Cervical Cancer Control in Minnesota: 
Assessing its Effectiveness with Data from the Minnesota Cancer Surveillance System

MCSS Epidemiology Report 05:2

Minnesota Department of Health
December 2005
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Table of Contents

Acknowledgements ........................................................................................................................................ ii
Executive Summary ..................................................................................................................................... iii
Introduction ............................................................................................................................................... 1
Terminology and Methods ........................................................................................................................ 4
The Burden of Cervical Cancer in Minnesota ............................................................................................. 7
Cervical Cancer in Minnesota and the U.S. ................................................................................................. 9
  Race/Ethnic Disparities .......................................................................................................................... 10
  Trends ...................................................................................................................................................... 11
  Stage at Diagnosis .................................................................................................................................. 12
  Age at Diagnosis .................................................................................................................................... 14
  Histology ................................................................................................................................................ 15
Disparities in Cervical Cancer in Minnesota
  Race/Ethnic Disparities .......................................................................................................................... 18
  Geographic Disparities ........................................................................................................................... 23
Conclusions .................................................................................................................................................. 27
The Sage Screening Program .................................................................................................................... 28
Minnesota Cancer Alliance ..................................................................................................................... 30
References ................................................................................................................................................... 31
Acknowledgements

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Executive Summary

- This report is the most detailed examination of cervical cancer in Minnesota published to date, and uses data from the Minnesota Cancer Surveillance System to assess the effectiveness of cervical cancer control efforts in our state.

- The incidence of invasive cervical cancer and mortality from this disease are significantly lower in Minnesota than in the U.S. as a whole. Based on this criterion alone, cervical cancer control in our state is highly effective.

- Nonetheless, about 175 Minnesota women are diagnosed with this preventable disease each year, and about 35 die. The burden of cervical cancer is greater than indicated by its frequency relative to other cancers because over half of the women are less than 45 years of age when diagnosed. Every invasive cervical cancer represents one of three failures: a failure to screen, a failure to detect abnormalities when screened, or a failure to adequately follow-up on detected abnormalities.

- Despite the overall effectiveness of cervical cancer control, women of color in Minnesota are two times more likely to be diagnosed with an invasive cervical cancer than non-Hispanic white women, and are three times more likely to die of this disease; they are more likely to be diagnosed at a later stage, at an older age, and with a squamous cell carcinoma. This pattern indicates that race/ethnic disparities in cervical cancer occurrence in Minnesota are primarily due to less effective screening among women of color.

- Women living outside the seven-county Metro Area are 30 percent more likely to be diagnosed with an invasive cervical cancer than women living in the Metro Area, and are also somewhat more likely to be diagnosed at a later stage, at an older age, and with a squamous cell carcinoma. Although urban/rural differences are less consistent and are of a smaller magnitude than race/ethnic differences, this pattern is also indicative of less effective cervical cancer screening outside of the seven-county Metro Area.

- Whether these race/ethnic and geographic disparities result from limited access to or utilization of cervical cancer screening, poorer quality of screening, or a lower likelihood of receiving timely and recommended treatment of detected abnormalities cannot be determined from the available data. A study to collect information on the health insurance, screening, and medical histories of women diagnosed with cervical cancer in Minnesota is needed to better understand why this preventable disease is still being diagnosed in our state.
Cervical Cancer Control in Minnesota: Assessing its Effectiveness with Data from the Minnesota Cancer Surveillance System

Introduction

Almost all invasive cervical cancers can be prevented. An estimated 95 to 100 percent of cervical cancers result from persistent infection of the cervix with one of the cancer-causing strains of the human papillomavirus (HPV) (1). Abnormalities caused by HPV can be found through routine screening with the Papanicolaou (Pap) test and can be eliminated before they become malignant.

Because it is relatively inexpensive and can be administered in a clinic setting, the Pap test has become a part of standard medical practice in the U.S. since it was introduced more than 50 years ago, and remains the most widely used method to screen for cancer (2).

Cervical cancer is the second most common cancer among women worldwide and the most commonly diagnosed cancer among women in many developing countries (3) where even the modest medical infrastructure required is unavailable. However, cervical cancer rates in the U.S. decreased by more than 70 percent between 1950 and 1970 and by an additional 40 percent between 1970 and 1999 (4).

In 2002, invasive cervical cancer was the twelfth most commonly diagnosed cancer among women in the U.S. and the fourteenth leading cause of cancer death (5, 6). Nonetheless, in 2005 an estimated 10,370 women will be diagnosed with an invasive cervical cancer in the U.S., and 3,710 women will die from this preventable disease (7).

Genital HPV infections may be the most common sexually transmitted disease in the U.S. (8). However, only a limited number of the 30 or more genital HPV types are thought to cause cancer (1). Based on extrapolations from epidemiologic studies, from 4.6 million to 9.2 million young adults ages 15 to 24 years old in the U.S. were infected in 2000 (9), and 7-11 percent of the adult population are currently infected with a potentially cancer-causing HPV type (8).

No curative treatment is available to eliminate the virus, but the vast majority of infections cause no symptoms in either men or women and are eliminated by the body’s natural defenses. The factors that increase the likelihood that the infection will persist in women may include older age, infection with high-risk types and/or multiple HPV types, other genital infections, and immune suppression (10, 11).

The American Cancer Society estimates that 10,370 women will be diagnosed with an invasive cervical cancer in 2005 in the United States, and that 3,710 women will die from this preventable disease.

Additional factors such as smoking, long-term use of oral contraceptives, and multiparity are thought to increase the likelihood that persistent HPV infections progress to cancer (12). However, the role of cofactors is not well understood. The prevalence of the DNA of oncogenic HPV types in cervical specimens has been shown to vary ten-fold worldwide (1), but the degree to which the prevalence of high-risk HPV types and persistent HPV infections vary within the U.S. is not well established. HPV infection rates in Minnesota have not been published.
The qualification that “almost all” invasive cervical cancers can be prevented by routine Pap testing is necessary because certain types of cervical cancer – adenocarcinomas and adenosquamous carcinomas – are more difficult to identify as precancerous lesions. Adenocarcinomas currently represent 10-12 percent of cervical cancers (1). The Pap test was primarily developed to identify the more common abnormalities of squamous cells occurring in the epithelial tissue of the cervix.

