high score reflects better perceptions of one's health status.	"My health is excellent."	83.6	47.8	A 5-point difference = the effect of having been diagnosed as having hypertension.	

^{*}Mean scores for the healthiest 40 per cent of the distribution.

[†]Mean scores for the sickest 20 per cent of the distribution.

[‡]Among participants in the experiment, adjusted for age and sex.

[§]Classification is based on the person's responding yes to questions about ever having acute or chronic pain, aching, swelling, or stiffness in fingers, hip, or knee.

[¶]Classification is based on the person's responding yes to a question about ever having been diagnosed as having high blood pressure and yes to a question about having been so diagnosed more than once or to a question about having had pills or medicines prescribed for high blood pressure.

Table 2. Operational Definitions and Mean Values for Health Habits and Physiologic Measures.

HEALTH VARIABLE AND OPERATIONAL DEFINITION	MEAN VALUE FOR PERSONS AT ELEVATED RISK *	SPECIFIC SCORING
Smoking: A six-level measure of the risk of death due to smoking relative to not smoking. ²⁶	1.89	Never smoked/exsmoker Pipe/cigar smoker only Cigarette smoker <1 pack/day 1.57 1 pack/day 2 packs/day 2 2.07 >2 packs/day 2 .20
Weight (kg) †	88.4	Standardized for height (in meters) by multiplying by (1.75/height) ² for men and by (1.65/height) ^{1.5} for women. Standardized for sex by summing 0.5 (average value for men) and 0.5 (average value for women). ²⁷
Serum cholesterol level (mg/dl)	242	
Diastolic blood pressure (mm Hg)	88	
Functional far vision: Measured in no. of Snellen lines. "Functional" means with whatever correction (if any) used by the person to improve vision.	2.95 ‡	Line 2 = 20/20 Line 3 = 20/25 Line 4 = 20/30
Risk of dying: The risk of dying from any cause relative to that of persons with average values of major risk factors: 100 exp(Index)/(1 + exp(Index)), where Index = 1.28 smoking scale + 0.0023 cholesterol + 0.023 systolic blood pressure - 9.52.	2.02	The coefficients of the risk factors are median values of the coefficients in the logistic regressions for death from any cause in five studies of heart disease in middleaged men. ²⁸

^{*}Means for the sickest 25 per cent of the distribution except for functional far vision. Enrollment values are given for smoking and weight. Predicted exit values are given for cholesterol level, blood pressure, vision, and risk of dying.

were too infrequent to allow meaningful analysis, we calculated an index predicting the extent to which eventual mortality would be affected by the specified risk factors. ¹⁸ In this paper we analyze 11 measures from the four categories (Tables 1 and 2). A number of other physiologic measures, as well as measures of dental health, have yet to be examined.

Data on general health (such as physical health, role functioning, and health perceptions) and health habits (such as smoking) were collected from a medical-history questionnaire that was self-administered at the beginning of the experiment (enrollment) and three or five years later (exit); the reliability, validity, and other psychometric properties of these measures have been reported elsewhere. ^{19-27,29} Blood pressure, serum cholesterol level, and visual acuity were measured at medical screening examinations that were given at enrollment to a randomly selected 60 per cent of the sample and at exit to the entire sample. ³⁰⁻³²

Methods of Analysis

To answer the question "Did the free plan improve health more than the cost-sharing plans?" we began by identifying certain variables that could be expected to affect the results and could be used in developing health-care policy. We then employed regression methods to estimate the influence of the "explanatory" variables (such as cost of care under each plan, family income adjusted for size and composition of the family, and initial state of health) on the "response" variable — namely, health status at exit. ²⁸

To interpret these effects we then used the regression equations to predict the health status at exit of people with any given set of characteristics at entry. In particular, we calculated health status for the average participant and for those in certain subgroups with relatively high or low incomes and with good or poor health.

Because we especially wanted to know the effect of cost sharing on people with poor health or low income, we measured all interactions between these factors and the various insurance plans. A score on each of the five general-health measures was determined for a permental for a permental forms as the contract of the five general forms as the contract of th

defined as being in the lowest fifth of the distribution of health status at enrollment, being in "good health" as being in the highest two fifths (Table 1). The effect of "low" or "high" income at enrollment was also tested. A "low" income was one in the lowest one fifth (a mean of \$7,300 for a family of four in 1982 dollars), a "high" income was one in the highest two fifths (a mean of \$40,000). For all the remaining explanatory variables, we used mean population values in the regressions when generating the predictions.

Medical care could be expected to have the most benefit for people with a health problem, but plan effects might be obscured if data on this subsample were pooled with those on the whole group. Accordingly, for each indicator of physiologic health (blood pressure, vision), health habits (smoking, weight, and cholesterol level), or risk of dying (Table 2), we divided our sample into those likely, by the time of exit, to have abnormal or normal values on the basis of data from the initial examination and responses to the questionnaire. We could detect no significant effects of the insurance plan on values for the group that was expected to have normal values at exit, so we focused the analysis on the group that was expected to be least healthy or at an elevated risk of dying (the least healthy quarter of the sample). For visual problems, we defined persons at high risk as those with an acuity at exit that was worse than 20/20 in the better eye without glasses (roughly half the sample).

