

A Critical Review of Periodic Health Screening Using Specific Screening Criteria

Part 4: Selected Miscellaneous Diseases

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Despite the increasing interest in recent years in prevention and early recognition of asymptomatic disease, an objectively based program for periodic health screening of asymptomatic adults has yet to be proposed for the primary care physician. This is the last in a series of four articles which have critically examined the feasibility of screening procedures for 36 selected diseases. Six basic criteria are adopted as necessary to justify periodic screening. Specific screening recommendations are made for each disease, and a longitudinal screening program for asymptomatic adults is proposed. Cost and patient education are two important factors in any viable screening program.

This is the last in a series of four articles which are intended to evaluate what information is available concerning screening procedures for selected diseases. Our goal is to construct a longitudinal screening program or "life flow sheet" for *asymptomatic adult patients* in our own model family practice unit. Several other life flow sheets have already been published,¹ but none have included the data and rationale behind each recommendation. This series specifically includes a discussion of the rationale for each recommended screening test. Furthermore, it provides an extensive bibliography so that the reader may critically re-evaluate each area and reach his own conclusions.

Methods

The following criteria are generally deemed necessary to justify screening for a given disease:

1. The disease must have a significant effect on quality or quantity of life.
2. Acceptable methods of treatment must be available.

3. The disease must have an asymptomatic period during which detection and treatment significantly reduce morbidity and/or mortality.
4. Treatment in the asymptomatic phase must yield a therapeutic result superior to that obtained by delaying treatment until symptoms appear.
5. Tests must be available at reasonable cost to detect the condition in the asymptomatic period.
6. The incidence of the condition must be sufficient to justify the cost of screening.

Using the "Geller Tables,"² American Cancer Society statistics³ and other sources, we tabulated a list of 36 diseases which were then evaluated according to the above criteria. We arbitrarily considered only diseases affecting adults. The following facts about each disease were specifically sought:

1. Incidence and prevalence of the disease, age and sex specific, if possible.
2. Progression of the disease both with and without treatment, to include morbidity, mortality, and the length of the early asymptomatic period.
3. Risk factors associated with development of the disease.
4. Availability of screening tests, their

safety, sensitivity and specificity in the early stages of the disease and their unit cost.

A brief discussion of each disease was then formulated and conclusions were made regarding the suitability and type of screening to be done. This article will deal with seven miscellaneous diseases whose prevalence is shown in Table 1. A longitudinal screening program is proposed based upon the six basic criteria we have adopted to justify screening in asymptomatic adults for the 36 selected diseases discussed.

Chronic Open-Angle Glaucoma

Occurrence:

Chronic open-angle glaucoma is usually a disease of persons over 40 and prevalence data are expressed in terms of this age group. There is wide variation among prevalence data due partly to differences in criteria for diagnosing the disease. Some figures use ocular hypertension alone to determine prevalence, while other authors may insist on visual field deficits and changes in the optic disk before diagnosing glaucoma. Estimates of prevalence range from 0.36 percent to 2.4 percent of the population over age 40.⁴ The peak incidence is between ages 60 and 70.⁵ In our area about one third of the population is over 40, which would make the overall prevalence roughly 360 per 100,000.

Progression and Benefit from Treatment:

Data on the progression of glaucoma with or without treatment is scanty, a surprising fact considering the high incidence of the disease. Graham followed 232 patients with ocular hypertension for 43 months without treatment and only one

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Table 1. Selected Miscellaneous Diseases

| Disease | Occurrence per 100,000 |
|-------------------------|------------------------|
| Anemia | 5,000 (P) |
| Alcoholism | 4,200 (P) |
| Glaucoma | 360 (P) |
| Breast cancer | 73 (I-W) |
| *Depression (psychotic) | 70 (P) |
| Lymphoma | 6 (I) |
| Chronic leukemia | 4 (I) |

I = Incidence P = Prevalence
W = Women

*The relative prevalence of this disease is probably understated in this table due to difficulties in determining true prevalence rates.

developed visual field loss.⁶ We could find no specific data on the natural course after field loss occurs, but general statements are made such as "gradual progression to blindness occurs in many cases."⁵ One study comparing medical versus surgical treatment started with two groups of patients with 76 percent normal visual acuity, and 67 percent normal visual fields; after two years the visual acuity of both the medically and surgically treated groups had decreased to about 50 percent of normal while visual fields had decreased only slightly.⁷ More critical evaluation of the natural course of the disease and benefit from therapy is needed.