Although adenocarcinomas and adenosquamous carcinomas are also caused by persistent infection with HPV, they arise in the glandular cells of the endocervix, a location that is more difficult to sample and in which abnormalities can be more difficult to evaluate. It also appears that HPV-18 may be responsible for a higher proportion of adenocarcinomas than squamous cell carcinomas (1).

In the past, adenocarcinomas and adenosquamous carcinomas of the cervix were not generally considered screening-sensitive (13). That is, it appeared that Pap testing did not reduce the risk of being diagnosed with an invasive adenocarcinoma or adenosquamous carcinoma of the cervix because it could not find precancerous lesions of these histologic types.

Assuming that the proportion of HPV infections that develop in the endocervix is relatively constant, comparing the incidence of adenocarcinomas of the cervix in various populations would provide indirect evidence about the relative frequency of persistent HPV infections.

However, recently developed techniques such as the endocervical brush and liquid based cytology and the recently adopted practice of reporting the absence of endocervical cells in the cytological sample may be improving the detection of precancerous changes of these cell types (14, 15).

The diagnosis of an invasive cervical cancer results from one of three failures: a failure to be screened, a failure to have an abnormality detected when screened, or a failure to receive adequate follow-up or treatment of a detected abnormality.

To the extent that adenocarcinomas are screening-sensitive, differences in the rate of adenocarcinomas in two groups of women will be influenced by the adoption of these sampling techniques as well as by the underlying rate of persistent HPV infection.

Therefore, when the overall rate of invasive cervical cancer incidence is markedly lower in one population than another, it may result from lower rates of persistent HPV infection, more widespread screening with the Pap test, better medical practice, or some combination of these factors.

Because it is largely preventable, the diagnosis of an invasive cervical cancer results from one of three failures: a failure to be screened, a failure to have an abnormality detected when screened, or a failure to receive adequate follow-up or treatment of a detected abnormality (16). Any of these three failures will reduce the overall effectiveness of cervical cancer screening.

A limited number of relatively large studies conducted in a variety of settings in the U.S. have indicated that about 50-55 percent of women diagnosed with an invasive cervical cancer hadn’t been screened in the previous three years, roughly 30 percent had abnormalities that were not detected, and another 15-20 percent hadn’t received timely or recommended follow-up of identified abnormalities (16-20).

However, the most recent of these studies were conducted in populations with long-term access to health care (16, 17).
and the population-based studies (18-20) were cases diagnosed in the 1980s prior to recent improvements in screening techniques. In addition, the relative importance of different failures varies by age, histology, geographic location, and socioeconomic factors (16).

The one study conducted in Minnesota (21) with information on this subject used claims data primarily to measure screening frequency from 1986 to 1990 among approximately 23,000 women continuously enrolled in a large health maintenance organization. In this highly screened group, 32 women were diagnosed with invasive cervical cancer during the study period, among whom only 34 percent had not been screened in the previous three years; medical record and cytology slide review were not conducted, so other types of failures could not be delineated.

For the reasons discussed above, cervical cancer can be considered a marker for access to quality health care and the success of cancer control efforts (22).

This report examines the occurrence of cervical cancer in Minnesota using data from the Minnesota Cancer Surveillance System (MCSS), the statewide, population-based cancer registry implemented in 1988, to assess the effectiveness of current efforts to eliminate this preventable disease and to help stakeholders in cancer control identify areas in which increased efforts are needed.

A recent study by the National Cancer Institute concluded that cervical cancer can be considered a marker for access to quality health care and the success of cancer control efforts.
Terminology and Methods

**Incidence** is the number of new cases of a disease that are diagnosed during a specified period of time. To adjust for population size, an **incidence rate** is calculated by dividing the number of new cases by the size of the population from which the cases were identified.

To additionally adjust for differences in age distribution between populations, rates are often **age-adjusted** to a standard population. Incidence rates in this report are either age-specific (i.e., the number of cases diagnosed in a specific age category divided by the number of women in that age category) or age-adjusted to the 2000 U.S. population, and are presented as the number of new cases per 100,000 females per year.

**Mortality** is the number of deaths with a given disease listed as the underlying cause of death on the death certificate during a specified period of time, regardless of when the disease may have been diagnosed.

**Mortality rates** in this report are either age-specific (i.e., the number of deaths in a specific age category divided by the number of women in that age category) or age-adjusted to the 2000 U.S. population, and are presented as the number of deaths per 100,000 females per year.

A **rate ratio** is calculated by dividing the rate in one population by the rate in another population. It provides a summary measure of the relative difference in rates between the two populations.

If the rates are the same in both populations, the rate ratio is 1.00; rate ratios less than 1.00 indicate that the rate is lower in the population in the numerator of the rate ratio; rate ratios greater than 1.00 indicate that the rate is higher in the population in the numerator of the rate ratio.

For example, if the age-adjusted incidence rate of cervical cancer is 10.0 new cases per 100,000 females per year in Population A and 7.5 per 100,000 in Population B, the rate ratio comparing population A to B is 10.0 divided by 7.5, or 1.3.

If the rate ratio is 1.3, one can say that the incidence rate (i.e., risk of being diagnosed with cervical cancer) is 30 percent higher in Population A than in Population B.

Conversely, if one wanted to reverse the comparison to compare Population B to Population A, the rate ratio would be 7.5 divided by 10.0 or 0.75; one could then equivalently say that the risk of being diagnosed with cervical cancer in Population B is 25 percent lower than in Population A.
Data on the incidence of cervical cancer in Minnesota are from cases reported as of April 2005 to MCSS. MCSS does not have information on stage at diagnosis or reliable race/ethnicity data on cases diagnosed prior to 1995.

Information on MCSS data collection and quality can be found in *Cancer in Minnesota, 1988-2002* (23), available online at [http://www.health.state.mn.us/divs/hpcd/cdee/mcss](http://www.health.state.mn.us/divs/hpcd/cdee/mcss).

Data on women with cervical cancer as the underlying cause of death are from death certificates reported to the Minnesota Center for Health Statistics and provided in electronic format to MCSS for analysis.

Although most states now require newly diagnosed cancers to be reported to a statewide registry, a nationwide cancer registry does not exist. Furthermore, the completeness and quality of data varies considerably from state to state and in many states has only been collected for a limited period of time (24).

