CAUSAL INTERPRETATIONS FROM CROSS-SECTIONAL DATA*

AN EXAMINATION OF THE STOCHASTIC PROCESSES INVOLVED IN THE RELATIONSHIP BETWEEN A PERSONALITY CHARACTERISTIC AND CORONARY HEART DISEASE

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AMONG scientists there is a constant striving to find simple inexpensive ways to arrive at desired answers. It would be desirable to be able to draw inferences about a sequence of events and possible causal relationships among them from cross-sectional data. Recently, IBRAHIM et al. [1] proposed an approach to this problem. It is our present purpose to examine some simple stochastic models based on their data and show that the method they have proposed is not quite up to the task in hand.

For present purposes, a factor is acceptable as contributing to etiology when one is satisfied that it regularly increases the probability of the subsequent occurrence of the disease in question. There are many ways of demonstrating this regularity beginning with replication of simple sequential associations down to demonstrating dose response relationships and consistent time relationships which are referred to as incubation periods. HYMAN has presented an excellent treatment of the analysis of relationships ordered in time. [2]

The important point is that sequential association in time is always relevant to the determination of cause. With this in mind we have worked with stochastic models in our examination of the method proposed by Ibrahim et al.

In developing a system for study we consider four main states or categories: low, medium and high risk of developing coronary heart disease (CHD) and a state involving CHD itself. These risk categories are those used by Ibrahim et al.; low risks denotes low values of both blood pressure and serum cholesterol; medium risk denotes low values of one and high values of the other; high risk denotes high values of both. In order to consider the effects of time on such a system, we need to add three more states, or categories: new persons entering the system, persons leaving the system by death from CHD, and persons dying from other causes.

Of central concern in this type of model is the probability of moving from each state to each other state during a specified time interval. In this paper it will be more convenient to consider the expected number of people making each such transition, rather than the probability of doing so. The expected number is one particular type of

weighted average; here it will suffice to think of it as the "average" number of people making the transition during one time interval.

A TYPOLOGY OF MODELS

We wish to consider the relationship of an additional variable, personality, to the system previously described. Following Ibrahim *et al.*, we shall treat personality as a dichotomous variable, selecting a specific personality pattern and classifying each person as either with or without this pattern. The selected personality pattern is characterized as "a level of manifest hostility below the levels of anxiety and re-pression". [1]

On the basis of earlier studies [3–9], Ibrahim *et al.* had entertained the hypothesis that this pattern is associated with, and precedes, CHD. However, they observed that the proportion of persons with this personality pattern in the CHD category was much higher than the proportions in any of the pre-CHD risk categories. They used this observation and their method of interpretation as a basis for rejecting the hypothesis stated above. Their rationale for doing so, we feel, fails properly to take account of the stochastic nature of the process being observed. We hope to take this into account in explicitly formulated models. The probabilistic models we will consider fall into three broad types.

Type I. The additional variable under consideration has no over-all effect on CHD. In other words, a person with the specified type of personality is neither more nor less likely than others in his risk category to develop, or die from, CHD.

Type II. A person with the specified personality pattern is more likely than others in the same risk category to develop, or die from, the disease.

Type III. A person with the selected personality pattern is less likely to develop or die from CHD.

These types are not exhaustive. It is conceivable that the personality pattern would make one more likely to develop the disease but less likely to die from it, or *vice versa*. But these possibilities don't seem likely. In addition, it is possible that the specified personality pattern is so unstable (i.e. people develop or lose the pattern with such frequency) as to make a knowledge of its presence or absence completely useless. However, we will confine our attention to one example of each of these three types They are sufficiently rich in possibilities for the purposes of this paper.

ILLUSTRATIVE GENERAL MODEL FOR CHD

In order to explore alternative interpretations of the Ibrahim data, we first construct a model for the development of CHD, for a population of 10,000 persons age 40 and above. For purposes of illustration we assume this population is distributed into the four main categories (low risk, medium risk, high risk, CHD) in the proportions observed by MCDONOUGH *et al.* [10] in the larger study of CHD in Evans County, Georgia. We examine the behavior of this system during a period of time in which 100 new persons enter the system. At the beginning of this time period, the distribution of the 10,100 persons involved will be as shown in Table 1.

