Time trends in mortality associated with depression: findings from the Stirling County study

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Time Trends in Mortality Associated with Depression: Findings from the Stirling County Study

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Abstract

Objective—The question addressed is whether a mortality risk associated with depression in a 1952 representative sample of Stirling County adults changed in a new sample of 1970 and whether there was a change in relationships to cigarette smoking and alcoholism.

Method—Sample members were interviewed about depression and cigarette smoking. General physicians were interviewed by psychiatrists regarding alcoholism. Information about death as of December 31, 1992 was provided by Statistics Canada. Proportional hazards models were fitted in the two samples to assess the mortality risks associated with depression among men and women over 20 years of follow-up, and additionally among men with heavy smoking and alcoholism. Specific causes of death were investigated.

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Results—Hazard ratios representing the association between depression and premature death among men were 2.6 (95%CI 1.4 to 4.9) and 2.8 (95%CI 1.5 to 5.1) respectively in the 1952 and 1970 samples for the first 10 years of follow-up. Hazard ratios for women were 1.4 (95%CI 0.6 to 3.2) and 1.2 (95%CI 0.5 to 2.9). The risk associated with depression among men was independent of alcoholism and heavy smoking. Depression and alcoholism were significantly associated with death due to external causes and to circulatory disease; heavy smoking with malignant neoplasms.

Conclusion—The mortality associated with depression did not change over the period of 1952 to 1970. Depressed men experienced a significant mortality risk that was not matched among depressed women and also was not due to alcoholism and heavy smoking.

Keywords

Mortality Risks; Depression; Alcoholism; Smoking; Sex differences; Epidemiology; Time-trends; Proportional hazards models

INTRODUCTION

In 1974, Marc Lalonde, Minister of National Health and Welfare, observed that “Canada has a male mortality problem of great significance”.[1] Using the census of 1971, he pointed out that two men for every woman died in the prime of life (ages 15–70). In discussing this, he paid considerable attention to the mortality consequences of smoking, alcoholism, and suicide.

For numbers of years, reports have appeared showing an elevated mortality risk among psychiatric patients.[2–6] Reports based on psychiatric epidemiologic studies of general populations have also pointed to increased risk.[7–12] Among ongoing population studies, the Stirling County Study was the first to have used a contemporary method of gathering data and a diagnostic approach that is reasonably similar to current standards.[13–14] It is the only study with such historical depth that has followed the population by drawing new samples at different points of time as well as following individuals for re-interview or death information.

Based on the sample of adults selected in 1952 and interviewed concerning depression and anxiety at that time, four reports about mortality risk have been published. The first was based on follow-up in 1968 when the original search for re-interviews and death certificates began.[15] Depressed men showed a significantly elevated risk for all-cause mortality while depressed women did not. Pure anxiety did not appear to carry such a risk.

The second report was based on information about the full range of psychiatric disorders provided by general physicians about the same persons. All types of psychiatric disorders other than anxiety were associated with elevated risk.[16] The third report combined the sources of information and indicated that while agreement between self-report and physician-report was low, the disorders identified by the different sources exhibited similar mortality risk.[17]

In the fourth report, we expanded the purview to include the 40 years of follow-up from 1952 to 1992.[18] Based on hypotheses that depressed men might be heavy users of alcohol and cigarettes and that these substances might be more lethal than depression itself, we investigated the mortality risks associated with all three conditions.[19–22] We found that there was very little comorbidity among them in 1952 and that each carried an independent risk of approximately the same magnitude. Further, we found that depression and alcoholism had most effect in the earlier years of follow-up while that associated with smoking was more delayed.

This evidence suggested that depression might not have been fully recognized as a factor related to Canada's "male mortality problem". This is not to say that the Lalonde report failed to take official records of suicide into account but simply to say that information about depression in the general population was not then available.

In this paper we address a new question. Did the longevity consequences of depression remain constant over time or did they change? For this we compare information about the sample selected in 1952 with that of a new sample selected in 1970, the mortality experiences of which have not previously been reported. In order to see if comorbidity levels may have changed over the intervening years, we continue to focus on depression, alcoholism, and smoking.

