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# Glucose Intolerance as Contributor to Noncommunicable Disease Morbidity and Mortality

## WHO Integrated Program for Community Health in Noncommunicable Diseases

**The World Health Organization (WHO) has considerable evidence that several interrelated factors (e.g., smoking, hypertension, cholesterol, and obesity) contribute to total mortality. Data are presented documenting that glucose intolerance is also a risk factor for total mortality, as well as for cancer and cardiovascular mortality. The Kaunas-Rotterdam Intervention Study, which documented glucose tolerance and mortality in a cohort of men, shows a linear increase in total mortality with increasing blood glucose levels. By use of multiple logistic regressions, glucose was shown to be a significant risk factor ($c$ = .2534, $t$ = 4.0) for total mortality. A paradigm is presented in which diabetes is placed as a disease and glucose intolerance as a risk factor within the total scheme for the development of noncommunicable diseases. The WHO action plan for integrated programs in noncommunicable diseases is discussed. The program expands on the experience gained by WHO investigators in community programs and proposes a cooperative effort globally in community-based programming. *Diabetes Care* 11:253–57, 1988**

Traditionally, major noncommunicable disease (NCD) prevention and control programs have been created as disease-specific entities despite growing evidence that several key factors related to prevention and control are common for some of these diseases. The World Health Organization (WHO) estimates that up to 90% of lung cancer cases and up to 25% of cardiovascular diseases are attributable to smoking tobacco (1). The interaction of diabetes and cigarette smoking increases cardiovascular mortality by 65% (2). Additionally, nutritional imbalance combined with decreased physical activity results in obesity, which contributes to diabetes, hypertension, coronary heart disease, and stroke (3–7).

Data have been published that relate total mortality to a set of conventional cardiovascular risk factors (i.e., smoking, hypertension, cholesterol, obesity; 8–10). Studies have also demonstrated that reduction of major risk factor levels (i.e., smoking, hypertension, cholesterol and total lipids, and obesity) is feasible and leads to a decrease in cardiovascular and total mortality (9,11,12).

## DIABETES AND ITS CONTRIBUTION TO ILL HEALTH

Non-insulin-dependent diabetes mellitus (NIDDM) is the disease of major concern in an integrated NCD program. Like cardiovascular disease, NIDDM occurs in relation to certain life-styles, the most obvious of which are obesity and rapid socioeconomic development. Table 1 documents the prevalence of diabetes in certain populations and the incidence in two well-studied groups. These studies document the effects of cultural change and obesity on the development of diabetes (13).

Thus, diabetes fits the developmental trend of other NCDs traditionally related to life-styles, e.g., hypertension, coronary heart disease, and certain cancers. For other NCDs, attempts have been made in primary prevention, i.e., prevention of the disease itself. Although the possibility of preventing NIDDM through efficient body mass control is unproven, good data exist for pre-

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**TABLE 1**
**Prevalence and incidence of NIDDM in certain populations determined by WHO criteria**

| Location/population | Age group (yr) | Rate (%) |
|---|---|---|
| Prevalence | | |
| Fiji Indians | 20+ | 13.5 |
| Indonesia | 15+ | 1.7 |
| Israel | 40–70 | 15.9 |
| Malta | 15+ | 7.7 |
| Mexican Americans (USA) | 25–64 | 17.0 |
| Nauru | 20+ | 24.3 |
| Pima Indians (USA) | 25+ | 25.5 |
| USA* | 20–74 | 6.9 |
| Incidence | | |
| Pima Indians (USA) | 15+ | 1.6/yr |
| Nauru | 20+ | 1.6/yr |

*Prevalence of diabetes ascertained either from medical records and use of antidiabetic preparations or from records of newly diagnosed diabetic subjects with venous plasma glucose ≥11.1 mM 2 h after standard 75-g oral glucose load. (From ref. 13.)

**TABLE 2**
**Costs of diabetes**

| |
|---|
| Mortality excessive by factor of 2–3 |
| Heart disease and stroke excessive by factor of 2–3 |
| Blindness 10 times more common than in general population |
| Gangrene and amputation ~20 times more common than in general population |
| Second leading cause of fatal kidney diseases |
| Other chronic disabilities (e.g., neuropathy, infections, and sexual dysfunction) |
| Hospitalization increased about twofold compared with age-matched elements of the general population |
| Direct costs to medical care system for professional time, drugs, and rehabilitative services (e.g., for blind diabetic people) and other services and materials |
| Other costs to society include costs of medical services, pensions, and loss in productivity and earnings due to both disability and premature death |
| Lifetime risk of diabetes 2–12% (variation by country) |

From ref. 15.

venting complications of the disease (secondary prevention; 14).