Next we make some assumptions regarding the behavior of this system over time. Some of these assumptions are crucial; others are made only to give specific numbers for the appropriate tables. Each assumption will be discussed as it is presented.

1. The distribution in Table 1, of the total number of persons in each category, is in

TABLE 1. DISTRIBUTION OF 10,100 PERSONS AT BEGINNING OF TIME PERIOD, WITH NUMBER OF PERSONS IN EACH CATEGORY WHO HAVE THE SELECTED PERSONALITY PATTERN (The upper number in each block is the number in the category who have the personality pattern; the lower number is the total number in the category)

New	X
	100
Low	1232
	5092
Medium	812
	3471
High	109
	764
CHD	449
	673
CHD death	0
	0
Other death	0
	0
Total	10,100

equilibrium, i.e. at the end of a time period, the four main categories will contain the same number of individuals they did at the beginning. The main implication of this assumption is that this distribution is typical, and not the result of a freak observation. This is a crucial assumption. Some assumption of this type must be made if available data is to be of any use. It is of no consequence to know that, in some particular population at some particular time some specific percentage of the population had a certain characteristic, if this percentage fluctuates markedly in some unknown fashion. On the other hand, small deviations from this assumption will be of minor concern, since in this paper we consider only relatively short periods of time. In particular, population growth can safely be ignored.

2. One third of the deaths in this population are from CHD. This corresponds to the figure cited by STAMLER. [11] This exact figure is not crucial; it serves only to give specific numbers for our models.

3. The rate of death from causes other than CHD is the same throughout the four main categories. In other words, neither high cholesterol, high blood pressure nor CHD makes one more likely to die of cancer or some other cause. This assumption seems reasonable except for deaths from cerebro-vascular accident, which constitute only a small part of the total death rate. Again, this assumption is not crucial, but we must have some specific assumption about the incidence of non-CHD deaths in the various categories or states.

4. For each risk category, 25–30 per cent of CHD cases result in "immediate" death. These figures were cited by STAMLER [11] as the over-all proportions. While this specific assumption is not crucial, but only for the purposes of giving a concrete numerical example, it does point out an interesting question which might be a topic for future research: are persons from the low risk group more (or less) likely to survive

an initial occurrence of CHD, if it were to occur, than persons from the high risk group; and if so, how much more (or less) likely? Lacking such information we assume there is no difference; however slight differences would make little change in our model.

5.   The rates of CHD incidence from the low, medium, and high risk categories are in the ratio 1 : 2 : 4. This assumption borders on the *ad hoc*; however, the proportions of surviving CHD patients having the blood pressure and cholesterol characteristics of the various risk categories were in this ratio in the study by McDONOUGH *et al.* [10] Also, the authors have investigated other ratios (such as 1 : 1.5 : 2) and found that they made no basic differences in the model for our purposes. Hence this assumption is not crucial.

6.   No person can go from CHD to one of the pre-CHD risk categories, nor from a higher to a lower risk category. The latter part of this assumption implies that blood pressure and serum cholesterol increase if they change at all. This is not strictly true, but, for our purposes, exceptions are infrequent enough to be regarded as measure-ment errors in a population such as that of Evans County, Georgia, which is unlikely to be treated for asymptomatic hypertension or hypor-cholesteremia. Zero is more convenient than some very small positive number, even if the latter were known. This figure is not exact, but, like other specific figures being used, is not crucial.

7.   No person will develop both high cholesterol and high blood pressure during one time period. On the basis of the previous assumptions, with an average CHD incidence in excess of 10/1000/yr for this age group [12], one of our time periods corresponds to approximately 4 months, so that this assumption should be quite realistic. (We started with an interval of time during which 100 persons would enter the system, and it turns out that 38 persons would develop CHD during such a time interval—see Table 2 below. On the other hand, in a population of 10,000 subject to an incidence rate of 10/1000/yr, 100 persons would develop CHD during one year. Hence our time period must be about 38/100 of a year, or approximately 4 months.) The previous comment about zero, as opposed to some very small positive number, applies here as well.

