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A COMPARISON OF THE 12-YEAR MORTALITY AND PREDICTIVE FACTORS OF CORONARY HEART DISEASE AMONG JAPANESE MEN IN JAPAN AND HAWAII

日本，ハワイ在住の日本人男性における虚血性心疾患の
12年間の死亡率と予測因子の比較

KATSUHIKO YANO, M.D. 矢野勝彦
CHARLES J. MACLEAN, Ph.D.
DWAYNE M. REED, Ph.D.
YUKIKO SHIMIZU, D.M.Sc. 清水由紀子
HIDEO SASAKI, M.D. 佐々木英夫
KAZUNORI KODAMA, M.D. 児玉和紀
HIROO KATO, M.D. 加藤寛夫
ABRAHAM KAGAN, M.D.

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日本，ハワイ在住の日本人男性における虚血性心疾患の12年間の死亡率と予測因子の比較

KATSUHIKO YANO, M.D. (矢野勝彦)*; CHARLES J. MACLEAN, Ph.D.[1]; DWAYNE M. REED, Ph.D.[2]; YUKIKO SHIMIZU, D.M.Sc. (清水由紀子)[3]; HIDEO SASAKI, M.D. (佐々木英夫)[4]; KAZUNORI KODAMA, M.D. (児玉和紀)[4]; HIROO KATO, M.D. (加藤寛夫)[3]; ABRAHAM KAGAN, M.D.[1]**

Honolulu Heart Program, Honolulu [1]; National Heart, Lung and Blood Institute, Honolulu Heart Program, Honolulu [2]; and RERF Departments of Epidemiology [3] and Clinical Studies [4]

Honolulu 心臓調査班[1]; 米国心臓，肺，血液研究所 Honolulu 心臓調査班[2]; 放影研統計部[3] 及び臨床研究部[4]

SUMMARY

The mortality and predictive factors of coronary heart disease (CHD) among men of Japanese ancestry in Japan and Hawaii were compared on the basis of 12-year follow-up data using comparable methods of case ascertainment and risk factor measurements. Among 1,687 men (Japan) and 7,536 men (Hawaii) who were free of CHD and aged 45-69 at baseline examination, 20 (Japan) and 123 (Hawaii) cases of fatal CHD were identified. The age-adjusted mortality rate was 40% higher in Hawaii than in Japan. The difference was not statistically significant, but consistent with earlier studies. More than half of this difference in mortality rate was attributed to different levels of known risk factors in the two cohorts. In multivariate analysis using the combined population, age, blood pressure, serum cholesterol, serum glucose, cigarette smoking, and alcohol intake (inversely) remained as significant predictors of CHD mortality. Although the associations of risk factors with CHD tended to be stronger in Hawaii than in Japan, there was no statistically significant difference in regression coefficient for any of the risk factors studied. These findings cannot be claimed definitive because of the small number of cases, especially in Japan.

要 約

日本，ハワイ在住の日本人男性における虚血性心疾患(CHD)の死亡率及び予測因子を12年間の追跡調査資料に基づき，症例確認及び危険因子測定の比較可能な方法を用いて比較した．CHD に罹患していない，初診時年齢が45～69歳の日本の対象者1,687名及びハワイの対象者7,536名のうち，致死性 CHD 症例が日本で20例，ハワイで123例確認された．年齢調整した死亡率は日本よりもハワイの方が40%高かった．この差異は統計的に有意ではなかったが，初期の調査と一致していた．この死亡率の差の半分以上は二つのコホートの既知の危険因子のレベルが異なるためであった．二つの母集団を合わせた多変量解析によれば，年齢，血圧，血清コレステロール，血糖，喫煙，アルコール摂取量(逆相関)が依然 CHD 死亡の重要な予測因子であった．CHD と危険因子との関連は，日本よりもハワイの方が強い傾向にあったが，調査されたどの危険因子についても回帰係数間の差は統計的に有意ではなかった．特に日本において症例数が少ないためこれらの所見が確定的であると断定することはできない．

Former ABCC Research Associate 元 ABCC 研究員

**Former RERF Vice-Chairman* 元放影研副理事長

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INTRODUCTION

The reported mortality rate from CHD in Japan is the lowest among the industrialized countries in the world.[1] Early studies based on autopsy examinations, clinical experiences, and vital statistics[2-5] suggested that the frequency of CHD in Japanese immigrants to the United States and their offspring was intermediate between the low rate in the native Japanese and the high rate in the US whites.

In 1965, a tripartite prospective epidemiologic investigation named "NI-HON-SAN" Study (acronyms of NIppon, HONolulu and SAN Francisco) was initiated to verify the reported differences in cardiovascular disease rates between Japanese men living in Japan and those in the United States. The populations under investigation included men of Japanese ancestry who were born in 1900-1919 and residing in Hiroshima and Nagasaki, Japan, Oahu Island, Hawaii, and the San Francisco Bay Area, California. Defined samples of men in these locations have been examined and followed up for the development of CHD and stroke using a common protocol designed to minimize methodological differences.[6]

In an earlier report from the NI-HON-SAN Study, Robertson et al[7,8] indicated that the age-adjusted annual incidence rate of definite CHD was twice as high in Hawaii as in Japan, and that this difference in CHD rate was largely attributed to different distributions of a few risk factors such as serum cholesterol and obesity in the two populations. These findings were, however, based on only 16 cases including fatal CHD and nonfatal myocardial infarction (MI) in Japan and 47 in Hawaii who were identified during relatively short follow-up periods (six years in Japan and two years in Hawaii).

Stimulated by the need for more conclusive results, the present study was conducted to make a comparison of CHD mortality and risk factor effects in the Japanese and Hawaiian cohorts of the NI-HON-SAN Study based on the 12-year follow-up data. The Japanese men in California were excluded from this study because the follow-up was discontinued early in the period.

MATERIALS AND METHODS

Study Population

In Japan the study population included approximately 2,400 Japanese men who were born between 1 January 1900 and 31 December 1919 among the

緒　言

日本のCHD死亡率は世界の先進国の中で最も低いと報告されている.[1] 剖検，臨床検査及び人口動態統計に基づく初期の調査[2-5]では，日本人の米国移住者及びその子孫におけるCHDの頻度は低率な本国の日本人と高率な米国白人との中間であることが示唆された.

日本在住の日本人男性と米国在住の日本人男性との間に心臓血管疾患罹患率の差があるという報告を検証するために，"NI-HON-SAN"（NIppon, HONolulu及びSAN Franciscoの頭文字）調査と称する三地区の疫学的計画調査を1965年に開始した．調査対象集団は1900－1919年に生まれた広島・長崎，ハワイのOahu島及びCaliforniaのSan Francisco湾地域に在住する日本人男性であった．これらの地区の限定された男性を対象として，方法論的な違いをできるだけ少なくするよう作られた共通の研究計画書を用いて，CHD及び脳卒中の発生を追跡調査してきた.[6]

NI-HON-SAN調査の初期の報告書においてRobertsonら[7,8]は，診断確実なCHD症例の年齢訂正年間発生率はハワイが日本の2倍であり，このCHD発生率の差の主な原因は二つの集団の血清コレステロール及び肥満など，幾つかの危険因子の分布の差であることを示した．しかし，これらの所見は，比較的短期間の追跡調査期間（日本6年，ハワイ2年）に確認された日本の致死性CHD及び非致死性心筋梗塞（MI）などわずか16例及びハワイの47例に基づいて得られたものであった.

今回更に確定的な結果が必要とされたため，調査を実施し，12年間の追跡調査資料に基づくNI-HON-SAN調査の日本及びハワイのコホートのCHD死亡率と危険因子効果の比較を行った．Californiaの日本人男性は早い時期に追跡調査が中止されたので今回の調査から除外した.

