# Decline in Mortality From Carcinoma of the Cervix in Beverly, Mass.

LESLIE LIPWORTH, M.B., Ch.B., HUMPHREY E. D. LLOYD, M.D., M.R.C.P., and ROBERT FIENBERG, M.D.

IN 1967 approximately 500,000 Massachusetts women underwent exfoliative cytological examination for uterine neoplasm (unpublished data from Massachusetts Laboratory Survey, Massachusetts Department of Public Health, 1968). These examinations entailed a large investment of time and effort of already overburdened physicians. The need to evaluate cervical cytology as a screening procedure with regard to death rates for cancer of the cervix has been documented recently (*1*, *2*). This paper discusses the decline in mortality from cancer of the cervix in Beverly, Mass.

A cervical cytology screening program began in Beverly in 1955. An investigation conducted by Fienberg and Lloyd showed that up to 1961, 62 cases of invasive and in situ cancer of the cervix had been detected at the Beverly Hospital laboratory among patients from Beverly and the surrounding towns. No decrease in the annual incidence of invasive cancer in the period 1955–61 was found when compared to the years preceding the screening program. Some cases of invasive cancer were discovered as a result of cytological screening, and discovery of these cases was associated with a decrease in the average age of patients with invasive cancers and with a larger number of patients with localized cancers.

An eventual decrease in the incidence of invasive cancers was, however, predicted in the written description of the investigation. In the years following 1961, we noted an increase in the proportion of patients with carcinoma in situ among those with newly diagnosed cancer of the cervix treated at the hospital. In 1967 this proportion was 90 percent or 18 patients with in situ cancer compared with two patients with invasive cancer of the cervix. A second study of the data to include the years following 1961 was therefore undertaken.

Investigation of the effect of cervical cytological screening is particularly appropriate in Beverly for the following reasons. All physicians in Beverly are associated with the Beverly Hospital, and the number of smears they sent to the pathology division increased from 24 in 1955 to more than 6,000 by 1966. Since 1958 cervical smear examination has been recommended for all women admitted to the hospital.

Detailed records extending back many years are maintained both in the hospital record room and in the pathology division. The hospital has had a tumor registry since 1908. In 1955–56 an average annual total of 122 new cases of malig-

*Dr. Lipworth is medical director of the statistical unit, bureau of chronic disease control, Massachusetts Department of Public Health. Dr. Lloyd is pathologist, and Dr. Fienberg is chief pathologist, pathology department, Beverly Hospital, Beverly, Mass.* *The statistical analysis was assisted by project PH 43–64–13 of the End Results Section of the National Cancer Institute, Public Health Service.*

nant disease of all sites among the 31,000 Beverly residents was reported to the hospital tumor registry—an annual incidence of nearly 3.9 per 1,000. Compared with an incidence of 3.4 in 1960 reported to the Connecticut registry, which has nearly complete coverage for that State (*3*), the reported incidence in Beverly indicates that a very high proportion of cancer patients in Beverly are known to the hospital.

## Method

*Collection and interpretation of smears.* Two vaginal smears were obtained from each patient: one specimen was taken from the vaginal pool and the other by scraping the region of the external uterine os with a wooden spatula. Immediate fixation of the wet smear in 95 percent ethanol was followed by routine hematoxylin and eosin staining. This technique is similar to that used in the cytology laboratory of the Mayo Clinic (*4*). One of three diagnoses was rendered:

1. Negative for neoplastic cells. This group included Papanicolaou classes I and II.
2. Positive for atypical cells. This was equivalent to Papanicolaou class III.
3. Positive for neoplastic cells. This group included Papanicolaou classes IV and V.

When smears were positive, a course of action was suggested to the referring physician. Cold-knife conization rather than punch biopsy of cervix was recommended for patients with positive smears. For patients with atypical cells we proposed repeated smears followed by biopsy if atypical cells persisted.

Analyses of doubtful and positive smears taken in 1955–61 showed that 29 percent of the doubtful and 74 percent of the positive smears were from patients later shown to have carcinoma in situ or invasive cancer of the cervix. The 74 percent of the smears classified as positive correspond roughly to Papanicolaou class IV (*4*). Since 1961 the proportion of positive smears from patients later shown to have carcinoma in situ has increased to more than 90 percent.