Because we had no prior expectation that cost sharing would affect health either favorably or adversely, we used two-tailed tests of

significance throughout. We have followed the convention of labeling a result "significant" if it was likely to occur by chance no more often than 1 time in 20. However, results falling short of this criterion should not necessarily be ignored. In some cases, although the calculated result is statistically insignificant, the confidence interval indicates that its actual value could plausibly have some clinical importance; that is, the range of values having 95 per cent certainty of bracketing the real one could include some that are medically important. All statistical tests were corrected for correlation of the error term within each family and for the nonconstant variance of the error term.^{28,33}

Possible Artifacts and Biases

We anticipated three problems that may have led to biased estimates or erroneous inferences. First of all, the various plan offerings may have been accepted by different kinds of people, whose health or other characteristics would have biased the outcome. Secondly, participants may have dropped out of the various plans at different rates as a function of their current health. Either factor could have distorted our picture of the actual effects of being enrolled in a particular plan. Thirdly, certain data were missing: some gaps were "unplanned" (for example, participants occasionally did not complete all questions on the exit questionnaire), and some were "planned" (certain participants, for example, were not asked to take an enrollment screening examination). Only the unplanned loss of data carried the potential for bias, because the planned gaps were known to have been distributed randomly.

We adopted several strategies to counter the potential for bias. First of all, we compared health-status values at enrollment for participants in each plan, and we compared selected characteristics of the people who refused the offer with those of the people who accepted. If these groups had similar values, we would have little reason to suspect bias.

each of the five general-health measures was determined for a permal of Medicine Councilly, in the regression models we included initial values of son who was initially defined in a case of the permanent of the council measures with the council measures and the council measures with the council measures the council measure

[†]Values exclude those for persons 14 to 17 years of age at enrollment and pregnant women.

[‡]Value represents the mean corrected score for vision of those whose uncorrected vision in the better eye was worse than 20/20; i.e., the mean for the worst 53 per cent of the distribution.

known to influence the response under study. (For example, high blood pressure at entry predicted high blood pressure at exit.) We thereby controlled statistically for any effect of nonrandom composition of the sample with respect to these explanatory variables.

Thirdly, through questionnaires we obtained longitudinal information on general health measures and smoking for people who voluntarily withdrew from the experiment and for those who did not complete the experiment for other reasons. Thus, we were able to include many of the dropouts in the analysis. We did not attempt to recover information on physiologic measures from participants who left the sample prematurely; results for these measures were based only on values for those who completed the experiment.

Data missing as a result of unplanned nonresponse never amounted to more than 2 per cent for any one question, so bias from this source should have been negligible. Nevertheless, in order to include people with missing data in the analysis, we imputed scores to them. ^{28,34}

RESULTS

Threats to Validity

Acceptance of the Enrollment Offer

Acceptance rates varied as a function of plan: 92 per cent of the families accepted the offer to join the free plan, 83 per cent the individual-deductible plan, 89 per cent the intermediate plans, and 75 per cent the catastrophic plans. To determine whether these different acceptance rates may have biased our results, we examined the health status of all enrollees at the start of the experiment and detected no significant differences among plans in any health measure at enrollment or in family income, education, or age (Table 3). Only the proportion of female family members was slightly different according to plan, and one significant difference would be expected to occur by chance among the 20 comparisons made.

We also compared people who refused the enrollment offer with those who accepted.²⁸ Results of this comparison established that the different acceptance rates were unlikely to have affected our conclusions.

Retention in the Experiment

During the experiment, each plan lost some of its participants because of voluntary withdrawal (including withdrawal to join the military) involves and former distributions.

Table 3. Values of Demographic, Study, and Health-Status Measures at Enrollment, According to Type of Experimental Insurance Plan.*