WHO has documented the burdens of diabetes to the person with diabetes and society as a whole (Table 2). Diabetes management and care consume a significant proportion of health resources. The total mortality in diabetic people greatly exceeds that of the general population; risk of cardiovascular diseases is increased two- to threefold. Complications absorb large proportions of health budgets (15).

## CONTRIBUTION OF GLUCOSE INTOLERANCE TO TOTAL MORTALITY

WHO coordinated the Kaunas (USSR) population study, known as the Kaunas-Rotterdam Intervention Study (KRIS). At initial screening, the study enrolled 2455 men, 45–59 yr of age at entry. The design and follow-up have been extensively documented (16). The cohort has been followed up for 10 yr through myocardial infarction, stroke, and mortality registers operating in Kaunas.

Although not a major variable of interest at the outset, glucose tolerance was measured by standard WHO criteria with a 75-g load and a 2-h glucose level. The cause-specific mortality rates measured in quintiles of blood glucose values have a tendency to increase with increasing blood glucose values; the all-cause mortality rates, both in blood glucose quintiles and by absolute glucose values distribution, have a strong positive linear relationship with blood glucose level (Table 3; Fig. 1). Interestingly, the mortality for cancer and the expected mortality for cardiovascular diseases show this increasing relationship with increasing blood glucose quintiles. As expected, the relationship does not follow for traumas, perhaps reinforcing the relationship between the above-mentioned causes and blood glucose levels.

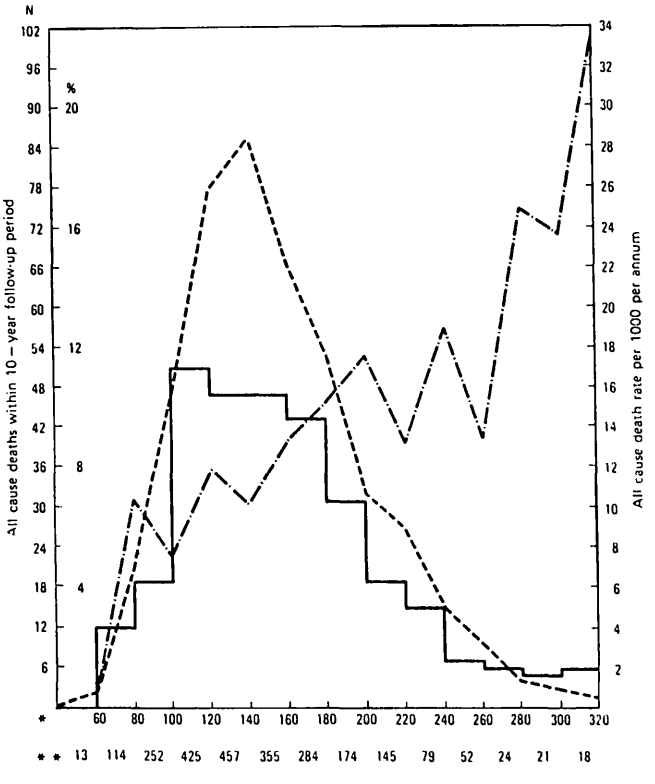


**FIG. 1. Relative risk and absolute risk of all causes of death in relation to blood glucose level in male population of Kaunas, USSR, from Kaunas-Rotterdam Intervention Study 10-yr follow-up. Blood glucose intervals (*) in milligrams per deciliter, and total numbers at risk in each blood glucose interval (**) are indicated. Frequency distribution in percent of average blood glucose (*dashed line*), frequency distribution of all causes of death in numbers by blood glucose level over 10-yr follow-up (*solid line*), and relative risk of all causes of death by blood glucose level per 1000 at risk per year (*dotted and dashed line*) are shown.**