*Analysis.* The death records of all Beverly residents who died between January 1, 1955, and December 31, 1967, were searched to determine which deaths were due to carcinoma of the cervix. Beverly Hospital tumor registry data were examined to find the annual incidence in Beverly of both invasive carcinoma of the cervix and carcinoma in situ during the same period. The same sources of information were used to obtain incidence and mortality figures for cancer of the uterine body. Nosological separation of endocervical cancers, which were included among cervical cancers, from cancers of the uterine body was made by the pathologist, who discussed with the gynecologist all cases in which uncertainty arose.

Sections of specimens from all patients with invasive carcinoma of the cervix were reexamined microscopically, and those with limited invasion, defined as less than 1 low-power field beyond the epithelium, were separated from those with more extensive invasion.

The numbers of women given exfoliative cytological examinations of the cervix each year were obtained from the laboratory records. These records included those of all patients whose smears were processed at the hospital laboratory and were therefore not restricted to Beverly residents, as were the figures for deaths and new cases of uterine cancer. Random samples were taken from the laboratory data of patients who had exfoliative cytological examinations in 1960 and 1965. Fifty-five percent of the patients so examined in 1960 were Beverly residents, as were 56 percent in 1965. The average ages of these Beverly patients were 46 years in 1960 and 41 years in 1965.

The number of women who have undergone a total hysterectomy in the area covered by a study such as this is important. If this number is large enough, it could affect the incidence rate both for cancer of the uterine cervix and uterine body. Therefore, the hospital records were searched to obtain an estimate of the number of such women.

## Results

The chart shows the numbers of cytological examinations of the cervix in the Beverly Hospital laboratory since 1955, the incidence of new cases of invasive and in situ cancer of the cervix in Beverly residents as reported to the hospital tumor registry, and the numbers of Beverly residents whose deaths were attributed to cancer of the cervix. There were 16 deaths during the period of the first investigation, that

is, in the 7 years 1955–61. In the subsequent 6 years there were two deaths compared with 13.7 expected on the basis of the 16 deaths reported for the earlier period ($P<0.01$).

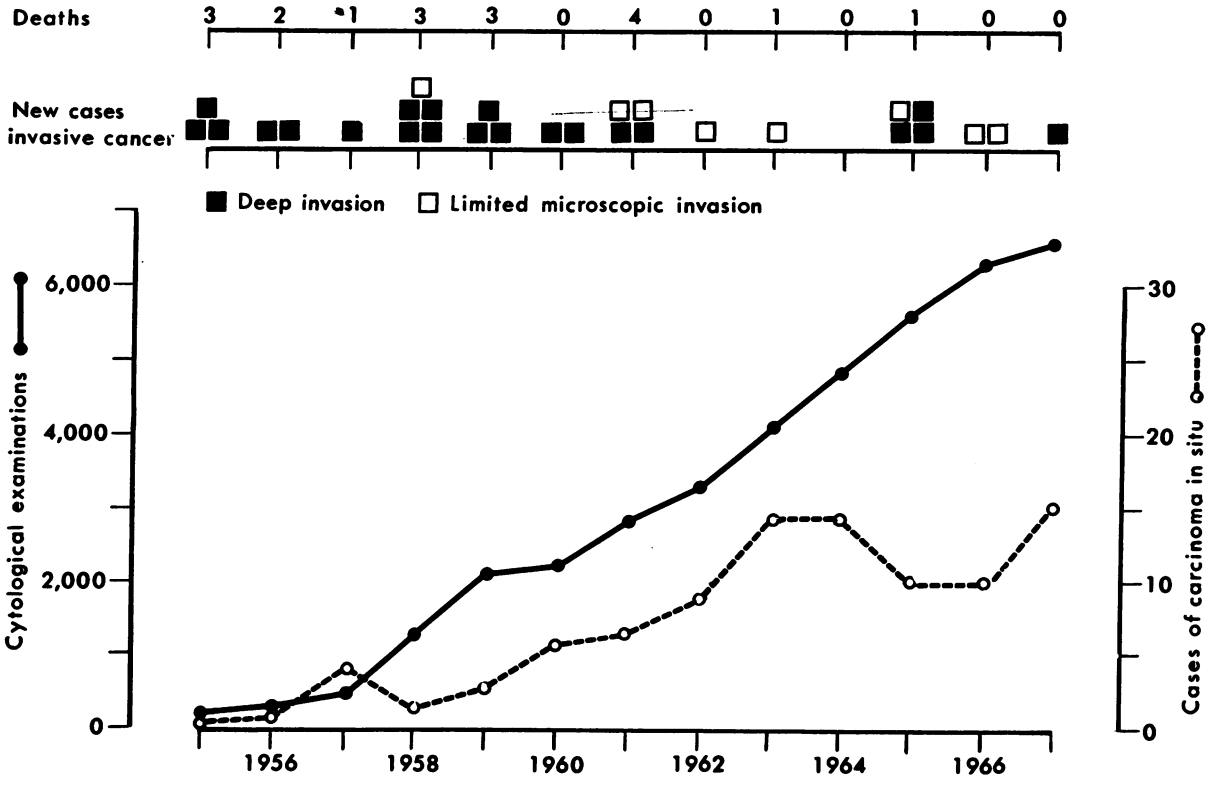
No adjustment was made for the population growth, which for Beverly women over 20 years of age increased from 10,800 in 1955 to 12,200 in 1965. According to the latest available figures for cervical cancer mortality in Massachusetts, an 8 percent decline in the age-adjusted mortality occurred in the period 1962–65 when compared with 1958–61. The corresponding figures for Beverly over the same periods show a decrease of 80 percent.

