The Duration of Unrecognized Diabetes Mellitus

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SUMMARY

If the age specific prevalence rates for known and unrecognized diabetics are known, deduction can be made of the rates at which cases are moving in and out of these categories and, therefore, the average time spent in each category. For example, if between the age of forty and fifty the number of known diabetics in a population increased from 300 to 600, then the increase (300 over ten years) indicates that previously unrecognized diabetics have become recognized at an average rate of thirty per year. Similarly, if the number of unrecognized diabetics has increased from 400 to 900, the unrecognized group has been increasing at an average rate of fifty per year. If the rate at which death has been removing persons from each group is known, it is possible to form a theoretical model and calculate approximately how long a person is likely to remain in the unrecognized category.

When the calculations are carried through, it appears that the average length of time spent in the unrecognized category is of the order of ten to twelve years. Unfortunately, some of the steps in the calculations are based on unknown factors, and in assuming arbitrary values for these factors, there will be some error introduced into the final estimate. Since the method of calculation may be of interest and value, however, the argument will be presented in detail.

When a new case of diabetes mellitus is diagnosed, it is not known how long the disease has been present. In this paper an attempt is made to deduce from epidemiological data the average length of time between development of impaired carbohydrate tolerance and diagnosis. DIABETES *15*: **160-63, March, 1966.**

Detailed Argument

The prevalence rates employed are those found in the 1962 survey of the British College of General Practice in Birmingham.[1] This survey is used because of its large size (18,500 persons tested) and because of the very thorough coverage (over 95 per cent) of the local population. The screening method employed was the postprandial testing of urine by the glucose oxidase method. Diabetes was diagnosed if after 50 gm. of glucose orally the capillary blood sugar level exceeded a peak of 180 mg. per 100 ml. and was above 120 mg. per 100 ml. at two hours.

Figures 1 and 2 show the age specific prevalence rates obtained in the Birmingham survey.[1,6] The regression lines have been obtained by the method of least squares, with weighting of the points according to the number of persons in each age group. Persons under the age of thirty have not been included in the calculations.

It will be noted that the age specific prevalence rates approximate straight lines on a linear scale in the case of the unrecognized cases and on a semilogarithmic scale in the case of the known diabetics.

The regression equations are:

Known cases:

Log Rate (per thousand) = 0.945 + .0273 (Age—55 yrs.).

Unrecognized cases:

Rate (per thousand) = 11.96 + 0.497 (Age —55 yrs.).

For age forty and age fifty, the estimated prevalence rates are:

Age forty:
Known 3.44 per thousand.
Unrecognized 4.51 per thousand.

Age fifty:
Known 6.44 per thousand.
Unrecognized 9.48 per thousand.

For convenience in handling these figures let us apply them to a very large group and suppose that we can survey 100,000 people, all in their fortieth year of life. We should then find that there are 344 known and 451 unrecognized cases of diabetes. At the end of ten years if no deaths had occurred, there would be 644 known and 948 unrecognized cases (prevalence rates at age fifty). In fact, however, the original group of 100,000 will be smaller at the end of ten years due to deaths from all causes. On the basis of the death rates for England and Wales[5] for the years 1950-1960, we

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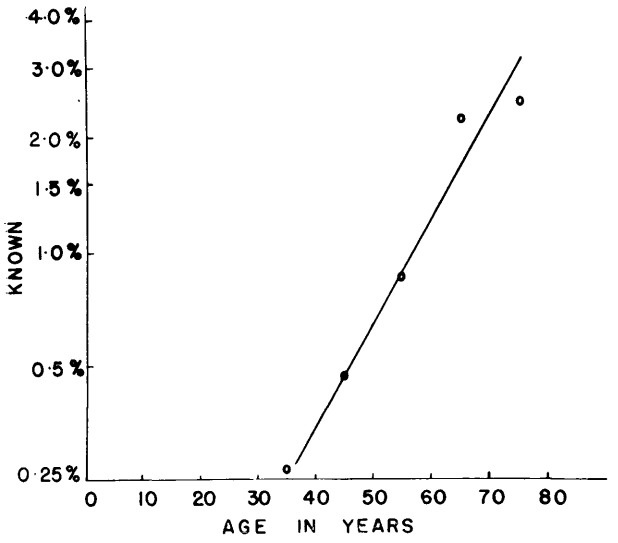

FIG. 1. Age specific prevalence rates for known diabetics. The regression line is calculated on the rates found in persons over thirty years of age.

calculate that there will have been about 3,600 deaths, so that the group will actually number about 96,400. This means that the prevalence rates for the 50-year old already quoted represent 620 known and 914 unrecognized in a group of 96,400.

Diagrammatically the situation at the beginning and end of the decade can be represented as in figure 3 (a) and (c). The shift from one category to another during the ten years is indicated in figure 3 (b). It is evident that the total deaths over the ten years is the sum of DU, DK and DN, so that DU + DK + DN = 3,600 (where DU, DK, and DN are the number of deaths which have occurred among the unrecognized, the known and the nondiabetic groups).

