Special Article

THE RELATION BETWEEN FUNDING BY THE NATIONAL INSTITUTES OF HEALTH AND THE BURDEN OF DISEASE

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ABSTRACT

Background The Institute of Medicine has proposed that the amount of disease-specific research funding provided by the National Institutes of Health (NIH) be systematically and consistently compared with the burden of disease for society.

Methods We performed a cross-sectional study comparing estimates of disease-specific funding in 1996 with data on six measures of the burden of disease. The measures were total mortality, years of life lost, and number of hospital days in 1994 and incidence, prevalence, and disability-adjusted life-years (one disability-adjusted life-year is defined as the loss of one year of healthy life to disease) in 1990. With the use of these measures as explanatory variables in a regression analysis, predicted funding was calculated and compared with actual funding.

Results There was no relation between the amount of NIH funding and the incidence, prevalence, or number of hospital days attributed to each condition or disease ($P=0.82$, $P=0.23$, and $P=0.21$, respectively). The numbers of deaths ($r=0.40$, $P=0.03$) and years of life lost ($r=0.42$, $P=0.02$) were weakly associated with funding, whereas the number of disability-adjusted life-years was strongly predictive of funding ($r=0.62$, $P<0.001$). When the latter three measures were used to predict expected funding, the conclusions about the appropriateness of funding for some diseases varied according to the measure used. However, the acquired immunodeficiency syndrome, breast cancer, diabetes mellitus, and dementia all received relatively generous funding, regardless of which measure was used as the basis for calculating support. Research on chronic obstructive pulmonary disease, perinatal conditions, and peptic ulcer was relatively underfunded.

Conclusions The amount of NIH funding for research on a disease is associated with the burden of the disease; however, different measures of the burden of disease may yield different conclusions about the appropriateness of disease-specific funding levels. (N Engl J Med 1999;340:1881-7).

THE research programs of the National Institutes of Health (NIH) have been remarkably successful over the past 50 years. NIH-funded scientists have made substantial progress in understanding the basic mechanisms of disease and have vastly improved the preventive, diagnostic, and therapeutic options available.[1] However, the NIH is able to fund less than 30 percent of extramural grant applications; this fact has led scientists, patients, and other advocates of biomedical research to question how research funds are allocated to research on various diseases.[2-6]

The NIH working group on the setting of priorities has listed five major criteria for the allocation of research funds: public health needs, the scientific quality of research, the probability of success, the maintenance of a diverse portfolio, and the maintenance of an adequate scientific infrastructure.[7] An Institute of Medicine panel recently embraced these criteria as an appropriate framework for funding.[8] However, the panel also concluded that the NIH does not adequately describe how public health need is assessed, and it recommended that "in setting priorities, the NIH should strengthen its analysis and use of health data, such as burdens and costs of diseases."[8]

We performed this study to determine whether the amount of funding the NIH allocates to research on particular diseases is associated with commonly available measures of the burden of disease.

METHODS

Study Design

This was a cross-sectional study relating different measures of the burden of disease to the magnitude of NIH research funding. Diseases that were included in our study were those for which estimates of NIH funding, definitions from the *International Clas-*

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TABLE 1. NIH RESEARCH FUNDS AND MEASURES OF DISEASE BURDEN FOR 29 CONDITIONS.