Variable and Brief		Cost-Si	IARING PLANS		Free	T-Test
Description †	CATA- STROPHIC	INTER- MEDIATE	INDIVIDUAL DEDUCTIBLE	total ‡	Plan	VALUE ¶
No. of enrollees ≥14 years of age	759	1024	881	2664	1294	
Mean age (yr)	32.8	33.8	33.6	33.4	33.3	-0.0
Sex (% female)	56.1	53.5	53.8	54.4	52.2	-2.1
Race (% nonwhite)	20.8	17.4	18.3	18.9	16.6	-1.2
Mean family income adjusted for family size (1982 dollars) §	21,500	22,800	23,300	22,500	22,100	-0.5
% Hospitalized in year before enrollment	11.5	11.2	12.0	11.6	11.7	0.1
Mean no. of physician visits in year before enrollment	4.49	4.23	4.80	4.51	4.55	0.2
Mean education (yr)	11.9	12.0	12.0	12.0	11.8	-1.4
% Taking enrollment screening examination	59.1	57.8	58.6	58.5	62.5	1.6
% Enrolled for 3 years	69.8	67.4	71.3	69.5	68.9	-0.3
Physical functioning (mean score, 0-100) Enrollees	89.6	88.7	89.1	89.1	88.9	-0.2
Analytic sample	89.6	89.0	89.6	89.4	89.0	-0.5
Role functioning (mean score, %) Enrollees	94.8	91.9	91.8	92.8	93.1	0.3
Analytic sample	94.8	92.1	92.5	93.1	93.0	-0.2
Mental health (mean score, 0–100)	73.8	75.0	72 7	74.2	74.7	0.0
Enrollees Analytic sample	73.8	75.0 75.1	73.7 73.9	74.2 74.3	74.7 74.7	0.9 0.8
Social contacts (mean score, 0–100)						
Enrollees Analytic sample	72.8 72.6	72.1 72.2	72.3 72.0	72.4 72.2	72.5 72.5	0.1 0.3
Health perceptions (mean score, 0–100)	.2.0	, _,_	.2.0	72.2	, 2.0	0.5
Enrollees Analytic sample	70.5 70.4	71.1 71.2	69.4 69.7	70.4 70.4	69.7 69.8	-1.2 -1.2
Smoking scale (mean score, 1–2.20)	70.4	/1.2	07.7	70.4	U7.0	-1.2
Enrollees	1.29	1.30	1.32	1.30	1.29	-0.7
Analytic sample	1.28	1.29	1.30	1.29	1.29	-0.3
Mean standardized weight (kg) Enrollees	71.5	71.3	71.0	71.3	71.3	0.0
Analytic sample	71.6	71.3	71.6	71.5	71.6	0.2
Mean cholesterol level (mg/dl) Enrollees Analytic sample	207 208	205 205	206 207	206 207	202 204	-1.9 -1.5
Mean diastolic blood pressure (mm Hg)	200	203	207	207	407	1.5
Enrollees Analytic sample	75.2 76.0	75.3 75.4	75.4 75.7	75.3 75.7	74.6 74.7	-1.4 -1.9
Functional far vision (mean						
no. of lines) Enrollees Analytic sample	2.28 2.28	2.39 2.37	2.42 2.41	2.37 2.35	2.33 2.32	-0.9 -0.9
Risk of dying (mean score)						
Enrollees Analytic sample	0.99 0.99	1.04 1.06	1.13 1.13	1.05 1.06	1.03 1.03	-0.6 -0.8

^{*}Values are adjusted for differences according to site.

[†]For demographic data, table entries include everyone with valid enrollment data. For health measures, the mean score for enrollees excludes persons who did not have valid enrollment data because of the study design (e.g., they were not assigned to an initial screening examination) or to missing data, and the mean score for analytic samples excludes the same persons plus those who did not have valid exit data.

[‡]Values represent equally weighted averages of the three types of cost-sharing plans.

[§]For an explanation and rationale of the adjustment, see Brook et al. 28

tary), involuntary factors (such image at UNIV OF WALL CALL HER THE THE METERS Society. All rights reserved.

Table 4. Numbers of Adult Enrollees According to Category of Participation in Experiment and Plan.

CATEGORY OF PARTICIPATION				Cost-Shari	ng Plans				Free	Plan	Тот	TAL
		ATA- ROPHIC	INT MED	ER-		IDUAL CTIBLE	тот	AL				
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Total enrolled	759	100.0	1024	100.0	881	100.0	2664	100.0	1294	100.0	3958	100.0
Completed enrollment and exited normally	642	84.6	926	90.4	772	87.6	2340	87.8	1225	94.7	3565 *	90.1
Left experiment voluntarily	83	10.9	43	4.2	53	6.0	179	6.7	5	0.4	184	4.7
Terminated for health reasons †	3	0.4	13	1.3	11	1.3	27	1.0	15	1.2	42	1.1
Terminated for non- health reasons †	24	3.2	31	3.0	34	3.9	89	3.3	38	2.9	127	3.2
Died	7	0.9	11	1.1	11	1.3	29	1.1	11	0.9	40	1.0
Recovered for analysis ‡	94	80.3 §	84	85.7	69	63.3	247	76.2	54	78.3	301	76.6

^{*}The actual analyses are based on a slightly smaller sample, because forms were not available for under 1 per cent of this sample

incarceration), health reasons (mainly, becoming eligible for disability Medicare), or death. The latter two health-related factors did not differ materially as a function of plan (Table 4). In all, 95 per cent of those in the free plan completed the experiment normally by filling out the medical-history questionnaire and going through the final screening examination, as did 88 per cent of those in the individual-deductible plan, 90 per cent in the intermediate plans, and 85 per cent in the catastrophic plans.

To test whether these differences affected our results, we collected data on general health measures and smoking behavior of people who had terminated for various reasons and ran our analyses with and without them. Our findings were not altered by including or excluding these data, which were obtained from 73 per cent of those who withdrew voluntarily, 83 per cent of those who terminated for health reasons, 78 per cent of those who died, and 82 per cent of those who terminated for reasons not related to health. Thus, data from these people were included, and the final sample used for the questionnaire-based analyses comprised 99 per cent of the participants in the free and intermediate plans, 97 per cent of those in the catastrophic plan, and 95 per cent of those in the individual-deductible plan. The percentages with complete data on physiologic measures (as well as weight) were lower because after enrollment no screening examination was administered to the participants who left the experiment early.