8.   Of the 40-yr-olds entering the system, 70, 25 and 5 per cent go into the low, medium, and high risk categories respectively. If we assume that no persons have CHD or die within one time period of their entry into the system, then the earlier assumptions provide constraints for these figures: 48–1000, 0–52, and 0–12 per cent respectively. Here we are merely picking a specific number near the middle of the various possibilities. Also, the exact figures we use here have little over-all effect on the system: if fewer enter at the high risk category, then more will move into it from the medium risk category, etc.

Assumptions 1–8 uniquely determine the expected number from each category that will move to each other category during one time period. These transitions are shown in Table 2. The method by which they were derived from the assumptions is explained in the Appendix.

Next we consider the prevalence of the selected personality pattern in the various categories at the beginning of the time period. To illustrate, we suppose that, in each category, it exists in the proportions observed by Ibrahim, *et al.*, namely 0.242, 0.234, 0.143 and 0.667 in the low, medium, high and CHD categories respectively. These proportions came from a small sample, but for illustrative purposes their accuracy is unimportant. The number in each category who have the personality pattern is shown

TABLE 2. TRANSITIONS OF 10,100 PERSONS DURING ONE TIME PERIOD

To:	New	Low	Medium	High	CHD	CHD death	Other death	Totals
From:								
New	0	70	25	5	0	0	0	100
Low	0	5022	23	0	9	4	34	5092
Medium	0	0	3423	8	12	5	23	3471
High	0	0	0	751	6	2	5	764
CHD	0	0	0	0	646	22	5	673
CHD death	0	0	0	0	0	—	0	0
Other death	0	0	0	0	0	0	—	0
Totals	0	5092	3471	764	673	33	67	10,100

in Table 1, where we denote by X the number of new persons having this pattern. Later we shall consider various values of X. Finally, we make one assumption regarding the personality pattern:

9. A patient does not develop or lose the selected personality pattern unless he has had CHD. This implies the pattern is relatively stable—a drastic development is required in order to change it. If this were not true or nearly so, then the data on the personality pattern would be worthless, as far as relating it to CHD is concerned. This assumption is crucial, not only for our models, but for any attempt to etiologically relate the personality pattern to CHD. If this personality pattern is developed or lost with any sizeable frequency it would be of little value as an indicator of proneness to CHD or anything else.

Now, within the framework of this general model, we develop several specific models, for each of which a different interpretation is appropriate. The further assumptions used in these specific models are of a different type than the assumptions above. We believe that assumptions 1–8 are reasonable approximations to the actual development of CHD within the population of white American males over 40 yr of age. Assumption 9 is necessary but is not a fact in evidence. In any serious study of this matter, this assumption must be proven to be correct.

Thus assumptions 1–9 are being used as reasonable approximations to reality. The further assumptions below, however, are designed to be substituted into the formula, "Let us suppose . . . . is true, and determine what results would occur." It should be noted that the three models are contradictory; no more than one of the three could be a good approximation to the situation actually in operation. However, as we shall see, these three different models could produce the same data in a cross-sectional study.

MODEL A: NO EFFECT FROM PERSONALITY

For this model, we add the assumptions:

A1. The number of persons making each possible transition is independent of the personality pattern i.e. for each possible transition, the average proportion of those

with the pattern who make the transition is equal to the average proportion without the pattern who make the transition. This is equivalent to saying the personality pattern has no effect with regard to CHD.

A2. The distribution of persons with the personality pattern, shown in Table 1, is in equilibrium. This is analogous to the first assumption of the general model, which concerned the total number (rather than the number with the personality pattern) in each category.