CONDITION OR DISEASE	NIH RESEARCH FUNDS	MEASURE OF DISEASE BURDEN*					
		INCIDENCE	PREVALENCE	HOSPITAL DAYS	MORTALITY	YEARS OF LIFE LOST	DISABILITY-ADJUSTED LIFE-YEARS†
	thousands of dollars (% of total)	thousands (rank)					
AIDS	1,410,925 (28.7)	138 (20)	1,303 (17)	329 (20)	42 (10)	979 (4)	1267 (15)
Breast cancer	381,880 (7.8)	523 (12)	2,262 (13)	525 (18)	44 (9)	426 (8)	1421 (14)
Dementia	304,411 (6.2)	959 (9)	7,082 (8)	841 (16)	34 (12)	99 (14)	2866 (7)
Diabetes mellitus	298,920 (6.1)	2,308 (6)	37,850 (1)	3,181 (8)	57 (8)	407 (9)	2357 (8)
Ischemic heart disease	269,100 (5.5)	2,216 (7)	8,976 (6)	11,815 (2)	481 (1)	2973 (2)	8876 (1)
Alcohol abuse	256,600 (5.2)	11,085 (3)	18,092 (2)	2,563 (9)	7 (18)	98 (15)	4690 (5)
Injuries	198,700 (4.0)			15,218 (1)	149 (4)	3109 (1)	8608 (2)
Dental and oral disorders	187,100 (3.8)			158 (25)	0.1 (28)	0.9 (28)	870 (18)
Cirrhosis	169,800 (3.4)	168 (17)	1,238 (18)	869 (15)	31 (13)	380 (11)	1584 (13)
Depression	143,800 (2.9)	20,622 (2)	12,785 (4)	8,409 (4)	8 (17)	23 (24)	8393 (3)
Lung cancer	127,796 (2.6)	430 (16)	874 (19)	1,536 (12)	149 (3)	1158 (3)	2987 (6)
Stroke	120,280 (2.4)	1,282 (8)	9,467 (5)	6,450 (5)	153 (2)	746 (5)	4977 (4)
Schizophrenia	111,479 (2.3)	162 (18)	7,164 (7)	4,129 (6)	0.4 (26)	2 (27)	2249 (10)
Colorectal cancer	105,525 (2.1)	499 (14)	1,926 (15)	1,600 (11)	58 (7)	391 (10)	1626 (12)
Sexually transmitted diseases	102,583 (2.1)			69 (29)	0.3 (27)	28 (26)	404 (22)
Prostate cancer	92,661 (1.9)	452 (15)	2,020 (14)	585 (17)	35 (11)	153 (13)	574 (19)
Multiple sclerosis	82,800 (1.7)	16 (24)	461 (21)	149 (26)	2 (23)	28 (21)	236 (25)
Asthma	81,600 (1.7)	3,594 (5)	15,919 (3)	1,820 (10)	5 (20)	65 (16)	1236 (17)
Parkinson's disease	77,158 (1.6)	136 (21)	1,849 (16)	162 (24)	10 (16)	36 (19)	447 (21)
Tuberculosis	64,125 (1.3)	155 (19)	39 (25)	163 (23)	2 (24)	15 (25)	118 (28)
Chronic obstructive pulmonary disease	62,400 (1.3)	670 (11)	4,271 (11)	3,537 (7)	96 (5)	518 (6)	2284 (9)
Pneumonia	61,900 (1.3)	9,257 (4)	178 (23)	8,625 (3)	81 (6)	363 (12)	1263 (16)
Cervical cancer	60,180 (1.2)	4 (25)	164 (24)	94 (28)	5 (21)	63 (17)	192 (26)
Epilepsy	55,100 (1.1)	504 (13)	4,511 (10)	483 (19)	1 (25)	25 (22)	505 (20)
Ovarian cancer	42,168 (0.8)	74 (23)	247 (22)	325 (21)	14 (15)	48 (18)	375 (23)
Perinatal conditions	26,400 (0.5)			1,382 (14)	14 (14)	473 (7)	1767 (11)
Uterine cancer	13,956 (0.3)	133 (22)	599 (20)	199 (22)	3 (22)	23 (23)	185 (27)
Otitis media	9,100 (0.2)	40,424 (1)	3,110 (12)	100 (27)	0.04 (29)	0.7 (29)	8 (29)
Peptic ulcer	6,000 (0.1)	944 (10)	5,005 (9)	1,440 (13)	6 (19)	35 (20)	239 (24)

*Estimates of incidence and prevalence were obtained from the Global Burden of Disease Study and apply to established market economies in 1990. All other estimates are specific to the United States for 1994.

†One disability-adjusted life-year is defined as the loss of one year of healthy life to disease.

sification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM), and potential measures of the burden of disease were available.[7,9,10]

Measures of the Burden of Disease

Number of People Affected

Two of the more frequently cited measures of the burden of disease are the total number of people with a disease (prevalence) and the frequency of new cases (incidence).

Use of Resources and Cost

Several methods have been proposed for estimating the financial burden imposed by various diseases on the health care system.[11-13] As a proxy for financial burden, we estimated the number of hospital days attributed to each disease as the principal diagnosis.