On the other hand, the National Cancer Institute has collected population-based cancer incidence data in nine geographic areas covering about ten percent of the U.S. population since 1973 through the Surveillance, Epidemiology and End Results (SEER) Program. The SEER Program expanded to 13 geographic areas covering 14 percent of the U.S. population in 1992.

Minnesota does not participate in the SEER Program, but follows many of the same standards. In this report, cervical cancer incidence in Minnesota is compared to that in the SEER Program because the data are believed to be of comparable quality and completeness.

From 1973-1992, race-specific data from the SEER Program are only available for the categories white and black; more detailed race/ethnic categories, including non-Hispanic white, are only available since 1992.

For long-term trends in cancer incidence, data from the nine SEER regions are presented, limited to the white population to minimize differences due to the racial compositions of Minnesota and SEER. For more recent time periods and race-specific rates, Minnesota is compared to data from the 13 SEER regions except where noted otherwise.

Information on cervical cancer mortality is available for the entire U.S. through the reporting of deaths to the National Center for Health Statistics by each state.

Following SEER conventions based on their assessment of the comparability of race and ethnicity coding, SEER incidence for Hispanics and non-Hispanic whites excludes SEER regions in Detroit, Hawaii, Alaska Native Registry and Rural Georgia; U.S. mortality for Hispanics and non-Hispanic whites excludes the states of Connecticut, Maine, Maryland, Minnesota, New Hampshire, New York, North Dakota, Oklahoma and Vermont.

"Cervical Cancer Control in Minnesota"
Data on cancer incidence in the geographic areas reporting to the SEER Program and cancer mortality in the U.S. were obtained from SEER public use files. More information on these files is available on the SEER website [http://seer.cancer.gov](http://seer.cancer.gov).

This report does not include in situ cervical cancer, the immediate predecessor to invasive disease. MCSS, along with most other cancer registries in the U.S., discontinued registering in situ cervical cancers in the mid-1990s. This decision resulted from lack of consensus on categorizing intraepithelial neoplasms and in situ disease, and the expense of continuing to register the large number of pre-invasive cervical cancers of questionable comparability. In 1995, the last year during which in situ cervical cancers were reported by the SEER Program, approximately seven in situ tumors were reported for each invasive cervical cancer (5).

Cancer incidence and mortality rates were calculated using the software program SEER*Stat (25). Rates with 95 percent confidence intervals that did not overlap were considered statistically significantly different, or in other words, to not have occurred by chance.

The software program Joinpoint Regression (26) was used to assess trends and changes in the trends of cancer rates. Through an iterative process, Joinpoint identifies points in time where trends significantly change direction and calculates the average annual percent change (APC) in the age-adjusted rate during the interval between these changes and its statistical significance.
The Burden of Cervical Cancer in Minnesota

In 2002, the most recent year for which cancer reporting is complete, 172 women in Minnesota were diagnosed with invasive cervical cancer (Figure 1). It was the fourteenth most common cancer diagnosed among women in the state.

In the same year, 34 women in Minnesota died with cervical cancer as the underlying cause of death (Figure 1). It was the seventeenth most common cause of cancer death among women in the state.

The age-adjusted cervical cancer incidence and mortality rates in 2002 in Minnesota were 6.8 new cases per 100,000 females and 1.3 deaths per 100,000 females, respectively.

Despite its relative rarity, current rates lead to an average of one out of every 167 women being diagnosed with this preventable disease during her lifetime (23).

An estimated 3,340 Minnesota women were living with a history of invasive cervical cancer on January 1, 2002, or nearly 20 women for every newly diagnosed case (23).

On average, women are diagnosed with cervical cancer at a younger age than other cancers, and because of this, the impact of cervical cancer on individuals, families, and communities is greater than indicated by its frequency relative to other cancers.

A young age at diagnosis is consistent with exposure to HPV around the time that one becomes sexually active and a 10-15 year period during which the infection becomes persistent and cell abnormalities progress to become cancerous if not removed (27).

The median age at diagnosis for cervical cancer in Minnesota from 2000 to 2002 was 44 years (23); that is, half of the women diagnosed were 44 years of age or younger. The median age at death for cervical cancer was 60 years, the youngest age for any of the fifteen most commonly diagnosed cancers among women (23).

Women are diagnosed with cervical cancer at a younger age than other cancers, and because of this, the impact of cervical cancer on individuals, families, and communities is greater than indicated by its frequency relative to other cancers.

Cervical Cancer Control in Minnesota
From 1998 to 2002, 18 percent of all invasive cervical cancers in Minnesota were diagnosed among women less than 35 years of age and 18 percent among women ages 65 and older, while women between the ages of 35 and 44 years accounted for nearly 30 percent of cases (Figure 2).

In contrast, fewer than five percent of cervical cancer deaths occurred among women under 35 years of age, and 42 percent of deaths occurred among women 65 years of age or older (Figure 3). Nonetheless, the majority of deaths (58 percent) occurred among women under the age of 65.

Follow-up information is not sufficiently complete on MCSS to calculate survival rates for Minnesotans diagnosed with cancer. However, in the geographic areas participating in the SEER Program, the five-year relative survival rate among women diagnosed with cervical cancer between 1995 and 2001 was 92.4 percent when the cancer was still confined to the cervix at diagnosis (localized stage), 54.7 percent when the cancer had already spread to nearby lymph nodes and/or adjacent tissues (regional disease), and 16.5 percent when the cancer had spread to distant organs (distant stage)(28).
Cervical Cancer in Minnesota and the U.S.

On average, women in Minnesota have a significantly lower risk of being diagnosed with an invasive cervical cancer and dying from this disease than in the U.S. as a whole. Over the five-year period 1998-2002, the age-adjusted cervical cancer incidence rate was 25 percent lower in Minnesota than in the SEER Program (Table 1, Figure 4). During the same period, cervical cancer mortality in Minnesota was 46 percent lower than in the U.S. as a whole (Table 1, Figure 4).