MATERIALS AND METHODS

Site and Design

The research site is a county of 20,000 located in Atlantic Canada and named by the pseudonym "Stirling" to protect identity. The study combines two longitudinal strategies: 1.) repeated cross-sectional surveys conducted with new samples in 1952, 1970, and 1992; and 2.) follow-up of sample participants in order to re-interview survivors and collect information about decedents. In addition, information has been sought from two sources: 1.) interviews with sample members conducted in their homes by trained personnel who administered a structured interview schedule; and 2.) interviews carried out by psychiatrists with the county's general physicians about the sample members.

Sampling and Completion Rates

The sampling frame for 1952 selected heads of households while the 1970 sample consisted of a systematic sample drawn from a research census of individual residents 18 years of age and older. These procedures have been described in detail elsewhere.[23–24] We found that position in household was not related to the prevalence of depression or anxiety.[25]

While the Stirling Study as a whole includes three samples selected at different times, this report is limited to those of 1952 and 1970 because we do not yet have death information about the 1992 sample. However, this report draws on both self-report and physician-report information (Table 1). We selected a somewhat larger sample in 1970 than in 1952 (1369 compared to 1098). The completion rates ranged from 88% to 94% across the two sources of information and the two samples.

Data Analyzed

All variables used in the analysis characterize the subjects at time of interview. This means that the subjects were or were not experiencing the condition of interest at the baseline from which survival time is calculated.

Information about depression derived from the answers to direct and simply-stated questions asked in face-to-face interviews. A four-step computerized algorithm named DPAX (DP for depression and AX for anxiety) provides diagnostic classification.[26] The algorithm requires the "essential feature" of mood disturbance as well as the associated symptoms of disturbances in appetite, sleep, and energy, It establishes that the depression persisted for a minimum of one month and that it involved impairment in everyday functioning. While the algorithm identifies cases of depression that had recovered by the time of interview (as in a lifetime rate), the depressions selected here were "current" but most of them had lasted much longer than required. We have suggested that our methods represent the chronic

underpinning of what has been called “double depression” without identifying the episodic variations as well as do more recent methods.[27–29]

Evidence of cigarette smoking also came from the self-report interview in response to questions about the level of daily smoking. Because this report concerns mortality risk and because cigarette smoking was very common in these years, our variable identifies those who smoked “more than 20 cigarettes a day” compared to everyone else. We describe this as “heavy smoking”.

Alcoholism was covered in the interviews with general physicians. They were not asked to distinguish between abuse and dependence, and thus we use the term “alcoholism”. Cases of alcoholism were selected for this analysis if the interviewing psychiatrist indicated that he/she was highly confident that the description was indeed a case of alcoholism; that the time of occurrence was current; that the condition had persisted for at least a month; and that it was associated with everyday impairment.[16]

The information on mortality was mainly provided by record linkage searches conducted by Statistics Canada using the Generalized Record Linkage System as applied to the Canadian Mortality Data Base that records deaths in Canada from 1950 onwards.[30–32] Searches were also made through the United States and the United Kingdom as needed. As of the common closing date of December 31, 1992, death information was complete for the 1952 sample but vital status remained unknown for 4 persons of the 1970 sample.

Time Comparisons

Because earlier evidence indicated that depression and alcoholism had a more immediate mortality effect and cigarette smoking a more delayed one, the analysis for this paper used two follow-up periods: the first 10 years after interview, and the second 10 years after interview. For the first 10 years, all individuals of a given sample were included. For the second 10 years, only the individuals of that sample who had survived the first period were included.

However, the central comparison in this paper refers to the passage of historical time in population terms and its effect on the mortality risk among persons selected to represent the population in 1952 compared to those selected for 1970. The population perspective will be referred to as “historical time” or “1952/1970 comparisons” while the individual perspective will be referred to as “follow-up period” or “survival time”.