Mortality

The most readily available and frequently cited measure for assessing the burden of disease is total mortality.[14] For each death, the underlying cause is determined on the basis of conditions reported in the death certificate with the use of an algorithm described in the ICD-9-CM.[15] Because statistics on total mortality do not take age into account, another measure has been developed, called years of life lost, which is calculated by subtracting a person's age at death from his or her life expectancy in the absence of a given disease.[16] We calculated years of life lost using the methods described in the Global Burden of Disease Study.[17]

The Global Burden of Disease Study was a five-year effort sponsored in part by the World Bank and the World Health Organization.[18] The goal was to develop a comprehensive and objective set of estimates of current patterns of morbidity and mortality due to disease and injury for all regions of the world. The investigators used a systematic and exhaustive approach to esti-

mate prevalence, incidence, and mortality and developed a new composite measure for assessing health status.[9]

Composite Measures

It is a widely held belief that increases in both the length and the quality of life are important.[19] Therefore, measures were developed that took into account the notion that the value of a year of life spent in perfect health is greater than the value of a year spent in less than perfect health.[20-22] The problem is how to ascertain the appropriate balance between the duration and the quality of life by converting time spent in various states of health to their "healthy-year equivalents."[23] Disability-adjusted life-years is the composite measure developed by the authors of the Global Burden of Disease Study; it incorporates the social values placed on various aspects of physical, mental, and social function.[17,24] These social values were derived from a formal exercise involving health workers from throughout the world.[25] The results of this analysis were subsequently validated by nine additional exercises with other participants that used the same protocol.[25] One disability-adjusted life-year is defined as one year of healthy life that has been lost because of either disability or death.[17]

Sources of Data and Construction of Variables

Estimates of disease-specific research funding for all awards and contracts in fiscal year 1996 were obtained from an NIH report compiled in response to a request from the House Committee on Appropriations.[26] Constructing annual budgets for the NIH is a complex process that begins approximately two years before each fiscal year.[27] We wanted to examine the relation between NIH allocations and the burden of disease at the time funding decisions were made. Hence, we compared 1996 NIH funding with measures of the burden of disease in 1994, when possible.

The number of deaths attributed to each disease in 1994 was obtained from the National Center for Health Statistics.[28] Data from the National Hospital Discharge Survey were used to estimate the number of hospital days attributed to each disease in 1994.[29] For disability-adjusted life-years, incidence, and prevalence in 1990, we used the estimates from the Global Burden of Disease Study for what is referred to as "established market economies," which includes western Europe, the United States, Canada, Japan, Australia, and New Zealand.[25] Specific estimates of disability-adjusted life-years are not yet available for the United States.

Statistical Analysis

The dependent variable was NIH funding for research on specific medical conditions, and the independent variables were measures of the burden of disease. Correlations between funding and measures of the burden of disease were assessed with Spearman's rho test. Because the data were not normally distributed, we also performed logarithmic transformations and used the Shapiro–Wilk W statistic to confirm reasonable normality of the log-transformed data. We performed simple linear regression analyses with funding as the dependent variable and a measure of the burden of disease as the independent variable. For each measure that had a statistically significant association with funding, we used the regression-derived estimates to predict the expected NIH funding for each disease. We then compared the expected funding with the actual funding.

RESULTS

Disease-Specific Funding

Estimates of NIH funding and measures of the burden of disease were available for 29 diseases. Funding for fiscal year 1996 and the various measures of the burden of these diseases are shown in Table 1. Total NIH research funding in 1996 was $11.9 billion, of which approximately $4.9 billion was for the diseases included in our analysis. Estimates of incidence and prevalence were not available for 4 of the 29 conditions (injuries, dental and oral disorders, sexually transmitted diseases, and perinatal conditions). Funding varied markedly, ranging from $6 million for peptic ulcer to $1.4 billion for the acquired immunodeficiency syndrome (AIDS).

Measures of the Burden of Disease

The relation between each of the measures of the burden of disease and the amount of NIH funding, as determined by simple linear regression of the log-transformed data, is shown in Table 2. Neither the incidence nor the prevalence of disease was predictive of the amount of NIH funding ($P=0.82$ and $P=0.23$, respectively). The number of hospital days was also not predictive of NIH funding ($P=0.21$), suggesting that the consumption of resources for specific illnesses may not be a major factor in the allocation of NIH funds.