Diagnosis:

Glaucoma is diagnosed by a combination of findings including: (1) elevated intraocular pressure, (2) visual field loss and later decreased acuity, and (3) enlargement of the optic cup to greater than one third the disk diameter. No one finding is pathognomonic of the disease. This fact is one of the major impediments to an effective screening program.

Tonometry is the most widely used screening test for glaucoma. It is fast, painless, inexpensive (the cost of a paramedic visit), and can be done by paramedics. Unfortunately, many patients without glaucoma have elevated pressures and worse, and many patients with glaucoma have normal pressures. Using 25 mmHg as an abnormal pressure, a Florida screening study

had about 50 percent false positives. When the cutoff pressure was lowered to 23.7 mmHg there were 91 percent false positives.⁸ Of more concern are reports that there will be 60 percent false negatives (ie, 60 percent of glaucoma cases will be missed) when 24 mmHg is used as the upper limit of normal.⁹ If 21 mmHg is the upper limit, there will be 39 percent false negatives.⁹

Tonography is an adaptation of tonometry in which an indentation tonometer is left on the eye for four minutes. The initial and final pressure readings are observed and from these the rate of aqueous outflow (outflow facility) is calculated. Being related to tonometry, it has the same drawbacks and wide overlap of normal and abnormal values.⁹

Measurement of visual fields has not been frequently used as a screening test for glaucoma because it is more time-consuming than tonometry. Several automated rapid field screeners are available to reduce the required time, but these have an increased incidence of false positive results.¹⁰ It may be possible for a paramedic to do visual fields in ten minutes on a young, cooperative patient, but it may take 45 minutes on older or senile patients — the ones most likely to have glaucoma. There is no data concerning the number of false positives and false negatives because no large-scale study has been done using visual fields alone to screen for glaucoma.

Examination of the optic disks is another method of diagnosing glaucoma. Ophthalmoscopy is not time-consuming, but it does require a skilled observer, probably a physician or specially trained physician's assistant. Again, little data is available concerning the accuracy or sensitivity of examining the optic disks as a sole screen for glaucoma.

Conclusion:

Glaucoma is an extremely difficult disease for which to decide whether to screen, how to screen, and how often. Superficially, the condition is an ideal one for screening. It has a high prevalence, a long asymptomatic course, significant morbidity and "common knowledge" says that treatment is effective in changing its course if started early (although good data are lacking).

The problem is that no single diagnostic test is sufficiently sensitive and specific. Tonometry is the most commonly used screen and, while the expense of completely evaluating the 50 to 90 percent who are false positives might be justified, it is unacceptable that 40 to 60 percent of patients with glaucoma will be falsely reassured that they do not have the disease. There is no ideal compromise between complete evaluation of everyone and no screening at all, but we have chosen to recommend tonometry plus ophthalmoscopy every four years after age 40.

Breast Cancer

Occurrence:

Breast cancer is the leading cause of death due to cancer in women. Its incidence has increased in the past decade to the current level of 73 per 100,000 women.³ It is rare before age 25, but after this age it becomes increasingly common, reaching an incidence of 150 to 200 per 100,000 in the 45 to 65 age group.¹¹

Progression:

The untreated five-year survival for breast cancer is 15 to 20 percent.¹² Histologic studies have shown an average tumor doubling time of 28 days, while other studies reported an average tumor growth rate of one centimeter every three months.¹³ The rate of growth and progression, however, is exceedingly variable depending on histologic type and grade, and average figures may be meaningless in the individual case.

Diagnosis:

Physician examination, self-examination, and mammography are three widely used methods of detecting breast cancer.

Self-examination by the patient is the way 90 percent of breast malignancies are detected,¹¹ whether or not the patient has been instructed in systematic, periodic examination of her breasts. In fact, in a study of women receiving yearly physician examinations, 38 percent of all tumors were discovered by the patients themselves at times other than the physician exam.¹⁴

There are several problems with self-examination:

1. Patient compliance — only 30 to 35 percent of women with breast tumors, discovered by any method, claimed to be doing routine examinations.¹¹
2. There is a lag, averaging ten months in one study, between the time of detection of a lesion and the first physician contact.¹⁵
3. Small breasts are more easily examined than larger, pendulous or fatty breasts.¹¹

The advantages of self-examination are:

1. It is inexpensive, the only cost being the initial educational session and occasional follow-up reminders.
2. It can be done frequently and at any desired interval.
3. It requires minimal physician or paramedical time.