Table 1. Cervical cancer incidence and mortality by race and ethnicity, Minnesota and the U.S., 1998-2002

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Minnesota</th>
<th>SEER</th>
<th>Rate Ratio</th>
<th>Mn/SEER</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Races Combined</td>
<td>843</td>
<td>6.7 (6.3, 7.2)</td>
<td>8.9 (8.8, 9.1)</td>
<td>0.75</td>
</tr>
<tr>
<td>American Indian</td>
<td>14</td>
<td>12.2 (6.1, 24.4)</td>
<td>4.9 (3.7, 6.5)</td>
<td>2.47</td>
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<tr>
<td>Asian/Pacific Islander</td>
<td>29</td>
<td>13.6 (8.8, 21.3)</td>
<td>8.9 (8.3, 9.5)</td>
<td>1.53</td>
</tr>
<tr>
<td>Black</td>
<td>30</td>
<td>10.3 (6.5, 16.5)</td>
<td>11.1 (10.5, 11.8)</td>
<td>0.93</td>
</tr>
<tr>
<td>Hispanic (all races)</td>
<td>25</td>
<td>11.0 (6.8, 19.4)</td>
<td>15.8 (15.1, 16.6)</td>
<td>0.70</td>
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<td>Non-Hispanic White</td>
<td>717</td>
<td>6.2 (5.7, 6.7)</td>
<td>7.1 (6.9, 7.4)</td>
<td>0.87</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Mortality</th>
<th>Minnesota</th>
<th>US</th>
<th>Rate Ratio</th>
<th>Mn/US</th>
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</thead>
<tbody>
<tr>
<td>All Races Combined</td>
<td>197</td>
<td>1.5 (1.3, 1.7)</td>
<td>2.8 (2.8, 2.8)</td>
<td>0.54</td>
</tr>
<tr>
<td>American Indian</td>
<td>4</td>
<td>~</td>
<td>2.6 (2.2, 3.1)</td>
<td>-</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>11</td>
<td>6.0 (2.8, 12.3)</td>
<td>2.7 (2.5, 2.9)</td>
<td>2.22</td>
</tr>
<tr>
<td>Black</td>
<td>9</td>
<td>~</td>
<td>5.3 (5.1, 5.5)</td>
<td>-</td>
</tr>
<tr>
<td>Hispanic (all races)</td>
<td>3</td>
<td>~</td>
<td>3.5 (3.3, 3.7)</td>
<td>-</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>170</td>
<td>1.4 (1.2, 1.6)</td>
<td>2.4 (2.4, 2.5)</td>
<td>0.58</td>
</tr>
</tbody>
</table>

Source: Minnesota Cancer Surveillance System (April 2005) and SEER public use files (November 2004). SEER incidence is for the 13 SEER Regions covering 14% of the nation; national mortality is for the entire U.S.
CI is confidence interval.
~ Race-specific rates based on fewer than ten cases or deaths are not presented.
Rates are per 100,000 females per year and age-adjusted to the US 2000 standard population (19 age groups).
Race/Ethnic Disparities

To some extent, lower statewide rates reflect that the Minnesota population has a higher proportion of non-Hispanic white women and higher average income and education levels than national averages, all of which are associated with lower cervical cancer risk (29).

However, limiting the comparison to non-Hispanic white women diagnosed in 1998-2002, the invasive cervical cancer incidence rate remained a statistically significant 13 percent lower in Minnesota than in the SEER Program and the mortality rate was a statistically significant 42 percent lower than in the U.S. as a whole (Table 1, Figure 5).

Comparisons of cervical cancer occurrence among populations other than non-Hispanic white women in Minnesota and the U.S. are limited by the relatively small number of cases and deaths in Minnesota (Table 1).

For example, the differences between American Indian, Asian/Pacific Islander, black and Hispanic women living in Minnesota and in the geographic areas participating in the SEER Program shown in Figure 5 are nearly as large as, or larger than, those for non-Hispanic white women, but because the numbers of cases are small, it cannot be ruled out that the differences occurred by chance.

However, it should be noted that in the SEER Program, American Indian women had the lowest incidence of invasive cervical cancer, while in Minnesota the rate among American Indian women was more than twice as high as among non-Hispanic white women and was comparable to the rates in Asian/Pacific Islander, black, and Hispanic women (Table 1).

It is also important to note that, although the difference was not statistically significant, the cervical cancer mortality rate among Asian/Pacific Islander women was more than twice as high in Minnesota as in the U.S. as a whole (Table 1).
Cervical Cancer in Minnesota and the U.S., continued

Trends

Lower cervical cancer occurrence in Minnesota does not appear to be a recent phenomenon.

Cervical cancer mortality has been consistently lower in Minnesota than in the U.S. as a whole going back to 1975 (Figure 6). The cervical cancer mortality rate in Minnesota decreased consistently by 2.8 percent per year between 1975 and 2002, closely matching the national decline.

Minnesota has one of the lowest cervical cancer mortality rates in the nation and since 1997 has met the Healthy People 2010 objective to reduce the rate of cervical cancer mortality to 2.0 deaths per 100,000 females. Nationally this objective has not yet been achieved (Figure 6).

Although cancer incidence data for Minnesota are only available since statewide cancer reporting was implemented in 1988, the cervical cancer incidence rate has also tended to be lower in Minnesota than in the SEER Program, and has declined at a similar or more rapid rate (Figure 6).

Figure 6. Trends in Cervical Cancer in Minnesota and the US, 1975-2002

Source: Minnesota Cancer Surveillance System (April 2005) and SEER public use files (November 2004). Minnesota rates are for all races combined. SEER incidence is for white women, including Hispanic white women, in the 9 SEER Regions covering about 10% of the US population; national mortality is for the US white population. Dotted bars note where the SEER/US trends changed significantly. Percents are the SEER/US APCs during the years between significant changes in trends. * APC is statistically significant.
Cervical Cancer in Minnesota and the U.S., continued

**Stage at diagnosis**

As the proportion of women in a population receiving effective cervical cancer screening increases, one would expect the rate of invasive cervical cancer incidence to decrease, as demonstrated in Figure 6. One would also expect that as screening continues, the proportion and rate of cancers diagnosed at a late stage would decrease and the proportion and rate of cancers diagnosed at an early stage would increase. The comparison of cervical cancer stage at diagnosis shows that 59 percent of cervical cancers in Minnesota were diagnosed at the earliest (localized) stage, compared to 52 percent in the SEER Program, and that a lower proportion of Minnesota women were diagnosed at later stages (Table 2, Figure 7).