Statistical Procedures

The prevalence rates of depression, alcoholism, and heavy smoking are background for analysis of the mortality risk associated with each condition. Earlier we presented time-trend information about depression and cigarette smoking across all the three of the Stirling Study samples.[33–34] For this paper we used logistic regression in SAS procedure GENMOD to assess the effect of the 1952/1970 comparison on the prevalence of each of the conditions.[35] Each was considered to be the outcome variable in a regression where the predictors were sex, age, and historical time with 1952 as the reference. Pairwise interactions were also tested.

Assessment of mortality risk was based on proportional hazards models implemented in the SAS procedure PHREG.[36–37] Hazard ratios with 95% confidence intervals were calculated. Where depression was concerned, two approaches were used. First, we investigated the mortality risks associated with depression in the 1952 and 1970 samples separately; proportional hazards models stratified by sex within each sample were fitted in which time to death (or censoring) was the outcome variable. Second, we analyzed the mortality risks

associated with depression in both samples combined, in which we were able to test the interaction between depression and sample (1952 vs 1970), and thereby determine whether the association between depression and mortality changed over time. These procedures were carried out for both the first 10 year follow-up period and the second 10 year follow-up period.

The prevalence of alcoholism and heavy smoking among women in both samples was too low to warrant statistical analysis. Thus, the procedures for these conditions were limited to men. The same procedures were used as for depression. In addition, a model was fitted in which the three conditions were entered simultaneously. Because the latter controlled for the effects of each condition, the resulting hazard ratios could be compared to those based on the separate analyses. A model was then run in which pairwise interactions between the conditions were tested.

As a final step, proportional hazards models were fitted for each of four categories of specific causes: circulatory diseases; external causes (including suicide and accidental deaths); malignant neoplasms; and “other” causes. Such models were investigated separately for each of the three conditions. For each specific cause, the person-years for subjects who did not die from this cause were included in the analysis until being censored either at the end of the follow-up period or at the time of death from another cause.

RESULTS

In regard to the background features of prevalence, the passage of time from 1952 to 1970 did not change significantly the rates of any one of the three conditions (Table 2). The point prevalence of depression and alcoholism remained stable between 4% and 6% while the prevalence of heavy smoking was stable at a rate twice as high. Where depression was concerned, sex was not a significant predictor in these years but older persons, both men and women, had significantly higher prevalence than younger persons. The subject's age did not significantly influence the prevalence of alcoholism but this condition was predominantly and significantly a condition of men. Similarly, heavy smoking was significantly more common among men than women and also among younger people. The only significant interaction with historical time was an increase of heavy smoking among women by 1970.

In regard to the main question addressed, the pattern of mortality risk associated with depression did not change in the historical comparison of 1952 to 1970 (Table 3). Depressed men from both samples carried a significant risk for death over the first 10 years of follow-up as indicated by hazard ratios of 2.6 and 2.8 but the risk did not continue at this level into the second 10 years of follow-up (hazard ratios of 1.4 and 1.3). Depression-related change was not observed among women in either of the two periods of individual follow-up (hazard ratios of 1.4 and 1.3 in the first 10 years; and 0.9 and 1.0 in the second 10 years).

In regard to the three conditions considered for men, we found that depression was rarely accompanied by alcoholism or heavy smoking in the years of these samples. In 1952 one depressed man was alcoholic and two others were heavy smokers; in 1970 these numbers were five and seven respectively. The most common form of comorbidity was that between alcoholism and heavy smoking with 15 men in 1952 and 26 in 1970 exhibiting this combination.

Results of proportional hazards models based on analyzing the three conditions in combination indicated that the elevated 10-year mortality risk associated with depression adjusted for alcoholism and heavy smoking was significant for men in both the 1952 and 1970 samples (Table 4). Alcoholic men in the 1952 sample were also shown to carry a significant mortality risk in the first 10 year period. According to the analysis carried out for

alcoholism and heavy smoking separately, both were found to carry a significant mortality risk in the second 10-year period but when adjusted for the other conditions the risks were attenuated. One significant interaction indicated that the combination of depression and heavy smoking was associated with a substantially elevated risk. The broad confidence interval for this interaction reflected the unreliability of small numbers since it pertained to only two men.