Mortality

Ischemic heart disease, stroke, and lung cancer were, respectively, the first, second, and third leading causes of death in the United States in 1994. There was a positive association between total mortality from disease and the amount of funding ($r=0.40$, $P=0.03$). Although the ranking of diseases according to mortality was somewhat different from that according to years of life lost (Table 1), the direction and magnitude of the association between each of these two variables and the amount of NIH funding were similar.

Disability-Adjusted Life-Years

The relation between NIH funding and disability-adjusted life-years was significant ($r=0.62$, $P<0.001$).

TABLE 2. ASSOCIATION OF MEASURES OF THE BURDEN OF DISEASE WITH AMOUNT OF RESEARCH FUNDING BY THE NIH.*

MEASURE (YEAR ASSESSED)	UNITS	CORRELATION COEFFICIENT (r)	P VALUE
Incidence (1990)	No. of new cases per year	−0.05	0.82
Prevalence (1990)	No. of existing cases	0.25	0.23
Hospital days (1994)	Days in acute care hospitals	0.24	0.21
Mortality (1994)	Deaths per year	0.40	0.03
Years of life lost (1994)	Years	0.42	0.02
Disability-adjusted life-years (1990)†	Years	0.62	<0.001

*Research funding was measured in dollars, with logarithmic transformation of data. Estimates were available for all measures of the burden of disease for 25 diseases. For an additional four diseases, estimates were available of all measures except incidence and prevalence.

†One disability-adjusted life-year is defined as the loss of one year of healthy life to disease.

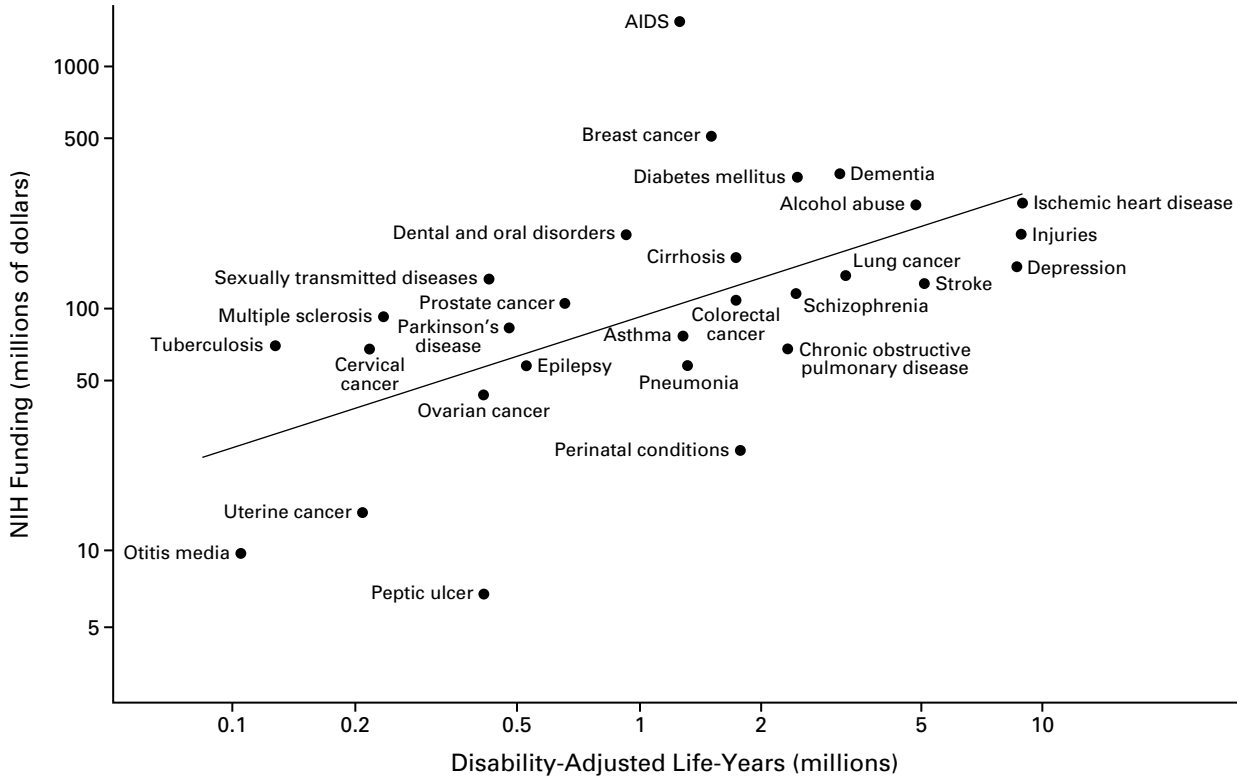

Figure 1. Relation between NIH Disease-Specific Research Funding in 1996 and Disability-Adjusted Life-Years for 29 Conditions in 1990.

