Limitations of a biomedical model to explain socioeconomic disparities in mortality of rheumatic and cardiovascular diseases

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Medical care advanced spectacularly over the 20th century, largely on the basis of a "biomedical model" paradigm (1-3). This paradigm applies "reductionism" to identify a single primary physical or somatic cause of a disease, leading to a pharmacological treatment (Table I). Laboratory tests and other information from high-technology sources are considered the most important data for diagnosis and prognosis. Mind and body are regarded as distinct in the pathogenesis, morbidity and mortality of most diseases. Management of health and disease is determined by health professionals and the medical care system, with little contribution from an individual in self-management of her/his health.

A biomedical model has been eminently successful in acute diseases – vaccines and antibiotics for infectious disease present some of the most striking examples. Steady improvement was seen over the 20th century in outcomes of acute problems ranging from pneumonia to myocardial infarction to major trauma and many others. These improvements depend almost entirely on decisions and actions of health professionals, with minimal contribution of the patient.

Application of a biomedical model to rheumatic diseases led to the discovery of rheumatoid factor (4, 5) and anti-nuclear antibodies (6) in the mid 20th century, which established rheumatology as a scientific field. A biomedical model provides the primary foundation for understanding pathogenetic mechanisms and development of advances in pharmacologic management of rheumatic diseases, ranging from methotrexate and biological agents in rheumatoid arthritis (RA) (7) to cyclophosphamide and mycophenolate mofetil in systemic lupus erythematosus (SLE) nephritis (8). Further biomedical research according to a biomedical model clearly is prerequisite to future advances in prevention and therapy of rheumatic (and other) diseases.

Nonetheless, despite its inestimable value, a biomedical model has many limitations to understand health, particularly in chronic diseases, the primary concern of most contemporary medical care in Western countries. A biomedical model presents an oversimplification, even in simple situations. For example, while a tubercle bacillus is the obvious "cause" of tuberculosis, an identical dose of tubercle bacilli may initiate a wide spectrum of results in different individuals, ranging from no disease to death. A single, simple "cause" of disease cannot fully explain pathogenesis without consideration of the host – genetic susceptibility and resistance, age, comorbidities and other variables.

Limitations of a biomedical model led to description of a complementary view of health and disease, termed a "biopsychosocial model," by Engel in 1978 (1, 9) (Table I). A biopsychosocial model suggests that the etiology of disease is multi-factorial, recognizing host variables – genes, age, behaviors, social support – in addition to external causes. A patient history may provide most of the information needed for diagnosis and many management decisions, without high-technology data. Information provided by patients often may be the most valuable data to estimate a prognosis. Mind-body interactions are recognized as affecting the etiology, course, and outcomes of most diseases. Health and outcomes of chronic diseases are determined as much by actions of an individual and her/his social milieu as by actions of health professionals and the medical care system.

Perhaps a most powerful example of limitations of a biomedical model involves disparities in health according to socioeconomic status variables such as formal education level, occupation, and

Table I. Features of a biomedical model and biopsychosocial model.

	Biomedical model	Biopsychosocial model
Cause	Each disease has a single "cause" to identify a single "cure"	Disease etiology is multifactorial: external pathogens, toxins, and internal host milieu, genes, behavior, social support
Diagnosis	Identified primarily through laboratory tests, radiographs, scans; information from patients is of value primarily (or only) to suggest appropriate tests	A patient medical history provides 50-90% of the information needed to make many, perhaps most, diagnoses
Prognosis	Also established most accurately on the basis of information from high-technology sources.	Information reported by patients often provides the most valuable data to establish a prognosis
Mind-body interactions	Mind and body are largely independent in the etiology and outcomes of most diseases	Mind-body interactions affect health, including etiology, course, and outcomes of most diseases
Treatment	Involves only actions of health professionals, e.g., medications, surgery	Includes actions of patient, family, social structure
Outcome	Health and outcomes are determined primarily by decisions and actions of health professionals.	Health and outcomes of chronic diseases are determined as much by actions of individual patients as by health professionals.

income. Such disparities have been observed for many decades in many studies in the United States (10-17), United Kingdom (18-22), Spain (23), Italy (24), the Netherlands (25), Belgium (26), Norway (27, 28), Sweden (29, 30), Finland (31-33), Denmark (34), Lithuania (35), Russia (36), Japan (37), Australia (38), and New Zealand (39). Similar clinical and epidemiologic findings in rheumatic and cardiovascular diseases are consistent with emerging data concerning similar pathogenetic mechanisms (40). A few of many reports are summarized below.