As a further check for possible bias, we examined the values for health status at enrollment in the actual sample used for each analysis. We detected no differences according to plan (Table 3).

Effects on Health Status

Exit Values According to Plan

For the average person enrolled in the experiment, vals for subgroup analyses were, of course, wider than the only significant positive effect of free are APS of Objy 15, 20 for the east amplie one was whole; whence, we cannot be as

was that for corrected far vision, although the difference in diastolic blood pressure approached statistical significance (P = 0.06) (Table 5). The corrected vision of those enrolled in the free plan was better (2.4 vs. 2.5 Snellen lines, or an acuity of about 20/22 vs. 20/22.5).

No other health measure showed a significant difference between the free and the cost-sharing plans. Furthermore, only for hypertension, the risk of dying, and role functioning did the direction of the overall (main) effect favor the free plan (see the two rightmost columns of Table 5). For the remaining measures, the direction of the main effect favored the cost-sharing plans.

Confidence limits for the differences between the free and the other plans were relatively narrow in all cases; thus, it is unlikely that our conclusion that there was little or no effect is far off the mark. To verify that this conclusion did not depend on our method of prediction, we compared the predicted differences with the differences between the raw means of the two groups. The predicted differences and the differences in the raw means scarcely diverged (see the two rightmost columns of Table 5), although precision was better for the predicted values.

Within the cost-sharing group of plans, outcomes were more similar than between the free-care plan and the cost-sharing plans. Such an outcome is not surprising because differences in use were greater between the free-care plan and the cost-sharing plans than within the group of cost-sharing plans.¹²

The Influence of Income and Health Status on General Health

In addition to detecting no significant effect on five general measures of health for the average person (Table 5), we were unable to detect any significant differences among subgroups that differed in income and initial health status (Table 6). Confidence intervals for subgroup analyses were, of course, wider than

[†]Participation ended because the person no longer fulfilled criteria for participation eligibility. Health reasons included becoming eligible for disability Medicare and being institutionalized; nonhealth reasons included joining the military and failure to complete data-collection forms.

[‡]Form nonresponse not included. The number analyzed equals the number completed plus the number recovered minus the number of nonresponses.

[§]Percentages in this row are based on the number of enrollees in each plan who did not complete enrollment.

certain as with the entire sample that clinically important effects did not occur in these subgroups.

The Elevated-Risk Groups

At the end of the experiment, neither smoking status, cholesterol level, nor weight differed as a function of plan, even among participants judged to be at elevated risk on these measures (Table 7). Diastolic blood pressure among those who were hypertensive or nearly hypertensive was 1.4 mm Hg lower on the free plan than on the cost-sharing plans (P = 0.07). Among those whose uncorrected far vision was worse than 20/20, corrected vision was, collectively, about 0.2 Snellen lines better — an improvement in visual acuity from 20/25 to 20/24 (P<0.05).

For the average person at exit, the risk of dying from any cause (on the basis of smoking habits, cholesterol level, and systolic blood pressure) was set arbitrarily at 1.0. By comparison, the relative risk of dying for someone in the group at elevated risk (generally the upper quartile of the distribution of risk factors) was, on average, 2.02; that is, a member of this group would have been twice as likely to die during the subsequent year as the average person of the same age and sex. For high-risk members of the free-care plan at exit, the relative risk of dying was 1.90, as contrasted with 2.11 for those in the cost-sharing plans (Table 7). This 10 per cent difference in favor of free care was significant (P<0.05) and was principally attributable to the improved control of high blood pressure among those in the free plan.

The improvements in vision, blood pressure, and risk of dying were largest in the group with low income and elevated risk (see the first column of Table 8). For

them, the differences between the free and the costsharing plans were significant for blood pressure and the risk of dying, whereas neither of these differences was significant for the higher-income group. For instance, the difference in diastolic blood pressure for persons of low income who were judged initially to be at increased risk of hypertension was 3.3 mm Hg (P = 0.02); for such persons of high income it was only 0.4 mm Hg (P > 0.05).

At this point, it is tempting to infer that free care improved the health of the poor but not of the rich. Unfortunately, our data do not permit quite such a blunt summary. If we begin with the (null) hypothesis that free care makes no difference to the poor who are at elevated risk, our findings permit us to reject it; free care does make a difference, as shown by the two significant values in Table 8. On the other hand, we were unable to demonstrate that free care benefited people with a high income and high risk; here we cannot reject the null hypothesis. Given the conditions of our experiment, free care made no detectable difference to this group. Now, however, a paradox emerges. If we start with another null hypothesis — that the two income groups responded in the same way to the various plans — we would expect to see it rejected, but because the differences between the two groups are not significant, we cannot reject this hypothesis.

Thus, we are reasonably confident that poor people at elevated risk benefited from receiving free care, but we cannot draw any conclusion about the higherincome group. We cannot say that they benefited from receiving free care, but we also cannot show that they responded differently from the lower-income group, who were benefited.