Such an equilibrium assumption is typically made because of the unpleasant amount of anarchy among the alternatives: if the system is not in equilibrium, then there are infinitely many non-equilibrium processes as alternatives, and cross sectional data provides no information as to which process is actually occurring. Thus we wouldn't like to discard this assumption unless we had reason to choose one *specific* alternative assumption from among the many possible alternatives.

TABLE 3. TRANSITIONS DURING ONE TIME PERIOD, FOR MODEL A, WITH NUMBER OF PERSONS IN EACH TRANSITION WHO HAVE THE SELECTED PERSONALITY PATTERN (See explanation with Table 1)

To:	New	Low	Medium	High	CHD	CHD death	Other death	Totals
From:								
New	0	17	5	0	0	0	0	22
	0	70	25	5	0	0	0	100
Low	0	1215	6	0	2	1	8	1232
	0	5022	23	0	9	4	34	5092
Medium	0	0	801	2	3	1	5	812
	0	0	3423	8	12	5	23	3471
High	0	0	0	107	1	0	1	109
	0	0	0	751	6	2	5	764
CHD	0	0	0	0	431	15	3	449
	0	0	0	0	646	22	5	673
CHD death	0	0	0	0	0	—	0	0
	0	0	0	0	0	—	0	0
Other death	0	0	0	0	0	0	—	0
	0	0	0	0	0	0	—	0
Totals	0	1232	812	109	(427)	17	17	
	0	5092	3471	764	673	33	67	10,100

Assumption A1, together with the general model, determines the entire transition matrix shown in Table 3, with the exception of the top row (new persons who have the personality pattern). Assumption A2 (equilibrium) requires a distribution of 17, 5, and 0 of the latter into the low, medium, and high risk categories to replace the 22 persons with the personality pattern who have moved further along in the system. This gives a 22 percent over-all prevalence of the personality pattern among the new patients, with a slightly higher percentage among those entering the low risk group and a slightly lower percentage among those entering the high risk group.

However, the resulting distribution is still not in equilibrium: at the end of one time period the CHD category has 12 less persons with the personality pattern that it had at the beginning of the time period, since a total of 34 died but only 22 entered the system. Equilibrium will be restored if during one time period there are 12 "conversions"—12 people with CHD who didn't have the personality pattern develop the personality pattern during the time period.

This is precisely the conclusion reached by Ibrahim, *et al.* Their rationale seems to implicitly involve our assumptions A1 and A2. But Assumption A1 is not forced on us, however plausible it may seem, and having to resort to "conversions" may be a good reason to question this assumption. If, as in this model, some people without the personality pattern develop the pattern after having developed CHD, then we should wonder why. We will discuss this question later, after presenting a second model.

MODEL B: PERSONALITY WITH BENEFICIAL EFFECT

For this model, we modify the assumptions of Model A to the following:

B1. The number of persons making each possible transition is independent of the personality pattern, with the exception of the transitions to CHD death.

B2. The distribution of personality patterns is in equilibrium (same as A2).

When we make a loophole in an assumption (as in B1) we don't have a complete model again until we plug it. In this case, there are several conceivable ways to complete the model. The ones with which we are concerned here have the characteristic that those persons with the personality pattern are less likely than others to die from CHD. For illustrative purposes, we will look at the situation where no conversions occur and each of the possible CHD death rates, for those with the personality pattern, is reduced proportionally to bring the system back in equilibrium.

B3. A person with CHD doesn't develop or lose the personality pattern.

B4. All the CHD death rates for persons with the personality pattern are proportional to the corresponding rates in Model A.

These assumptions require that CHD death be only about one fifth as likely, for those with the personality pattern, as it would be in Model A. Thus in this model the personality pattern has a marked favorable effect. The transition matrix for this model is shown in Table 4. The equilibrium assumption requires a prevalence of 20 per cent for the personality pattern among the new entrants to the system, somewhat lower than the prevalence required in Model A and the prevalences observed in the low and medium risk categories.