Socioeconomic status and mortality in rheumatic diseases

Formal education level was found to be a significant predictor of morbidity and mortality in a cohort of 75 patients with RA analyzed over nine years from 1973-1982 (41). Survival over nine years was about 95% in patients with more than 12 years of education, compared to about 80% in patients with 9-12 years of formal education, and 65% in patients with fewer than eight years of education (41) (Fig. 1). In addition, declines in functional status, which were seen at that time in almost all patients, were substantially greater in those with fewer than eight years of education than for patients with 9-12 years of education, which were in turn greater than those seen in patients with more than 12 years of formal education (41).

Overall, almost half of the patients with fewer than eight years of education died over the 9-year study period, while fewer than 10% had the best outcome of less than a 20% functional loss, in contrast to patients with more than 12 years of education, among whom half had less than 20% functional loss, and very few died (Fig. 2). Associations of low education level with mortality outcomes were explained only in small part by age, race, duration of disease, or any biomedical marker (41).

A second cohort of patients with RA was recruited from 15 private practices in the United States in 1985, designed to analyze whether observations of disparities in mortality rates according to formal education level seen in a tertiary university clinic in the United States (41) would also be seen in U.S. private practice settings (42). The standard mortality ratio was 1.5 over 5 years (43) and 1.6 over 10 years (42). Formal education level was a significant predictor of mortality in univariate and multivariate analyses, in which the associations were explained in part by helplessness scores (Fig. 3).

In the United Kingdom, Young *et al.* (44) found that the Carstairs Index – an index of social deprivation based on four census indicators, low social class, lack of ownership of a car, overcrowding, and male unemployment (45) – was significant in predicting mortality in the Early Rheumatoid Arthritis Study (ERAS) between 1986 and 2004 (Table II). In a Cox regression which included age, erythrocyte sedimentation rate (ESR), sex, health assessment questionnaire (HAQ) score and baseline hemoglobin, all of which were significant

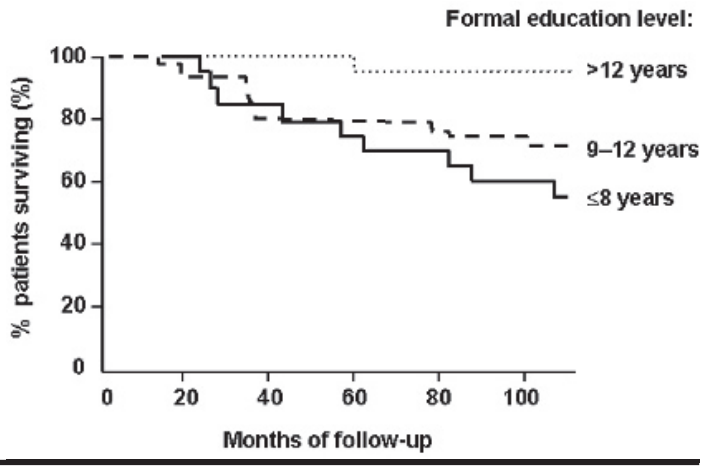

Fig. 1. Survival over 108 months (1973-1982) according to years of formal education in 75 patients with rheumatoid arthritis (RA) (41).

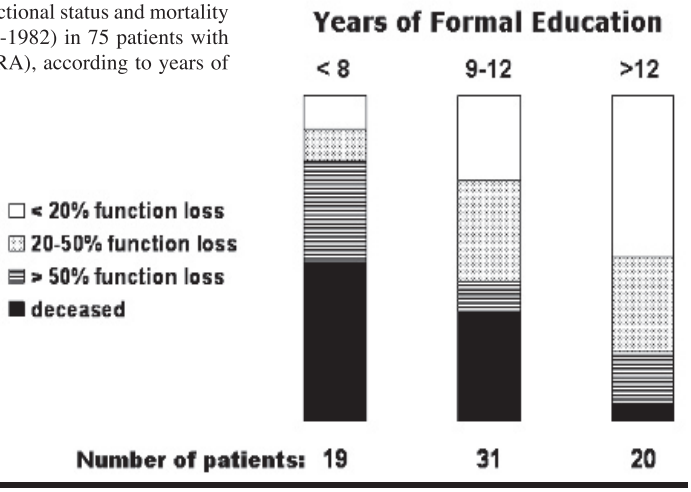

Fig. 2. Change in functional status and mortality over nine years (1973-1982) in 75 patients with rheumatoid arthritis (RA), according to years of formal education (41).

predictors of mortality, the highest odds ratio was seen for the Carstairs Index. Socioeconomic status is an important predictor of mortality in RA outside the United States.