<table>
<thead>
<tr>
<th></th>
<th>Minnesota</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Percent</td>
<td>Rate</td>
<td>(95% CI)</td>
<td>Percent</td>
<td>Rate</td>
<td>(95% CI)</td>
</tr>
<tr>
<td>All Races Combined</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Localized</td>
<td>59.3</td>
<td>4.0</td>
<td>(3.7, 4.4)</td>
<td>51.8</td>
<td>4.6</td>
<td>(4.5, 4.8)</td>
</tr>
<tr>
<td>Regional</td>
<td>28.8</td>
<td>1.9</td>
<td>(1.7, 2.2)</td>
<td>32.3</td>
<td>2.9</td>
<td>(2.8, 3.0)</td>
</tr>
<tr>
<td>Distant</td>
<td>9.4</td>
<td>0.6</td>
<td>(0.5, 0.8)</td>
<td>10.6</td>
<td>1.0</td>
<td>(0.9, 1.0)</td>
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<tr>
<td>Unknown</td>
<td>2.5</td>
<td>0.2</td>
<td>(0.1, 0.2)</td>
<td>5.3</td>
<td>0.5</td>
<td>(0.4, 0.5)</td>
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<tr>
<td>Non-Hispanic White</td>
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<td></td>
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<td></td>
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<tr>
<td>Localized</td>
<td>59.3</td>
<td>3.7</td>
<td>(3.2, 4.1)</td>
<td>53.9</td>
<td>4.0</td>
<td>(3.8, 4.1)</td>
</tr>
<tr>
<td>Regional</td>
<td>28.9</td>
<td>1.7</td>
<td>(1.5, 2.0)</td>
<td>30.1</td>
<td>2.1</td>
<td>(2.0, 2.2)</td>
</tr>
<tr>
<td>Distant</td>
<td>9.5</td>
<td>0.6</td>
<td>(0.4, 0.7)</td>
<td>11.1</td>
<td>0.8</td>
<td>(0.7, 0.8)</td>
</tr>
<tr>
<td>Unknown</td>
<td>2.4</td>
<td>0.1</td>
<td>(0.1, 0.2)</td>
<td>4.9</td>
<td>0.3</td>
<td>(0.3, 0.4)</td>
</tr>
</tbody>
</table>

Source: Minnesota Cancer Surveillance System (April 2005) and SEER public use files (November 2004). SEER incidence is for the 13 Regions covering 14% of the US population with exclusions for Hispanics and non-Hispanic whites noted in the Terminology and Methods section.

CI is confidence interval.

Rates are per 100,000 females per year and age-adjusted to the US 2000 standard population (19 age groups).
Another way to evaluate differences in stage at diagnosis is to compare the age-adjusted rates for each stage.

While Minnesota had significantly lower rates of cervical cancer at each stage, the differences were larger for regional and distant stage than for localized stage (Table 2, Figure 8).

This confirms that the stage distribution shown in Figure 7 is not biased by differences in the age distribution in Minnesota and SEER. The same relationships were seen when analyses were limited to non-Hispanic white women (Table 2).

An earlier stage at diagnosis for cervical cancers in Minnesota is consistent with more effective screening in Minnesota than in the geographic areas participating in the SEER Program.
Cervical Cancer in Minnesota and the U.S., continued

Age at diagnosis

In addition to diagnosing cancer at an earlier stage, effective screening programs would also be expected to diagnose women at a younger age, since the majority of HPV infections are acquired in early adulthood (1).

Figure 9 shows the age-specific cervical cancer incidence rates in Minnesota and SEER over the five-year period 1998-2002, and Figure 10 summarizes these data by showing the age-specific rate ratios (the Minnesota rate divided by the SEER rate).

Although the overall cervical cancer incidence rate was 25 percent lower in Minnesota than SEER, Minnesota rates became lower relative to rates in SEER as age at diagnosis increased until they were about 45 percent lower among women ages 75 and older.

Unless the average age of exposure to HPV is younger in Minnesota, a shift to an earlier age at diagnosis is also consistent with more effective screening in Minnesota than in the geographic areas participating in the SEER Program.

Figure 9. Cervical Cancer Incidence by Age at Diagnosis, Minnesota and SEER, 1998-2002

Figure 10. Cervical Cancer Incidence Rate Ratios by Age at Diagnosis, Minnesota / SEER, 1998-2002
Histology

In sum, Minnesota women are diagnosed with invasive cervical cancer less frequently, and at an earlier stage and younger age, than in the geographic areas participating in the SEER Program, all of which are consistent with more effective screening in Minnesota.

The extent to which the overall lower risk of invasive cervical cancer may additionally be related to a lower frequency of persistent HPV infection among women in Minnesota is not known, but can be indirectly evaluated by comparing rates of adenocarcinomas and adenosquamous carcinomas of the cervix in Minnesota and the SEER Program.

During the most recent five-year period 1998-2002, the combined rate of adenocarcinomas and adenosquamous carcinomas of the cervix was 25 percent lower in Minnesota than among white women in the SEER Program, while rates of squamous cell carcinomas were only marginally lower (Table 3, Figure 11).

If this were the only information available, it might therefore appear that persistent HPV infection was less common in Minnesota.

### Table 3. Cervical cancer incidence by histologic type, Minnesota and SEER, 1998-2002

<table>
<thead>
<tr>
<th>Histology</th>
<th>Minnesota Cases</th>
<th>Rate (95% CI)</th>
<th>SEER Cases</th>
<th>Rate (95% CI)</th>
<th>Rate Ratio Mn/SEER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous cell</td>
<td>609</td>
<td>4.8 (4.4, 5.2)</td>
<td>2,708</td>
<td>5.0 (4.9, 5.2)</td>
<td>0.96</td>
</tr>
<tr>
<td>Adenocarcinomas</td>
<td>155</td>
<td>1.2 (1.0, 1.4)</td>
<td>904</td>
<td>1.7 (1.6, 1.8)</td>
<td>0.71</td>
</tr>
<tr>
<td>Adenosquamous cell carcinomas</td>
<td>41</td>
<td>0.3 (0.2, 0.4)</td>
<td>182</td>
<td>0.3 (0.3, 0.4)</td>
<td>1.00</td>
</tr>
<tr>
<td>Other/NOS</td>
<td>38</td>
<td>0.3 (0.2, 0.5)</td>
<td>276</td>
<td>0.5 (0.4, 0.6)</td>
<td>0.60</td>
</tr>
<tr>
<td>Total</td>
<td>843</td>
<td>6.7 (6.3, 7.2)</td>
<td>4,073</td>
<td>7.5 (7.3, 7.8)</td>
<td>0.89</td>
</tr>
</tbody>
</table>

Source: Minnesota Cancer Surveillance System (April 2005) and SEER public use files (November 2004). SEER incidence is for white women, including Hispanic white women, in the 9 SEER Regions covering 10% of the nation.