DISCUSSION OF CONVERSIONS, A MIXED MODEL

In the section on Model A we posed—but did not answer—the question: If it actually does happen, why is it that some people without the personality pattern develop this pattern after they have CHD? IBRAHIM, *et al.* [1] have some relevant remarks:

> "In the light of the high case–fatality ratio of coronary disease, as well as the various degrees of disability which often require patients to modify their usual ways of life, it is conceivable that this threatening disease results in tension, general emotional upset, worry, feelings of unhappiness, and feelings of pessimism. The medical recommendation as well as the popular advice usually given to coronary victims is to avoid situations of emotional excitement, to try not to get 'angry' etc., in order to avoid

TABLE 4. TRANSITIONS DURING ONE TIME PERIOD, FOR MODEL B, WITH NUMBER OF PERSONS IN EACH
TRANSITION WHO HAVE THE SELECTED PERSONALITY PATTERN

To:	New	Low	Medium	High	CHD	CHD death	Other death	Totals
From:								
New	0	16	4	0	0	0	0	20
	0	70	25	5	0	0	0	100
Low	0	1216	6	0	2	0	8	1232
	0	5022	23	0	9	4	34	5092
Medium	0	0	802	2	3	0	5	812
	0	0	3423	8	12	5	23	3471
High	0	0	0	107	1	0	1	109
	0	0	0	751	6	2	5	764
CHD	0	0	0	0	443	3	3	449
	0	0	0	0	646	22	5	673
CHD death	0	0	0	0	0	—	0	0
	0	0	0	0	0	—	0	0
Other death	0	0	0	0	0	0	—	0
	0	0	0	0	0	0	—	0
Totals	0	1232	812	109	449	3	17	2622
	0	5092	3471	764	673	33	67	10,100

complications of their heart condition. It is, therefore, expected that coronary patients may not express their aggressive feelings, anger, or hostility. They may also deny these feelings in order not to contradict the advice offered to them."

This leads in a circle: If the personality pattern has no effect, then we must have conversions to account for observed data. Why should conversions occur? Because the doctor recommends them. Why should he recommend them? Because, as a result of his training and experience, he believes that the personality pattern *does* have an effect. The Ibrahim formulation of the problem is not sufficiently explicit to show that this circle exists; at least they make no mention of it.

To break this circle, we can suppose that the doctor's advice is unfounded—that although he *thinks* the personality pattern helps, it really doesn't. Alternatively, we can use a mixed model—a model somewhere between Models A and B. In such a model the high prevalence of the personality pattern among CHD survivors would be due to two things: those with the pattern tend to remain alive while those without it are dying off, and those without this personality pattern tend to develop it at the recommendation of their doctors and friends.

In such a model, the transition rates to CHD death, for those with the personality pattern, would be lower than in Model A but not as low as in Model B, and enough conversions would take place to give equilibrium. For example, the CHD death rates for those with the personality pattern might decrease (from those given by independence) only one half as much as required in Model B, with the remainder of the equilibrium being restored by about one half as many conversions as required in Model A.

Such a mixed model seems more plausible than either Model A or Model B. However, the observed data can also be interpreted in terms of a quite different model, as we now show.

MODEL C: PERSONALITY WITH HARMFUL EFFECT

This model differs drastically from the previous ones—yet would give rise to the same cross-sectional data. We begin with the assumptions:

C1.   The selected personality pattern operates as an independent risk factor, which doubles the chances of developing CHD, for a person in one of the three risk categories (as compared with the over-all risk in the risk category). The factor of 2 in this assumption was chosen arbitrarily, but with two things in mind: to make the added risk small enough that its effects could reasonably remain unnoticed, but to make it large enough to be worth finding. Effects of factors other than 2 will be noted below.

C2.   The transitions from low to medium and from medium to high risk are independent of the personality pattern, in the sense of assumption A1.

C3.   The distribution of personality patterns is in equilibrium.

C4.   No person with CHD develops or loses the personality pattern.