材料及び方法

調査対象集団

日本における調査対象集団は，広島・長崎の放影研成人健康調査集団のうち1900年1月1日から1919年

RERF Adult Health Study population in Hiroshima and Nagasaki. These men have been examined biennially since 1958 to study the late effects of atomic bomb exposure. Among these men, 1,818 participated in the initial examination of the NI-HON-SAN Study.

In Hawaii over 11,000 men of Japanese ancestry who were born in 1900-1919 and residing on Oahu Island as of 1 January 1965 were identified and located through an updated record of the World War II Selective Service Registration. Among these men, 8,006 participated in the initial examination of the NI-HON-SAN Study. Details of the recruiting method and population characteristics for the cohorts in Japan and Hawaii have been published elsewhere.[9,10]

Baseline Examination

The baseline examination for the NI-HON-SAN Study was conducted during 1965-66 in Japan and 1965-68 in Hawaii. All participants were interviewed to obtain information on socio-demographic variables, past medical history, family medical history, smoking habit, alcohol consumption, and dietary intake. They also had anthropometric measurements, three blood pressure determinations, measurements of hematocrit, serum cholesterol, triglycerides, uric acid, and glucose one hour after ingestion of 50 g glucose on nonfasting blood specimens, spirometry, and a resting 12-lead electrocardiogram (ECG). Physical examination focusing on the cardiovascular system was also performed. Details of the examination procedures have been described in the common protocol.[6] The values recorded at this baseline examination were used as risk factor levels throughout the present paper.

Population at Risk

The population at risk was defined as men who were examined (with ECG) at baseline examination during 1965-66 in Japan and 1965-68 in Hawaii, excluding those who met the following criteria:

1) Prevalent cases of CHD (definite history of any type of CHD or definite ECG evidence of an old MI) or stroke (definite history alone or suggestive history plus physical signs of neurological deficit). The reason for excluding stroke was that in many cases of stroke, CHD may coexist either clinically or subclinically, and that some risk factors for CHD may have been altered by the existing stroke.

12月31日に生まれた約2,400名の日本人男性である．これらの男性を1958年以来2年ごとに検診し，原爆被爆の後影響を調べた．これらの男性のうち1,818名がNI-HON-SAN調査の最初の検査を受けた．

ハワイでは，第二次世界大戦時の選抜徴兵登録の最新記録によって，1900－1919年に生まれた，1965年1月1日現在Oahu島在住の11,000名以上の日系男性を確認した．これらの男性のうち8,006名がNI-HON-SAN調査の最初の検査を受けた．日本及びハワイのコホートの選定方法及び各集団の特性の詳細はよそで発表している．[9,10]

初　診

NI-HON-SAN調査の初診は日本では1965－66年，ハワイでは1965－68年に行われた．被検者全員を面接し，社会人口学的因子，既往歴，家族の既往歴，喫煙，飲酒及び食餌に関する情報を得た．被検者はまた，身体計測，3回の血圧測定，ヘマトクリット，血清コレステロール，トリグリセライド，尿酸，及びグルコース50 gを摂取して1時間後非空腹時に採取された血糖の測定，肺活量測定及び安静時の12誘導心電図検査（ECG）も受けた．心臓血管系に重点をおいた理学的検査も行った．検査手順の詳細は共通の研究計画書に記述されている．[6] この初診時に記録された測定値を本報では危険因子として使用した．

観察集団

観察集団は，日本では1965－66年，ハワイでは1965－68年の初診時に検査（ECG）を受けた男性により構成されるが，以下の基準に合致する者を除外した：

1）CHD（あらゆる種類の確実なCHDの既往歴のある者又は以前MIに罹患したことを示す確実なECG所見がある者），又は脳卒中（確実な既往歴のみの者又は不確実な既往歴があって神経系欠損の身体的徴候のある者）の罹患症例．脳卒中を除外する理由は，多くの脳卒中症例では臨床的に又は潜在的にCHDが共存する可能性があり，またCHDの危険因子の一部が脳卒中罹患によって変化したかもしれないからである．

2) Doubtful old MI by ECG without supportive history, or other ECG abnormalities such as complete left bundle branch block, Wolff-Parkinson-White syndrome, and complete atrioventricular block. The reason for excluding men with these ECG abnormalities was that these findings may interfere with ECG temporal changes required to identify new cases of MI.

Follow-up and Case Ascertainment

The method of follow-up and case ascertainment for fatal CHD was essentially the same in Japan and Hawaii. All men who died within 12 years after the date of baseline examination (up to 1978 in Japan and 1980 in Hawaii) were identified by community surveillance. The ascertainment of death due to acute or chronic CHD was made by a panel of study physicians on the basis of all available information from hospital or clinic records, death certificates, autopsy reports, family physicians, and surviving relatives.

In the original study protocol a comparison of the incidence of nonfatal MI was also planned. However, different methods of case ascertainment made a valid comparison difficult. In Japan cases of nonfatal MI were identified only by temporal changes of ECG (development of new Q/QS) between biennial examinations, and no hospital surveillance was conducted. In Hawaii, follow-up examinations were performed two and six years after baseline examination for the entire cohort, and further examinations were done only for a 30% subsample. In addition, a continuous morbidity surveillance through monitoring hospital discharges of cardiovascular events has been conducted for the entire cohort since 1965. Thus, case ascertainment for nonfatal MI in Hawaii was based on both temporal changes of ECG at follow-up examinations and hospital surveillance. Efforts were made to reconcile this discrepancy in methods of case ascertainment, but no satisfactory solution could be found. In the present report, therefore, the comparison had to be restricted to fatal CHD cases which were ascertained in a strictly comparable manner.

In order to assure the comparability of case ascertainment, one of the staff physicians from each study group visited the other study site and independently reviewed all potential cases in each cohort. Only those cases with a diagnosis agreed upon by physicians of both groups were accepted for the study.

2）裏付けとなる既往歴はないが，ECG でかって MI の存在が疑われた者，又は完全左脚ブロック，Wolff-Parkinson-White 症候群及び完全房室ブロックなどその他の ECG 異常．これらの ECG 異常のある者を除外する理由は，これらの所見が新たな MI 症例を確認するために必要な ECG の経時的変化に影響を及ぼす可能性があるからである．

追跡調査及び症例確認

致死性 CHD の追跡調査及び症例確認方法は日本とハワイでは本質的に同じである．初診時から12年以内（日本1978年まで，ハワイ1980年まで）に死亡した全男性が各地域の調査で確認された．急性又は慢性 CHD による死亡の確認は，病院又は医院の記録，死亡診断書，剖検報告書，家庭医及び生存している親戚など，あらゆる情報に基づき調査医師団が行った．

当初の調査計画では非致死性 MI の発生率の比較も予定されていた．しかし，症例確認方法が異なるため有効な比較は困難であった．日本では2年ごとの調査で得られた調査の間の ECG の経時的変化（新しい Q/QS の発生）によってのみ非致死性 MI 症例が確認され，病院での調査は行われなかった．ハワイでは初診から2年後及び6年後にコホート全体の追跡調査を行い，そのうち30％についてのみ更に追跡調査を行った．更に，1965年以来心臓血管疾患患者の退院状況を調査することによってコホート全体の罹患率の継続的調査が行われた．このように，ハワイにおける非致死性 MI の症例確認は追跡調査時の ECG の経時的変化及び病院調査に基づいて行われた．この症例確認方法の相違を調整する努力をしたが，満足のいく解決法は見つからなかった．したがって，本報では完全に比較可能な方法で確認した致死性 CHD 症例に限定して比較を行った．

症例確認が比較可能であることを保証するために，各調査グループの医師の一人が他の調査地区を訪れ，各コホートの症例をすべて独自に調べた．両グループの医師の診断が一致した症例のみを調査対象として認めた．

Definition of Cases

Fatal CHD cases were defined as deaths due to acute CHD (including MI, coronary insufficiency, and sudden death with coronary type chest pain) or to chronic CHD (including congestive heart failure and severe arrhythmia with prior history of CHD).