Physician examination and mammography are the other two methods of detection. In Shapiro's prospective study of yearly screening for breast cancer, palpation detected 67 percent of lesions. Forty-five percent were also detected by mammography, but 22 percent would have been missed using mammography alone. On the other hand, 33 percent of all tumors were found only by mammography.¹⁴

Age and breast size are important variables in the relative yield from mammography and palpation. In women under age 50, 61 percent of cancers were found by palpation alone, while only 19 percent were detected by mammography alone. Over age 50, 42 percent of tumors were detected only by mammography and about the same number, 40 percent, were found only by palpation.¹⁴ Mammography is most useful for detecting lesions in large, fatty breasts, especially in the lower quadrants.¹¹

The biggest drawback to mammography is its cost (\$40 in our area). By contrast, palpation by a physician or paramedic should cost no more than \$5 if combined with other studies, eg, pap smear, at the same visit.

Benefit from Treatment:

There is little question that treatment improves the survival of Stage I breast cancer. The untreated five-year survival is 15 to 20 percent. The overall five-year survival for treated breast cancer is 54 percent with a ten-year survival of 40 percent. Stage I disease is where most of the improve-

ment occurs; treatment produces a five-year survival of 74 percent. By contrast, the five-year survival with treatment of Stage II disease is 28 percent, that is, not much better than the overall untreated survival.¹²

The crucial question is "Does periodic screening improve survival?" No study has shown that screening by a single modality improves survival. Venet and Shapiro, in an ongoing prospective study of annual palpation plus mammography, have shown a significantly decreased 3½ year case fatality rate in women 50 to 60 years old. They were unable to demonstrate an improved survival with screening in women under age 50.¹⁴

Conclusion:

Early Stage I breast cancer has a much better prognosis with treatment than other stages. There is some evidence that screening improves survival in women over 50. Self-examination is inexpensive. Mammography is expensive. Given these facts, we recommend:

1. At age 20, women should be given detailed instruction in self-examination. This instruction should be repeated every ten years.
2. Women should be encouraged to do systematic self-examination at monthly intervals.
3. A physician examination should take place every two years until age 50, and every year thereafter.
4. Mammography should be used routinely only in women over 50 with large, fatty breasts on an annual or biannual basis.

Alcoholism

Occurrence:

Alcoholism is an extremely common problem with a reported incidence of 4,200 per 100,000. It primarily affects middle-aged persons in the 30 to 50 age group. Men are affected six times as often as women,¹⁶ although some experts feel the true incidence in women is understated.

Progression and Benefit from Treatment:

Alcoholism develops slowly over a period of years. Pfeffer¹⁷ describes four distinct phases of this progression: (1) the pre-alcoholic phase last-

ing several months to two years, (2) the prodromal phase lasting six months to four or five years characterized by a preoccupation with drinking, (3) the crucial phase where loss of control occurs, and (4) the chronic phase which includes periods of prolonged intoxication, morning drinking, etc. The complications of alcoholism include liver, gastrointestinal, cardiac, and neural damage, as well as psychic, financial, and social disruption of the patient and his family.

Treatment of alcoholics is limited to arrest of the disease by abstinence from drinking. There is no cure. Without any formal treatment program, five to ten percent of alcoholics will spontaneously stop drinking for significant periods of time.¹⁷

With treatment, including residential centers, Alcoholics Anonymous, counseling, etc, the eventual prognosis is good for the 70 percent of alcoholics who are married and have a family and a job. Twenty percent of these will remain abstinent for three to five years, and 60 percent achieve abstinence "most of the time."¹⁸

Diagnosis:

There is no single test to diagnose alcoholism. The diagnosis is made from the history and, to a lesser extent, by physician examination. Major and minor criteria have been established to aid in identification of alcoholics.¹⁹ History can also be obtained from the patient's family and close friends. No studies have shown that early diagnosis of alcoholism will lead to earlier arrest of the disease. The patient must want to stop drinking before treatment can be effective. Just being told he has a disease may not make him want to stop. On the other hand, the sooner the disease is detected the sooner it can be faced squarely, if not by the patient, at least by family and friends.