The drop in the annual incidence of invasive cervical cancer is less marked than that of the mortality from this tumor (see chart). This decline was not unexpected because many women were having their first cytological examination each year, leading to the detection of some growths that, in the absence of screening, would have been diagnosed later. This assumption is supported by the large number of patients found in the later years with limited invasion but no symptoms (see chart). Twenty patients with invasive cancer were treated in 1955–61 compared with nine (17 expected) treated subsequently. There were 17 patients with deep invasion in 1955–61 and four (14.6 expected) in 1962–67.

Three patients were admitted for invasive cancer of the cervix within 12 months of a negative smear and one after 17 months. The patient admitted after 17 months was the only one with limited invasion. The appearance of invasive cancer in patients between annual screenings is not infrequent and has been reported before (*5*).

There were 13 deaths among the 29 patients reported to the hospital registry with cancer of the cervix in the period 1955–67. All the dead patients were known to the registry and were known to have died with recurrence or further spread of the neoplasm. As a test of the accuracy of death certification and coding relevant to the study, the identification data of these pa-

**Cervical cytological examinations by Beverly Hospital laboratory, incidence of carcinoma of the cervix, and deaths due to uterine cancer, Beverly, Mass., residents, 1955–67**



tients were matched with the death records. All 13 deaths had been coded to cancer of the cervix in these records and are included among the 18 deaths from 1965 to 1967. Similarly, all 18 deaths, with the exception of one patient who died in 1965, were of patients who had been registered with cancer of the cervix in the hospital.

Five deaths of Beverly residents in the period 1955–67 were attributed to carcinoma of corpus uteri, three before 1961 and two after that year. Seven other patients who died were known to the hospital tumor registry as having had treatment for cancer of the uterine body. The deaths of six of these patients, three of whom had an autopsy, were thought to be due to other causes, and the seventh patient died of uterine cancer while residing elsewhere. Twenty-four patients with cancer of the uterine body were reported to the tumor registry in 1955–61 and 19 (20.6 expected) in 1962–67.

The average annual numbers of total hysterectomies at the Beverly Hospital in successive quinquennia were 40 in 1941–45, 68 in 1946–50, 107 in 1951–55, 114 in 1956–60, and 126 in 1961–65. If allowance is made for population growth in Beverly and the surrounding towns, there has been little or no increase in the hysterectomy rate after 1950.

A sample consisting of all patients who had a total hysterectomy in the years 1956 and 1960 showed that 54 percent were Beverly residents. Thus, in the period of the study an estimated average of 64 hysterectomies were performed on Beverly women each year at the Beverly Hospital. Although we do not know how many Beverly residents had total hysterectomies at other centers, judging by the coverage of the hospital cancer registry, apparently the great majority of Beverly patients elected to have surgical procedures at the Beverly Hospital.

## Discussion

In Beverly deaths due to cervical cancer decreased after 1961, the seventh year of a cervical cytology program. Three factors may have accounted for the decrease.

First, there was the detection of patients with carcinoma in situ of the cervix. Lange's study (*6*) showed that the risk of developing invasive cancer of the cervix is greater for older patients with carcinoma in situ of the cervix. The average age of patients with carcinoma in situ in the period 1955–61 in our study was 41 years. In the majority of the studies reviewed by Lange, the average age of patients with carcinoma in situ was 35–40 years.

The second factor is the discovery through the screening program of patients with limited cancerous invasion of the cervix that was not clinically detectable and of patients with localized invasive cancer of the cervix.