CI is confidence interval.

Rates are per 100,000 females per year and age-adjusted to the US 2000 standard population (19 age groups).
However, examining the trends of cervical cancer in Minnesota and SEER by histologic type reveals a somewhat different picture.

In the SEER Program, most of the reduction in overall cervical cancer incidence has been limited to squamous cell carcinomas, which decreased significantly by 3.4 percent per year from 1991 to 2002; in contrast, the rate for adenocarcinomas and adenosquamous carcinomas combined increased by two percent a year until 1997, and only then began decreasing (Figure 12).

In Minnesota, the rate for adenocarcinomas and adenosquamous carcinomas decreased by 3.5 percent per year over the entire fifteen-year period 1988-2002, outstripping the decline in squamous cell carcinomas (Figure 12).

Because of these contrasting trends, the combined rate of adenocarcinomas and adenosquamous carcinomas of the cervix was 15 percent higher in Minnesota than in the SEER program at the beginning of the fifteen year period (1988-1992), five percent lower in 1993-1997, and 25 percent lower at the end of the fifteen year period (1998-2002) (Figure 13).

Source: Minnesota Cancer Surveillance System (April 2005) and SEER public use files (November 2004). Minnesota rates are for all races combined. SEER incidence is for white women, including Hispanic white women, in the 9 SEER Regions covering about 10% of the US population. Dotted bars note where the SEER trend changed significantly. Percents are the SEER APCs during the years between significant changes in trends.

* APC is statistically significant.
The trends and relative rates of squamous cell and adenocarcinomas of the cervix indicate that persistent HPV infection rates may be similar in Minnesota and the SEER Program, but that the more rapid adoption of new medical techniques to better detect precancerous adenocarcinomas has reduced the rate of invasive adenocarcinomas at an earlier date in Minnesota than in the rest of the nation.

In summary, it appears that lower rates of invasive cervical cancer incidence in Minnesota may result primarily from a combination of both more widespread screening and better medical technique in conducting Pap tests.

Direct information on the frequency of persistent HPV infections in Minnesota is not available, and a lower prevalence in Minnesota cannot be ruled out. However, the fact that rates of adenocarcinomas were as high as or higher in Minnesota in 1988-1992 compared to the SEER Program argues against this interpretation.

Earlier stage at diagnosis and earlier age at diagnosis both contribute to better survival and contribute to a substantially lower cervical cancer mortality rate in Minnesota than in the U.S. as a whole.
Disparities in Cervical Cancer in Minnesota

Race/Ethnic Disparities

Aggregating data over the most recent five-year period 1998-2002, the cervical cancer incidence rate in Minnesota was significantly higher for Asian/Pacific Islander and Hispanic women than for non-Hispanic white women (Table 1).

Rates among black and American Indian women were similar to those for Asian/Pacific Islander and Hispanic women, but comparisons to non-Hispanic white women were not statistically significant (Table 1).

The cervical cancer mortality rate was significantly higher among Asian/Pacific Islander women than non-Hispanic white women; there were too few deaths among American Indian, black, and Hispanic women to present mortality rates.

Combining data for American Indian, Asian/Pacific Islander, black and Hispanic women, women of color in Minnesota were approximately two times more likely to be diagnosed with an invasive cervical cancer than non-Hispanic white women, and three times more likely to die from this preventable disease (Table 4, Figure 14), and both comparisons were statistically significant.

Figure 14. Cervical Cancer Incidence and Mortality by Race and Ethnicity, Minnesota, 1998-2002

![Graph showing cervical cancer incidence and mortality by race and ethnicity]

Table 4. Cervical cancer incidence and mortality by race and ethnicity, Minnesota, 1998-2002

<table>
<thead>
<tr>
<th></th>
<th>Incidence</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Rate (95% CI)</td>
</tr>
<tr>
<td>All Races Combined</td>
<td>843</td>
<td>6.7 (6.3, 7.2)</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>717</td>
<td>6.2 (5.7, 6.7)</td>
</tr>
<tr>
<td>Women of Color</td>
<td>98</td>
<td>12.3 (9.6, 15.6)</td>
</tr>
</tbody>
</table>

Source: Minnesota Cancer Surveillance System (April 2005) and Minnesota Center for Health Statistics. Analyses performed by MCSS. Women of color are American Indian, Asian/Pacific Islander, black, or Hispanic.

CI is confidence interval; RR is the ratio of rates among women of color to the non-Hispanic white rate.

Race-specific rates based on fewer than ten cases or deaths are not presented.

Rates are per 100,000 females per year and are age-adjusted to the US 2000 standard population (19 age groups).
The age distribution of cervical cancer incidence for all races combined shown in Figure 2 obscures race/ethnic differences in the impact of age on the risk of being diagnosed with an invasive cervical cancer.

Among non-Hispanic white women, risk increased until about 30 years of age, and then remained relatively stable with increasing age (Figure 15). Among women of color, risk continued to increase sharply with age. Because of these differences, by 80 years of age the incidence of invasive cervical cancer was more than five times higher among women of color than non-Hispanic white women (Figure 15).

Similarly, the risk of dying from cervical cancer increased three-fold between 40 and 80 years of age among non-Hispanic white women, but increased five-fold among women of color (Figure 16).
Minnesota women of color are more likely to be diagnosed with cervical cancer at a later stage than non-Hispanic white women, although the differences are based on a relatively small number of cases among women of color.

Among non-Hispanic white women, 59.3 percent of invasive cervical cancers were diagnosed at the earlier (localized) stage, compared to 53.1 percent among women of color (Figure 17).

