The population of adults age 65 or older in Canada and most industrialized nations continues to increase, in both absolute terms and as a proportion of the overall population. Just under 60% of all malignancies, and 71% of all cancer-related deaths, occur in people aged 65 or older. Stated differently, adults age 65 or older have a 16-fold greater risk of dying from cancer than younger people. Against this background, numerous studies have demonstrated that older adults, particularly age 75 or older, often do not undergo cancer screening tests. For example, in a retrospective cohort study...
an Update on Cancer Screening among American women aged 65 or older, 52%, 41%, and 11% of women aged 65-69, 75-79, and 85+, respectively, received a screening mammogram.\(^5\)

Table 1 summarizes the guidelines from three major agencies (the American Cancer Society (ACS), the Canadian Task Force for Preventive Health Care (CTFPHC), and the United States Preventive Services Task Force (USPSTF)) for four of the most common malignancies that will be the focus of this article. The full text of the guidelines can be found on the websites of each organization. Notably, the CTFPHC and the USPSTF guidelines are very similar to one another and differ significantly from the ACS guidelines in several areas. Where there are differences, recommendations from the CTFPHC and the USPSTF tend to be more conservative than the ACS.

Most Canadian primary care physicians are familiar with the recommendations of the CTFPHC. As such, their practices probably mirror these guidelines most closely. It is therefore instructive to note that the CTFPHC does not recommend screening for three of the four cancers in Table 1 for adults age 70 or over. To better understand these issues, I will briefly review the evidence that led to the formulation of the guidelines for each of the four cancers, and then discuss issues specific to seniors for each cancer. Throughout this article I will focus only on average risk individuals.

**Breast Cancer**

Breast cancer remains the most common non–skin cancer and the second highest cause of cancer deaths in Canadian women. With increasing age, there is an increase in both breast cancer incidence and mortality.\(^6\)

The most widely utilized screening manoeuvre consists of screening mammography and clinical breast examination (CBE). At least 8 randomized controlled trials (RCTs) have been conducted on breast cancer screening using mammography with or without CBE.\(^7\) For women aged 50 to 69 years, mammography reduces breast cancer mortality by 26% (95% confidence interval 17-34%).\(^8\) Self breast examination has not been demonstrated in RCTs to reduce breast cancer mortality and is not recommended as a stand-alone screening manoeuvre.\(^9\) A recent study from Ontario suggested that mammography plus CBE was associated with improved screening sensitivity and cancer detection rates compared to mammography alone, but at a cost of more false positive diagnoses and a greater rate of referral for further investigation.

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**Key Point**

The most widely utilized screening manoeuvre for breast cancer consists of screening mammography and clinical breast examination (CBE).
breast self-exam
The breasts should be checked for shape and size and any changes in colour or texture. This exam should be performed with arms down at the side and repeated with arms above the head. Use the pads of the fingers to manually inspect each breast for any changes or lumps by following the three patterns illustrated above.

incidence
The spectrum of breast disease changes substantially between age 45 and 55 years. The graph shows that at age 45-55 the most likely causes of a discrete breast lump are cysts, cancer, or localized benign change. In women 55 years and older, the most likely cause of a discrete lump is cancer.

With aging, breasts become easier to examine because glandular tissue is replaced by fat. As a consequence, the sensitivity of mammography increases slightly in older women. However, the rate of false-positive mammograms increases, as does the incidence of ductal carcinoma in situ (DCIS). DCIS is generally considered a low lethality malignant condition for which treatment in older women is unlikely to improve mortality.

Two RCTs of screening mammography included relatively women aged 50-74, but subgroup analyses were not provided for women over age 70. Pooled results from the Swedish RCTs of mammography in women older than 70 years did not show any reduction in breast cancer mortality, but the trials included few women over age 70 and were consequently underpowered. Long-term follow-up suggests that any mortality benefits from mammography begin to appear after at least 5-7 years of follow-up.

Extrapolating data from other sources of evidence, at least two cost-effectiveness analyses have looked at continuing mammography beyond age 70. These have suggested that continuing with screening mammography up to age 80 among women who were otherwise healthy or had minimal comorbidity was associated with reduction in breast cancer mortality at a reasonable cost per life year gained.

Thus, based on the evidence to date, it is reasonable to continue breast cancer screening with biennial mammography with or without annual CBE for women up to age 80 as long as the remaining life expectancy is at least 5-7 years. Estimating remaining life expectancy by examining age, comorbidity, and functional status was reviewed in detail in my prior article.

Cervical Cancer

Cervical cancer is the third most common gynecologic malignancy and thirteenth overall in Canada. The Papanicolaou (Pap) test is the standard screening test for cervical cancer.