Table 5. Predicted Exit Values of Health-Status Measures for an Average Person According to Measure and Plan, and Raw Mean Difference.

HEALTH-STATUS MEASURES	No. *		Cost-Sh	IARING PLANS		Free Plan	P	REDICTED MEAN DIFFERENCE (free minus	RAW MEAN DIFFERENCE (free minus
		CATA- STROPHIC	INTER- MEDIATE	INDIVIDUAL DEDUCTIBLE	TOTAL			cost-sharing) †	cost-sharing)
General health (score, 1-100)									
Physical functioning	3862	86.0	85.0	84.9	85.3	85.3	0.0	(-1.6, 1.5)	-0.3 (-2.3, 1.7)
Role functioning	3861	95.5	95.0	94.7	95.1	95.4	0.3	(-0.6, 1.2)	-0.3 (-2.2, 1.6)
Mental health	3862	75.6	75.5	75.8	75.6	75.5	-0.2	(-1.1, 0.8)	-0.1 (-1.1, 1.0)
Social contacts	3827	69.3	70.2	69.8	69.8	69.4	-0.3	(-2.3, 1.6)	-0.2 (-2.4, 2.0)
Health perceptions	3843	68.1	68.0	67.9	68.0	67.4	-0.6	(-1.5, 0.3)	-0.9 (-2.1, 0.3)
Health habits									
Smoking (scale, 1-2.20)	3758	1.28	1.29	1.29	1.29	1.29	0.0	(-0.02, 0.02)	-0.00 (-0.03, 0.03)
Weight (kg)	2804	72.8	72.6	73.1	72.8	72.8	0	(-0.5, 0.5)	0.0 (-1.0, 1.0)
Cholesterol level (mg/dl)	3381	202	200	204	202	203	1.0	(-1, 3)	1 (-2, 4)
Physiologic health									
Diastolic blood pres- sure (mm Hg)	3232	79.2	79.1	79.3	79.2	78.5	-0.7	(-1.5, 0.02) ‡	-0.8 § (-1.7, -0.02)
Functional far vision (no. of Snellen lines)	3477	2.55	2.50	2.51	2.52	2.42	-0.1	(−0.16, −0.04) ¶	-0.13 (-0.20, -0.06)
Risk of dying (score)	3317	1.01	0.98	1.03	1.01	0.99	-0.02	2 (-0.05, 0.02)	-0.03 (-0.07, 0.02)

^{*}Numbers of persons in various parts of the analysis are dissimilar because noncompleters were not included for physiologic health, weight, or cholesterol level and because of differences among measures in the number of persons with valid enrollment or exit data

[†]Numbers in parentheses are 95 per cent confidence intervals; an approximate confidence interval is given for role functioning.

[‡]t = 1.89, P = 0.06.
\$Although Tensor Variation is a fair in the case of differences in base-line blood-pressure values, it cannot be relied on.

¶t = 3.29; P = 0.001. Persons with normal vision were included and without permission.

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Table 6. Predicted Exit Values of Self-Assessed General Health Measures According to Measure, Plan, Income, and Initial Health Status.*

GENERAL HEALTH-	TOTAL	FREE	FREE MINUS	TOTAL	FREE	FREE MINUS
STATUS MEASURE	Cost- Sharing	Plan	Cost-Sharing †	COST- Sharing	Plan	Cost-Sharing †
	Low Inc	ome and	l Initial Ill Health	Low Income	e and In	itial Good Health
Physical functioning	60.3	65.9	5.6 (-2.9, 14.0)	89.8	91.2	1.4 (-1.6, 4.4)
Role functioning	69.0	46.3	-22.7 (-53.2, 7.8)	95.0	96.1	1.1 (-1.8, 4.0)
Mental health	65.6	67.0	1.4 (-1.8, 4.7)	81.1	79.3	-1.8 (-4.1, 0.6)
Social contacts	51.8	55.3	3.5 (-5.2, 12.2)	77.7	77.9	0.2 (-4.1, 4.5)
Health perceptions	54.2	54.6	0.3 (-3.0, 3.7)	74.7	72.4	-2.3 (~4.8, 0.1)
	High Inc	come and	d Initial Ill Health	High Incon	ne and I	nitial Good Health
Physical functioning	59.9	55.6	-4.3 (-9.8, 1.2)	92.6	91.9	-0.6 (-2.8, 1.6)
Role functioning	60.3	56.0	-4.3 (-24.1, 15.5)	96.3	96.3	0.0 (-2.0, 2.0)
Mental health	63.3	64.5	1.3 (-1.6, 4.1)	82.7	82.1	-0.6 (-1.9, 0.7)
Social contacts	47.3	47.6	-0.3 (-5.0, 5.5)	82.2	80.1	-2.1 (-5.1, 1.0)
Health perceptions	52.8	52.1	-0.7 (-3.1, 1.7)	77.7	77.8	0.1 (-1.4, 1.6)

^{*}Initial health status is defined with respect to the individual health measure denoted in each row

DISCUSSION

One purpose of the Rand Health Insurance Experiment was to learn whether the direct cost of medical care, when borne by consumers, affects their health. Participants in the experiment received one of a graded set of insurance plans; for some, medical care was absolutely free, whereas for others the annual cost could range up to as much as 15 per cent of family income. The experiment was designed to be as "realistic" as possible. The sample was typical of a general population of adults with two major exceptions: it excluded severely disabled persons who were eligible for Medicare and those over age 61 at the start. Moreover, the study was conducted at sites representing a cross-section of American medicine; participants could, and did, choose their own physicians.