The axes are drawn to logarithmic scale. The line represents funding predicted on the basis of a linear regression with disability-adjusted life-years as the explanatory variable. One disability-adjusted life-year is defined as the loss of one year of healthy life to disease.

The amount of predicted and actual NIH funding as a function of disability-adjusted life-years is shown in Figure 1. The line represents the amount of funding that would be predicted if the number of disability-adjusted life-years were the sole criterion for funding.

Differences between Actual and Predicted Funding

The difference between actual and predicted funding for each disease, with mortality, disability-adjusted life-years, and years of life lost used as explanatory variables, is shown in Table 3 (negative values indicate that the disease received less funding than predicted). Research in the areas of chronic obstructive pulmonary disease, perinatal conditions, and peptic ulcer was underfunded according to all three measures. On the other hand, AIDS, breast cancer, dementia, and diabetes mellitus all received more than the predicted amount of research funding, regardless of which measure of the burden of disease was used. However, for some diseases, the conclusions about the appropriateness of funding differ depending on which measure is chosen. For example, if the number of disability-adjusted life-years is used as the sole funding criterion, then ischemic heart disease, schizophrenia, and depression received less funding than predicted. If mortality-based measures (total mortality or years of life lost) are used as funding criteria, these diseases received more funding than predicted.

Sensitivity Analysis

Because the discrepancy between actual and predicted funding was far higher for AIDS than for any other disease, we repeated the analyses after excluding AIDS. There was no significant change in the relation of actual to predicted funding with any of the measures of burden of disease (data not shown).

DISCUSSION

Although it is arguable whether the burden of disease should assume priority in NIH funding decisions, the NIH's allocation process has been criticized as being arbitrary and insensitive to the burden of disease.[2,3,8,30] However, only a few diseases have been analyzed, and often only one measure of the burden of disease has been assessed. Our analysis re-

vealed a significant relation between NIH research funding and measures of the burden of disease. Disability-adjusted life-years, a measure that takes into account the age of those affected, the degree of disability, and the number of deaths, was most strongly associated with the amount of funding. The number of years of life lost was not substantially more predictive of funding than total mortality. This result suggests that all deaths are treated as having equal importance, regardless of the age at death.

However, the prevalence of a disease, its incidence, and the number of hospital days attributed to a disease were not associated with the amount of funding. The lack of association of prevalence and incidence with funding may be due to the fact that these measures do not take into account the severity of illness. These measures assign a higher burden to mild but widespread diseases such as otitis media than to severe but less common diseases, such as breast cancer.

Our data demonstrate how policy makers could be misled by using a single measure of the burden of disease, because the ranking of diseases according to their burden varies with the different measures used. Comparison of actual and predicted funding based on mortality, years of life lost, and disability-adjusted life-years led to similar conclusions (i.e., that actual funding was above or below predicted funding) for 21 of the 29 diseases. As a result, advocates interested in promoting research on particular diseases could select measures that best support their cause.

The burden of disease is only one of the five criteria used by the NIH to set priorities; all should be considered when research funds are allocated.[7] Scientific opportunity is a particularly important factor to consider, because recent discoveries may make some areas of research more "ripe" for success. However, external pressure can also influence funding priorities. It was partially in response to such pressure that the Institute of Medicine panel recommended that the NIH explicitly compare the burden of disease and the amount of research funding.[8]

Policy makers are faced with two main problems when choosing among alternative measures of the burden of disease. The first is the availability and quality of the data. For many measures, there is no central repository of data, and advocacy groups can select or emphasize data derived by a variety of methods.[31] The second, and far more important, problem is the social values incorporated into various measures. Some may argue that all lives are equal in importance and that total mortality should therefore be used to guide allocation decisions.[16,32] Others may contend that the equitable distribution of resources requires attention to any incremental improvement in health status. For this purpose, disability-adjusted life-years may be a more appropriate measure.[19,24] The relations among different measures should also be considered by policy makers, because some measures may be negatively correlated.[33] For example, improved treatment of a disease could decrease mortality due to the disease but increase its prevalence by increasing the number of survivors.