From both samples, the most common specific cause of death for men was the category for circulatory diseases (72% of all male deaths in 1952 and 58% in 1970). The decline of circulatory deaths over time was offset by an increase in deaths due to malignant neoplasms. Death due to external causes remained the rarest specific cause. The division of all-cause mortality into these specific causes meant that the numbers were small and in some cases non-existent for a particular category. Because of this and because the effect of depression was seen mainly in the first 10 years, the cause-specific analysis is presented only for the first 10 years (Table 5).

Significant relationships were found for external causes relevant to depression (1970) and to alcoholism (1952). The hazard ratios were large but the confidence intervals broad. In the 1952 sample both depression and alcoholism were significantly related to death due to circulatory diseases but these associations were not statistically significant in the 1970 sample. Heavy smoking was related to malignant neoplasms in the 1970 sample. Both depression and alcoholism were significantly associated with “other” causes in the 1970 sample.

DISCUSSION

The most prominent finding of this report is that there were no significant changes in the profile of mortality risk associated with depression over the period of 1952 to 1970. Depressed men from both the 1952 and 1970 samples exhibited a significantly elevated mortality risk and depressed women did not. Further, the effect of depression among men continued to show little confounding due either to alcoholism or to cigarette smoking. Similarly, the prevalence of the three conditions and the levels of comorbidity among them exhibited relatively little change.

A question that arises from these findings is why there was so little change when health care has consistently improved. Universal medical service for Atlantic Canada was instituted in 1969.[38] In other words, this change in health delivery got started close to the time when members of the 1970 sample were selected and interviewed. While psychotropic medications became available in the 1950s, antidepressants were not commonly prescribed by the general physicians until after national health insurance was in place. Thus it is unlikely that members of the 1970 sample had benefitted from this form of improved health care at the time they were giving information about the conditions analyzed in this report. On the other hand, in the period following the interviews, some of the depressed subjects may have received a type of care that had not been available earlier. Such care may have reduced the mortality risk or retarded its effects in ways that our data do not convey. While we interviewed survivors of both the 1952 and 1970 samples at later points in time, this report stems from a single baseline interview with the decedents. In other words, we do not have information about the course of depression right up to the time of death.

The fact that depressed women of both the 1952 and 1970 samples did not exhibit the mortality risk that characterized men during these years raises still other questions. It can be hypothesized that part of the explanation for male mortality in this regard may be that suicide attempts among men are more likely to be fatal than those among women.[39–40] Such

an explanation would, however, account for only a small portion of the deaths because of the rarity of suicide compared to the prevalence of depression.

While the difference between depressed men and women in this regard needs further research, a factor that our earlier work suggests may be pertinent concerns the likelihood that men deny depression. We found that, over the years from 1952 to 1970, depressed men very rarely discussed depressive symptoms with a family physician while the opposite was true for women.[41] This suggests that denial of depression with its characteristic disinclination to look after oneself may be related to the mortality risk among men.

With regard to the specific causes of death, a limitation of our study is small numbers and even the absence of subjects when divided into four categories of specific causes. In addition, it is recognized that death certificates themselves are based on different levels of knowledge.[42] In some instances, the certifying physician has little background information about the decedent's mental and physical health status, a factor which may contribute to death due to circulatory diseases being the most common cause.

Despite these limitations, some of the findings about the causes of death were in line with general expectation. The well-known associations of depression and alcoholism with suicide were borne out in the link to external causes. This category also includes accidental deaths which are now recognized as sometimes being a masked form of suicide.[43–46] The fact that heavy smoking was associated with death due to malignant neoplasms fits with knowledge of the relationship between smoking and cancer.[47] Evidence that alcoholism was associated with death due to circulatory diseases is in line with evidence that heavy alcohol consumption can lead to accelerated atherosclerosis or deadly arrhythmia.[48–49]

Recently interest has grown in the possibility that depression may be related to abnormalities in the cardiovascular system.[50–54] We found that mortality risk for death due to circulatory diseases pertained significantly to depression as well as alcoholism. We suggest that these findings contribute to the need for further research about the relationship between cardiovascular malfunction and depression.