Analyses of clinical status in patients with RA indicated disparities according to formal education levels. In 385 patients with RA, all clinical measures studied, including a tender joint count, erythrocyte sedimentation rate (ESR), and patient self-report questionnaire scores for activities of daily living and pain, differed significantly in patients with fewer than 8, 9-11, 12, or more than 12 years of formal medication (46) (Table III). Patients with fewer than 11 years of education had at least a two-fold higher likelihood of poor clinical status than those with 12 or more years of education, according to all measures studied (46).

In other studies, functional status and pain scores in patients with five different rheumatic diseases, RA, osteoarthritis, fibromyalgia, SLE, and systemic sclerosis, differed at higher levels of significance according to education level than age or duration of disease (47) (Table IV). Disparities in clinical status in RA, SLE and other rheumatic

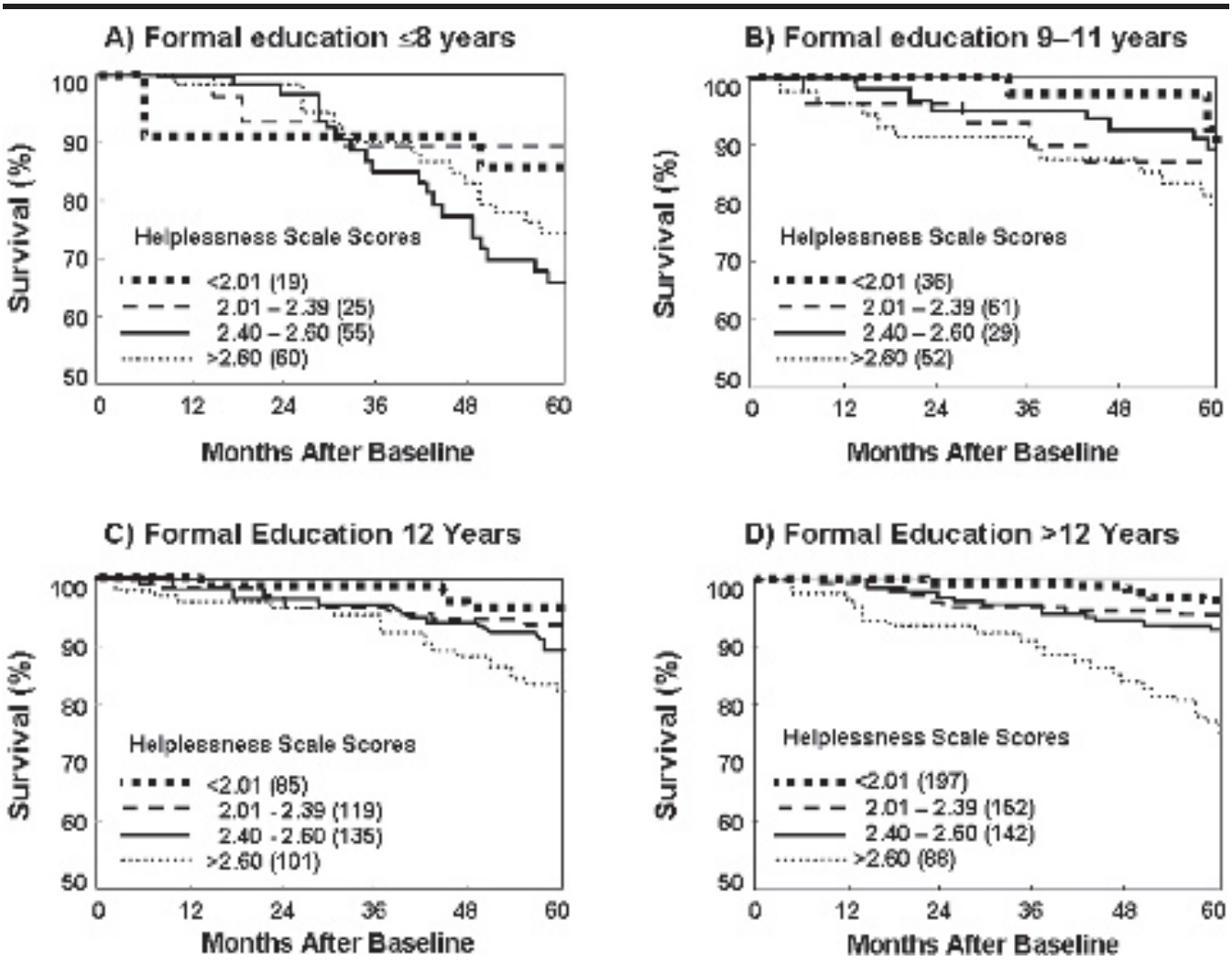

Fig. 3. Survival analysis over 5 years of 1,384 patients with rheumatoid arthritis (RA) according to helplessness scale scores, grouped by formal education level (1985-1990) (43).

Table II. Risk factors for mortality in Early Rheumatoid Arthritis Study (ERAS) between 1986 and 2004 using Cox regression [Adapted from Young A *et al*. *Rheumatology* (Oxford) 2007 (44)].

Variables in the equation	Wald	Significance	OR	95% CI for OR
Age onset	188.87	0.000	1.081	1.06-1.09
ESR (baseline)	10.897	0.001	1.008	1.00-1.01
Sex	4.771	0.029	1.331	1.03-1.72
HAQ (year 1)	25.088	0.000	1.047	1.02-1.06
Carstairs Index	8.338	0.004	1.542	1.14-2.06
Hb (baseline	6.378	0.012	1.012	1.00-1.02

OR: Odds ratio based on Exp (B); CI: confidence interval.

diseases have been described in many reports in the United States (48-51), the Netherlands (52), Sweden (53), and Denmark (54). Lee and Kavanaugh have presented an eloquent plea for more reporting of socioeconomic status and race in clinical trials (55), which may apply to all clinical research (56).

Socioeconomic status and cardiovascular and other diseases

Analyses of cardiovascular mortality in 17,530 London civil servants during the 1970s were conducted over a 7-year period in the "Whitehall study" (18). The civil servants were classified into four categories on the basis of employment, including administrative, professional-executive, clerical, and un-skilled workers known as "other." Cardiovascular mortality over the 7-year period was seen in 4% of unskilled workers, compared to 3% of clerical workers, 2% of professional-executive workers and fewer than 1% of administrative workers, with trends seen as early as 2 years after the baseline evaluation, with continuing divergence over time (Fig. 4). Fewer than one-third of the differences in mortality in the four groups classified by occupation could be explained by traditional cardiovascular risk factors such as cholesterol, blood pressure or smoking, and more than two-thirds of these differences were unexplained (Fig. 5).