The third factor relates to the decline in mortality from cervical cancer which has preceded the commencement of cervical cytology screening in many areas. For example, in Massachusetts the age-standardized death rate from cancer of the cervix has decreased by 36 percent from 1947 to 1965(*7*). Examination of the decrease in different age groups shows that the greatest decline has been in women over 60 years of age. Further, the mortality from cervical cancer was already decreasing before 1955 when exfoliative cytology was less widely practiced.

Other factors besides screening procedures are therefore likely to be partly responsible for the decrease in mortality from cervical cancer. Possibly, a considerable number of women have had total hysterectomies. In this study, however, the number of deaths due to cervical cancer appears to have decreased suddenly after 1961 and is therefore likely to be associated with the marked increase in cervical cytological screening during 1958–59.

The decline in mortality rates for cervical cancer in Massachusetts after 1961 was small by comparison. Some idea of the effect of total hysterectomies can also be gained from the following reasoning. If the yearly number of total hysterectomies exceeds the natural increase of women, the number of women at risk of cervical cancer would decrease and consequently so would the crude numbers of new cases of this disease.

The average annual number of hysterectomies performed on Beverly residents in their hospital, namely 64, can be compared with the average annual increase in Beverly of women over 20 years of age, which was 140 during the period of the study. Assuming that only 50 percent of hysterectomies on Beverly residents

were performed in the Beverly Hospital, there would still have been as many women at risk of cancer of the cervix from 1955 to 1961 as from 1962 to 1967.

A recent report of data from the National Health Survey (*8*) shows that women from lower socioeconomic areas, who have a higher incidence rate of cancer of the cervix than the female population as a whole, are not more likely to have had a total hysterectomy.

If no other factors were operative, a decline in the incidence of cervical cancer after cytological screening, which was not accompanied by a corresponding drop in the incidence of cancer of the uterine body, would indicate that hysterectomies were not responsible for the decline. The numbers of new cases of invasive cancer of the uterine body reported to the Beverly Hospital tumor registry did not decrease after 1961 to the same extent as the cervical cancers, but this difference was not significant.

Further, the incidence of cancer of the uterine body probably was affected by the large numbers of women being screened for the first time in the later years of the study, as explained in the case of cervical cancer. Thus, the comparison of the trends shown by these two forms of uterine cancer cannot, by itself, be used to indicate that the incidence of hysterectomies did not contribute to the decline of the death rate due to malignant disease of the cervix.

## Conclusion and Summary

A cervical cytology program was introduced in Beverly, Mass., in 1955. A preliminary study of the program's data up to December 1961 showed no decrease in the incidence of invasive cancer of the cervix in Beverly after 1955. However, in the period 1962–67 there was a statistically significant decrease in the mortality from this disease. This decrease could not be accounted for by the estimated numbers of women who had undergone a hysterectomy.

Further analysis of the data after 1967 should show the importance of detection of cases of in situ carcinoma of the cervix as compared with the importance of detecting patients with early invasion in preventing deaths from cancer of the cervix.

Studies in small areas like Beverly have some obvious advantages but, because of the correspondingly small number of women involved, these studies require repetition elsewhere before final conclusions can be drawn concerning the value of cervical cytology screening programs.

## REFERENCES


(*1*) Dunn, J. E., Jr.: Presymptomatic diagnosis of cancer with special reference to cervical cancer. Symposium No. 8. Proc Roy Soc Med 59: 1198–1204 (1966).

(*2*) Ahlawalia, H. S., and Doll, R.: Mortality from cancer of the cervix uteri in British Columbia and other parts of Canada. Brit J Prev Soc Med 22: 161–164, July 1968.

(*3*) Connecticut State Department of Health: Cancer in Connecticut. Hartford, 1960.

(*4*) Soule, E. H., and Dahlin, D. C.: Cytodetection of preclinical carcinoma of the cervix: Twelve years' experience with initial screening and repeat cervical smears. Proc Staff Meetings of Mayo Clinic 35: 508–513, Aug. 31, 1960.

(*5*) Dunn, J. E., Jr.: Preliminary findings of the Memphis-Shelby County uterine cancer study and their interpretation. Amer J Public Health 48: 861–873, July 1958.

(*6*) Lange, P.: Clinical and histological studies on cervical carcinoma. Acta Path Microbiol Scand 50: (Supp 143), 1960.

(*7*) Annual report on the vital statistics of Massachusetts. Public Document No. 1. Commonwealth of Massachusetts, Department of Public Health, Boston, 1947–65.

(*8*) U.S. National Center for Health Statistics: Age at menopause, 1960–62. PHS Publication No. 1000, Series 11, No. 19. U.S. Government Printing Office, Washington, D.C., 1966.