Substitutes for NIH funding also need to be considered. For instance, private industry now funds nearly twice as much biomedical research as does the NIH.[8,34] Research on pneumonia may receive relatively low funding from the NIH because the pharmaceutical industry is keenly interested in developing new antibiotics. Although research performed by industry may be distinct from NIH-funded research in a number of ways, it is important for policy

TABLE 3. DIFFERENCE BETWEEN ACTUAL AND PREDICTED FUNDING BY THE NIH, ACCORDING TO THE MEASURE USED TO PREDICT FUNDING.*

CONDITION OR DISEASE	MORTALITY	DISABILITY-ADJUSTED LIFE-YEARS†	YEARS OF LIFE LOST
	millions of dollars		
Chronic obstructive pulmonary disease	−83	−79	−76
Perinatal conditions	−81	−97	−109
Peptic ulcer	−79	−36	−72
Pneumonia	−79	−41	−66
Uterine cancer	−61	−23	−58
Ovarian cancer	−57	−12	−41
Stroke	−39	−95	−29
Lung cancer	−31	−36	−36
Prostate cancer	−27	25	−14
Colorectal cancer	−27	−13	−25
Otitis media	−23	−15	−25
Cervical cancer	−21	22	−28
Parkinson's disease	−17	18	−1
Epilepsy	−9	−8	−17
Asthma	−2	−20	−7
Tuberculosis	−2	35	−1
Multiple sclerosis	14	41	9
Cirrhosis	53	53	40
Depression	53	−140	72
Injuries	54	−89	−4
Sexually transmitted diseases	56	46	57
Schizophrenia	61	−29	68
Ischemic heart disease	70	−24	68
Dental and oral disorders	149	102	152
Diabetes mellitus	167	155	168
Alcohol abuse	170	48	160
Dementia	185	144	207
Breast cancer	257	272	249
AIDS	1,287	1,307	1,252

*Negative numbers indicate that research on a condition was underfunded in relation to the burden of disease, and positive numbers that it was overfunded.

†One disability-adjusted life-year is defined as the loss of one year of healthy life to disease.

makers to consider these substantial efforts when allocating funds. Trends in NIH-funded research should also be considered, since diseases that have been underfunded in earlier years may deserve additional funding.

Our study has several limitations. First, the serendipitous nature of science must be considered; investigations in one area frequently yield fruitful results in another. Research done by a virologist, for example, may produce information that is immediately and directly beneficial in cancer research. Hence, it may be overly simplistic to link funding to specific diseases. However, awareness of this factor does not preclude the need for rational methods to assign priorities and continue goal-directed initiatives.

Second, all measures of the burden of disease in our analysis are imperfect, since reporting errors, improper coding, and the use of proxy measures contribute to potential bias. For example, the death certificate is not always a reliable record of the cause of death. Improved diagnostic techniques may lead to increased recognition and diagnosis of some diseases. In addition, data may not accurately reflect the true burden of each disease, because many diseases contribute to the morbidity caused by other diseases.

Third, it was not possible to analyze all diseases, since we were constrained by the availability of data. However, the diseases in our study represented a substantial proportion of the total burden of disease. For instance, the sum of the mortality attributed to the 29 diseases and conditions we studied represents 63 percent of all deaths reported in 1994. Similarly, the sum of the disability-adjusted life-years for these 29 diseases represents 62 percent of the total estimate.

Fourth, our conclusions are based on estimates of disability-adjusted life-years for industrialized countries. The United States has a higher incidence of AIDS than most other countries in this group. However, even when we tripled the estimated number of disability-adjusted life-years attributed to AIDS, our results did not change substantially.

Finally, some funds may be assigned to more than one disease. For instance, a grant to investigate heart disease in patients with diabetes would be included in both categories.[7] There may be disagreement about how some research expenditures are assigned to particular diseases.

Despite past criticisms, the allocation of research funds to specific diseases by the NIH is not arbitrary in relation to the burden of disease. The number of disability-adjusted life-years is strongly associated with funding levels. However, conclusions about the degree of matching between NIH funding and the burden of disease are extremely sensitive to the measure used, and assessments of the appropriateness of funding levels should be interpreted with great caution.

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