We found that the more people had to pay for medical care, the less of it they used. Adults who had to

Table 7. Predicted Exit Values for Physiologic Measures and Health Habits in Elevated-Risk Groups, According to Measure and Plan.

HEALTH HABITS AND PHYSIOLOGIC MEASURES	Definition of Elevated-Risk Group *	TOTAL COST- SHARING	Free Plan	Free Minus Cost-Sharing †
Smoking	≥1.79 (≥1 pack per day)	1.75	1.73	-0.02 (-0.06, 0.03)
Weight	20% over ideal weight (kg)	89.1	89.4	0.3 (-1.1, 1.7)
Cholesterol level	≥220 mg/dl	242	244	2 (-3, 7)
Diastolic blood pressure	>83 mm Hg or taking hypertension drugs at enrollment	89.3	87.9	-1.4 (-3.0, +0.1) ‡
Functional far vision	Line 3 (20/25) or worse for better eye	2.98	2.78	-0.2 (-0.3, -0.1) §
Risk of dying	Risk >1.42	1.42	1.90	-0.21 (-0.39, -0.04) ¶

^{*}Elevated-risk groups are the least healthy 25 per cent of the people as defined with respect to the individual health measure denoted in each row. For functional far vision, all persons with uncorrected natural vision worse than 20/20 are included. †Numbers in parentheses are 95 per cent confidence intervals.

share the cost of care made about a third fewer ambulatory visits and were hospitalized about a third less often.12 We might have expected that differences of this magnitude in their use of medical resources would have influenced the participants' health.

From our data we can draw three conclusions about what the influence was. We can, therefore, narrow the range of speculation about the relation between cost-sharing and health status.

First of all, free care had no effect on the major health habits that are associated with cardiovascular disease and some types of cancer. Enrollment in a more generous insurance plan, resulting in an average of one to two more encounters with a physician each year for several

years, had no impact on smoking, weight (of either the average or the overweight), or cholesterol levels (average or elevated). Moreover, these habits, especially smoking, were at levels at which substantial health benefit from behavior change was possible.

Secondly, we detected no effects of free care for the average enrollee on any of five general self-assessed measures of health; and the confidence intervals in Table 5 rule out the possibility of anything beyond a minimal effect. We can be less certain of this interpretation of the findings with regard to subgroups differing in income or initial state of health, because the smaller samples yield wider confidence intervals

Thirdly, people with specific conditions that physicians have been trained to diagnose and treat (myopia, hypertension) benefit from free care. At the end of the experiment, persons receiving free care had better visual acuity, and some of them had lower blood

pressure. From the latter improvement we infer that their risk of early death had been diminished. Although differences between income groups were insignificant, the improvements appeared to be greater among the poor.

To illustrate the magnitude of the gains, consider an average 50-year-old man, who in the late 1970s had approximately a 5 per cent chance of dying within five years.²⁸ A 50-year-old man at elevated risk had approximately double that chance of dying. If 1000 50-year-old men at elevated risk were enrolled in a free insurance plan, we could anticipate that 10.5 of them, who would otherwise have died, would be alive five years later

[†]Numbers in parentheses are 95 per cent confidence intervals; approximate confidence intervals are given for role functioning

^{0.07}. § t=-3.29; P=0.004 New England Journal of Metrieine-2.41; P=0.02. Downloaded from nejm.org at UNIV OF MANITOBA LIBRARIES on February 15, 2015. For personal use only. No other t = -1.79; P = 0.07.

Table 8. Differences between Free and Cost-Sharing Plans in Predicted Exit Values of Blood Pressure and Vision and the Risk of Dying, According to Initial Health Status and Income.

Physiologic Measures	ELEVATED RISK *				
	LOW INCOME	HIGH INCOME			
Diastolic blood pressure	-3.3 (-5.9, -0.7)	-0.4 (-2.6, 1.8)			
Functional far vision	(-0.3 (-0.6, +0.02)	-0.1 (-0.4, 0.2)			
Risk of dying	-0.30 (-0.60, -0.04)	-0.13 (-0.40, 0.10)			

*For definitions of elevated risk for diastolic blood pressure and risk of dying, see Table 7. For functional far vision, elevated risk in this table refers only to the upper one quarter of the distribution of values for uncorrected natural vision. Predictions in these two columns were made with use of the mean value of the elevated-risk group. Numbers in parentheses are 95 per cent confidence intervals. All intervals that do not include 0 are significant at P<0.05.

 $(1000 \times 0.05 \times (2.11 - 1.90) = 10.5)$. An average 39-year-old woman, on the other hand, had only a one per cent chance of dying within five years²⁸; free care given to 1000 high-risk women would be expected to keep only two more women alive than would care provided under cost-sharing arrangements.