CONCLUSION

This report indicated that men and women differed in the mortality risk associated with depression and that the difference did not change from 1952 to 1970. Another aspect of history that has not changed is that women continue to live longer than men.[55] Canada still has a “male mortality problem”. Further Canada is not alone in experiencing this problem. It is almost a global phenomenon.[56]

It is well recognized that cigarette smoking and alcoholism reduce longevity among men. The evidence given here indicates that the problem also involves depression and that the risk is not limited to suicide and is not confounded by alcoholism and heavy smoking. The stability of heightened risk strengthens the need for further research aimed at understanding reasons that may explain the association.

The findings presented here stem from information gathered by interviewing representative subjects of a community population. Men in these samples responded to questions about moods and symptoms in the setting of an interview conducted by a professionally trained person. On the other hand, men infrequently indicated that they had talked to a doctor about such feelings. It is possible that male longevity would benefit if physicians more frequently took the initiative to ask about depressed mood among male patients since diminished value of life may be an especially strong hallmark of depression among men.

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Clinical Implications

- Increased proaction to identify depression among men
- Outreach to general physicians as front line caregivers for men
- Engage family members in encouraging depressed men to seek help

Limitations

- Sparse numbers especially for analysis of specific causes of death
- Mortality information not available for more recent period
- Recorded causes of death vary according to certifying physicians' knowledge of health status of decedents.

Table 1

Sources of information and number of subjects by sex and age for two representative samples of adults, one selected in 1952 and the other selected in 1970.

Subjects	1952 Sample Number Selected: 1098		1970 Sample Number selected: 1369	
	Self-Report (%)*	Physician-Report (%)*	Self-Report (%)*	Physician-Report (%)*
Men	456 (45)	469 (46)	598 (50)	588 (48)
<45	197 (43)	203 (43)	247 (41)	222 (38)
45 +	259 (57)	266 (57)	351 (59)	366 (62)
Women	547 (55)	560 (54)	605 (50)	631 (52)
<45	284 (52)	279 (50)	276 (46)	274 (43)
45 +	263 (48)	281 (50)	329 (54)	357 (57)
All Subjects	1003	1029	1203	1219

* Percentages show the proportions of men and women in the samples as wholes and those for age show the proportions <45 and 45+ within the given sex categories. Self-report provided information about depression and heavy smoking while physician-report gave information about alcoholism.

Table 2

Standardized prevalence rates per 100 at baseline for depression, alcoholism, and heavy cigarette smoking for two representative samples of adult men and women, one selected in 1952 and the other selected in 1970. *

	Depression		Alcoholism		Heavy Smoking	
	1952	**1970**	**1952**	**1970**	**1952**	**1970**
Men	4.3	5.5	8.0	11.2	21.5	20.9
<45 years	2.2	3.5	7.2	11.4	26.4	23.4
45+ years	6.2	7.3	8.8	11.1	16.6	18.4
Women	6.2	5.7	0.6	1.0	1.3	4.1
<45 years	4.8	3.8	0.8	0.7	1.6	5.5
45+ years	7.5	7.5	0.4	1.4	0.9	2.8
All subjects	5.2	5.6	4.3	6.1	11.4	12.5

* These rates have been standardized by the direct method using as the external standard the pooled population of all adults in the census of the county for 1952 and 1970 divided into three units representing the socioeconomic diversity of the county. The effects of historical time, sex, and age are conveyed in the following: Depression: time (p=0.78), sex (p=0.45), age (p<.002). Alcoholism: time (p=0.08), sex (p<.0001), age (p=0.87). Heavy smoking: time (p=0.30), sex (p=<.0001), age(p<.0001). One interaction was significant: increase of heavy smoking among women (p=0.02).