Key Point

The Papanicolaou (Pap) test is the standard screening test for cervical cancer.

Although the incidence and mortality of invasive cervical cancer increases with age up to at least age 60, both incidence and mortality rates have been declining in Canada since 1960. About one-half of all cases are diagnosed in women who have never been screened.

The Papanicolaou (Pap) test is the standard screening test for cervical cancer. No RCTs have directly demonstrated a reduction in cervi-
Table 1: Recommendations for Cancer Screening from Major Medical Organizations for 4 Common Malignancies

<table>
<thead>
<tr>
<th>Malignancy</th>
<th>ACS</th>
<th>CTFPHC</th>
<th>USPSTF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>Annual clinical breast exam and mammography after age 40 <em>(may be in the process of changing to age 50)</em></td>
<td>Clinical breast exam and mammogram every 1-2 years ages 50-69</td>
<td>Mammogram every 1-2 years, ages 50-69; do not recommend clinical breast exam</td>
</tr>
<tr>
<td>Cervical</td>
<td>Pap test every 2-3 years after age 30 if three prior normal results; may stop at age 70 if three normal prior Pap tests and no abnormal results in the last 10 years</td>
<td>Pap test every 3 years 3 years up to age 69 if three normal prior Pap tests</td>
<td>Pap test every 3 years up to age 65</td>
</tr>
<tr>
<td>Colorectal</td>
<td>Starting at age 50: FOBT annually OR flexible sigmoidoscopy every 5 years OR colonoscopy every 10 years OR double contrast barium enema every 5 years</td>
<td>Starting at age 50 FOBT every 1-2 years with or without flexible sigmoidoscopy (interval not specified)</td>
<td>Starting at age 50 yearly FOBT and/or sigmoidoscopy (interval not specified); <em>not routinely advised age 75; stop after age 85</em></td>
</tr>
<tr>
<td>Prostate</td>
<td>Annual PSA and DRE starting at age 50 if life expectancy at least 10 years</td>
<td>Not routinely recommended; discuss pros and cons with patient, <em>but stop after age 75</em></td>
<td>Not routinely recommended; discuss pros and cons with patient</td>
</tr>
</tbody>
</table>

ACS = American Cancer Society; CTFPHC = Canadian Task Force on Preventive Health Care; USPSTF = United States Preventive Services Task Force.

cal cancer mortality with screening. That being said, there is a large body of evidence from cohort and case-control studies supporting the effectiveness of cervical cancer screening. Newer cytologic techniques, such as using liquid-based thin-layer slide preparation, may
be associated with higher sensitivity and may therefore require less frequent screening intervals. It is anticipated that the introduction of a vaccine against human papillomavirus (HPV) in young women will significantly decrease the incidence and mortality of invasive cervical cancer among vaccinated women, but whether screening guidelines for middle-aged and older women (who are not currently receiving the vaccine) will change is not presently clear.

**Issues in older women**

Canadian data suggests that 45-60% of women aged 60-69 have not had a Pap test in the last 3 years. All three agencies recommend that screening be stopped in average risk women (i.e. those without prior abnormal cytology results or who are positive for HPV) at the age of 70 provided they have had at least 3 normal Pap tests in recent years. Since cervical cancer is rare among average risk women over age 70 who have been screened in the past it still appears reasonable to stop screening at age 70 in these women.

**Colorectal Cancer**

Colorectal cancer is the second and third most common cause of cancer death in men and women, respectively, and the prevalence of colorectal cancer increases markedly among persons beyond 50 years of age. Several different screening manoeuvres have been considered, including the fecal occult blood test (FOBT), sigmoidoscopy, double contrast barium enema (DCBE), and colonoscopy. The strongest evidence exists for FOBT although colonoscopy is becoming very popular. RCTs have demonstrated that annual screening with the FOBT is associated with a 15-33% reduction in colorectal cancer mortality and a 17-20% reduction in incidence. Retrospective case-control studies have shown that flexible sigmoidoscopy reduces mortality from colorectal cancer. A small RCT demonstrated reduced incidence of colorectal cancer but no reduction in cancer mortality was noted. Two large RCTs of flexible sigmoidoscopy are underway. It is unclear how frequently flexible sigmoidoscopy should be performed; many experts suggest every 5 years, although this has not directly been compared to other intervals in RCTs. There are no RCTs of either colonoscopy or DCBE that demonstrate reductions in colorectal cancer mortality. However, many experts argue that colonoscopy is very likely to be an effective screening test for several reasons. First, colonoscopy is the gold standard for full visualization of the colon, and can facilitate diagnosis and removal of polyps. Second, the ben-
Figure 2: Screening for Colorectal Cancer
benefits of other screening tests such as the FOBT or flexible sigmoidoscopy are most likely due to follow-up colonoscopy in screen-positive patients. Additionally, colorectal cancer incidence was decreased in two large cohort studies of adults with adenomatous polyps removed at colonoscopy.\textsuperscript{24} Third, cross-sectional studies have demonstrated that colonoscopy is more sensitive (and thus likely more efficacious as a screening measure) than flexible sigmoidoscopy and/or FOBT.\textsuperscript{24} In a recent modelling study, the cost of screening per life-year saved with colonoscopy was better than either FOBT or sigmoidoscopy.\textsuperscript{25} These factors have recently led the USPSTF to include colonoscopy as an option instead of FOBT. Colonoscopy seems to be particularly effective at detecting and decreasing mortality from left-sided tumours.\textsuperscript{26}