**TABLE 3**
**Cause-specific and total mortality in entire initially screened Kaunas male population sample within 10-yr follow-up period by level of glucose at entry**

| | Quintiles of blood glucose level | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | Total | |
| Disease outcome | *n* | % | *n* | % | *n* | % | *n* | % | *n* | % | *n* | % |
| Coronary heart disease | 12 | 2.50 | 6 | 1.20 | 15 | 3.22 | 16 | 3.34 | 20 | 4.09 | 69 | 2.86 |
| Other cardiovascular disease | 4 | 0.83 | 5 | 1.00 | 7 | 1.50 | 12 | 2.51 | 17 | 3.48 | 45 | 1.86 |
| All cardiovascular disease | 16 | 3.33 | 11 | 2.20 | 22 | 4.72 | 28 | 5.85 | 37 | 7.57 | 114 | 4.72 |
| Cancer | 14 | 2.92 | 12 | 2.40 | 15 | 3.22 | 21 | 4.38 | 21 | 4.29 | 83 | 3.44 |
| Other diseases | 5 | 1.04 | 11 | 2.20 | 10 | 2.15 | 9 | 1.88 | 14 | 2.86 | 49 | 2.03 |
| Trauma | 9 | 1.87 | 12 | 2.40 | 12 | 2.58 | 10 | 2.09 | 10 | 2.04 | 53 | 2.20 |
| All causes | 45 | 9.38 | 48 | 9.62 | 64 | 13.73 | 68 | 14.20 | 83 | 16.97 | 308 | 12.76 |

## CONCEPT OF MULTIPLE RISK FACTORS AND THEIR INTERRELATIONSHIP

KRIS was primarily designed to study methodological aspects in designing community intervention programs for the prevention of cardiovascular diseases. However, looking at the totality of health problems in this particular population, as expressed by mortality indices within a 10-yr follow-up period, it became clear that coronary heart disease deaths accounted for only 21.8% of the total mortality. Utilizing multiple logistic regressions for risk factors usually considered traditional for cardiovascular disease, standardized multiple logistic function coefficients and *t* values were generated (Table 4). Age, systolic blood pressure, cholesterol, and smoking were significantly related to the incidence of fatal coronary heart disease. Significant contributors to other cardiovascular mortality were age, systolic blood pressure, cholesterol (inversely), and glucose tolerance. Cancer deaths were significantly related to age and smoking; deaths caused by other diseases were related to cholesterol (inversely) and glucose intolerance. The significant contributors to total mortality were age, smoking, and glucose intolerance.

The data can also be expressed as a paradigm that links smoking, blood pressure, cholesterol, obesity, and glucose levels as risk factors for the development of major NCDs and their complications (Fig. 2). The data presented suggest the inclusion of glucose intolerance as a risk factor for more than just diabetes mellitus; therefore, glucose fits into the whole scheme for NCD prevention and control.

The major prevention and control activities for diabetes mellitus relate to the prevention of complications of the disease. These complications primarily affect the vascular system. This argument for including risk factors traditionally considered for cardiovascular programs in the diabetes aspect of an NCD program seems very logical.

**TABLE 4**
**Standardized multiple logistic function coefficients (c) and *t* values for selected risk factors predicting cause-specific and total mortality within 10-yr follow-up period**

| | Coronary heart disease | | Other cardiovascular disease | | Cancers | | Other diseases | | Accidents | | All causes of death | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Risk factors | c | *t* | c | *t* | c | *t* | c | *t* | c | *t* | c | *t* |
| Age | .3908 | 2.3 | .5141 | 3.2 | .5598 | 4.73 | .2772 | 1.8 | .0301 | 0.2 | .4417 | 6.8 |
| Systolic blood pressure | .4781 | 2.1 | .6226 | 2.8 | −.0217 | −0.1 | −.2504 | −1.2 | −.0857 | −0.4 | .1518 | 1.7 |
| Diastolic blood pressure | −.1623 | −0.7 | .1043 | 0.5 | −.0652 | −0.4 | .2778 | 1.3 | .2426 | 1.2 | .0765 | 0.8 |
| Cholesterol | .8367 | 5.0 | −.4087 | −2.6 | .0952 | 0.8 | −.4550 | −3.1 | −.0475 | −0.3 | .0077 | 0.1 |
| Glucose | .0321 | 0.2 | .5887 | 3.7 | .1822 | 1.6 | .3667 | 2.5 | −.0239 | −0.2 | .2534 | 4.0 |
| Body mass index | .1550 | 0.9 | −.0276 | −0.2 | .0247 | 0.2 | −.0733 | −0.5 | −.2421 | −1.6 | −.0440 | −0.6 |
| Height | −.0086 | −0.1 | −.1343 | −0.8 | .0308 | 0.3 | −.1249 | −0.8 | .0340 | 0.2 | −.0738 | 1.2 |
| Smoking | .5321 | 3.1 | .0263 | 0.2 | .5183 | 4.3 | −.0191 | −0.8 | .5246 | 3.6 | .3546 | 5.4 |
| Education | .0583 | 0.3 | −.2830 | −1.5 | .2169 | 1.5 | .0915 | 0.5 | −.2744 | −1.6 | −.0168 | 0.2 |
| Occupation | −.0204 | −0.1 | .0061 | 0.0 | −.3427 | −2.4 | −.1504 | −0.8 | .1720 | 1.0 | −.0756 | −1.0 |
| Alcohol | .0652 | 0.4 | −.2299 | −1.46 | −.0274 | −0.2 | .1747 | 1.2 | .1684 | 1.0 | .0304 | 0.5 |