Sudden deaths within one hour after the onset of symptoms without clear evidence of CHD (by ECG, cardiac enzyme, or chest pain), and in the absence of other attributable causes, are usually regarded as fatal CHD in the United States. However, the proportion of CHD proved to be the cause of death in autopsied cases of sudden death within one hour was only 14% (1/7) in the Japanese cohort, while it was 72% (33/46) in the Hawaiian cohort. It was decided therefore to exclude this category in the present comparative study. Old MIs found incidentally at autopsy without clinical history of CHD were also excluded because it was difficult to determine whether the MI occurred before or after the baseline examination. Another category of exclusion was CHD death diagnosed only by death certificate without supportive evidence from either clinical or autopsy findings.

Statistical Analysis

The purpose of the present study was to compare the Japanese and Hawaiian cohorts. Comparison was complicated by the different follow-up periods used in the two cohorts. In order to account for follow-up differences, all analyses were performed by life table regression methods, familiarly known as Cox proportional hazards model.[12] This procedure enabled adjustment for the particular follow-up duration of each subject, and also the adjustment for confounders such as age and other risk factors by the method of analysis of covariance.

Because the cohort sample sizes were quite different, the significance level of risk factor effect was much higher in Hawaii than in Japan for nearly all risk factors. The Japanese sample was too small to yield significant rates. However, since all the variables employed were well-known risk factors for CHD from previous studies, significance was assumed, and attention was focused on differences between the cohorts with overall effect estimated from the combined data.

Age Adjustment. Since CHD mortality increased substantially for older men within both cohorts,

症例の定義

致死性CHD症例は，急性CHD（MI，冠不全及び冠状動脈型胸痛を伴う突然死など）又は慢性CHD（CHD既往歴のあるうっ血性心不全及び重度の不整脈）による死亡と定義した．

CHDの明瞭な証拠（ECG，心臓酵素又は胸痛による）もなく，またほかの原因も認められず，症状の発症後1時間以内に突然死亡した場合，米国では普通，致死性CHDとみなす．しかし，1時間以内の突然死の剖検症例においてCHDが死因であることが証明された割合は，日本のコホートではわずか14%（1／7）であり，ハワイのコホートでは72%（33/46）であった．したがって，今回の比較調査ではこのカテゴリーを除外することにした．CHDの臨床歴がなく剖検時に偶然見つかった以前のMIは，初診時以前に起こったものか初診時以降に起こったものか決定しにくいためこれも除外した．除外したもう一つのカテゴリーは，臨床又は剖検所見による裏付け証拠がなく，死亡診断書だけで診断されたCHD死亡である．

統計解析

今回の調査目的は日本のコホートとハワイのコホートの比較であった．二つのコホートの追跡調査方法が異なるため比較は複雑であった．追跡調査の差を説明するために，Cox比例ハザードモデルとしてよく知られている生命表の回帰分析法を用いて全解析を行った．[12] この方法によって各対象者の追跡調査期間の訂正と共分散解析法による年齢及びその他の危険因子などの交絡因子の訂正が可能となった．

コホート集団の大きさが非常に異なるため，ほぼすべての危険因子について危険因子効果の有意性レベルは日本よりもハワイの方がはるかに高かった．日本の集団は小さすぎて統計的に有意性を示すに至らなかった．しかし，使用した変数はすべて過去の調査からよく知られたCHDの危険因子だったので，有意性があると想定し，コホート間の差に注目し二つのデータを合併して全体的な効果を推定した．

年齢の訂正． 両コホート内の高齢者のCHD死亡率が大幅に増加したので，年齢訂正が極めて重要に

age adjustment became quite important. The age-specific rates, shown in Table 1, were compared by life table regression (see Figure 1). There was no evidence of departure from log-linearity of age effect in either cohort. CHD mortality rates increased 7% and 8% per year of age at risk in Japan and Hawaii, respectively (see Table 3). The same rate of increase (7.5% per year) is shown superimposed on age-specific data in Figure 1. Since age effect appeared so similar, the same adjustment for age was applied throughout subsequent risk factor analyses.

なった．表1の年齢別死亡率を生命表回帰分析法を用いて比較した（図1参照）．いずれのコホートも年齢効果の対数線形性からの偏りは認められなかった．CHD死亡率は日本及びハワイでそれぞれ観察年齢1年当たり7％～8％増加した（表3参照）．図1に同じ増加率（1年当たり7.5％）を年齢別データの上に重ねて示している．年齢効果は酷似しているように思われたので，以下の危険因子解析でも同じ年齢訂正を行った．

TABLE 1 AVERAGE ANNUAL MORTALITY RATE/1000 OF CORONARY HEART DISEASE (CHD) BY AGE AT RISK DURING 12 YEARS OF FOLLOW-UP AMONG JAPANESE MEN IN HAWAII AND JAPAN, 1965-80

表1　ハワイ及び日本の日本人男性における12年間の追跡調査期間中の観察年齢別虚血性心疾患（CHD）の1000人当たりの年間平均死亡率，1965－80年

	Hawaii			Japan		
Age at risk (1965-80)	Person-years of follow-up	No. of CHD cases	Rate	Person-years of follow-up	No. of CHD cases	Rate
45-49	2667	0	0	620	0	0
50-54	15741	10	0.63	2539	0	0
55-59	25159	30	1.19	4321	5	1.16
60-64	21731	28	1.29	4796	4	0.83
65-69	13455	24	1.78	4032	7	1.74
70-74	6459	25	3.87	1836	4	2.18
75-79	1396	6	4.30	230	0	0
Total No. of men	7536			1687		
Total No. of follow-up	86612	123	1.42	18374	20	1.09
Age-adjusted rate*			1.44			1.00

*The Hawaii/Japan rate ratio calculated by life table regression was 1.41 (p=0.15) (95% confidence limits: 0.87, 2.29).

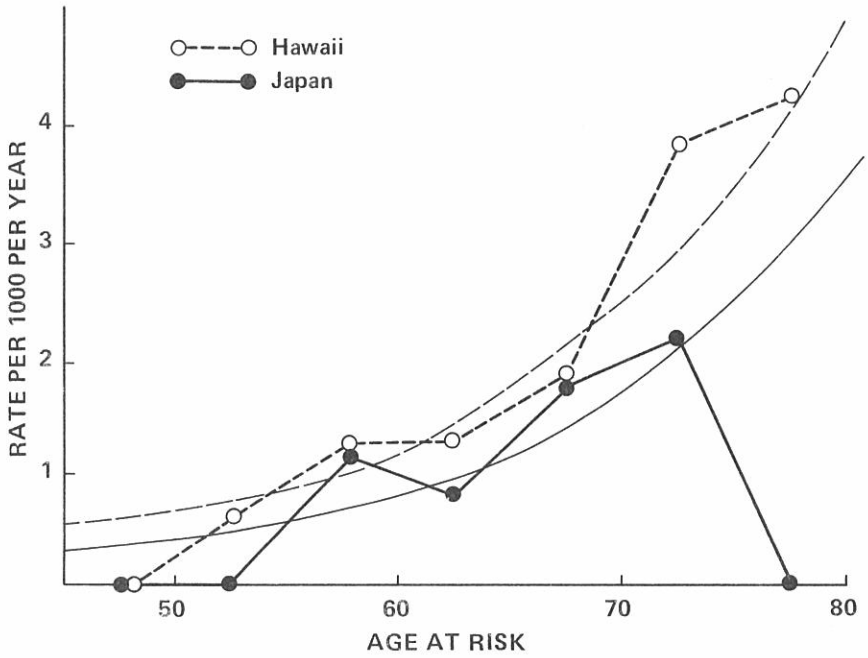
生命表回帰分析により算出されたハワイ/日本の死亡率比は1.41（p＝0.15）（95％信頼限界：0.87，2.29）．