Another classic study indicating associations of mortality in cardiovascular disease with socioeconomic status is seen in the beta-blocker heart attack trial (BHAT), a clinical trial designed to compare the efficacy of a beta-blocker drug, propanolol, to placebo in preventing death from a second heart attack in 2,320 male survivors of an initial myocardial infarction (57). Mortality was 8% in those who took propanolol, compared to 12% in those who took placebo, indicating the efficacy of this beta-blocker drug to prevent a second myocardial infarction (Fig. 6). However, differences between drug and placebo were considerably lower than differences according to formal education level, regardless of treatment group. Differences according to education level were explained by two variables, life stress and social isolation, defined according to several simple questionnaires shorter than a health assessment questionnaire (HAQ).

These reports are but two examples from an extensive literature concerning associations of socioeconomic status with cardiovascular disease (58-61).

Socioeconomic disparities in health in the general population

Most chronic diseases in people in the United States age 18 to 65 are found 3 times more commonly in those who have not versus those who have completed 11 years of formal education (Table V) (14). For example, the two most common conditions in the United States population under age 65, arthritis and hypertension, were reported by about 25% of people with fewer than 8 years of education (about 10% of the 1978 total United States population less than age 65), 13-15% of people with 9 to 11 years of education (about 15% of the 1978 United States population), 9-11% of people with 12 years of education (about 38% of the 1978 United States population), and 6-7% of people with more than 12 years of formal education (about 37% of the 1978 United States population) (14). Similar ratios were seen for most diseases, including back pain, heart attack, diabetes, renal

Table III. Mean values for laboratory, physician/assessor and self-report measures of disease status in 385 patients with rheumatoid arthritis, classified according to level of formal education [Adapted from Callahan LF, Pincus T: *Arthritis Rheum* 1988 (46)].