If the death rate among the known diabetics was the same as for the other categories, the number of known diabetics dying during the ten years would be in the same ratio as the size of the two groups. At the beginning of the period this is 344/100,000, but the ratio changes gradually during the decade until at the age of fifty it is 620/96,400. Thus we can calculate the simple average of the diabetics as 482, and of the total population as 98,200. The rates are changing in a logarithmic fashion, however, the appearance of diabetics becoming more frequent and the size of the total population shrinking more rapidly as the years go by. It is, therefore, more accurate to use the logarithmic means, and these are found to be 470 and 97,700. Since 3,600 deaths have occurred in an average population of 97,700, we would expect the number of deaths in a group of 470 to be (470 ÷ 97,700) × 3,600 = 17.3.

This figure of 17.3 is based on the assumption that the death rate among diabetics is no higher than that among the general population but actually Joslin[4] found that the death rate among diabetics was 3.1 times higher than normal at the age of 45. (The effect of

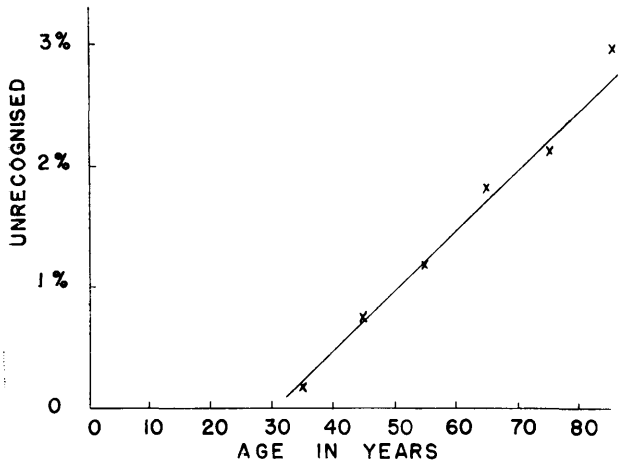

FIG. 2. Age specific prevalence rates for unrecognized diabetics. The regression line is calculated on the rates found in persons over thirty years of age.

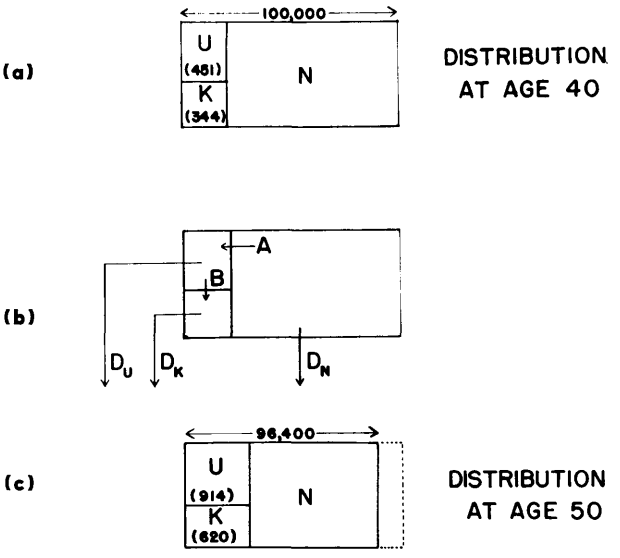

FIG. 3. Diagrammatic representation of the changing distribution of diabetics (known and unrecognized) between the ages of forty and fifty years. During the ten years the deaths from each category are DU (unrecognized), DK (known), and DN (nondiabetic). The number of nondiabetics becoming diabetic (initially unrecognized) is represented as A, and the number of unrecognized diabetics becoming known is represented as B.

TABLE 1

Birmingham survey
(1961)

Age group	Number tested	Number diabetics	New diabetics
0-9	2,654	0	1
10-19	2,737	6	3
20-29	2,092	2	2
30-39	2,573	6	4
40-49	2,558	12	19
50-59	2,727	24	32
60-69	1,614	36	29
70-79	1,136	28	24
80-89	422	5	13
90-99	19	0	0
TOTAL	18,532	119	127

altering the size of this factor will be examined later in the discussion.) With this factor the number of deaths among the known diabetics will be 54 (53.7).

By applying the same calculations to the group of unrecognized diabetics and using a factor of 2.0 instead of 3.1 (see Discussion), the number of deaths among the unrecognized diabetics (DU) is found to be 50 (50.2).

Reference to figure 3(b) shows that the increase in the number of known diabetics over the ten-year period is the resultant of the addition of new cases (B) and the losses through deaths (DK). Thus

$$K50 - K40 = B - DK$$

$$\text{or } B = K50 - K40 + DK$$

(where K50 is the number of known cases at age fifty, etc.).

Since K50 is 620, K40 is 344 and DK is 54, B is calculated as 330.

Thus, 330 previously unrecognized diabetics have become recognized during the ten-year period, an average of thirty-three persons each year.