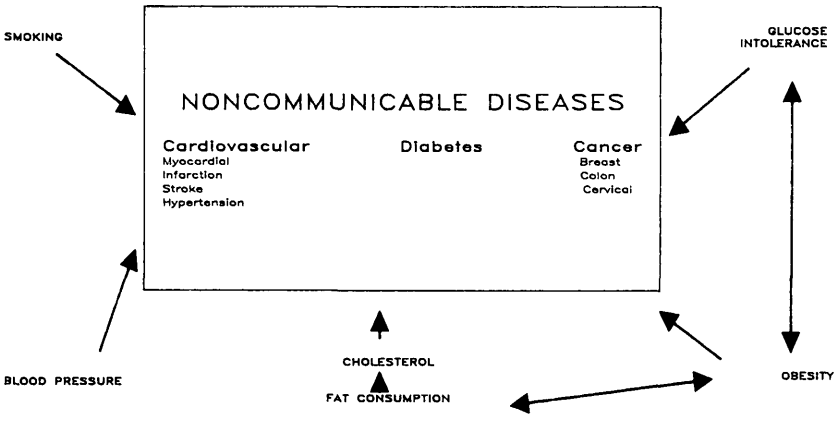


**FIG. 2. Paradigm for risk factors and their relationships to development of noncommunicable diseases.**

The WHO integrated program for NCDs is based on the above-listed data and tenets. This conceptual thinking provides a useful framework for further research needed to prove the hypothesis of life-style influences on major chronic disease morbidity and mortality patterns. The Alameda County Study is similar to KRIS in that the data suggest that simple measurement of certain characteristics creates the possibility of identifying a segment of the population that is at increased risk for both cause-specific and total mortality (8).

Moreover, the Alameda County Study points out common risk factors for NCDs and their complications and suggests the potential benefits of integrated management of these conditions. Programs should be moved from a categorical disease approach to a more integrated approach, as suggested by groups of WHO investigators (16,17). Further research is definitely needed, but studies in North Karelia and other areas have given the indication that health intervention programs covering total communities are feasible (9,12).

## WHO ACTION AT GLOBAL, REGIONAL, AND NATIONAL LEVELS

The concept of integration is attractive from the logistical, economic, and, to a large extent, scientific points of view but requires further development and operational testing because there is a lack of experience in implementing such integrated programs (17–22). On the other hand, several proven program components, such as certain diabetes control activities, smoking control, or high blood pressure control, do not require substantial further research and make implementation on a national level desirable.

One of the most important tasks for WHO is to continue its global advocacy role in introducing this innovative approach. For this purpose, WHO believes a regular review of the state of the art of existing knowledge in the causation of a group of major NCDs, effective health intervention technologies, dissemination of this information to those interested, and the exchange of experiences would contribute considerably to fulfill the global advocacy role.

There is a clear need for more specific research to be carried out in a cooperative manner. The aim of this research is evaluation of these proposed integrated programs. WHO intends to have a core group of countries and centers representing all WHO regions work together with a standard protocol. The protocol should contain the necessary minimum requirements for program planning and design, core information collection, and program evaluation. This cooperative activity should provide ongoing data to aid WHO as it continues its role of helping reduce the burden of NCDs on both the individual and society.

Community-based prevention and control programs can logically be linked in an integrated NCD program. Disease-specific data and expertise is necessary as programs evolve, but current morbidity and mortality rates demand action.

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