Interquartile Relative Risk. Risk factors such as blood pressure, body mass index, and serum cholesterol were treated as numerical variables adjusted for age by standard life table regression methods.[13] All significance values were calculated from the usual regression equations. However, ordinarily, results of life table regression are presented in a

四分位数間相対危険度． 血圧，肥満指数及び血清コレステロールなどの危険因子は，通常の生命表回帰分析法で年齢を訂正し，数値変数として扱った．[13] 有意性はすべて通常の回帰方程式から算出した．しかし，普通，生命表回帰分析法から得た結果は

FIGURE 1 AVERAGE ANNUAL MORTALITY RATES OF CORONARY HEART DISEASE BY AGE AT RISK DURING 12 YEARS OF FOLLOW-UP AMONG JAPANESE MEN IN JAPAN AND HAWAII

図1　日本及びハワイの日本人男性における12年間の追跡調査期間中の観察年齢別 CHD 年間平均死亡率



list of coefficients corresponding to estimated increments in relative log hazard rate, which have very little intuitive meaning. Therefore, for the purpose of presentation, we have transformed coefficients by solving the log hazard equation at both the 25th percentile and 75th percentile values of the corresponding risk factor, and taking the ratio to form an "interquartile relative risk." If the samples were divided in half on the basis of the risk factor, these two values (the 25th and 75th percentile values) would represent the median averages of the two groups. Therefore, the interquartile relative risk compares the upper half with the lower half of the data, for each risk factor. Since the cohorts have somewhat different ranges for several risk factors, a weighted average value was employed. In cases of highly skewed risk factors, e.g., serum triglycerides and glucose as well as cigarette smoking and alcohol intake, the regression was performed on logarithms of the risk factors. In the case of age, the distribution was not natural, but rather artificially selected

相対対数ハザードの増加分の推定値に対応する係数で示されるが，それにはほとんど直観的な意味がない．したがって，説明上，対応する危険因子の25及び75パーセンタイルで対数ハザード方程式を解き，その比を「四分位数間相対危険度」とすることにより係数を変換した．危険因子に基づいて集団を二つに分けると，これらの二つの数値（25及び75パーセンタイル）は二つのグループの中央平均値を示すことになる．したがって，四分位数間相対危険度は，各危険因子についてデータの上半分と下半分とを比較するものである．各コホートでは幾つかの危険因子の範囲が若干異なるので，加重平均値を用いた．歪度の大きい危険因子，例えば血清トリグリセライド，血糖，喫煙及びアルコール摂取量の場合には，危険因子の対数に対して回帰分析を行った．年齢については，分布は自然ではなく，むしろ実験計画によって人為的に選択された．したがって，四分位数間の範囲は

by experimental design. Therefore, the interquartile range would be inappropriate for expression, and instead we used 10 years as the arbitrary base. This provided a convenient scale in that both cohorts originally ranged over about 20 years and were followed up for about 12 years.

Risk Factor Quintiles. Life table regressions are difficult to display graphically. Therefore, for Figure 2 we sorted each risk factor into quintiles for either cohort, and age-adjusted mortality rates of CHD calculated for these categories. Moreover, since the number of cases was so small, random variation in the figures was reduced by a simple smoothing technique. Each pair of contiguous quintiles was averaged to yield one point so that quintiles were represented by only four overlapping values. For cigarette smoking and alcohol intake, which had a large proportion of nonusers, values at zero (nonusers) were plotted without smoothing. Then the users were grouped into quartiles and these four points were smoothed by pairs to yield three additional points.

RESULTS

Table 1 presents the numbers of person-years of follow-up and cases of CHD and the mortality rates (per 1,000 per year) by age at risk, as well as the total number of men at risk, the total number of person-years of follow-up, and the age-adjusted mortality rates in Japan and Hawaii.

In Japan, a total of 1,818 eligible men were examined at baseline examination during the period 1965-66. Among these men, 131 were excluded because they had either prevalent CHD, specified ECG abnormalities or prevalent stroke. The remaining 1,687 men thus formed the population at risk. In Hawaii, among the 8,006 men who were examined at baseline examination during 1965-68, 470 were excluded for the same reasons as in Japan. The remaining 7,536 men thus formed the population at risk. The total numbers of fatal CHD cases were 20 in Japan and 123 in Hawaii. The age-adjusted rates were calculated by the direct method using the age structure of the combined population (Japan + Hawaii).

The age-specific mortality rates were not appreciably different between the two cohorts until age 70, after which the rates became substantially higher in Hawaii than in Japan. However, the follow-up of subjects over 70 years of age was quite sparse,

不適切なので，その代わりに任意に10年を用いた．両コホートの年齢範囲は当初約20年であり，約12年間追跡調査が行われたことからこれは便利な尺度となった．

危険因子五分位数． 生命表回帰分析の結果は図式的に表示しにくい．したがって，図2ではいずれのコホートも各危険因子を五分位数に分類し，これらのカテゴリーについて年齢訂正したCHD死亡率を算出した．更に，症例数が大変少ないので，各図の確率変動は単純な平滑法で小さくした．隣接する二つの五分位数を平均して1点を出し，五分位数は四つの重複値だけで表されるようにした．非摂取者の比率が高い喫煙及びアルコール摂取量では，ゼロ値（非摂取者）は平滑化を行わずにプロットした．次に摂取者を四分位数に分け，これらの4点を対で平滑化して更に3点をだした．