Since there were 451 unrecognized cases at the start of the decade, of whom fifty have died, and *if no new cases entered this category,* it would take 401 ÷ 33, or 12.2 yrs. for the survivors to become recognized, and the mean length of time spent in the unrecognized phase would be half this, or 6.1 yrs.

To this figure must be added two corrections: First, the length of time spent by persons in the unrecognized category before the age of forty must be considered. As a first approximation, one can say that the length of time spent before the age of forty will be the same as that spent after the age of forty. The reasoning is as follows: Let us suppose that there are ten persons aged forty who have unrecognized diabetes, that each of them spends ten years in the unrecognized category, and that they become recognized at one-year intervals. Five of the ten will have become recognized in five years, so that this is the mean length of time spent in the unrecognized category, *after the age of forty.* The actual length of time spent in this category was originally stated, however, as ten years, so that it is necessary to double the apparent duration to arrive at a true figure for the total duration of this phase. Similarly, if we consider groups of people instead of single individuals, the apparent length of the unrecognized phase must be doubled to arrive at the true figure.

The second correction which should be made concerns the failure to recognize that new cases enter the category. The pool of unrecognized diabetics is constantly being diluted by new cases, and some of these may spend a very short time in this category before moving into the known category so that the *original* group of 401 will be reduced by less than thirty-three per year, resulting in a longer time for them all to become recognized. Unfortunately, there is no way of knowing the shape of the frequency distribution curve for lengths of time spent in the unrecognized phase, so that we are only able to say that the average time spent in the unrecognized phase is something *greater* than 12.2 yrs.

Similar calculations can be used for examining the pattern of diabetes in other decades of life. For the decade 50 to 60 yrs., the mean time spent in the unrecognized phase appears to be at least 10.0 yrs. and for the decade 60 to 70, to be 3.3 yrs.

DISCUSSION

Several assumptions have been made in the course of the calculations which deserve to be examined more closely.

First, it is assumed that the prevalence rates found are static and that, for example, the prevalence rates found for age fifty this year will be the same as that found for age fifty in ten years' time. While this assumption probably is not entirely justified, it seems reasonable to suppose that changes in prevalence rates will be occurring slowly, and that any error introduced by this assumption will be of small magnitude.

Second, the calculation of expected deaths among diabetics during the ten-year period is based on assumptions which, if false, may have a substantial effect on the calculations, particularly in the older age groups. The factors used are based on the experience of Joslin

around 1950, and it may well be argued that improved treatment will have reduced this factor by the present day.

Similarly, the assumption that the death rate for unrecognized diabetics is twice that of the nondiabetic population is also open to question. On the one hand, the fact that the diabetes is unrecognized should mean that these individuals are at greater risk than those in whom the disease is known and (presumably) under control. On the other hand, the fact that the disease remains unrecognized may imply that it is not of such severity and, therefore, the death rate should tend to be lower than in the known group. On the whole, it seems reasonable to favor this latter view and to take a factor slightly lower than that used for the known group. For this reason a factor of 2 has been used. If we were to take the position of assuming no excess of deaths in either the known or the unrecognized groups, the figures become:

Decade 40 — 50: 14.7 (previously 12.2 yrs.)
Decade 50 — 60: 15.4 (previously 10.0 yrs.)
Decade 60 — 70: 10.2 (previously 3.3 yrs.)

It will be noted that the effect of changing the death rate factors is comparatively small in the 40- to 50-yr. age group but becomes quite large in the older age groups. Accordingly, it is not possible to say with certainty that the mean duration becomes less with advancing age, since the apparent reduction may be entirely due to errors introduced by false assumptions about the death rate among the diabetic groups at different ages. As far as age groups under forty are concerned, the occurrence of unrecognized diabetes is so small below the age of thirty (less than 0.1 per cent) that no valid age specific prevalence rates can be calculated and, therefore, no estimate of duration can be made.

A third point to be discussed is whether the prevalence rates used are in fact reliable estimates of the true prevalence of known and unrecognized diabetes. It is of interest to consider the effect on the calculations of using the much higher rates of unrecognized diabetics found in some recent surveys which used a 50 gm. dose of glucose followed by a blood sugar reading at two hours as the *screening* test.[2,3] Under these circumstances the number of unrecognized diabetics was found to be very high (an over-all figure of roughly 10 per cent as against 1 per cent). If these prevalence rates were to be used in the calculations, the average duration is found to be in the order of 40 to 50 yrs.—in other words, the majority of cases would never be discovered during their lifetime. It is important to bear in mind, however, that the majority of these cases are borderline diabetics and that almost all the "florid" cases (needing active treatment) will be discovered on postprandial urine testing.

CONCLUSION

From the findings of the 1962 Birmingham diabetic survey, it would appear that for persons in their forties and fifties the mean length of time spent between the appearance of impaired carbohydrate tolerance and the time of diagnosis of diabetes is at least ten to twelve years.

ACKNOWLEDGMENT

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