Table 3

Mortality risks associated with depression comparing men and women from two representative samples, one selected in 1952 and the other selected in 1970, showing results for the first 10 years and second 10 years of follow-up.*

	Men		Women	
	1952	**1970**	**1952**	**1970**
Depression	Hazard Ratio 95% CI	Hazard Ratio 95% CI	Hazard Ratio 95% CI	Hazard Ratio 95% CI
First 10 Years of follow-up	**2.6 1.4 to 4.9**	**2.8 1.5 to 5.1**	1.4 0.6 to 3.2	1.2 0.5 to 2.9
Second 10 Years of follow-up	1.4 0.5 to 3.9	1.3 0.5 to 3.1	0.9 0.4 to 2.3	1.0 0.4 to 2.4

* In analysis combining the samples of 1952 and 1970, historical time was not significant in either of the individual follow-up periods (first 10 years, men (p=0.25) and women (p=0.57): second 10 years: men (p=0.79) and women (p=0.79). The overall hazard ratio for depressed men in the first 10 years was 2.8 (1.8 to 4.4) and for depressed women 1.3 (0.7 to 2.4). Comparable figures for the second period were depressed men 1.2 (0.7 to 2.6) and depressed women 1.0 (0.5 to 1.8). No interactions were significant.

Table 4

Mortality risks associated with depression, alcoholism, and heavy smoking among men in two representative samples, one selected in 1952 and the other selected in 1970, showing results for a first 10 years and a second 10 years of follow-up.*

	1952 Sample Men		1970 Sample Men	
	First 10 Years of Follow-up	Second 10 Years of Follow-up	First 10 Years of Follow-up	Second 10 Years of Follow-up
	Hazard Ratio 95% CI	Hazard Ratio 95% CI	Hazard Ratio 95% CI	Hazard Ratio 95% CI
Depression	**2.6 1.3 to 5.3**	1.1 0.3 to 4.6	**2.8 1.4 to 5.8**	1.1 0.3 to 3.6
Alcoholism	**2.5 1.2 to 5.4**	1.4 0.3 to 5.9	1.7 0.8 to 3.7	0.9 0.4 to 2.2
Heavy Smoking	1.2 0.5 to 2.8	1.5 0.7 to 2.9	1.4 0.8 to 2.6	1.5 0.8 to 2.7

*The results derive from analysis in which all three conditions were entered simultaneously in order to provide adjustment for each, thus accounting for small differences regarding depression comparing this Table with Table 3. Also this analysis was based on subjects who had both self-report and physician-report information. Age as a continuous variable was a predictor variable. One interaction was significant at the p = 0.04 level (HR 10.6, 95%CI 1.1 to >10). The interaction pertained to two men who were both depressed and heavy smokers.

Table 5

Mortality risks for specific causes of death associated with depression, heavy smoking, and alcoholism among men in two representative samples, one selected in 1952 and the other selected in 1970, showing results for the first 10 years of follow-up.*

	Depression		Alcoholism		Heavy Smoking	
	1952	1970	1952	1970	1952	1970
Specific Causes of Death	**Hazard Ratio 95%CI**	**Hazard Ratio 95%CI**	**Hazard Ratio 95%CI**	**Hazard Ratio 95%CI**	**Hazard Ratio 95%CI**	**Hazard Ratio 95%CI**
Circulatory Diseases	**2.2** **1.0–4.9**	1.3 0.4–4.4	**2.2** **1.1–4.2**	1.7 0.8–3.5	0.7 0.3–19	0.8 0.4–1.8
External Causes		**10.5** **2.5–>10**	**21.5** **1.9–>10**	1.0 0.1–8.2		0.5 0.1–4.5
Malignant Neoplasms		0.9 0.1–6.5		1.9 0.6–5.6	1.3 0.2–>10	**3.4** **1.4–8.2**
Other	3.8 0.8–>10	**9.0** **3.0–>10**		**3.5** **1.3–9.9**	2.1 0.4–>10	1.5 0.5–4.6

*An empty cell means that there were no cases in this category or that the number of cases was so small that the statistical assessment was meaningless. The analysis controlled for age as a continuous variable. For the sample based on self-report (depression and heavy smoking) in 1952 the total number of men who died in the first 10 years of follow-up was 78 with 57 who died of circulatory diseases, 2 of external causes, 9 of malignant neoplasms and 10 of other causes. Comparable figures for physician report (alcoholism) in 1952 were: 86; 61; 3; 12; 10. For 1970, the self-report figures were: 120; 68; 8; 24; 20. For physician-report they were: 133: 77; 9; 26; 21.