These mortality reductions, in and of themselves, are not sufficient to justify free care for all adults; investing in more targeted programs such as hypertension detection and screening would be a more cost-effective method of saving lives. ²⁸ If there are other life-saving benefits that free care yielded — for example, a reduction in cancer deaths because of increased or more appropriate screening — such a conclusion could change.

Precisely how increased use of care led to improvement in some measures of health status and why it did not in others are not yet known. Future analysis of data collected during the experiment will examine the use of services and the quality of care provided to patients with hypertension and visual impairments, as well as to persons with a host of other conditions or problems not reported on here.

Our results must be used with caution to derive policies for special groups in the population. In our study, poor families were protected by an incomerelated ceiling on their out-of-pocket medical expenses. The aged and those too disabled to work were not included in the experiment, and in any event additional medical care for such persons may provide benefits that a young, relatively healthy population does not experience.

Future studies will evaluate the benefits of free care that have already been observed, as well as other possible benefits, relative to their costs. At this juncture, however, we conclude that although free care did not improve health status across the entire range of measures or income groups examined, it did confer demonstrable benefits for patients with selected conditions that physicians are trained to manage.

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REFERENCES

- Benham L, Benham A. The impact of incremental medical services on health status, 1963-1970. In: Andersen R, Kravits J, Anderson OW, eds. Equity in health services: empirical analyses in social policy. Cambridge, Mass.: Ballinger, 1975:217-28.
- Rice DP, Wilson D. The American medical economy: problems and perspectives. J Health Polit Policy Law 1976; 1:151-72.
- Miller MK, Stokes CS. Health status, health resources, and consolidated structural parameters: implications for public health care policy. J Health Soc Behav 1978; 19:263-79.
- Miller AE, Miller MG. Options for health and health care: the coming of post-clinical medicine. New York: John Wiley, 1981.
- Cochrane AL, St. Leger AS, Moore F. Health service 'input' and mortality 'output' in developed countries. J Epidemiol Commun Health 1978; 32: 200-5.
- Newhouse JP, Friedlander LJ. The relationship between medical resources and measures of health: some additional evidence. J Hum Res 1980; 15:200-18.
- Hadley J. More medical care, better health? Washington, D.C.: The Urban Institute, 1982.
- Illich I. Medical nemesis: the expropriation of health. New York: Pantheon, 1977.
- 9. Carlson RJ. The end of medicine. New York: John Wiley, 1975.
- Starr P. The politics of therapeutic nihilism. Working Papers for a New Society 1976; IV(2):48-55.
- Rogers DE, Blendon RJ. The changing American health scene: sometimes things get better. JAMA 1977; 237:1710-4.
- Newhouse JP, Manning WG, Morris CN, et al. Some interim results from a controlled trial of cost sharing in health insurance. N Engl J Med 1981; 205:1501.7
- Keeler EB, Rolph JE. How cost sharing reduced medical spending of participants in the health insurance experiment. JAMA 1983; 249:2220-
- Newhouse JP. A design for a health insurance experiment. Inquiry 1974; 11:5-27.
- Newhouse J, Manning W, Morris C, et al. Some interim results from a controlled trial of cost sharing health insurance. Santa Monica, Calif.: Rand Corporation, 1982. (Rand publication no. R-2847-HHS).
- Morris CN. A finite selection model for experimental design of the health insurance study. J Econometrics 1979; 11:43-61.
- Constitution of the World Health Organization. In: Basic documents. Geneva: World Health Organization, 1948.
- McGee D, Gordon T. The results of the Framingham Study applied to four other US-based epidemiologic studies of cardiovascular disease. In: Kannel WB, Gordon T, eds. The Framingham Study: an epidemiologic investigation of cardiovascular disease, section 31. Washington, D.C.: National Institutes of Health, April 1976. (DHEW publication no. (NIH)76-1083)
- Stewart A, Ware JE Jr, Brook RH. Construction and scoring of aggregate functional status measures. Vol. 1. Santa Monica, Calif.: Rand Corporation, 1982. (Rand publication no. R-2551-1-HHS)
- Stewart A, Ware JE Jr, Brook RH. Construction and scoring of aggregate functional status indexes. Vol. 2. Appendixes. Santa Monica, Calif.: Rand Corporation, 1982. (Rand publication no. N-1706-1-HHS).
- Ware JE Jr, Johnston SA, Davies-Avery A, Brook RH. Conceptualization and measurement of health for adults in the health insurance study. Vol. 3. Mental health. Santa Monica, Calif.: Rand Corporation, 1979. (Rand publication no. R-1987/3-HEW).
- Veit CT, Ware JE Jr. The structure of psychological distress and well-being in general populations. J Consult Clin Psychol 1983; 51:730-42.
- Ware JE Jr, Manning WG, Duan N, Wells KB, Newhouse JP. Health status and the use of ambulatory mental health services. Am Psychol (in press).
- Donald CA, Ware JE Jr. The quantification of social contacts and resources. Santa Monica, Calif.: Rand Corporation, 1982. (Rand publication no. R-2937-HHS).