結　果

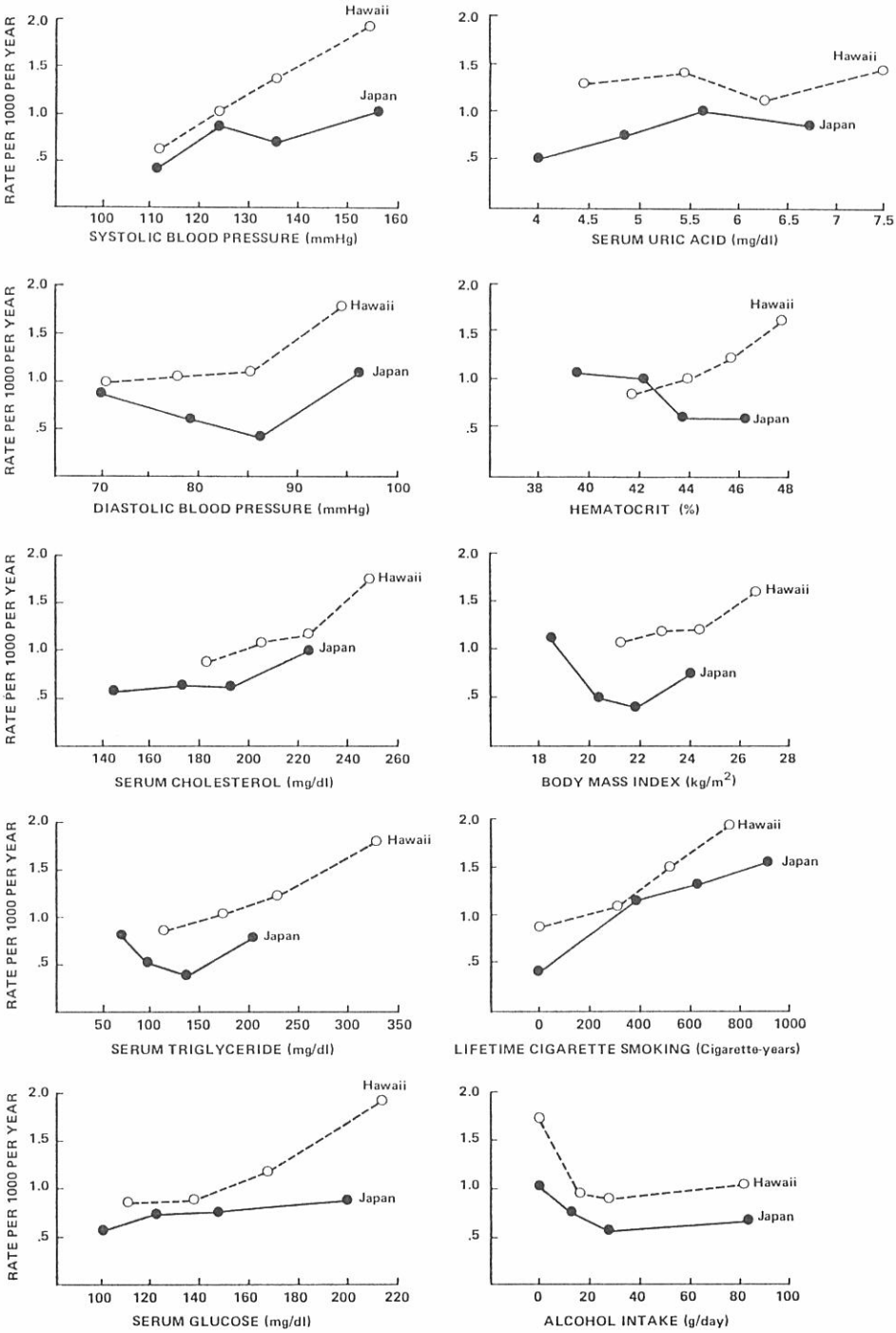
表1は，日本及びハワイにおける観察年齢別追跡調査人年数，CHD症例数及び死亡率（1,000人年当たり）並びに観察対象者総数，追跡調査人年総数及び年齢訂正死亡率を示す．

日本では，1965～66年の初診時に総数1,818名を検査した．これらのうち131名は，CHD，特定のECG異常又は脳卒中に罹患していたので除外した．したがって残り1,687名が観察集団となった．ハワイでは，1965－68年の初診時に受診した8,006名のうち470名は日本の場合と同じ理由で除外した．したがって残り7,536名が観察集団となった．致死性CHDの総数は日本で20名，ハワイで123名であった．二つ合わせた集団（日本＋ハワイ）の年齢構成を用いて直接法により年齢訂正死亡率を算出した．

年齢別死亡率は70歳までは二つのコホート間で大きく異なることはなかったが，70歳以上では日本よりもハワイの方がかなり高くなった．しかし，70歳以上の対象者の追跡調査は特に日本では極めて少ない．

FIGURE 2 AGE-ADJUSTED MORTALITY RATES OF CORONARY HEART DISEASE BY QUINTILES OF BASELINE RISK FACTOR LEVELS AMONG JAPANESE MEN IN JAPAN AND HAWAII

図2　日本及びハワイの日本人男性における危険因子レベル五分位数別年齢訂正 CHD 死亡率



especially in Japan. There were 31 deaths among the Hawaiian cohort over 70 years of age in 7,855 person-years of follow-up, whereas there were only 4 deaths in 2,066 comparable person-years in the Japanese cohort. Had there been nine such deaths in Japan, the rates would be identical. Thus, there is no evidence of any difference other than random variation in a small sample. The age-adjusted rate was 1.44 for Hawaii and 1.00 for Japan, with the rate ratio of 1.41 (95% confidence limits: 0.87, 2.29) calculated by a life table regression. While this trend was in the expected direction, the difference was not statistically significant (p=0.15). The trend of mortality rates of CHD by age at risk in the two cohorts is essentially the same as shown by Figure 1 in which age-specific mortality rates were superimposed by mortality curves obtained from the life table regressions (7.5% increase by age at risk, see Table 3).

The next step was to examine the relationship of risk factors to the CHD mortality during 12 years of follow-up. Risk factors included body mass index, as expressed by body weight (kg)/height^2(m), systolic blood pressure, diastolic blood pressure, serum cholesterol, serum triglyceride, serum uric acid, serum glucose (one hour after 50 g glucose load), hematocrit, lifetime cigarette smoking (cigarette-years), and alcohol intake (g/day, based on 24-hour diet recalls). Table 2 shows age-adjusted mean values of the risk factors at baseline examination. The mean age and diastolic blood pressure were greater in Japan than in Hawaii, while body mass index, serum cholesterol, triglyceride, glucose, uric acid, and hematocrit were greater in Hawaii than in Japan. The mean systolic blood pressure was equal in the two cohorts. The percentages of cigarette smokers and alcohol drinkers were greater in Japan than in Hawaii, but the average amount of lifetime smoking for smokers was greater in Hawaii because of a higher percentage of heavy smokers. The average intake of alcohol for drinkers was greater in Japan than in Hawaii, but the difference was not statistically significant. Thus, except for blood pressure and alcohol intake, the mean level of known risk factors was significantly higher in Hawaii than in Japan.

The relationship of risk factors to fatal CHD was then examined separately in each cohort. As noted in the methods, the emphasis of statistical testing was placed upon whether there was a difference in the regression coefficient for any specific risk

ハワイのコホート中70歳以上の7,855追跡調査人年のうち死亡者は31名であるのに対し，日本のコホート中70歳以上の2,066人年のうち死亡者はわずか4名であった．日本で死亡者が9名であったら死亡率は等しくなる．このように，小集団では確率変動以外の差のある証拠は認められない．年齢調整死亡率はハワイで1.44，日本で1.00であり，生命表回帰分析で算出した死亡率比は1.41（95％信頼限界：0.87，2.29）であった．この傾向は予測した方向に沿うものであったが，差は統計的に有意ではなかった（p＝0.15）．二つのコホートの観察年齢別CHD死亡率の傾向は図1で示されるとおり実質的に同じである．この図には年齢別死亡率の上に生命表回帰分析から得た死亡率曲線を重ねて示した（観察年齢別増加7.5％，表3参照）．

次に12年間の追跡調査期間中のCHD死亡率と危険因子との関係を調べた．危険因子は，体重（kg）/身長^2（m）で表される肥満指数，収縮期血圧，拡張期血圧，血清コレステロール，血清トリグリセライド，血清尿酸，血糖（50ｇグルコース負荷1時間後の値），ヘマトクリット，生涯喫煙量（本数-年）及びアルコール摂取量（g/日，24時間食餌記憶調査に基づく）であった．表2は，初診時の危険因子の年齢訂正平均値を示す．平均年齢及び平均拡張期血圧はハワイよりも日本の方が高かったが，肥満指数，血清コレステロール，トリグリセライド，血糖，尿酸及びヘマトクリットはハワイの方が大きかった．平均収縮期血圧は両コホートで等しかった．喫煙者及び飲酒者の割合はハワイよりも日本の方が高いが，喫煙者の平均生涯喫煙量は大量に喫煙する者の割合が高いハワイの方が多かった．飲酒者の平均アルコール摂取量はハワイよりも日本の方が多かったが，その差は統計的に有意ではなかった．したがって，血圧及びアルコール摂取量以外の既知の危険因子の平均レベルは日本よりもハワイの方が有意に高かった．