Disease status measure	Patients classified according to formal education level							*p*-value
	All patients	Grade school	Some high school	High school graduate	Some college	College graduate	Post-graduate	
ESR (mm/hr)	40.1	48.3	49.4	34.7	29.3	41.8	26.6	0.002*
Tender/painful joint count	12.1	163.	15.1	9.1	10.2	9.3	8.5	0.001**
Self-report measures								
MHAQ physical function (0-3)	0.97	1.26	1.04	0.86	0.73	0.99	0.70	0.000**
Pain VAS (0-10)	5.12	5.75	5.85	4.89	4.26	4.94	3.86	0.074
Global self-assessment (1-4)	2.68	3.09	2.70	2.55	2.43	2.61	2.25	0.000**

ESR: erythrocyte sedimentation rate; MHAQ: modified health assessment questionnaire; VAS: visual analog scale.
p-value by analysis of covariance, after controlling for age, sex, clinical setting, and disease duration.
*p <0.05 after adjustment for multiple comparisons.
**p<0.01 after adjustment for multiple comparisons.

Table IV. Regression analyses of responses of patients with one of five rheumatic diseases on self-report questionnaire scales analyzed according to age, disease duration, and formal education level [Adapted from Callahan LF *et al*. *Arthritis Care Res* 1989 (47)].

	Rheumatoid arthritis		Osteoarthritis		Fibromyalgia		Systemic lupus erythematosus		Systemic sclerosis	
	Beta	*p* -value	Beta	*p*-value	Beta	*p*-value	Beta	*p*-value	Beta	*p*-value
MDHAQ physical function										
Years of formal education	–0.17	0.05	–0.16	0.02	–0.33	<0.01	–0.37	<0.01	–0.16	0.32
Duration of disease	–0.06	0.54	–0.02	0.79	–0.02	0.88	–0.00	0.99	0.06	0.74
Age	0.10	0.30	–0.01	0.94	0.10	0.38	–0.01	0.89	–0.20	0.24
Pain visual analog scale										
Years of formal education	–0.05	0.54	–0.22	<0.01	–0.18	0.12	–0.16	0.08	–0.21	0.19
Duration of disease	–0.11	0.24	–0.01	0.90	–0.06	0.58	–0.07	0.42	–0.03	0.85
Age	–0.17	0.07	–0.02	0.79	0.19	0.09	–0.12	0.16	–0.05	0.79
Patient global estimate of status										
Years of formal education	–0.22	0.01	–0.27	<0.01	–0.24	0.03	–0.29	<0.01	–0.18	0.24
Duration of disease	–0.03	0.72	0.14	0.02	–0.04	0.71	0.08	0.35	–0.26	0.13
Age	0.10	0.30	0.01	0.92	0.20	0.08	0.10	0.26	0.15	0.36

disease, stroke, and tuberculosis (14). A few diseases, including allergies, and cancer, were exceptions to the patterns, and occur in similar percentages in individuals with fewer or more than 11 years of formal education. One disease, multiple sclerosis, was seen more commonly in individuals with more than 12 years of formal education than with fewer than 12 years (14). In the United States, the risk for cardiovascular or rheumatic diseases according to non-completion of high school is as great as any known "biomedical" risk factor, including elevated blood pressure or smoking.

Disparities in health according to socioeconomic status appear to be widening, rather than narrowing, over the last few decades in the United Kingdom (62), the Netherlands (25) and the United States (63-65). Unequal access to medical care may explain, in part, differences in the United States and the Netherlands. However, in the United Kingdom, all citizens have access to a common medical system, the National Health Service. The increases in health disparities according to socioeconomic status present a serious concern for modern societies throughout the world.