The transition matrix determined by these assumptions is shown in Table 5. With this additional risk factor, in order to retain equilibrium, we need a 31 per cent prevalence of the personality pattern among the new entrants to the system—substantially higher than the prevalence among the new persons of the other models and the prevalence among the three risk groups—since this model has those with the personality pattern dying off more rapidly than in the other models. We also examined some

TABLE 5.   TRANSITIONS DURING ONE TIME PERIOD FOR MODEL C, WITH THE NUMBER OF PERSONS IN EACH TRANSITION WHO HAVE THE SELECTED PERSONALITY PATTERN

To:	New	Low	Medium	High	CHD	CHD death	Other death	Totals
From:								
New	0	20	9	2	0	0	0	31
	0	70	25	5	0	0	0	100
Low	0	1212	6	0	4	2	8	1232
	0	5022	23	0	9	4	34	5092
Medium	0	0	797	2	6	2	5	812
	0	0	3423	8	12	5	23	3471
High	0	0	0	105	2	1	1	109
	0	0	0	751	6	2	5	764
CHD	0	0	0	0	437	9	3	449
	0	0	0	0	646	22	5	673
CHD death	0	0	0	0	0	—	0	0
	0	0	0	0	0	—	0	0
Other death	0	0	0	0	0	0	—	0
	0	0	0	0	0	0	—	0
Totals	0	1232	812	109	449	14	17	2633
	0	5092	3471	764	673	33	67	10,100

alternatives to double risk. A risk 1.3 times as high (instead of 2 times as high) could be balanced by a 25 per cent prevalence of the personality factor among the new patients—much closer to the prevalences in the other models and in the risk groups.

The interpretation of this model is that those with the personality pattern are more likely to develop CHD—and to die from CHD—than those without the pattern, but that the system stays in equilibrium because they are replaced with new entrants at a higher rate. Thus we see that it is possible to interpret the available cross-sectional data as consistent with a harmful effect of the personality pattern.

DISCUSSION AND SUGGESTIONS FOR RESEARCH

The models considered—and numerous possible variations of them—cover three different types of processes: one where the personality pattern has no effect on the development of CHD, one where it tends to prevent deaths from CHD, and one where it actually increases the probability of death from CHD.

Each of these models would perpetuate the same type of cross-sectional data, namely distributions in the proportions shown in Table 1. The reason is that each of these processes is in equilibrium. Thus, contrary to the Ibrahim conclusion, the observation of a distribution in these proportions is not sufficient reason to choose Model A over any of the other models. We repeat for emphasis: each of these models would produce the same type of cross-sectional data.

What, then, can be done to determine which type of process is actually at work? One obvious answer is a prospective study: if we examine enough people enough times during a sufficiently long period of time, we should learn much more about the process. However, it is worth asking what could be done short of a full prospective study, as the latter may not be feasible at present.

A mathematician might consider treating the process as a Markov Chain (using probabilities, rather than numbers of persons, to make a stochastic transition matrix) and determining what types of processes would give convergence to the observed distribution from various starting distributions. This approach would involve considerable work, and doesn't seem justified at this time, when we don't even have good assurance that the personality pattern being considered is stable. In addition, unless such convergence is rapid we would run into problems which have been avoided in our models by assuming equilibrium. This approach would assume constant transition probabilities, while over long periods of time these probabilities would actually change—but in ways not easily measured—with advances in heart medicine. In addition, such long run effects as population change, change in eating habits, and change in type of work for a general population cannot be ignored if the process is considered over very long periods of time. Here we are concerned with short term equilibrium only, as the entire process changes over longer periods of time.

However, there are some features of the system which would help to distinguish the correct type of model.

Model A requires conversions. It should be possible to go back to the original sample used in the Ibrahim study, and readminister the personality tests to those who have developed CHD since the tests were first administered, to determine whether any conversions have, in fact, taken place,. If the tests are readministered, they should be repeated for all the persons originally in the study, to determine the stability of the specified personality pattern, since this entire analysis—and, actually, any attempt to

relate CHD to this personality pattern—depends heavily on our assumption 9. If no conversions are observed, this would be some evidence against Model A; if conversions are observed only in those developing (or already having) CHD, this would be evidence in favor of a model like Model A or a mixed model.