Cervical cancer incidence was higher among women of color at each stage, but the relative increase was larger for regional disease (Figure 18).

Given that the five-year relative survival rate is 92.4 percent for localized cervical cancers and 54.7 percent for regional disease, this may contribute to the relatively greater increase in mortality than in incidence among women of color compared to non-Hispanic white women in Minnesota.

**Figure 17. Percent Distribution of Cervical Cancers by Stage at Diagnosis and Race/Ethnicity, Minnesota, 1998-2002**

- **Localized**: Non-Hispanic White (59.3%) vs. Women of Color (53.1%)
- **Regional**: Non-Hispanic White (28.9%) vs. Women of Color (32.7%)
- **Distant**: Non-Hispanic White (9.5%) vs. Women of Color (10.2%)
- **Unknown**: Non-Hispanic White (2.4%) vs. Women of Color (4.1%)

Source: Minnesota Cancer Surveillance System (April 2005). Women of color are American Indian, Asian/Pacific Islander, black, or Hispanic. Number of cases given in parentheses.

**Figure 18. Cervical Cancer Incidence by Stage at Diagnosis and Race/Ethnicity, Minnesota, 1998-2002**

- **Localized**: Non-Hispanic White (3.7) vs. Women of Color (1.7)
- **Regional**: Non-Hispanic White (4.5) vs. Women of Color (0.6)
- **Distant**: Non-Hispanic White (1.4)

Source: Minnesota Cancer Surveillance System (April 2005). Women of color are American Indian, Asian/Pacific Islander, black, or Hispanic.
Although based on a relatively small number of cases, almost all of the increased risk for being diagnosed with an invasive cervical cancer among women of color in Minnesota was limited to squamous cell carcinomas, which are more easily identified with routine Pap testing.

The combined rate of adenocarcinomas and adenosquamous cell carcinomas was only marginally higher among women of color compared to non-Hispanic white women in Minnesota, while the rate of squamous cell carcinomas was 2.3 times higher (Table 5, Figure 19).

Table 5. Invasive cervical cancer incidence by histologic type and race and ethnicity, Minnesota, 1998-2002

<table>
<thead>
<tr>
<th>Histology</th>
<th>Women of Color</th>
<th>Non-Hispanic White</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases Rate (95% CI)</td>
<td>Cases Rate (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Squamous cell</td>
<td>82 10.0 (7.7, 13.1)</td>
<td>510 4.4 (4.0, 4.8)</td>
<td>2.3</td>
</tr>
<tr>
<td>Adenocarcinomas</td>
<td>8 1.1 (0.4, 2.7)</td>
<td>138 1.2 (1.0, 1.4)</td>
<td>0.9</td>
</tr>
<tr>
<td>Adenosquamous cell carcinomas</td>
<td>5 0.5 (0.2,1.9)</td>
<td>36 0.3 (0.2, 0.4)</td>
<td>1.7</td>
</tr>
<tr>
<td>Other/NOS</td>
<td>3 0.7 (0.1, 2.3)</td>
<td>33 0.3 (0.2, 0.5)</td>
<td>2.3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>98 12.3 (9.6, 15.6)</strong></td>
<td><strong>717 6.2 (5.7, 6.7)</strong></td>
<td><strong>2.0</strong></td>
</tr>
</tbody>
</table>

Source: Minnesota Cancer Surveillance System (April 2005). CI is confidence interval; RR is the ratio of rates among women of color to the non-Hispanic white rate. Squamous cell carcinomas are ICD-O-3 histology codes 8050-8130; adenocarcinomas are ICD-O-3 histology codes 8140-8490; adenosquamous cell carcinomas are ICD-O-3 histology codes 8560-8570. Rates are per 100,000 females per year and are age-adjusted to the US 2000 standard population (19 age groups).
The characteristics of cervical cancer among women of color discussed above (higher overall risk, increasing risk with age, later stage at diagnosis, and concentration of increased risk in squamous cell carcinomas) are all consistent with lower utilization of or poorer quality in conducting and follow up of cervical cancer screening among women of color in Minnesota compared to non-Hispanic white women.

A higher rate of persistent HPV infection or co-factors that increase the likelihood of the infections persisting among women of color cannot be ruled out, but if this were an important factor, one would expect the incidence of adenocarcinomas to be higher relative to that of non-Hispanic white women.

After adjusting for population size and age distribution, women of color in Minnesota are two times more likely to be diagnosed with an invasive cervical cancer than non-Hispanic white women in the state, and are three times more likely to die of this preventable disease.
Table 6. Cervical cancer incidence and mortality among non-Hispanic white women by residence, Minnesota, 1998-2002

<table>
<thead>
<tr>
<th>Residence at Diagnosis</th>
<th>Incidence</th>
<th></th>
<th></th>
<th>Mortality</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Rate (95% CI)</td>
<td>RR</td>
<td>Deaths</td>
<td>Rate (95% CI)</td>
</tr>
<tr>
<td>Metro</td>
<td>328</td>
<td>5.5 (4.9, 6.1)</td>
<td>1.2</td>
<td>73</td>
<td>1.2 (0.9, 1.5)</td>
</tr>
<tr>
<td>Non-Metro</td>
<td>389</td>
<td>7.0 (6.3, 7.7)</td>
<td>1.3</td>
<td>97</td>
<td>1.5 (1.2, 1.9)</td>
</tr>
<tr>
<td>Non-Metro MSA</td>
<td>136</td>
<td>6.8 (5.7, 8.1)</td>
<td>1.2</td>
<td>41</td>
<td>2.0 (1.4, 2.7)</td>
</tr>
<tr>
<td>Rural</td>
<td>253</td>
<td>7.0 (6.2, 8.0)</td>
<td>1.3</td>
<td>56</td>
<td>1.3 (1.2, 1.6)</td>
</tr>
</tbody>
</table>

Source: Minnesota Cancer Surveillance System (April 2005) and Minnesota Center for Health Statistics. Analyses performed by MCSS.

Metro is the seven-county Twin Cities area (Anoka, Carver, Dakota, Hennepin, Ramsey, Scott, and Washington); non-Metro MSA is the 11 additional counties considered Metropolitan Statistical Areas in the 2000 Census (Benton, Chisago, Clay, Houston, Isanti, Olmstead, Polk, St Louis, Sherburne, Stearns, and Wright); rural is the remaining counties.