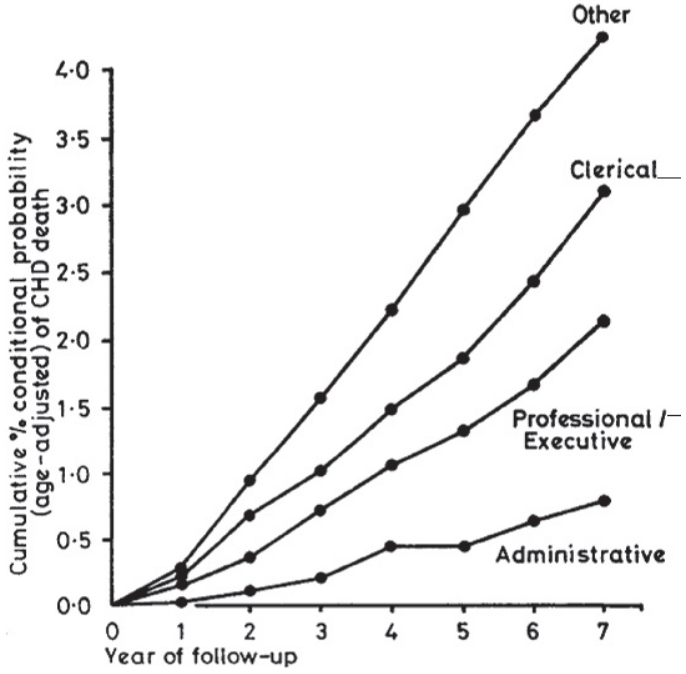

Fig. 4. Coronary heart disease (CHD) mortality among total population and four employment grades, by year of follow-up (18).

Why include these data in a journal supplement concerning mortality in rheumatic diseases?

Almost every clinical report concerning mortality includes the patient's age and duration of disease, but fewer than 20% include a measure of patient socioeconomic status, although differences in clinical status were explained as much by education as by age or duration of disease (47) (Table IV). Therefore, further observations concerning socioeconomic status and mortality in RA and cardiovascular disease appear needed to raise awareness in the rheumatology community of limitations of a strictly "biomedical model" to understand and improve mortality outcomes of most rheumatic (and other) diseases.

A biomedical model paradigm attempts to "explain" socioeconomic disparities in health on the basis of limited access to medical care, reflecting a view that health professionals are the primary determinants of health. Indeed, this "explanation" is prevalent among most health professionals, politicians and the general public. For example, a position paper of the American College of Physicians advocates improved access as the primary basis to improve socioeconomic disparities in health (66).

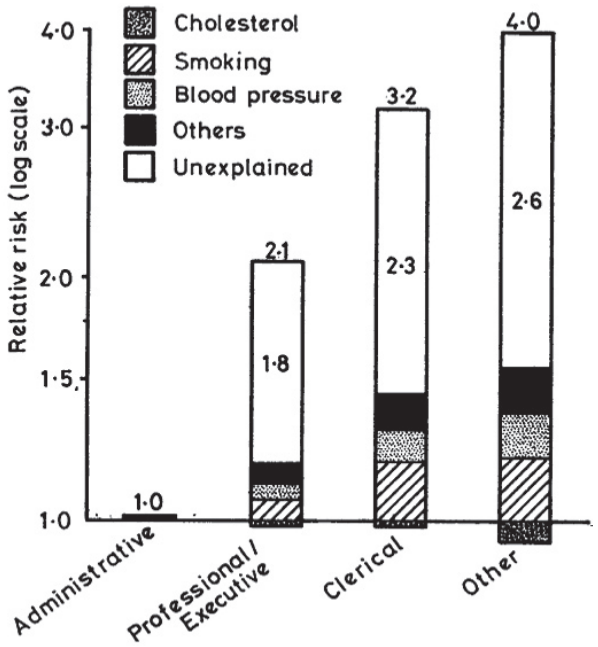

Fig. 5. Relative risk of death from coronary heart disease (CHD) in four different employment grades 'explained' by risk factors (age-standardized) (18).