Conclusions:

Alcoholism is an extremely common disease with a long presymptomatic (more correctly, pre-recognition) phase. It has serious morbidity, but with treatment the eventual prognosis for arrest of the drinking pattern is good in most people.

We recommend that appropriate questions be asked at infrequent intervals of five to ten years to all patients between 30 and 60 concerning their

drinking habits and those of their family.

Depression

Occurrence:

Depression, a most common psychiatric illness, is certainly significant in terms of numbers of cases. Exact incidence data is difficult to obtain because of problems in classifying depression, as well as its wide range of severity. In one study,²⁰ the prevalence of psychotic depression was 70 per 100,000, with an age-adjusted incidence of 33 per 100,000. The true overall incidence is probably considerably higher. Depression is more frequent in women than men by a ratio of 1.7 to one.^{20,21} Most depressed patients are over 35. In one study the mean age was 38,²¹ in another, 63 percent of patients were between 50 and 70.²⁰

Progression:

Depression may occur as an isolated episodic illness, but at least 50 percent of cases will have recurrent episodes interspersed with periods of improvement or remission. There is often a significant lag period averaging two to six years²¹ between the onset of symptoms and the seeking of psychiatric care. The ultimate progression of depression, suicide, occurred in 2.2 percent of a psychotically depressed population over five years, compared with an expected suicidal death rate of 0.4 percent for a non-depressed population.²⁰ Thus, psychotically depressed persons have several times the normal risk of suicide.

Diagnosis:

Depression is defined in terms of a symptom complex including: (1) alternation of mood, (2) pessimism, (3) ideas of guilt, (4) retardation or agitation, (5) self-punitive wishes or suicidal ideas, and (6) somatic changes.²² It is therefore difficult to talk about diagnosing depression in an asymptomatic phase — one can, however, talk about diagnosing “masked depression”²³ or uncovering depressive symptoms in the patient who does not realize he is depressed. Masked depression may include as many as 31 percent of depressed patients who usually express their depression through somatic symptoms.²³ Several questionnaires, including the “Index of

Depression,”²⁴ have been devised as quick methods for identifying masked depression. Although sensitive in identifying persons suspected of being depressed, the “Index of Depression” has not been used as a screening tool in asymptomatic persons. Other scales for measuring depression are probably either too complex or too long to be useful as a screening method.²⁴

Benefit from Treatment:

The treatment of acute depressive episodes is quite effective, with more than 90 percent of patients improving after psychiatric, pharmacologic, and electroconvulsive therapy in various combinations.²² However, a significant portion of patients will have a recurrence of symptoms. It is impossible to talk of treatment in the pre-symptomatic stage of the disease because treatment is defined in terms of relief of symptoms. As in all psychiatric diseases, the patient must feel he has a problem and desire help before treatment is likely to be effective.

Suicide:

Suicide is an event rather than a disease. In discussing screening for potential suicide we are, therefore, trying to prevent an event rather than detect a disease. The first problem is to identify those persons who will commit suicide — then one can try to evaluate whether therapy prevents the act. Unfortunately, if treatment does prevent suicide, there will always be uncertainty about whether the person was correctly identified as suicidal in the first place.

The demographic characteristics of those with the highest risk of suicide have been identified and include white males over age 45, separated, widowed, or divorced, who live alone and are unemployed or retired. However, most suicides do not fit these characteristics and most persons with these characteristics do not commit suicide.²⁵ Likewise, most suicides are committed by people not recognized as being depressed.

Murphy²⁵ shows by simple mathematical analysis that even a hypothetical predictive test that was 80 percent efficient would be only four percent correct in predicting suicide. Such a test is not currently available. There is no suitable method of predicting suicide at the present time.