- Davies AR, Ware JE Jr. Measuring health perceptions in the health insurance experiment. Santa Monica, Calif.: Rand Corporation, 1981. (Rand publication no. R-2711-HHS).
- Stewart AL, Brook RH, Kane RL. Conceptualization and measurement of health habits for adults in the health insurance study. Vol. 1. Smoking. Santa Monica, Calif.: Rand Corporation, 1979. (Rand publication no. R-2374/1-HEW).
- Stewart AL, Brook RH, Kane RL. Conceptualization and measurement of health habits for adults in the health insurance study. Vol. 2. Overweight. Santa Monica, Calif.: Rand Corporation, 1980. (Rand publication no. R-2374/2-HEW).
- Brook RH, Ware JE Jr, Rogers WH, et al. The effect of coinsurance on the health of adults: results from the Rand Health Insurance Experiment. Santa Monica, Calif.: Rand Corporation, (in press). (Rand publication no. R-3055-HHS)
- Stewart AL. The reliability and validity of self-reported weight and height.
 J Chronic Dis 1982; 35:295-309.

- Brook RH, Berman DM, Lohr KN, Goldberg GA, Applegate KH. Conceptualization and measurement of physiologic health for adults: hypertension. Santa Monica, Calif.: Rand Corporation, 1980. (Rand publication no. R-2262/3-HHS).
- Brook RH, Lohr KN, Keeler EB, Berman DM, Goldberg GA. Conceptualization and measurement of physiologic health for adults: hypercholesterolemia. Santa Monica, Calif.: Rand Corporation, 1981. (Rand publication no. R-2262/11-HHS).
- Rubenstein RS, Lohr KN, Brook RH, Goldberg GA. Conceptualization and measurement of physiologic health for adults: vision impairments. Santa Monica, Calif.: Rand Corporation, 1982. (Rand publication no. R-2262/12-HHS)
- Huber PJ. The behavior of maximum likelihood estimates under nonstandard conditions: fifth Berkeley Symposium, 1965. Berkeley, Calif.: University of California Press, 1967:221-33.
- Dagenais MG. Further suggestions concerning the utilization of incomplete observations in regression analysis. J Am Stat Assoc 1971; 66:93-8.

MEDICAL PROGRESS

VARICELLA AND HERPES ZOSTER

Changing Concepts of the Natural History, Control, and Importance of a Not-So-Benign Virus (Second of Two Parts)

THOMAS H. WELLER, M.D.

Patients at High Risk of Morbidity or Mortality from Varicella–Zoster Virus

Recognition of the potential severity of varicella in immunocompromised patients dates from our postmortem studies of two children who contracted chickenpox; one child had rheumatic fever and was receiving cortisone therapy, and the other was being treated for a neuroblastoma. ^{96,97} The latter case demonstrated that in such patients infections with varicella–zoster virus may be bizarre. When death occurred, in addition to the generalized lesions that had appeared in continued crops for 17 days, there was a zosteriform concentration of lesions over the right T-10 dermatome

The risk of severe infection is high when the immunologic insults of hematopoietic or reticuloendothelial cancer are compounded by those of cytotoxic or immunosuppressive therapy. Severe varicella–zoster occurs frequently in children being treated for Hodgkin's disease, non-Hodgkin's lymphoma, or lymphocytic leukemia. In Hodgkin's disease the frequency has been reported to be 22 and 35 per cent. ^{98,99} In one series of patients who contracted varicella while receiving therapy, 32 per cent had visceral involvement, with a mortality rate of 7 per cent. ¹⁰⁰ However, zoster in such patients is usually not fatal, ¹⁰¹ although death may follow visceral involvement, with pneumonia, hepatitis, or encephalitis predominant. Numerous

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studies suggest that an impaired cellular immune state is the major contributing factor. As in the immunocompetent patient, the risk of dissemination increases with age. Representative observations are that absolute leukopenia correlates with severe visceral involvement, 100 that patients with reticuloendothelial cancer frequently have a lowered response to the lymphocytetransformation test, 102,103 and that the viral-inactivating capacity of the white cells is low. 104 Gershon and Steinberg reported that all 12 of their patients had demonstrable humoral antibody, even though 4 died. 104 In a prospective study, suppression of specific cell-mediated immunity preceded each episode of reactivation. 105 Although defective cellular immunity has been established as a major factor in disseminated infections, the role of depressed humoral responses remains controversial. 106 After the appearance of localized zoster in the high-risk patient, administration of zoster immune globulin does not reduce the frequency of dissemination 107 or affect the clinical course after dissemination. 108 However, as described by Zaia, 109 extensive experience has established the value of passive immunization for modification of the primary attack of varicella in the exposed high-risk patient.

Infections with varicella-zoster virus are a major problem in the subset of patients with leukemia or aplastic anemia who receive marrow transplants after high-dosage radiochemotherapy. In a group of 140 marrow recipients, including 89 who survived longer than six months, 92, or 65 per cent, had a clinically apparent process; zoster developed in 77 patients, with dissemination in 22, and in 15 the first manifestation was a generalized rash. Seven patients with an active infection died, and most of them had pneumo-