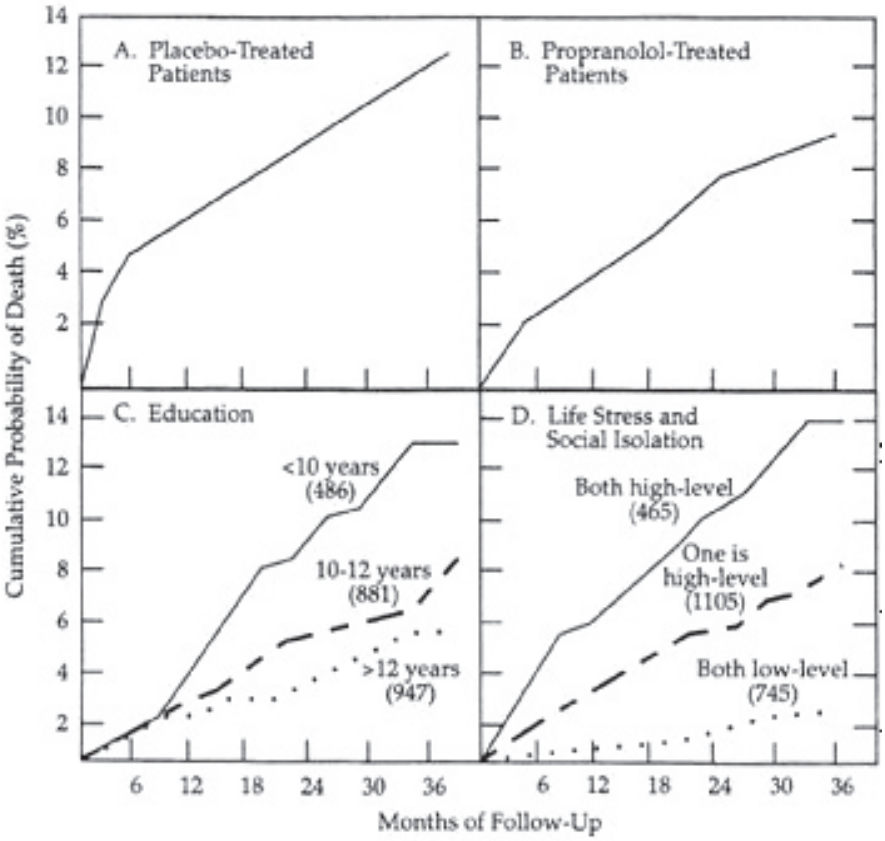

Fig. 6. Effects of placebo and drug on coronary deaths in a randomized clinical trial versus effects of education, life stress, and social isolation (57).

All RA patients in the studies summarized above (41-44, 46, 47) had access to care at a medical center. No differences were observed in prescribed treatments, although it might be suggested that differences may have been seen in how these treatments were used by the individual patients. The 17,530 London civil servants (18) all were working at baseline, and all had access to medical care through the National Health Service (NHS). A clinical trial provides extensive and equal access to medical care for all participants; substantial differences in results (57) could not be explained by differences in any physiologic measures at baseline. Socioeconomic disparities in the *prevalence* of most chronic diseases (14) cannot be explained on the basis of limited access to medical care.

Reduction of socioeconomic disparities in health may be expected *in part* by provision of greater access to medical care. However, strong evidence over more than 30 years indicates that improved access through Medicaid in the United States and universal insurance in many countries has not resulted in reduction of these disparities. Indeed, disparities in health according to socioeconomic status appear to be widening, rather than narrowing (25, 62-64). These data may be interpreted to suggest that reduction or elimination of health disparities according to socioeconomic status exclusively through strategies based on a biomedical model are likely to have limited effectiveness.

What explains socioeconomic disparities in health?

Neither limited access to medical care nor traditional biomedical risk factors can account for most of the disparities in prevalence, morbidity and mortality seen in rheumatic and cardiovascular diseases. Socioeconomic status may serve as a surrogate measure for self-management of behavioral, psychological, and cognitive variables, which are primary mediators affecting the incidence, prevalence, morbidity, and mortality of most chronic diseases (10, 67-71). The capacity of an individual to maintain health and cope with disease may be correlated with that individual's capacity to complete a high school education or obtain employment at a high level. Many potential behavioral mediational variables are associated with both socioeconomic and health status, including poor diet (72, 73), smoking (72-74), lack of exercise (72, 73), non-use of seat-belts (75), poor coping and problem-solving skills, and inefficiency in use of medical services (68). Psychological and cognitive constructs

Table V. Prevalence of health conditions in the 18- to 64-year-old United States population according to level of formal education [Adapted from Pincus T *et al: J Chronic Dis* 1987 (14)].