Conclusions:

Although it is possible that a screening test, such as the “Index of Depression” could unmask a significant number of depressed persons, there is no evidence that they would benefit from this revelation or be motivated to seek treatment. There is also no evidence that earlier detection of depression will significantly decrease the incidence of suicide. We, therefore, feel that periodic screening of asymptomatic patients specifically for depression is not indicated. (Fails criterion 4)

Anemia

Occurrence:

The incidence and prevalence of anemia in the population is directly related to the value defined as the lower limit of normal for hemoglobin, hematocrit, or red blood cell count. If based on usual statistical means of sampling a large population and determining the range of normal as the mean ± 2 standard deviations, then the prevalence of anemia will be 2.5 percent by definition. This does not imply, however, any significant correlation with a pathologic state. Textbook values for normal ranges are unrealistically high.^{26,27} Furthermore, individual laboratories have enormous variation in what they report as the normal range for hematologic values.²⁷ Population surveys to detect the prevalence of anemia generally select an arbitrary cutoff value without justifying why they chose that value.²⁸⁻³² Conventional definitions of anemia, when applied to large populations, lead to prevalence figures of the following magnitude: males one percent,³³ females ten percent,³³ pregnant females ten to 60 percent,³² elderly males ten percent,²⁹ and elderly females 15 percent.²⁹

Progression and Benefit from Treatment:

Anemia is not a disease per se, but rather a sign found in many diseases. No reference could be found wherein a large series of anemias was analyzed to determine relative frequency of various causes. It is generally agreed that the great majority (85 to 90 percent) are a result of iron deficiency.²⁸ The natural history, risk factors, and prognosis with treatment for anemia vary,

of course, with the specific etiology.

Elwood³³⁻³⁶ has refuted several common assumptions regarding anemia. His data show:

1. Symptoms thought to be associated with anemia show *no* correlation with hemoglobin level until values below 7-8 gm percent are reached.
2. Cardiovascular reserve and capacity for physical work show no relation with hemoglobin level until levels below 7-8 gm percent are reached.
3. The frequency with which "serious underlying disease" is associated with anemia is less than ten percent.
4. Although studies show that in cases of hemoglobin values less than 12 gm percent supplemental iron therapy will result in elevation of hemoglobin level at least 1-2 gm percent, double blind crossover trials of therapy show no correlation between improved hemoglobin levels and changes in symptoms or capacity for physical work.

Rapid reduction of hemoglobin level may produce symptoms at a higher level than if the anemia forms gradually. However, Conrad's study of the natural history of iron deficiency anemia also revealed that, even with acute reductions of hemoglobin level from 14.7 gm percent to 9.7 gm percent, each volunteer continued to perform daily activities without difficulties. Furthermore, all physiologic variables returned to normal with iron replenishment.³⁷

Conclusion:

Anemia, as commonly defined, is frequently asymptomatic. There is no evidence, however, that asymptomatic anemia per se is harmful, or that treatment in the asymptomatic phase is superior to waiting until symptoms appear. We, therefore, recommend no routine screening for anemia. (Fails criterion 4) The potential value of screening for anemia as a clue to other diseases must be considered in the overall context of screening asymptomatic persons for each specific disease according to our six screening criteria. This is done in other sections of this paper for diseases such as leukemia, chronic nephrosis, and cancers in which anemia may be present.

Lymphoma

Occurrence:

Lymphoma includes Hodgkin's disease, lymphosarcoma and reticulum

cell sarcoma. The overall incidence is six per 100,000 (three per 100,000 for Hodgkins, two per 100,000 for lymphosarcoma, one per 100,000 for reticulum cell sarcoma).³⁸ Hodgkin's disease occurs primarily in the second and third decades, while lymphosarcoma and reticulum cell sarcoma are diseases of older persons.

Progression and Benefit from Treatment:

Hodgkin's disease has the best prognosis of the group. The average untreated survival is two to three years, but with early treatment Stage I disease has a 90 to 100 percent five-year survival. Lymphosarcoma has a 25 percent five-year survival with treatment. Reticulum cell sarcoma has a 20 percent five-year survival with treatment.³⁸

Diagnosis:

Progressively enlarging, painless lymph nodes are the most common presenting sign of this group. Examination of the lymph nodes with subsequent biopsy of suspicious areas is the only feasible diagnostic screen. In Hodgkin's disease, cervical nodes are enlarged in 60 to 80 percent of cases, axillary in six to 20 percent, mediastinal in six to 11 percent and inguinal in six to 12 percent. Anemia is found in one third of cases, but this is a later sign.

Conclusions:

Hodgkin's disease is the lymphoma most attractive for potential screening. It occurs in younger people, has the highest incidence and, if the disease is detected early, the response to therapy is excellent. The disease is amenable to self-examination in that cervical nodes can be easily palpated by the person himself. Three per 100,000 is not a high enough incidence to justify repeated physician examinations.