次に危険因子と致死性CHDとの関係を各コホートで別々に調べた．方法の項で述べたように，統計解析で重視したのは，特定危険因子の回帰係数に日本，

TABLE 2 AGE-ADJUSTED MEAN VALUES AND STANDARD DEVIATIONS OF SLECTED RISK FACTORS AT BASELINE EXAMINATION AMONG JAPANESE MEN IN HAWAII AND JAPAN, 1965-68

表2 ハワイ及び日本の日本人男性における初診時危険因子の年齢訂正平均値及び標準偏差，1965－68年

Risk Factor	Hawaii		Japan	
	Mean	SD	Mean	SD
Age at entry (years)	54.8	5.5	56.2*	5.7
Systolic blood pressure (mmHg)	133	22	133	24
Diastolic blood pressure (mmHg)	82	13	83*	14
Body mass index (kg/m^2)	23.8*	3.1	21.3	2.9
Serum cholesterol (mg/100 ml)†	218*	38	185	42
Serum triglyceride (mg/100 ml)†	236*	203	136	88
Serum glucose (mg/100 ml)†	161.0*	58	145	64
Serum uric acid (mg/100 ml)†	6.0*	1.5	5.4	1.4
Hematocrit (%)	44.7*	3.0	43.0	3.8
Cigarette smokers (%)‡	69		86*	
Lifetime smoking§ (cigarette-years)	691*	447	567	349
Alcohol drinkers (%)ǁ	29		60*	
Alcohol intake (g/day)¶	46	42	49	43

*Significantly greater than the other cohort at $p<0.05$
$p < 0.05$でもう一方のコホートより有意に大きい

†Determinations of these blood chemical components were performed on blood specimens drawn one hour after ingestion of 50 g glucose in nonfasting subjects
空腹時でない対象者に50 g ブドウ糖を投与して1時間後に採取した血液標本にこれらの血液化学成分の測定を行った

‡Men who ever smoked cigarette
喫煙経験のある男性

§Cigarette smoked/day × years of smoking for smokers only
喫煙者のみを対象とした一日当たりの喫煙本数×喫煙年数

ǁMen who drank alcoholic beverages on the previous day
調査前日にアルコールを摂取した男性

¶Based on the 24-hour diet recall data for drinkers only
飲酒者のみを対象とした24時間食餌記憶調査に基づく

factor between Hawaii and Japan, rather than upon whether a regression coefficient was significantly different from zero within each cohort.

Figure 2 illustrates age-adjusted mortality rates (per 1,000 men per year) of CHD during 12 years of follow-up by quintile levels of selected risk factors at baseline in each cohort. The four points in each curve represent smoothed averages of two contiguous quintiles to reduce random variations due to the small number of cases, especially in Japan. For

ハワイ間で差があるかどうかであり，回帰係数が各コホート内でゼロと有意に異なるかどうかではない．

図2は，12年間の追跡調査期間中の年齢訂正CHD死亡率（1,000人年当たり）を各コホートにおいて初診時の選択危険因子の五分位数レベル別に示したものである．各曲線の4点は，症例数が少ない（特に日本において）ことによる確率変動を小さくするために隣接する二つの五分位数を平滑化した平均値を示す．

smoking and alcohol in which nonusers accounted for the large proportion, the mortality rate was first plotted for the nonusers without smoothing, and then three other points were plotted using smoothed averages of two contiguous quartiles of the users.

There was a general pattern of direct association with fatal CHD in both cohorts for systolic and diastolic blood pressure, serum cholesterol, glucose, uric acid, and cigarette smoking, while the association was inverse for alcohol intake. The Hawaiian cohort tended to have higher mortality rates at any given level of these risk factors. The patterns appeared to be different in the two cohorts for body mass index, serum triglyceride, and hematocrit. This is due partly to the different range of baseline levels of risk factors in the two cohorts and partly to the small number of cases in Japan. However, when the life table regression coefficients for individual risk factors were examined for differences between the two cohorts, no statistically significant difference was found for any of these risk factors (Table 3). The coefficients for all risk factors were statistically significant in Hawaii, whereas only the coefficient for systolic blood pressure was significant in Japan mainly due to the small sample size.

In order to aid comprehension, we transformed all regression results to "interquartile relative risk," as described in the Statistical Analysis section. Table 4 shows the interquartile relative risks of fatal CHD for individual risk factors after adjustment for age within each cohort, as well as the relative effects (Hawaii/Japan) of these risk factors, with their 95% confidence limits. In general, the relative risks were similar for most risk factors when they were compared between the two cohorts. In 8 out of the 11 risk factors the relative effect was greater in Hawaii than in Japan, but none of the differences were statistically significant mainly due to the small sample size in Japan. This tendency was reflected in the larger 95% confidence limits of the interquartile relative risks for all risk factors in Japan as compared with those in Hawaii (Table 4).

Since there were intercorrelations among these risk factors, multivariate life table regression analysis was performed to evaluate additive contributions of risk factors to the prediction of fatal CHD. In this analysis the two cohorts were combined and the cohort relative risk (Hawaii/Japan) was

非摂取者の比率が高い喫煙及びアルコールについては，まず非摂取者の死亡率を平滑化しないでプロットし，次に摂取者の隣接する二つの四分位数の平滑化した平均値を用いてほかの３点をプロットした．

収縮期及び拡張期の血圧，血清コレステロール，血糖，尿酸及び喫煙については両コホートとも致死性CHDとの直接の関連性を示す一般的パターンがあったが，アルコール摂取量は逆相関を示した．ハワイのコホートはこれらの危険因子のどのレベルでも死亡率が高い傾向があった．肥満指数，血清トリグリセライド及びヘマトクリットのパターンは二つのコホートで異なるようであった．これは一つには二つのコホートで危険因子のレベルの範囲が異なるためであり，また一つには日本で症例数が少ないためである．しかし，個々の危険因子の生命表回帰係数を二つのコホート間の差について調べると，これらのいずれの危険因子についても統計的に有意な差は認められなかった（表３）．ハワイでは全危険因子の係数が統計的に有意であったが，日本では収縮期血圧の係数のみが有意であった．これは主に日本の集団の大きさが小さかったためである．

理解しやすくするために，統計解析の項で示したように回帰解析結果をすべて「四分位数間相対危険度」に変換した．表４は，各コホート内で年齢訂正した後の各危険因子についての致死性CHDの四分位数間相対危険度，これらの危険因子の相対効果（ハワイ／日本），並びに，それぞれの95％信頼限界を示す．概して，二つのコホートを比較すると大半の危険因子について相対危険度は類似していた．11の危険因子中八つでは，相対効果は日本よりハワイの方が大きかったが，主に日本での集団の大きさが小さかったためいずれの差も統計的に有意ではなかった．この傾向は，全危険因子に対する四分位数間相対危険度の95％信頼限界がハワイよりも日本の方が大きいことに反映されていた（表４）．

これらの危険因子の間には相関関係が見られたので，多変量生命表回帰分析を行い危険因子の致死性CHDの予測に対する付加的な寄与を評価した．この解析では二つのコホートを合計し，年齢及び全危険因子をコントロールした後，コホート相対危険度（ハワイ／日本）を評価した．表５に示すように，年齢，収縮期

TABLE 3 LIFE TABLE REGRESSION COEFFICIENTS FOR FATAL CORONARY HEART DISEASE ONTO AGE AND SELECTED RISK FACTORS AMONG JAPANESE MEN IN HAWAII AND JAPAN, 1965-80