Similarly, the different models considered require different prevalences of the personality pattern among the 40-yr-olds entering the system. A "low" frequency of the personality pattern among 40-yr-olds would be evidence in favor of Model B; a "high" frequency would favor Model C; and a "medium" frequency would favor Model A. But before we try to define "low" and "high" as exact percentages, we should remember that our model contains many approximations, and some "nearly true" assumptions, so that the 22, 20, and 31 per cent frequencies in the three models should not be pressed too far.

We might do better to look at the age distribution of the personality pattern, provided that it is stable and provided that it has no secular trend. In such a case, under Model A we would expect approximately the same prevalence of the personality pattern for all age groups; under Model B, we would expect an increase in the prevalence with age, since those without the pattern die at a higher rate that those with it; under Model C, we would expect a decrease in the prevalence with age, since those with the pattern die at a higher rate. Thus, if these provisions are met, an observation of the age distribution of the personality pattern would help to determine the type of process occurring.

If these provisions are met, the age distribution would essentially give us the input and output data for the system: the age distribution at age 40 is the prevalence of the personality pattern among the new entrants, while the slope of the change in the distribution with age (if any) corresponds to the difference in death rates for those with and without the personality pattern.

It should be noted that the interpretations above differ from those often applied to age distributions in medical studies. If the prevalence of a disease increases with age, we interpret this as implying that the disease is developed with advance in age. However, such an interpretation is *not* implied by this data alone. The same age distribution would be observed if the presence or absence of the disease was determined by birth but that those *without* the disease died at a higher rate. For diseases we reject the second interpretation not because of the age distribution data observed, but because of two additional reasons: we know that persons without the disease can and do develop the disease (we don't currently know this about the personality pattern); and secondly, we have good reason to assume that "disease" necessarily involves harmful effects, not beneficial effects such as lower death rate. It is because of these two points, not the age distribution by itself, that we make the usual interpretation of age distribution data for diseases. While we have strong conclusive evidence on these points with regard to diseases, we have no evidence on these points with regard to the selected personality pattern.

One substantial problem here is that the criteria for the selected personality pattern, which was constructed by Ibrahim *et al.*, has apparently never been used elsewhere. Hence we know little or nothing about this pattern; in particular, we don't know whether (or under what circumstances) an individual may lose or develop this pattern, and we don't know whether the prevalences of the pattern in the population and various subpopulations are changing over time.

In general, in order to determine a process of this nature we must have more information than is provided by a cross-sectional study. Such a study tells only the content of each category at one particular time. In order to answer etiological questions we need to know (or have some way of determining) the input and output rates for each category (and how these rates change with time, if they do).

In the absence of such information, it is helpful to make assumptions (as we did in our three models) and compare predictions derived from them with available data, until further research provides the needed information—but we must remember that they *are* assumptions, and that alternative assumptions are also plausible. Furthermore, the reader must remember that the three models considered here are by no means an exhaustive set.

SUMMARY

We have shown that available data from a cross-sectional study is not sufficient to determine what, if any, causal relationship exists between selected personality traits and coronary heart disease. Specifically, we have shown that the observed data could have arisen from either a process where the personality trait has a beneficial effect (i.e. makes one less likely to die from CHD) or a process where it has a harmful effect (i.e. makes one more likely to develop CHD), as well as a process where it has no effect.

The assumptions which would be required to choose one interpretation over another have been explicitly pointed out and discussed. It is concluded that more information is required to make a valid choice between the many alternative processes that might be associated with the observed data.

Specifically, a conclusive causal analysis will always require a time variable. Mathematically stated: in a causal analysis of this type we are concerned with first derivatives with respect to time, while a cross-sectional study determines only the values of the corresponding variables at one specific time, not their derivatives. To estimate the derivatives from data requires a knowledge of the values at least two distinct times; without this an analysis depends on unverified assumptions about the derivatives.