Lymphosarcoma and reticulum cell sarcoma do not respond to treatment of early disease as well as Hodgkin's disease. They too, however, are amenable to self-examination.

We recommend that adults be taught to examine for and report any lymph node swelling unassociated with infection that is progressively enlarging or persists more than one month. We do not feel periodic physician exams are justified to screen for lymphoma in *asymptomatic* patients.

Chronic Leukemia

Occurrence:

Chronic lymphocytic (CLL) and chronic granulocytic leukemia (CGL) are felt to have about equal incidence of two per 100,000.³⁹ Each makes up about 20 percent of all leukemia.⁴⁰ The majority of patients with chronic granulocytic leukemia are between 25 and 60 with the peak incidence in the forties and fifties.⁴⁰ Ninety percent of patients with chronic lymphocytic leukemia are over age 50 and two thirds are over age 60.⁴¹ Men with CLL outnumber women two to one.

Progression and Benefit from Treatment:

Chronic granulocytic leukemia has an insidious onset over two to six months with symptoms of fatigue, malaise, fever, and weight loss. There is granulocytosis and anemia on peripheral blood count. There follows a three to six-year period with granulocytic proliferation, a chronic treatable phase of one to four years, and finally an acute terminal phase.⁴⁰ There is no known treatment in the early stages which will prevent progression of the disease. Chronic lymphocytic leukemia (with treatment) often has an even longer course of ten to 15 years before the terminal episode. Treatment is aimed at relieving symptoms and does not improve the eventual outcome.⁴¹

Diagnosis:

It is fairly unusual to diagnose chronic leukemia in an asymptomatic person and, if this does occur via incidental splenectomy or peripheral white count, symptoms usually are present within a matter of months. The white count is usually elevated early in the course of the disease and could possibly be used as a screening device.

Conclusions:

The main reason not to screen for chronic leukemia is that in both CLL and CGL early asymptomatic treatment does not affect the ultimate course and often is not indicated. In addition, the incidence of these conditions is low and CGL has only a short asymptomatic period of several months.

We do not recommend screening *asymptomatic* patients for chronic leukemia. (Fails criteria 4, 6)

We have attempted to strictly require that all criteria were fulfilled before recommending any particular screening test. Failing a single criterion was enough to disqualify a test or disease from screening. This is perhaps more rigid than many of us are in practice but was necessary to avoid the pitfall of being carried away by intuition, special interest group propaganda, "common practice," and personal emotional bias. Therefore, many commonly used reasons for doing screening tests such as, "The test has a high yield," "It is so easy to do," or "It's good to have a baseline value," were not sufficient.

It should also be emphasized that we are considering screening only the hypothetical *completely asymptomatic person*. This does not imply that the screening test is a sufficient work-up for the disease being screened once detected or that incidental symptoms should not be evaluated.

We have formulated a longitudinal screening program for asymptomatic adults based on the criteria used in this study and the conclusions of the individual sections. This longitudinal screening flow sheet, shown in Figure 1, is designed for use in the private physician's office on voluntary fee for service patients. Cost is, therefore, an important consideration if continued acceptance among the general population is to be obtained. The average cost for men is considerably less than for women. This difference is partly due to the pap smear and pelvic exam, but also reflects the fact that most of the male visits are done by paramedics.

Patient education and participation is an important part of the screening program. Patients should be educated regarding the general importance of preventive medicine, health screening, and risk factor reduction. The plan of the screening program should be explained in detail and patients should understand that specific diseases are being evaluated, rather than feeling it is an overall guarantee of good health. Providing them their own copy of the flow sheet might facilitate this understanding and improve motivation. Second, patients are to be instructed in specific techniques of self-diagnosis such as breast, lymph node, and testes examinations.

There are several reasons why health screening can best be done by

the family physician. He is less likely to repeat tests that have recently been done or screen for conditions already known to exist. Many screening visits can be included in visits for other, symptomatic problems. Patients can receive immediate follow-up for conditions detected.

We feel that health screening programs must be objectively based. As Cochrane has stated "... There is an ethical difference between everyday medical practice and screening. If a patient asks a medical practitioner for help, the doctor does the best he can. He is not responsible for defects of medical knowledge. If, however, the practitioner initiates screening procedures, he is in a very different situation. He should, in our view, have conclusive evidence that screening can alter the natural history of disease in a significant proportion of those screened."⁴³

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