Cancer Screening Recommendations in the United States: Progress and Process. Douglas L. Weed, M.D. Division of Cancer Prevention, National Cancer Institute, Bethesda, MD 20892, U.S.A.

In the past twenty-five years, cancer screening recommendations have been the subject of intense interest and controversy in the United States. The process of making recommendations is a complex one, involving science, medicine, ethics, and economics. Represented in this process are the interests of private and public institutions as well as the interests of health professionals and the public.

Cancer screening recommendations are intended for asymptomatic individuals who, although apparently healthy, undergo screening tests. Cancer screening tests, in turn, may change the status of these individuals from asymptomatic and healthy to patients in need of therapy. Cancer screening recommendations are made with extensive scientific knowledge of the risks and benefits of the screening test itself as well as knowledge of the risks and benefits of therapy. Scientific evidence pertinent to understanding these various risks and benefits is of many types and strengths. The strongest evidence is that of the randomized clinical trial. Observational evidence is also used in the process of making screening recommendations. Biases may affect the interpretation of scientific evidence: lead-time, length, and selection bias are important examples.

Implementing cancer screening recommendations typically involves the active support of programs by health care professionals as well as public and private institutions concerned with preventive medicine and public health. Understanding the risks and benefits of screening and accurately informing individuals who would undergo screening tests are important ethical norms for American health care professionals who promote specific screening tests. Decisions by asymptomatic individuals who undergo cancer screening tests or participate in cancer screening research must be informed and consented to without coercion or misrepresentation. Cancer screening recommendations may also take into account the financial costs of testing and resultant therapies when cancer is detected.

In the United States, cancer screening recommendations are produced by different organizations. There are no official national policies. Recommendations may differ across organizations, although consensus is possible and today is generally recognized for breast, cervical, and colorectal cancer screening. Organizations making recommendations include: societies representing medical specialties (e.g. the American College of Radiology, the American College of Physicians, and others), public institutions such as the U.S. Preventive Services Task Force, and non-profit organizations such as the American Cancer Society.

For reference, followings are the summaries of evidence of effectiveness of cancer screening of major cancers abstracted from recent PDQ of NCI.

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## Screening for cervical cancer

Evidence strongly suggests a decrease in mortality from regular screening with Pap tests in women who are sexually active or who have reached 18 years of age. The upper age limit at which such screening ceases to be effective is unknown.

The widespread acceptance of the Pap smear makes the possibility of testing the efficacy of cervical cytology by randomized trials remote. There is, nevertheless, substantial evidence from observational studies that mortality from cervical cancer can be reduced by screening.

Mortality from cervical cancer has decreased in several large populations following the introduction of well-run screening programs. Data from several large Scandinavian studies show sharp reductions in incidence and mortality following the initiation of organized screening programs. Iceland reduced mortality rates by 80% over 20 years, and Finland and Sweden reduced their mortality by 50% and 34%, respectively. Similar reductions have been found in large populations in the United States and Canada.

Reductions in incidence and mortality seem to be proportional to the intensity of screening efforts. The Scandinavian countries with the highest rates of screening activity reported greater reductions in mortality than those countries with lower rates of screening. Mortality in the Canadian provinces was reduced most remarkable in British Columbia, which had screening rates two to five times those of the other provinces.

Case-control studies have found that the risk of developing invasive cervical cancer is 3-10 times greater in women who have not been screened. Risk also increases with longer duration following the last normal Pap smear, or similarly, with decreasing frequency of screening. Screening every 2-3 years, however, has not been found to increase significantly the risk of finding invasive cervical cancer above the risk expected with annual screening.

The analysis of survival data shows that survival appears to be directly related to the stage of disease at diagnosis. The 5-year relative survival rate for cervical cancer is 88% for women with an initial diagnosis of localized disease. For those initially diagnosed with distant disease, the survival rate is only 13%. Early detection, using cervical cytology, is currently the only practical means of detecting cervical cancer in localized or premalignant stages.

## Screening for gastric cancer

There is insufficient evidence to establish that screening would result in a decrease in mortality from gastric cancer in the United States population.

There has been a significant decrease in the gastric cancer death rate in Japan. This has been attributed to the national mass screening program that was initiated in the 1960s, but clinical trial evidence is lacking. Most studies show at least a two-fold decrease in mortality in screened versus unscreened lacking. Most studies show at least a two-fold decrease in mortality in screened versus unscreened patients. These studies have included time-trend-analysis and case-control studies. While there have been no data from randomized studies, currently there is an ongoing Japanese study randomizing municipalities (not individual patients) within a single prefecture.

While there has been discussion about whether adenocarcinoma of the stomach in the Japanese is a different biological entity than that in the United States, there has been little evidence to support such a difference. The failure to discover gastric carcinoma in early stages in this country is most likely influenced by a low incidence, lack of aggressiveness in screening, and the use of different screening techniques. In one study, aggressive screening among Americans resulted in finding early lesions comparable to the Japanese experience, suggesting that the screen would be effective in finding early, possibly curable lesions if the incidence were higher and if screening techniques were more aggressive. However, no mortality differences were noted. There may be some justification for screening some populations of Americans at higher risk, although there is considerable discussion about how much incidence would make the examination worthwhile. Potential subgroups might include elderly with atrophic gastritis or pernicious anemia, patients with partial gastrectomy, patients with the diagnosis of sporadic adenomas and with familial polyposis, and immigrant ethic populations from countries with high rates of gastric carcinoma.

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## Screening for breast cancer

Aged 40-49 years:

Combined data from eight randomized controlled trials indicate a reduction in breast cancer mortality of about 17% for women entering the trials when they are 40-49 years of age. This estimated reduction occurs 15 years after the start of screening and is statistically significant, or nearly so. There is little or no reduction evident during the first 10 years after starting screening. Some of the observed reduction in breast cancer mortality may have been due to cases detected after women had passed their 50th birthday.

Aged 50-69 years:

There is strong evidence that regular mammographic screening of women aged 50-69 years leads to a reduction in breast cancer mortality of 25%-30% 10-12 years later. Benefits in breast cancer mortality begin about 5 years after initiation of screening.

Aged 70 years and older:

The risk of breast cancer increases with age. However, clinical trials offer insufficient information on the effectiveness of mammography in women aged 70 years and older. The small numbers of women who are older than 70 years of age at entry into randomized trials provide insufficient statistical power to allow assessment.

## Screening for colorectal cancer

Guaiac-based fecal occult blood testing either annually or biennially using rehydrated or nonrehydrated stool specimens in people age 50-80 decreases mortality from colorectal cancer.

Regular screening by sigmoidoscopy in people over the age of 50 may decrease mortality from colorectal cancer. There is insufficient evidence to determine the optimal interval for such screening.