表３　ハワイ及び日本の日本人男性における年齢及びその他の危険因子に対する致死性虚血性心疾患の生命表回帰係数，1965－80年

	Hawaii		Japan	
Risk factor†	β‡	(SE)§	β	(SE)
Age	0.070**	(0.015)	0.081	(0.042)
Systolic blood pressure	0.024**	(0.003)	0.018*	(0.008)
Diastolic blood pressure	0.031**	(0.006)	0.028	(0.015)
Body mass index	0.094**	(0.028)	0.030	(0.076)
Serum cholesterol	0.010**	(0.002)	0.005	(0.005)
Serum triglyceride	0.584**	(0.142)	0.446	(0.480)
Serum glucose (log)	1.665**	(0.254)	0.765	(0.658)
Serum uric acid (log)	0.139*	(0.057)	0.039	(0.153)
Hematocrit	0.063*	(0.029)	−0.030	(0.060)
Lifetime smoking (log)	0.267**	(0.029)	0.268	(0.206)
Alcohol intake (log)	−0.128*	(0.063)	−0.148	(0.124)

*$p<0.05$, **$p<0.01$

†Each risk factor was related one at a time to fatal CHD, with age as covariate.
各危険因子は，年齢を共変量として１回一つずつ致死性 CHD との関連を調べた．

‡Regression coefficient. 回帰係数

§Standard error. 標準偏差

None of the differences in β between two cohorts attained the statistically significant level ($p<0.05$).
二つのコホート間の β の差は統計的に有意なレベルに達しなかった（$p<0.05$）．

assessed after controling for age and all risk factors together. As shown in Table 5, age, systolic blood pressure, serum cholesterol, serum glucose, lifetime smoking, and alcohol intake (inversely) were significant predictors of fatal CHD. The cohort relative risk (Hawaii/Japan) was 1.17, indicating that fatal CHD risk was nearly 20% higher in Hawaii than in Japan when adjustment was made for all risk factors simultaneously. Since the cohort relative risk adjusted only for age was 1.41 (Table 1), more than half the difference in fatal CHD rate between the two cohorts was attributed to differences in all other risk factor levels at baseline examination.

血圧，血清コレステロール，血糖，生涯喫煙量及びアルコール摂取量（逆相関）は致死性 CHD の重要な予測因子であった．コホート相対危険度（ハワイ／日本）は1.17であり，危険因子をすべて同時に訂正した場合，致死性 CHD の危険度は日本よりもハワイの方が約20％高いことを示した．年齢のみの訂正を行ったコホート相対危険度は1.41であった（表1）ので，二つのコホート間の致死性 CHD 死亡率の差の半分以上は初診時の年齢以外の危険因子レベルの差によるものと考えられた．

TABLE 4 INTERQUARTILE RELATIVE RISKS OF FATAL CORONARY HEART DISEASE AND HAWAII/JAPAN RELATIVE EFFECTS FOR SELECTED RISK FACTORS AMONG JAPANESE MEN IN HAWAII AND JAPAN OF THESE RISK FACTORS, 1965-80

表 4　ハワイ及び日本の日本人男性における致死性 CHD の四分位数間相対危険度及び危険因子のハワイ/日本相対効果，1965－80年

Risk factor*	Interquartile relative risk (95% confidence limits)		Hawaii/Japan Relative effect (95% confidence limits)
	Hawaii	Japan	
Age†	2.02 (1.49, 2.72)	2.20 (0.97, 5.20)	0.90 (0.37, 2.18)
Systolic blood pressure	2.27 (1.85, 2.79)	1.88 (1.07, 3.19)	1.20 (0.67, 2.14)
Diastolic blood pressure	1.71 (1.38, 2.10)	1.63 (0.96, 2.73)	1.05 (0.59, 1.83)
Body mass index	1.51 (1.18, 1.93)	1.19 (0.58, 2.22)	1.26 (0.62, 2.56)
Serum cholesterol	1.64 (1.34, 2.00)	1.20 (0.78, 2.10)	1.36 (0.80, 2.31)
Serum triglyceride	1.74 (1.32, 2.27)	1.56 (0.61, 3.79)	1.11 (0.44, 2.86)
Serum glucose	2.53 (1.90, 3.35)	1.58 (0.73, 3.19)	1.60 (0.73, 3.51)
Serum uric acid	1.37 (1.05, 1.77)	1.04 (0.54, 2.18)	1.31 (0.59, 2.87)
Hematocrit	1.32 (1.02, 1.70)	0.88 (0.51, 1.48)	1.50 (0.83, 2.70)
Lifetime smoking	2.20 (1.85, 2.61)	2.26 (0.65, 7.44)	0.97 (0.30, 3.30)
Alcohol intake	0.61 (0.37, 0.99)	0.57 (0.21, 1.47)	0.93 (0.31, 2.72)

*All risk factors (except age) were adjusted for age alone.
危険因子はすべて（年齢は除く）年齢のみ訂正した．

†Relative risk per decade. 10年当たりの相対危険度．

TABLE 5 INTERQUARTILE RELATIVE RISKS OF FATAL CORONARY HEART DISEASE FOR SELECTED RISK FACTORS AND COHORT RELATIVE RISK IN MULTIVARIATE LIFE TABLE REGRESSION USING COMBINED POPULATION OF JAPANESE MEN IN JAPAN AND HAWAII, 1965-80

表5　日本及びハワイの日本人男性を合計した集団を用いた多変量生命表回帰分析における危険因子の致死性 CHD 四分位数間相対危険度及びコホート相対危険度，1965－80年

Risk factor*	Interquartile relative risk	p-values for difference from unity
Age†	1.64	0.001
Systolic blood pressure	1.96	0.0001
Body mass index	0.96	>0.10
Serum cholesterol	1.39	0.001
Serum triglyceride	1.24	>0.10
Serum uric acid	1.20	0.09
Serum glucose	2.25	0.0001
Hematocrit	0.91	>0.10
Lifetime smoking	1.97	0.001
Alcohol intake	0.54	0.001
Relative risk (Hawaii/Japan)‡	1.17	>0.10

*Adjusted for age and all other risk factors together
年齢及びその他すべての危険因子合わせて訂正した．

†Relative risk per decade
10年当たりの相対危険度．

‡Cohort relative risk after adjusting for age and all other risk factors
年齢及びその他すべての危険因子を訂正した後のコホート相対危険度．

DISCUSSION

One of the major purposes of the present study was to compare CHD mortality rates among Japanese men living in Japan and Hawaii based on the 12-year follow-up data using comparable methods of case ascertainment.

Earlier reports from the NI-HON-SAN Study demonstrated that Japanese men in Hawaii were more westernized in their biological and life-style characteristics than those in Japan[10] and that CHD mortality,[14] prevalence,[15] and incidence[7] rates and grades of atherosclerosis[16] were higher in Hawaii than in Japan.

In the present study based on the 12-year follow-up data we found that the mortality rate of CHD was about 40% higher in Hawaii than in Japan, with the 95% confidence limits: 0.87, 2.29 (p=0.15). This result is consistent with the earlier report which demonstrated a twofold difference (p<0.01) in the incidence of definite CHD (nonfatal MI + fatal CHD) which was higher in Hawaii than in Japan.[7]

考　察

今回の調査の主要目的の一つは，比較可能な症例確認法を用い，12年間の追跡調査データに基づき，日本及びハワイに在住する日本人男性の CHD 死亡率を比較することであった．

NI-HON-SAN 調査の初期の報告では，ハワイ在住の日本人男性の方が日本在住の日本人男性よりも生物学的にも生活様式においても，より西欧化していたこと，[10] また，CHD 死亡率，[14] 罹患率 [15] 及び発生率 [7] 並びにアテローム性動脈硬化症の進行度 [16] は日本よりもハワイの方が高いことが示された．

12年間の追跡調査資料に基づく今回の調査において，CHD 死亡率は日本よりもハワイの方が約40％高いことが分かり，95％信頼限界は 0.87，2.29（p＝0.15）であった．この結果は，確実な CHD（非致死性 MI＋致死性 CHD）の発生率において日本よりもハワイの方が高く，その差は2倍（p＜0.01）であることを示した初期の報告と一致している．[7]

If the smaller difference in CHD rate between the two cohorts in the present study as compared with the earlier studies is real, it may be attributed to several factors. First, in the earlier study both nonfatal MI and fatal CHD cases were included, while in the present study nonfatal MI cases were excluded because of different methods of case ascertainment. Looking at the development of new CHD by year of follow-up, the incidence rates of both nonfatal MI and fatal CHD tended to be much lower in Japan than in Hawaii during the first few years of follow-up. This trend of a particularly low incidence rate of CHD in Japan early in the study period may be responsible for the greater Hawaii-Japan difference in the earlier report.