	Total number (x 10^3)	% of total population	% in 4 categories by years of formal education			
			≤8 years	9 – 11 years	12 years	>12 years
Any disease	54,194	42.7%	64.7%	53.5%	41.3%	33.4%
Musculoskeletal						
Rheumatoid arthritis	2,366	1.9%	8.9%	4.4%	3.1%	1.7%
Osteoarthritis	4,261	3.4%	14.2%	9.7%	7.0%	4.3%
Any arthritis	14,215	11.3%	26.4%	13.1%	11.0%	6.8%
Back problems	9,901	7.9%	11.6%	10.5%	7.5%	6.1%
Cardiovascular						
Hypertension	14,015	11.1%	26.1%	15.1%	9.5%	7.2%
Heart attack	1,805	1.4%	4.9%	2.0%	1.2%	0.6%
Stroke	649	0.5%	1.2%	0.8%	0.4%	0.3%
Diabetes	3,205	2.5%	5.2%	3.6%	2.5%	1.4%
Other						
Renal disease	2,354	1.9%	5.1%	2.4%	1.4%	1.3%
Tuberculosis	261	0.2%	0.3%	0.4%	0.1%	0.2%
Cancer	837	0.7%	1.5%	0.6%	0.6%	0.5%
Allergies	5,313	4.2%	3.6%	3.3%	4.6%	4.4%
Multiple sclerosis	148	0.1%	0.0%	0.1%	0.1%	0.2%

associated with both socioeconomic and health status may serve as possible mediational variables including social support (76-79), anxiety (80), depression (80), learned helplessness (81-83), self-efficacy (84, 85), health locus of control (81), sense of coherence (86-88), optimism (89), time preference (90), and health knowledge (72, 85, 91).

Why does a biomedical model continue to dominate analyses of health and disease?

The continued domination of a biomedical model paradigm in analysis of health, disease and mortality may be based in large part on its value in clinical activities in acute-care inpatient hospitals, the setting of more than 95% of medical education, training and clinical research. The outcomes of acute somatic problems appear almost invariably to result from actions and decisions of health professionals, with minimal contribution from patients or their social milieus. Health professionals busily pursuing activities in medical education, care, research and policy continue to depend on traditional paradigms as guideposts.

A second explanation for continued dominance of a biomedical model and limited attention to a biopsychosocial model may result from the fact that relatively few reports include both biopsychosocial and rigorous biomedical data. Many concepts concerning assessment, prognosis, and outcomes according to a biopsychosocial model may be correct, but not necessarily (yet) supported by data from clinical care and other clinical research. The studies presented above concerning rheumatic and cardiovascular diseases indicate the potential value of adding perspectives of a biopsychosocial model to traditional biomedical research to explain the prognosis and course disease in individual patients. Rigorous statistical analyses, according to standards of a biomedical model (2, 41, 42, 92-102), are required to describe accurately biomedical and biopsychosocial risk factors for the pathogenesis, morbidity and mortality of diseases.

What recommendations for future studies emerge from these observations?

On the basis of the data presented, some recommendations might be offered to advance understanding of pathogenesis, course and outcomes, including premature mortality, in rheumatic diseases:

1) Any baseline database for clinical research should include a measure of socioeconomic status. The most easily assessed is formal education level, which has been included in all versions of the multidimensional HAQ used in all patients seen by the senior author since 1982 (103). Formal education level appears as good an indicator in regression models of health status as occupation or income, in the United States. Other measures of socioeconomic status may be more relevant than formal education level to answer certain questions or in other cultures.
2) Consider inclusion of feasible, non-biomedical data in any study. It is discouraging that more than two decades after documentation of the capacity of physical function on a questionnaire to significantly predict mortality in RA (at higher levels than joint counts, radiographs, or laboratory tests) (93), or of a half-page questionnaire for life stress and social support to predict mortality in cardiovascular disease with greater significance than beta blocker therapy (57), that these simple assessment tools remain unused in the majority of clinical studies. Clinical researchers may be depriving themselves of potentially important explanatory variables, which may enhance an accurate assessment of biomedical variables in research studies.

3) The need for long-term longitudinal databases to analyze chronic disease cannot be overemphasized. For many years, and even at this time, increased mortality rates seen in inflammatory rheumatic diseases have been greatly underestimated by the general medical community and the public, and probably by most rheumatologists as well. As discussed extensively in reports concerning specific diseases in this Supplement, it is not possible to recognize increased mortality rates in people with rheumatic diseases without availability of long-term longitudinal data.

   A long-term database is a relatively trivial undertaking in modern computer science technology, and can easily be maintained in any clinical unit with expenses that are more than justified by organization of data for the clinic. It is important to remember that a clinical tool including an electronic medical record is not a database, although a database is often easily maintained as an electronic record. Of course there are some expenses involved, just as are seen with an electronic medical record, but the ultimate saving of time in organization of the data more than justifies these expenses, in the experience of the senior author.

It is hoped that the information in this chapter may be borne in mind by readers of the other chapters, to add further understanding to the important subject of mortality in rheumatic diseases.

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