RR is the ratio of rates outside of the Metro area to the Metro rate.
Rates are per 100,000 females per year and are age-adjusted to the US 2000 standard population (19 age groups).
However, the relationship between residence and cervical cancer risk has not been consistent over time.

From 1990 to 1999, cervical cancer mortality among non-Hispanic white women in Metro and non-Metro Minnesota were about the same, and only became consistently lower in the Metro area over the last five years (Figure 21).

Except for the three-year period 1998-2000 when rates were considerably lower in the Metro area, incidence has been similar in the two areas as well (Figure 21).

It is not clear whether the geographic differences in risk over the most recent five-year period represent random variation or true differences.
Nonetheless, Figures 22 and 23 demonstrate that non-Hispanic white women living in Metro Minnesota are more likely to be diagnosed at an early stage, and conversely, that much of the increase in risk in non-Metro Minnesota is for tumors that have spread beyond the cervix to nearby lymph nodes or organs.


Unlike women of color, whose increase in risk compared to non-Hispanic white women increases with age (Figure 15), the excess of cervical cancer in non-Metro Minnesota, if it is real, appears to be primarily limited to women ages 30-69 (Figure 24). Similar to women of color, the excess risk of cervical cancer among non-Metro women is primarily limited to squamous cell carcinomas (Figure 25).

**Data on stage at diagnosis, age at diagnosis, and histologic type are consistent with somewhat less effective cervical cancer screening outside of the seven-county Metro area in Minnesota.**
Conclusions

• Minnesota has low cervical cancer incidence and mortality rates, among the lowest in the nation. Nonetheless, the burden of this disease is largely preventable.

• Comparisons of stage at diagnosis, age at diagnosis, and histologic type of invasive cervical cancers diagnosed in Minnesota and the geographic areas participating in the SEER Program are consistent with the explanation that this reduction is primarily due to more effective screening in Minnesota. More effective screening may include increased utilization, better medical techniques for identifying abnormalities, and better follow-up of identified abnormalities.

• Nonetheless, women of color in Minnesota are two times more likely to be diagnosed with an invasive cervical cancer than non-Hispanic white women in the state, and are three times more likely to die of this disease. Comparisons of stage at diagnosis, age at diagnosis, and histologic type are consistent with the explanation that this increase in risk is primarily due to less effective screening among women of color. Whether this is primarily due to less access to or utilization of screening, poorer quality of screening, or a lower likelihood of receiving timely and recommended treatment of detected abnormalities is unknown.

• Although based on a relatively small number of cases and deaths, it appears that American Indian and Asian/Pacific Islander women are at greater risk of cervical cancer in Minnesota than in the geographic areas participating in the SEER Program.

• Non-Hispanic white women living outside of the seven-county Metro area had a 30 percent increased risk of being diagnosed with and dying from this disease than non-Hispanic white women in Metro Minnesota during the five-year period 1998-2002. Whether this is a result of random variation or a true increase in risk is unclear. However, compared to women in Metro Minnesota, women in non-Metro Minnesota tend to be diagnosed at a later stage, at an older age, and with a higher proportion of squamous cell carcinomas, all of which are consistent with somewhat less effective cervical cancer screening. Again, whether this is primarily due to less access to or utilization of screening, poorer quality of screening, or a lower likelihood of receiving timely and recommended treatment of detected abnormalities is unknown.
Conclusions, continued

The impacts of income, education, and insurance status on the occurrence of cervical cancer in Minnesota could not be evaluated in this study, but are likely to be intertwined with and at least partially responsible for the race/ethnic and geographic disparities identified.

Collecting information on the health insurance, screening, and medical histories of women diagnosed with cervical cancer in Minnesota would require an independent study, but such a study is needed to better understand why this preventable disease is still being diagnosed in our state.

It is likely that a vaccine to protect against infection with HPV will be released in the near future. While clinical trials of vaccines indicate that they have the potential to greatly reduce the incidence of cervical cancer (30), they will not protect women who are already infected, and they will only prevent infection with the two most common HPV strains, thought to be responsible for about 75 percent of cervical cancers.

Pap testing will therefore remain an important component of cancer control for the foreseeable future. In addition, increasing the utilization of Pap testing in underserved communities could lay the groundwork for the health education efforts that would be needed to assure that vaccines are available to and accepted by these same communities.
The Sage Screening Program

Low income uninsured and underinsured Minnesota women age 40 or older can receive free cervical cancer screening through the Sage Program, formerly the Minnesota Breast and Cervical Cancer Control Program (MBCCCP). This program is funded by the Centers for Disease Control and Prevention and by the State of Minnesota.

Since 1991, this program has detected and treated about 3,400 precancerous cervical lesions and detected over 980 breast and cervical cancers in Minnesota women.

For more information about this program, or to find out if you or your patient are eligible for screening through this program, call

1-888-6-HEALTH (1-888-643-2584)

or view the Sage Program web site at http://www.health.state.mn.us/divs/hpcd/ccs/mbcccp.htm.
Minnesota Cancer Alliance

_Cancer Plan Minnesota 2005-2010_ is the state’s first comprehensive cancer control plan. Developed over a two-year period through a broad-based collaboration of public, private, and non-profit organizations, the plan was released in April 2005 and now serves as a common framework for action to reduce the burden of cancer for all Minnesotans. _Cancer Plan Minnesota_ identified four priorities, one of which is to reduce disparities in cancer screening and treatment.

Planning partners have formed the Minnesota Cancer Alliance to provide a forum through which cancer control activities can be better coordinated to make optimal use of limited resources and to more fully realize opportunities for innovation.

Volunteers representing a broad base of stakeholders are working together in project teams to take specific action to achieve the cancer plan’s objectives. If you or your organization are interested in joining the Alliance or one of its project teams, or to order a copy of _Cancer Plan Minnesota 2005-2010_, go to www.cancerplanmn.org or contact Elizabeth Moe, Project Coordinator, at (651) 201-3608.
References


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St. Paul, Minnesota 55164-0882
http://www.health.state.mn.us/divs/hpcd/cdee/mcss/T

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