Secondly, the criteria for fatal CHD employed in the present study were somewhat different from those in the earlier study. For example, sudden unexpected deaths within three hours of onset were included in the earlier study, while no such deaths were accepted unless there were clear evidence of acute coronary events (chest pain, ECG changes, or enzyme elevation) in the present study. Furthermore, some other categories of possible fatal CHD were excluded in the present study as described in the methods section. However, even if all these possible cases had been included, there would have been no significant difference in the CHD mortality rate between Japan and Hawaii. Instead, the difference became smaller: total numbers of excluded cases of possible fatal CHD were 26 in Japan and 96 in Hawaii in contrast to the numbers of accepted cases (20 in Japan and 123 in Hawaii).

Thirdly, it may be hypothesized that during the course of 12 years of follow-up rapid westernization of diet and other life-style characteristics in Japan may have increased the risk of CHD in Japan, resulting in the reduction of difference in CHD incidence and mortality between the two cohorts. However, this hypothesis is not substantiated by analysis of secular trends in the incidence rates of CHD which have shown little change in either mortality or incidence of CHD during the study period in both places.[17-19]

In regard to the relationship between CHD and risk factors, there was a general trend for the interquartile relative risks (75th/25th percentile) calculated from the life table regression to be similar between the two cohorts for all risk factors studied. In

初期の調査と比較して今回の調査で二つのコホート間のCHD死亡率の差が小さいことが事実であれば，それは幾つかの要因によるものと思われる．まず，初期の調査では非致死性MI症例及び致死性CHD症例のいずれも対象としていたが，今回の調査では，症例確認法が異なるため非致死性MI症例は除外した．追跡調査年別に新しいCHDの発生状況をみると，非致死性MI及び致死性CHDの発生率は追跡調査の最初の数年間ハワイよりも日本の方がかなり低い傾向にあった．このように調査期間の初期に日本のCHD発生率が特に低い傾向を示したのは初期の報告のときの方がハワイと日本との差が大きかった理由かもしれない．

第二に，今回の調査で使用した致死性CHDの基準は初期の調査で使用した基準と若干異なった．例えば，発病後3時間以内の不慮の突然死は初期の調査では対象に含められていたが，今回の調査では急性虚血性疾患の明白な証拠（胸痛，ECG変化又は酵素増加）がない限りそのような死亡は含めなかった．更に，方法の項で述べたとおり不確実な致死性CHDのその他の幾つかのカテゴリーは今回の調査では除外した．しかし，たとえこれらの不確実な症例をすべて含めたとしても，日本とハワイのCHD死亡率の差は有意ではなかったであろう．それどころかその差は小さくなった．除外された不確実な致死性CHD症例の総数は日本で26例，ハワイで96例であったのに対し，認められた症例の数は日本20例，ハワイ123例であった．

第三に，12年間の追跡調査期間中に日本の食生活及びその他の生活様式の特性が急速に西欧化したため日本のCHD危険度が上昇し，その結果二つのコホート間のCHD発生率及び死亡率の差が縮小したという仮説が立てられるかもしれない．しかし，CHD発生率の経時的傾向の解析では，日本，ハワイ両地での調査期間中CHDの死亡率も発生率もほとんど変化していないことが示されており，この仮説を実証することはできない．[17-19]

CHDと危険因子との関係に関しては，生命表回帰分析から得た四分位数間相対危険度（75/25パーセンタイル）は，調査したすべての危険因子について二つのコホート間で同様であるという一般的傾向が認め

other words, there was no statistically significant difference in the effect of each risk factor upon CHD mortality, mainly due to the small sample size in Japan, although most of the risk factors showed a greater effect in Hawaii than in Japan.

The earlier study[8] reported that significant predictors of CHD incidence in both Japan and Hawaii were systolic blood pressure, serum cholesterol, relative weight, and age, and that their regression coefficients did not differ significantly between the two cohorts. When the risk function based on these factors in Japan was applied to Hawaii, the estimated CHD incidence thus obtained did not differ significantly from that actually observed in Hawaii. Although analytical techniques employed in the present study differ from those in the earlier study, similar results were obtained with respect to the relationship between fatal CHD and risk factors.

The higher mortality rates of CHD in Hawaii than in Japan are consistent with higher average levels of most risk factors in Hawaii. It is noteworthy that established risk factors for CHD such as blood pressure, serum cholesterol, glucose intolerance, cigarette smoking, and alcohol intake (inversely) were related to CHD similarly for indigenous Japanese men and for American Japanese men in Hawaii, although CHD occurs much less commonly in these Japanese men than in Caucasian males.

In conclusion, age-adjusted mortality rates of CHD during 12 years of follow-up, using strictly comparable methods of case ascertainment, was approximately 40% higher (not statistically significant) among Japanese American men in Hawaii than among indigenous Japanese men. The relationships between fatal CHD and various risk factors were generally similar in the two cohorts, and more than half of the difference in CHD mortality rate was attributed to different baseline levels of known risk factors between the two cohorts. The implication of these findings is that the low rate of CHD observed in Japan is a realistic goal for Japanese and possibly other populations elsewhere. However, the small sample size in Japan appears to weaken the definitiveness of the present study findings.

られた．言い換えれば，大部分の危険因子が日本よりもハワイの方で大きな影響を示したにもかかわらず，日本の集団の大きさが小さかったということが主な原因となって，各危険因子がCHD死亡率に及ぼす影響は，両地域間で統計的に有意に異ならなかった．

初期の調査[8]では，日本及びハワイのCHD発生の重要な予測因子は収縮期血圧，血清コレステロール，比体重及び年齢であること，またそれらの回帰係数は二つのコホート間で有意に異ならないことが報告された．日本におけるこれらの予測因子に基づく危険度関数をハワイに適用した場合，得られた推定CHD発生率はハワイで実際に観察された発生率と有意に異ならなかった．今回の調査で用いた解析方法は初期の調査で用いた方法と異なるが，致死性CHDと危険因子との関係については同様の結果が得られた．

日本よりもハワイの方がCHD死亡率が高いことはハワイの方が大部分の危険因子の平均レベルが高いことと一致している．CHDの発生率は白人男性よりも日本人男性の方が通常低いが，血圧，血清コレステロール，耐糖能，喫煙及びアルコール摂取量（逆相関）などの確定したCHD危険因子とCHDとの関係は日本の日本人男性とハワイの日系アメリカ人男性のいずれにおいても同様であったことは注目に値する．

結論として，厳密に比較できる症例確認法を用いて調べた12年間の追跡調査期間中の年齢訂正CHD死亡率は日本の日本人男性よりもハワイ在住の日系アメリカ人男性の方が約40％高かった（統計的に有意ではない）．致死性CHDと種々の危険因子との関係は二つのコホートで概して同様であったが，CHD死亡率の差異の半分以上は既知の危険因子の基準レベルが二つのコホート間で異なるためであった．これらの所見は，日本で観察された低いCHD死亡率が日本及び恐らく他国の集団にとっての現実的な目標であることを示している．しかし，日本の集団の規模が小さいことが今回の調査所見の確実性を弱めているように思われる．

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