Of course, a cross-sectional study can be used to show that certain factors are unlikely to be causes of a given effect. Positive causal conclusions, however, will require observations over time.

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APPENDIX A
TRANSITION PROBABILITIES AND EXPECTED NUMBERS OF TRANSITIONS

Suppose that n_i is the number of persons in the ith state or category at the beginning of a time period, and that P_{ij} is the probability for an individual in state i to move to state j in one time period. Then the average, or expected value, of the number of persons moving from state i to state j (including the case where $j=i$) in one time period, is the product $n_i P_{ij}$.

The numbers shown in Tables 2–5 are these average numbers of transitions per time period. They, rather than the transition probabilities, are used for simplicity in interpreting the tables. In particular, while transition probabilities are additive horizontally in a transition matrix, they are not additive vertically; the expected number of persons making transitions is additive both horizontally and vertically, the total of a row being the number of persons in the particular state originally, and the total of the corresponding column being the expected number of persons in that state at the end of one time period.

APPENDIX B
DERIVATION OF TRANSITION MATRIX

For the reader who wonders how Tables 2–5 were derived from the various assumptions, we now present the derivation of Table 2, from assumptions 1–8, as an example. The other tables were derived similarly. The reader may find it helpful to construct a copy of the table, number by number, as he follows this explanation. Numbers actually appearing in the table are in boldface type; the other numbers are used only at intermediate stages of the derivation.

The *column* labeled "Totals" gives the number of persons in each category at the beginning of the time period. These are entered directly into Table 2 from Table 1. The *row* labeled "Totals" shows the expected number of persons in each category at the end of the time period. The new persons will have entered the risk categories during the time period, leaving **0** in the New category. By assumption 1, the totals in the three risk categories and the CHD category will be the same as previously, and 100 will die, so these totals also come from Table 1. By the second assumption, $(1/3)(100) = 33$ will die from CHD, leaving **67** deaths from other causes, for a grand total, again, of **10,100**. This completes the row and column of totals.

Assumption 8 gives the top row: **70**, **25**, and **5** respectively entering the three risk categories, and **0** of the new persons entering each other category. By assumption 3, the number from each remaining category who die from causes other than CHD is proportional to the total number in the category:

$(67)(5092/10,000) = $ **34** from the low risk group,
$(67)(3471/10,000) = $ **23** from the medium risk group,

(67)(764/10,000)=**5** from the high risk group, and
(67)(673/10,000)—**5** from the CHD group.
This completes the "Other death" column.

Obviously, nobody returns from the dead (we didn't bother to state this as a formal assumption); hence the **0**'s in the bottom two rows. Assumption 6 (that once a given category is reached there is no return) gives **0**'s in the rest of the positions below the diagonal. Assumption 7 (that it requires more than one time period to move from low risk to high risk) give the other **0** in the matrix. We now have 100 people entering the three risk categories, and $34+23+5=62$ people leaving these categories by death from causes other than CHD. Thus by assumption 1 (equilibrium) we must have a total of $100-62=38$ people leaving the three risk categories to enter the CHD and CHD death categories.

By assumption 5 (regarding the relative incidence in the several categories),

$$\frac{38\,[(5092)(1)]}{(5092)(1)+(3471)(2)+(764)(4)}=(38)(5092)/(15,090)=(5092)(0.002518), \text{ or } 13$$

of these 38 people will come from the low risk category. Similarly, $(3471)(2)(0.002518)=$ 17 will come from the medium risk category, and $(764)(4)(0.002518)=8$ will come from the high risk category. Of these 13, 17, and 8 persons from the respective categories, assumption **4** (regarding immediate mortality), with the fact that we are rounding to integers, requires that **4, 5,** and **2** go into the CHD death category, leaving **9, 12,** and **6** to go into the CHD category.

The remainder of the table is completed by starting with the blank in the CHD death column, and working diagonally up the table filling in the numbers required to give the proper column and row totals.