**Issues in older adults**

At least three issues are of specific relevance to older adults. First, are screening tests more or less sensitive with increasing age? With an increasing prevalence of diverticular disease as a cause of microscopic gastrointestinal bleeding, FOBT may have a higher sensitivity but lower specificity in older adults. However, this does not appear to have been directly evaluated in large studies. Second, are screening tests less safe? A major complication of flexible sigmoidoscopy and colonoscopy is bowel perforation. It occurs in about 1 in 10,000 adults with flexible sigmoidoscopy\textsuperscript{27} and about 1 in 3,000 with colonoscopy.\textsuperscript{28} It is even rarer with DCBE. Major complications after colonoscopy occur in about 0.3-0.6% of patients.\textsuperscript{28} Since my last review was published, a large study of 53,220 men and women aged 66 or older confirmed that increasing age and comorbidity were associated with greater risks of serious complications including perforation.\textsuperscript{29} Whether this means that the screening procedure should change with increasing age (i.e. colonoscopy for middle-aged patients but FOBT for more elderly patients) is unclear at this time. Third, when should screening stop? While screening studies have generally included adults up to age 79-85, benefit from screening appears within 5-10 years of follow-up.\textsuperscript{30,31} Thus, screening is likely to be of limited benefit and may be harmful in individuals with a remaining life expectancy of less than 5 years. As a consequence, the USPSTF revised its guidelines in 2008 to indicate an upper age limit of 75 years above which colorectal cancer screening was no longer routinely recom-
mended, and discouraged at age 86 or higher, due to limited benefit and increased risk of harms.\textsuperscript{32} Again, however, these guidelines fail to consider remaining life expectancy.

**Prostate Cancer**
Prostate cancer is the most common cancer in Canadian men and the second most common cause of cancer mortality.\textsuperscript{23} The prevalence increases with age, and the median age at diagnosis is 68 years. Although mortality from prostate cancer also increases with age, the risk of dying from prostate cancer is about 3% for a man aged 60 or older.\textsuperscript{19}

Of the four cancers reviewed thus far, prostate cancer screening remains the most controversial, despite recent publication of the first 2 RCTs examining the benefits and risks of screening for prostate cancer.\textsuperscript{33,34}

Both RCTs reported interim data after 7-9 years of follow-up. The first RCT, part of the massive US Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, enrolled 76,693 men ages 55-74 to annual screening with a prostate-specific antigen (PSA) test and digital rectal examination (DRE). Compliance was over 85% in the screening arm, but screening went from 40% to 52% in the control arm, significantly weakening the likelihood of finding any benefit of screening. Neither biopsies nor treatment were mandated if the PSA was above a specific threshold. After a median of 11 years of follow-up, there were 92 deaths from prostate cancer in screened patients and 82 in the control group (rate ratio 1.11, 95% confidence interval (CI) 0.83 to 1.50).

In contrast, in the European study, 182,000 men ages 55-69 in 7 European countries were offered PSA screening; most centres did not include DRE. In contrast to the US study, a biopsy was mandated if the PSA rose above 3.0 ng/mL, but no treatment was mandated if the biopsy was positive. After a median of 9 years of follow-up, 5,990 prostate cancers were diagnosed in the screening group compared to 4,307 among controls. More importantly, 214 prostate cancer deaths occurred in the screened group compared to 326 in the control group (rate ratio 0.80, 95% CI 0.67 to 0.95). Mortality curves did not separate between screened and unscreened groups until at least 10 years of follow-up. The absolute difference in prostate cancer deaths is about 0.71 per 1,000 men screened. Follow-up continues in both trials.

Interpretation of the 2 studies is challenging and controversial.\textsuperscript{35} It is clear that screening is associated with a significantly greater detection rate of prostate cancer but the 2 RCTs differ with respect to whether early detection improves cancer-specific mortal-
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Thus, screening is associated with an increased risk of overde-
tection (i.e. identifying tumours that are indolent and unlikely to be clinically important during a man’s remaining life). It also important to recognize that treatment is associated with significant long-term side effects such as incontinence and impotence.

None of the agencies have for-
mally revised their guidelines since the release of these 2 trials. The ACS recommends both the DRE and the PSA test annually in men age 50 or older. Given the lack of evidence, the CTFPHC and the USPSTF, in contrast to the ACS, have long concluded that there is insufficient evidence to recommend for or against screening for prostate cancer.

Issues in older adults

In the situation where a middle-aged man and his physician have agreed to start screening with annual PSA and DRE, when should he stop? Based on the recent European study data, mortality benefits were only seen after at least 10 years of follow-up. Most experts who recommend for prostate cancer screening suggest a remaining life expectancy of at least 15 years. In a similar vein, the USPSTF recently revised its guidelines to recommend not screening for prostate cancer in men age 75 or older, citing low likelihood of benefit and significant risks of overdetection and harm from overtreatment.

Remaining Life Expectancy

Critical to any discussion to continue screening in adults beyond age 70-75, where guidelines and the primary evidence are more likely to be silent, is understanding the patient’s remaining life expectancy. Clearly age is a factor, with the average 65 year old expected to

Figure 3: Screening for Prostate Cancer

- PSA/digital rectal exam
- Prostate biopsy to establish diagnosis of prostate cancer
- Metastatic work-up (laboratory tests, bone scan, imaging, etc.) to rule out metastatic, node-positive, and locally advanced disease
- Review disease factors and assess risk

Low risk:
- Stage: T1c or T2a AND
- Gleason: 2–6 AND
- PSA level: <10ng/ml

Intermediate risk:
- Stage: T2b OR
- Gleason: 7 OR
- PSA level: 10–20ng/ml

High risk:
- Stage: T2c OR
- Gleason: 8–10 OR
- PSA level: >20ng/ml

Need for local therapy?

Yes

Low risk:
- Expectant management
- Active surveillance
- RP
- EBRT
- Brachytherapy

Intermediate risk:
- RP
- EBRT
- Brachytherapy

High risk:
- RP +/- ADT
- EBRT + ADT

No

(advanced age, comorbidity) with life expectancy under 5–10 years

ADT = androgen deprivation therapy; EBRT = external beam radiotherapy; PSA = prostate-specific antigen; RP = radical prostatectomy
live longer than the average 70 or 75 year old. Yet there is tremendous heterogeneity in the older population. Estimating remaining life expectancy is not an easy or precise science, yet clinical decisions are made daily after implicitly considering remaining life expectancy. Beyond age, both comorbidity (the presence of one or more medical illnesses) and functional status (independent or dependent in basic or instrumental activities of daily living) impact upon remaining life expectancy.\textsuperscript{38,39} A useful framework discussing these issues was presented several years ago by Walter and Covinsky.\textsuperscript{40}

To make things more practical, in my previous article, I discussed a quantitative attempt to model and estimate remaining life expectancy using these factors.\textsuperscript{16} In the last few years, guidelines have remained silent about how to estimate remaining life expectancy, despite a growing awareness of its importance and a greater number of articles suggesting incorporating remaining life expectancy into clinical decision making. This area is a crucial one for future research. In the interim, clinicians are forced to use life-tables, clinical guess-timates, or model predictions to help make these challenging decisions.

**Summary**

Cancer remains a major cause of morbidity and mortality in older adults. This situation is likely to worsen given the demographic imperative and improving survival rates after a new cancer diagnosis. Cancer screening is an important tool to decrease the incidence and mortality from can-

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**SUMMARY OF KEY POINTS**

The most widely utilized screening manoeuvre for breast cancer consists of screening mammography and clinical breast examination (CBE).

The Papanicolaou (Pap) test is the standard screening test for cervical cancer.

Several different screening manoeuvres have been considered for colorectal cancer, including the fecal occult blood test (FOBT), sigmoidoscopy, double contrast barium enema (DCBE), and colonoscopy.

The standard for prostate cancer screening remains the prostate-specific antigen (PSA) test and digital rectal examination (DRE).
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In older adults. In particular, systematic screening for colorectal cancer in both sexes, breast cancer and cervical cancer in women, and possibly prostate cancer in men leads to decreased mortality from the respective cancers.

Clinical Pearls

Cancer screening is an important tool to decrease the incidence and mortality from cancer in older adults.

Systematic screening for colorectal cancer in both sexes, breast cancer and cervical cancer in women, and prostate cancer in men leads to decreased mortality from the respective cancers. I have reviewed the guidelines on cancer screening in general, updating my prior review in this area and highlighting specific issues that are germane to older adults and their clinicians. Any screening decision must incorporate patient preferences and consider the patient’s remaining life expectancy.

References:

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